Nursing Seminar

APPROACHING SEXUALITY IN CANCER NURSING CARE

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Cancer and its treatment tend to destroy both sexual function and sexual performance. In gynaecological oncology that applies even more because the sexual machinery is directly involved. As a result, sex for fun and sex for procreation will disappear from the couple’s menu. Bothering about possible sexual side effects seems not very relevant. That makes discussing this topic also absent from the menu of the oncology professionals, causing unnecessary additional sadness to the woman and her partner and potentially causing additional damage to their relationship.

This presentation will try to change the perspective and focus on integrating sexuality and intimacy in our care.

Fact 1: People have sex for many more reasons than only fun or procreation. It can reduce emotional stress and decrease mutual tension in the relationship. It can console and comfort and be important for female self respect. It can reduce depression and improve mood. It has physical benefits with muscle relaxation and an increased pain threshold. Next to these various aspects of care, there are some cure aspects, since regular sex improves vaginal circulation, reducing vaginal atrophy.

Fact 2: Not complaining is not a sign of ‘no problem’. Even when patients wholeheartedly want help for a serious sexual disturbance, the great majority will not raise the problem. So, starting that discussion is our task! Especially because our interventions are responsible for the majority of the sexual disturbances.

Fact 3: Sexual diversity. There is great diversity in the sexual relationships, sexual desires and sexual expression of people. Most probably, there is nothing wrong with our own sexual life, but it should not be the frame of reference for our patients. Outward appearance should nor guide us. Besides, even when single, aged, lesbian, from a traditional culture, or in the terminal stage of cancer, women can desire and need sexual expression for fulfillment.

Fact 4: The relevance of the sexual relationship. The great majority of our cancer patients has a partner. The majority of those partners is male, and for the majority of men sexual expression is an important aspect of their wellbeing. Preserving as good as possible sex is a relevant element in preserving the relationship.

Fact 5: Sexual medicine and oncosexology developed much expertise on the causes of sexual disturbances, providing information and education strategies to prevent serious damage, answers for the common questions, and treatment strategies for the common disturbances, allowing oncology professionals to adequately deal with sexuality and intimacy after cancer.
Fact 6: Over the last decade oncosexology developed various treatment strategies to handle the more complex cases. That back-up should create enough room for the oncology professional to inquire after the sexuality of their cancer patients.

No approach in oncology care deserves the term holistic as long as sexuality and intimacy have not been addressed.
SEXUAL CONSEQUENCES OF GYNAECOLOGICAL CANCER AND ITS TREATMENT

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Estimates of the prevalence of female sexual difficulties after treatment for gynaecological cancer vary markedly depending on primary diagnosis and treatment(s), problem definition and the scope and validity of the research instruments used. Recent reviews suggest that between 30-100% of women treated for gynaecological cancer experience some form of sexual difficulty (Abbott-Anderson & Kwekkeboom, 2012). Furthermore, radiotherapy morbidity studies indicate that women receiving primary or adjuvant pelvic radiotherapy experience greater and more prolonged disruption to their sexual well-being (Jensen et al. 2003; Davidson et al. 2003) than women after surgery alone (Leake et al. 2001; Juraskova et al. 2003, Song et al, 2012). Sexual difficulties may be transient or permanent and can be a consequence of biological, psychological and interpersonal factors, or a combination thereof. The empirical literature surrounding female sexuality in gynaecological cancer describes sexuality as a multidimensional construct that should be assessed in this way (Cleary & Hegarty, 2011). Research has predominantly focused upon the physical consequences of cancer treatment, neglecting the psychological and social experiences of changes to sexuality including anxiety, depression, distress, and negative perceptions of sexual identity and body image (Gilbert, Ussher & Perz, 2011). A theoretical framework for sexuality and adequate clinical interventions for treatment of difficulties after cancer treatment are currently lacking. This paper will outline the sexual consequences of gynaecological cancer treatment, current interventions and discuss the discourses surrounding sexual self schema, relationship context, sexual recovery and access to sexual support.
Nursing Seminar

SEXUALITY AFTER RADICAL TRACHELECTOMY SURGERY

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Radical trachelectomy surgery is a fertility sparing option for women with early stage cervical cancer. It involves removal of the cervix and re-anastomosis of the vagina to the womb, with insertion of a cerclage (stitch) to reduce the risk of miscarriage. US and Korean studies using Female Sexual Function Index (FSFI) scores indicate some sexual dysfunction after a radical trachelectomy which improves over time, but at 24 months remains slightly lower than the general public. There is little longer term research of sexuality beyond 24 months after trachelectomy and few in-depth qualitative reports including the impact on sexuality.

In-depth qualitative interviews explore sexuality in a UK sample of women who were between 1 and 10 years post trachelectomy. The outcomes indicate that sexual issues were not experienced as a long term concern for most, for example many developed techniques to reduce ‘feeling the stitch’ during intercourse. Single women disclosed more psychosexual issues, such as body image concerns related to the prospect of new sexual partners.

Sexuality after cancer treatment is a current cancer survivorship issue and awareness of current quantitative and qualitative studies related to sexuality after trachelectomy is important for health care professionals caring for this unique group. There is a need for further longer term quantitative and qualitative research on morbidity and quality of life after trachelectomy surgery, including the impact on sexuality.
DEVELOPING A FRAMEWORK FOR WORKING WITH PATIENTS WITH SEXUAL AND CANCER ISSUES

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One of the most sensitive questions which arise in cancer survivorship is what happens to the sexual relationship. The evidence from the UK, Europe & the USA shows that patients living with and beyond a diagnosis of cancer will have problems with sexuality, and in their sexual relationships. The cause of the problems may be due to the disease itself or the treatment modalities. As a UK nation, sexuality is seen as a private part of life but equally it underpins the sense of self (who we feel we are). Patients find it difficult to ask their healthcare professionals for help as shown in the Macmillan surveys, and equally health professionals find it difficult to raise the subject with patients, feeling deskilled and embarrassed as shown in The Christie Hospital survey. The questions that concern health professionals are ‘How to ask’, ‘What to ask’, ‘When to ask’ and ‘What to do with the answers’.

Cancer Survivorship (living with & beyond cancer) raised nationally by the Department of Health (DH), NICE (2004), Macmillan Cancer Support (2010) & The National Cancer Survivorship Initiative, looks to ensure survivors needs are identified, and long term effects of cancer and its' treatment managed.

Developing a framework for working with patients, which enables healthcare staff to deliver better communication, skills and knowledge, will improve the clinical care pathway for this group of patients.
EVALUATION OF THE GYNAECOLOGY BASIC SEXUAL HEALTH ASSESSMENT QUESTIONS INCLUDED IN THE SUPPORTIVE NEEDS SCREENING TOOL

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Introduction
Self-reported assessments and clinicians seeing results before consultation show increased communication about impacts of cancer and/or treatments on sexuality (Berry et al 2011). At Peter MacCallum Cancer Centre, a supportive needs screening tool (SNCT) containing one sexual health question is completed at first appointment. Typical questions for basic sexual health assessment (BSHA) were added.

Aims/ Method
A retrospective audit of notes was conducted to evaluate the added BSHA questions and describe results.

Results
All new referral notes (August 2010 to January 2012) were audited (n=151). Less than 4% (n=5) indicated discussion of sexual impact of treatment. Nurse coordinators completed BSHA for 74% (n=112). More than half (62% n=69) were in a relationship, 8% (n=9) same sex. 10% (n=11) reported decreased sexual interest, 20% (n=23) were sexually active. Under half (37% n=41) reported vaginal bleeding/discharge. Over half (55% n=62) reported discussions of treatment on fertility. Two thirds (69% n= 77) were post-menopausal, 4.5% (n=5) using hormone replacement. 37% (n=41) reported being made to feel uncomfortable about their body, possible sexual abuse indicated in 17% (n=7). Although sexual counselling was recommended for 3 women, only 1 accepted. 4 sets of notes contained documented sexual health self-help/management.

Conclusion
The addition of BSHA supports nurse-led sexual health discussions. Timing is critical, initial consultation may not always be appropriate. Recommendations include dedicated BSHA at several time points. Documentation is required indicating discussion of sexual impact of treatment covered in consent process and information provision to support patient decision making.
Plenary Session: BEST ORAL PRESENTATIONS

AGO-OVAR 12: A RANDOMIZED PLACEBO-CONTROLLED GCIG/ENGOT-INTERGROUP PHASE III TRIAL OF STANDARD FRONTLINE CHEMOTHERAPY +/− NINTEDANIB FOR ADVANCED OVARIAN CANCER

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Objectives
Angiogenesis plays an established role as target in the treatment of ovarian cancer (OC). Nintedanib (N), an oral inhibitor of VEGFR, PDGFR, and FGFR, has shown activity in OC in phase II Trials.

Methods
Pts with FIGO IIB-IV OC and upfront debulking surgery were randomized 2:1 to N 200 mg bid + Carboplatin (C AUC5 or 6) and Paclitaxel (T 175 mg/m2), or placebo (Pl) + TCq21. Primary endpoint was investigator assessed PFS, analysis of stratification factors were pre-planned.

Results
1,366 patients were recruited 12/2009 – 7/2011 by 9 study groups: 911 TC+N and 455 received TC+Pl. Overall, 39% had a very high risk with FIGO III and residuals >1cm or FIGO IV while 61% had FIGO III and residuals ≤1cm or FIGO II (283 in TC-Pl, 556 in TC+N). After 752 observed events, PFS was significantly longer with N+TC than Pl+TC (median 17.3 vs 16.6 months; HR 0.84; 95%CI:0.72 – 0.98; p=0.0239). Post-hoc analysis of pre-defined subgroups showed a higher benefit in patients of the low risk subgroup: median PFS 20.8 vs 27.1 months; HR 0.75 (0.61 – 0.92); p=0.005. OS data are still immature. Main adverse events were GI side effects.
Conclusions
Nintedanib in combination with TC significantly prolongs PFS in first-line OC; its impact was highest in pts with low post-OP tumor burden. Nintedanib appears to be a valuable treatment option in advanced OC, however, further studies should focus on patient selection and optimization of tolerability.
Plenary Session: BEST ORAL PRESENTATIONS

PHASE III TRIAL OF EVERY-3-WEEKS PACLITAXEL VS. DOSE DENSE WEEKLY PACLITAXEL WITH CARBOPLATIN +/- BEVACIZUMAB IN EPITHELIAL OVARIAN, PERITONEAL, FALLOPIAN TUBE CANCER: GOG 262 (NCT01167712)

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Objectives
In a randomized phase III trial of Japanese women with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, dose dense weekly paclitaxel and carboplatin (ddwT) improved the survival over conventional paclitaxel and carboplatin (q3T). We proposed to determine if ddwT improves progression-free survival (PFS) compared to q3T chemotherapy with or without bevacizumab (bev).

Methods
Eligible patients had newly diagnosed stage II, III or IV disease following surgery; stage III (macroscopic residual disease) or stage IV disease. Patients were randomly allocated to intravenous regimens (1) Paclitaxel 175 mg/m² q 3 weeks + Carboplatin (AUC=6) x 6 cycles vs. (2) Paclitaxel 80 mg/m² weekly + Carboplatin (AUC=6) IV x 6 cycles. Both arms have the option for bev 15 mg/kg q 3 weeks followed by maintenance bev until progression or adverse effects. The primary endpoint is PFS and secondary endpoints include overall survival, safety, and quality of life. Our sample size provides approximately a 90% chance of concluding that ddwT is more efficacious than q3T in reducing PFS rate by 25%.
Results
692 patients were enrolled from September 2010 to February 2012. 89%, 4%, 4%, and 2% were Whites, Blacks, Hispanics, and Asians/Pacific Islander. 46%, 47% and 7% of patients had performance status of 1, 2, and 3. Stage II, III, and IV disease comprised of 2%, 70%, and 28% of women. 84% of patients opted for

Conclusions
The primary PFS results are expected to mature in late summer 2013. An updated analysis will be submitted as a late breaking abstract.
Plenary Session: BEST ORAL PRESENTATIONS

PHASE 3 DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF WEEKLY FARLETUZUMAB WITH CARBOPLATIN/TAXANE IN SUBJECTS WITH PLATINUM-SENSITIVE OVARIAN CANCER IN FIRST RELAPSE

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Objectives
Farletuzumab (FAR) is a humanized monoclonal antibody that binds to folate receptor-α which is highly expressed in ovarian cancer and largely absent from normal tissue. FAR potentially has anti-tumor activity via antibody dependent cell cytotoxicity and complement-dependent cytotoxicity, and was studied in a Phase 3 platinum-sensitive ovarian cancer trial.

Methods
This was a global, double-blinded, randomized Phase 3 trial in 1100 women with platinum-sensitive first recurrent ovarian cancer 6-24 months following completion of first-line platinum-taxane based chemotherapy. All subjects received carboplatin and paclitaxel or docetaxel for 6 cycles combined with randomized test product (1:1:1 to FAR 1.25 mg/kg, 2.5 mg/kg, or placebo). Single agent test product was then continued weekly until disease progression. The primary endpoint was progression-free survival (PFS) by Response Evaluation Criteria in Solid Tumors via independent assessment.

Results
Subject length of first remission was 6≤12 months (45%), 12≤18 months (35%), and 18-24 months (19%) and similar in the 3 groups. Median PFS was 9.0 (placebo), 9.5 (FAR 1.25 mg/kg), and 9.7 (FAR 2.5 mg/kg) months with no statistically significant difference between arms (hazard ratio=0.86 [0.70, 1.06] for 2.5 versus placebo. The most commonly reported adverse events across arms were those known to be associated with the study chemotherapy agents. Subgroup analyses are ongoing and final overall survival data data are still pending.

Conclusions
Neither FAR dose met the study’s primary PFS endpoint. The most commonly reported adverse events across arms were those known to be associated with the study chemotherapy agents.
Plenary Session: BEST ORAL PRESENTATIONS

UK GYNAECOLOGICAL ONCOLOGY SURGICAL OUTCOMES AND COMPLICATIONS (UKGOSOC)

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Objectives
UKGOSOC study was set up to collect prospective data and set benchmarking standards on complication rates for Gynaecological Oncology surgery.

Methods
All patients undergoing major surgery in ten participating gynaecological cancer centres were approached for consent. Data on surgery and complications in hospital were contemporaneously recorded. Women were sent a follow-up letter >6 weeks following surgery to collect data on postoperative complications (POC) which were graded on a scale of I to V in increasing severity using Clavien-Dindo system. Multivariable regression was used to identify factors associated with intra-operative and postoperative complications. For intra-operative complications all surgeries were subjected to regression analysis, while for postoperative complications Grade II to V only those surgeries with both hospital and patient-reported data were included.

Results
Prospective data on 3026 surgeries was collected of which 2948 were eligible. In 139 surgeries (IOC rate 4.7%; 95% CI 4-5.7), 143 intraoperative complications were reported. Surgical complexity, diagnosis, diabetes, endocrine disorders (excluding diabetes) and previous abdominal surgery were independently associated with IOC risk.
Patient reported data was obtained for 1462 surgeries. In 379 surgeries (POC rate 26%; 95%CI, 24-28) there were 453 Grade II to V postoperative complications (200 hospital-reported and 253 patient only reported). Age, diabetes, presence of comorbidity, diagnosis, duration and surgical approach were significantly associated with POC risk.

**Conclusions**

This is the first large multi-centre prospective study to investigate morbidity associated with gynaecological oncology surgery. There are significant patient and surgical factors which increased risk of complications.
The cancer diagnosis is a stressful event that poses formidable and enduring challenges to the women and to their intimate partners. A conjoint process of mutual support has been suggested to be an effective coping strategy for patients who are in committed relationships. The primary aim of this study was to gather data on the potential benefits of a brief psychological intervention ("Side by Side") designed to assist women and their partners to cope with breast cancer.

Two randomized-controlled studies were conducted at two different time points. Study I: \( N = 72 \) couples were randomly assigned to either the couples’ component ("Side by Side"), or an information component directly after the diagnosis whereas in study II \( N = 45 \) couples were randomly assigned to "Side by Side" or relaxation after completing the medical treatment. Results of study I suggest that women receiving Side by Side showed larger reductions in cancer-related distress and fear of progression post-intervention compared to women in control group. Furthermore, couples in the Side by Side intervention showed less avoidance in dealing with the cancer, more posttraumatic growth, and better communication skills and dyadic coping relative to the control group. Study II showed a reduction of cancer-related distress in both groups but only in the Side by Side group improvements of relationship satisfaction occured. Short-term changes in cancer-related functioning may be improved by enhancing couples’ dyadic coping skills. The findings highlighted the importance of helping both, the woman and her partner, to effectively cope with cancer.
SPECIAL LECTURES

MANAGEMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Definitive chemoradiation is considered as the standard treatment for bulky cervical cancer by many European and Northern American teams. Universal use of chemoradiation, combining external radiation therapy, brachytherapy, and concurrent cisplatin is then apparently the best option.

However, several issues are still debated and deserve discussion, update of knowledge, and clinical trials, some of them under way: the preferred preoperative workup, the remaining place of upfront surgery, the place of completion surgery after chemoradiation, the place of pretherapeutic surgical staging using on modern minimal invasive surgery techniques, the role of extended field radiation, the impact of new techniques of radiation therapy, and the place of different drug regimens.

These issues will be the topic of the review.
SPECIAL LECTURES

HIPEC ROLE IN OVARIAN CANCER
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HIPEC is an innovative treatment that combines the pharmacokinetic advantage of intraperitoneal chemotherapy with hyperthermia. However, despite the established rationale and encouraging results of several independent studies, randomized controlled trials (RCTs) testing its efficacy have been requested by many scientists in all time points of the natural history of advanced epithelial ovarian cancer (AEOC). Nowadays there are no RCTs of AEOC treated with cytoreduction surgery and HIPEC in upfront setting. A criticism of this approach could be that the radical surgery is often associated with postoperative morbidity and mortality that could be even increased by the HIPEC procedure. Moreover, the direct administration of high dose HIPEC on residual tumor cells after upfront surgery for AEOC would be offered to a certain percentage of women with insensitive chemoresistant tumor cells.

However, HIPEC has been also employed for the treatment of recurrent ovarian cancer patient. During the past years, in the setting of platinum-sensitive recurrent disease, we presented two phase-II studies on the use of HIPEC following secondary cytoreduction (SCR), obtaining encouraging results.

Moreover, waiting for the results of a phase-III studies, comparing survival rates in women submitted to SCR plus HIPEC vs. SCR alone (HORSE trial), our group have carried out a case–control analysis demonstrating that the combination of SCR and HIPEC seems to improve survival rate in patients suffering from platinum-sensitive AEOC recurrence with respect to no-HIPEC treatments.
CHEMOTHERAPY OR UPFRONT SURGERY FOR NEWLY DIAGNOSED ADVANCED OVARIAN CANCER: RESULTS FROM THE MRC CHORUS TRAIL.
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CHORUS (CRUK 07/009) is the 2nd Phase III randomized controlled trial to investigate timing of initial surgery in OC.

Methods:
Patients with clinical FIGO stage III - IV OC (pelvic mass, extrapelvic metastases & CA125/CEA ratio >25) were randomized to standard treatment (PS followed by 6 cycles P-CT) or NACT (3 cycles P-CT either side of surgery). CHORUS was designed to demonstrate non-inferiority of NACT, excluding a 6% absolute detriment in 3yr survival from 50% expected with PS (1-sided alpha 10%). The primary outcome was overall survival (OS) & secondary outcomes were progression free survival ,toxicity & quality of life.

Results:
550 women (276 PS, 274 NACT) were randomized from 74 centres (72 UK, 2 NZ) between Mar 2004 & Aug 2010. Baseline characteristics were well balanced: median age 65yrs, median tumor size 80mm, 25% FIGO stage IV, 19% WHO PS 2. Median follow-up was 3yrs, 410 pts have died. Intention-to-treat analysis showed a median OS of 22.8 months for PS vs 24.5 months for NACT (hazard ratio (HR) 0.87 in favor of NACT, 80% CI 0.76 – 0.98) & a median PFS of 10.2 vs 11.7 months (HR 0.91, 0.81 – 1.02). OS results represent a 5% absolute benefit in 3yr survival for NACT to 37% & the upper 80% CI allows us to exclude there being any survival benefit for PS.

Conclusions:
NACT was associated with increased optimal debulking, less early mortality & similar survival in this poor prognosis group. CHORUS results are consistent with EORTC55971 & strengthen evidence that NACT is a viable alternative to PS.
Society Session: BRITISH GYNECOLOGICAL CANCER SOCIETY (BGCS) / NATIONAL CANCER RESEARCH INSTITUTE (NCRI)

EMBRACING NEW APPROACHES IN LOCALLY ADVANCED CERVICAL CANCER

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Embracing New Approaches In Locally Advanced Cervical Cancer

Over a decade ago chemoradiotherapy (CRT) was adopted in the UK and elsewhere as the new standard of care for women with locally advanced cervix cancer. A subsequent individual patient data (IPD) meta-analysis of CRT confirmed the benefit of adding chemotherapy to radiation. However, it showed that the improvement in 5-year overall survival (OS) was only 6% (i.e. from 60 to 66 %, HR 0.81). With a 5-year disease free survival (DFS) rate of 58%. A significant proportion of patients die from systemic disease with or without local failure. A single trial has reported a survival advantage from the addition of adjuvant chemotherapy after CRT but its findings await confirmation in additional randomised trials and it is not considered standard of care. Upfront or induction chemotherapy prior to radiation therapy has been the subject of several small trials with different methodologies and conflicting results. More recently a single arm phase II trial has demonstrated the feasibility of a short course of dose-dense weekly carboplatin and paclitaxel chemotherapy followed immediately by chemoradiation.

The rationale being that induction chemotherapy might reduce tumour volume while controlling micrometastatic disease. The use of weekly dose-dense chemotherapy in cervical cancer treatment is novel and could overcome tumour regrowth between cycles while limiting the proliferation of tumour cells resistant to both chemotherapy and radiotherapy. The INTERLACE trial, a multicentre randomised phase III trial is currently evaluating this approach.
LYMPHADENECTOMY FOR ENDOMETRIAL CANCER. WHY WE STILL NEED A TRIAL

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Randomised trials have indicated that pelvic lymphadenectomy for endometrial cancer is not associated with either a recurrence free or survival benefit. Criticism of these trials has emphasised the absence of a thorough para aortic lymphadenectomy, and the fact that the lymphadenectomy did not directly determine subsequent adjuvant therapy. Nonetheless, it appears very unlikely that lymphadenectomy will improve survival. If lymphadenectomy does have a role, it would be to differentiate those tumours with a higher risk of relapse from those with a much lower risk. Therefore a large trial is warranted which determines adjuvant therapy on the basis of lymph node status alone.

Through the GCIG, a trial design has been agreed, supported by several groups to undertake a trial which will randomise women with high risk endometrial cancer to have either no lymphadenectomy, or pelvic and para aortic lymphadenectomy. In the lymphadenectomy arm only those lymph node positive women will have adjuvant therapy, whereas in the other arm all women will have adjuvant therapy. The primary outcome will be overall survival, and powered to show non inferiority. Secondary outcomes will be toxicity and recurrence free survival. If non inferiority is shown together with reduced toxicity because of more selective adjuvant therapy, this would represent a strong rationale for lymphadenectomy. The trial would also incorporate a sentinel node study.
In advanced epithelial ovarian, the aim is complete cytoreduction of macroscopic visible disease since this has been shown to be associated with a significantly increased OS and PFS. Optimal cytoreduction is defined as total macroscopic tumor clearance with no residual visible disease. The value of systematic pelvic and paraaortic lymphonodectomy in advanced disease remains controversial. The timing of surgical cytoreduction in relation to chemotherapy is still debated. A large prospective trial showed that in advanced bulky disease three cycles of platinum-based neoadjuvant chemotherapy followed by interval debulking surgery was not inferior to primary debulking surgery followed by chemotherapy. Neoadjuvant chemotherapy, however, cannot be regarded as an adequate routine therapy strategy for advanced ovarian cancer should be limited to selected patients with very advanced disease and contraindication for upfront debulking surgery or tumor-dissemination.

Front-line chemotherapy for advanced epithelial ovarian cancer consists of a combination of paclitaxel and carboplatin, both administered intravenously every three weeks. Intraperitoneal chemotherapy and dose dense scheduling has demonstrated significant benefit in PFS and OS. However, due to higher toxicity, concerns about study design, and lack of evidence of efficacy in Caucasian population for dose-dense therapy these concepts cannot be considered as standard of care.

Angiogenesis is an important component to driving the growth of ovarian cancer. Two large randomized clinical trials have demonstrated an improvement of PFS by the addition of bevacizumab to chemotherapy in front-line therapy. The addition of bevacizumab is recommended for patients with advanced ovarian cancer with poor prognostic factors such as FIGO stage IIIB – IV.
Platinum-containing regimens are the mainstay of first-line treatment for ovarian cancer and also the referral therapy for platinum-sensitive recurrent disease. In the recurrent setting, the effectiveness of platinum retreatment is dependent on the relapse-free and treatment-free intervals. Platinum agents can be effectively re-administered to patients with disease that relapses >12 months after completion of a platinum regimen. Ovarian cancer that relapses between 6 to 12 months after treatment with a platinum regimen is considered partially platinum sensitive and represent a challenge with respect to treatment options. Phase III studies of combination platinum based regimens versus platinum monotherapy generally do not report separate data for partially platinum-sensitive patients but suggest a benefit of combination vs monotherapy regardless the platinum free interval. New non platinum combination seems better than monotherapy in this setting in term of overall and progression free survival. They may represent a way to artificially prolong platinum free interval and increase the subsequent response to platinum. Ongoing randomized prospective trials will better clarify the question.
State of the Art: OVARIAN CANCER

PLATINUM SENSITIVE RELAPSE: THE ROLE OF SURGERY AND CURRENT STATE OF THE ART OF SYSTEMIC THERAPY
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Platinum-sensitive relapse is defined as relapse at least 6 months after end of prior platinum based chemotherapy. Multiple treatment options have to be considered in the individual patient.

The DESKTOP I and II studies showed that selected patients have a significant survival benefit if complete resection is feasible compared to any residuals after end of therapy. The AGO score was successfully validated to identify patients in whom complete resection might be feasible. However, the potential benefit of surgery for recurrent ovarian cancer has to be proven within ongoing randomized trials (DESKTOP III, GOG 213). ICON 4/AGO OVAR 2.2 (carboplatin + paclitaxel versus platinum) and AGO-OVAR 2.5 (carboplatin + gemcitabine versus carboplatin) have shown superiority of platinum based combination chemotherapy. The subsequent CALYPSO trial comparing carboplatin + PLD versus carboplatin + paclitaxel showed superior PFS of carboplatin + PLD. The OCEANS study compared carboplatin + gemcitabine + bevacizumab versus carboplatin + gemcitabine and has also shown a significant benefit of PFS, but both trials did not report a significant OS difference. The results of the chemotherapy part of GOG 213 (carboplatin + paclitaxel versus carboplatin + paclitaxel + bevacizumab) are pending. The ongoing AGO-OVAR 2.21 trial compares carboplatin + PLD + bevacizumab versus carboplatin + gemcitabine + bevacizumab.

Conclusion: Multiple standard treatment options including surgery and platinum based chemotherapies with difference toxicity profiles allow individual counseling and treatment of patients. Further treatment options and optimizations are under investigation. The benefit of re-treatment after failure of bevacizumab is unknown.
Oral Presentation/Debate: CERVICAL CANCER I

ROBOTICALLY-ASSISTED PARA-AORTIC LYMPHADENECTOMY: SURGICAL RESULTS - A COHORT STUDY OF 487 PATIENTS

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Objectives
To report the feasibility of robotically-assisted laparoscopic para-aortic lymphadenectomy (PAL) in patients with gynecologic cancers, and to compare surgical results of different approaches if PAL is isolated (staging) or combined to another procedure.

Methods
Retrospective multi-centric study of patients who underwent robotically-assisted laparoscopic PAL between November 2004 and March 2012 (n=487). Twelve centers participated in the study, in Europe and USA. Patient’s characteristics, per operative data, definitive pathology and post operative complications were considered.

Results
Surgical procedures were performed for 12% (58/487) by extra-peritoneal approach and 88% (429/487) by trans-peritoneal approach. In the group trans-peritoneal approach, PAL was isolated in 17% (72/429) or combined with another surgical procedures in 83% (357/429) cases. For the whole population, mean lymph node removed was 12.6±8.1, operative time was 217±85 min, and hospital stay was 2.8±3.2 days. Four (0.8%) conversions to open and two (0.4%) conversions to laparoscopy were described. Seven (1.4%) vascular injuries and three (0.6%) urinary injuries occurred, and 10 (2.1%) patients were transfused. Post-operative lymphocysts occurred in 32 (6.6%) cases. For trans-peritoneal approach, the average number of lymph nodes removed was higher in isolated group than combined group (95% CI: -7.29 to -3.52, p=1.5.10⁻⁶).

Conclusions
Our series demonstrates the feasibility and safety of robotic PAL. The quality of transperitoneal PAL dissection (lymph node count) is significantly improved when PAL is isolated compared to PAL associated to another procedure. These results add to the importance of a dedicated docking to perform PAL: it suggests that a double-docking may improve the quality of PAL dissection in combined procedures.
Oral Presentation/Debate: CERVICAL CANCER I

CERVICAL CANCER SCREENING IN LOW RESOURCE COUNTRIES; EXPERIENCES FROM SOUTH SOUTH NIGERIA.

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Objectives
To present the experiences of the Centre for Gender Values and Culture with free cervical cancer screening exercise carried out between 2007 and 2011 in Bayelsa, South South Nigeria.

Methods
A prospective survey of the free cervical cancer awareness and screening campaign.

Results
A total of 6113 women were screened during the period. Over 90% were above 40 years of age. 98% of those screened never heard of cervical cancer before the awareness and screening campaign. Cytologic examination of the smears revealed inflammatory, high grade, low grade intraepithelial lesions as well as negative to intraepithelial lesions. The detailed results are to be presented at the conference.

Conclusions
Cervical Cancer Screening exercises have been carried out in South South Nigeria. Researchers can build up on these experiences to improve and increase the uptake of cervical cancer screening in low resource countries.
Oral Presentation/Debate: CERVICAL CANCER I

SQUAMOUS EPITHELIAL LESIONS IN PREGNANCY
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Objectives
The aim of this study was to evaluate the progression, persistence or regression of cervical lesions in pregnancy, and whether age or histologic grade influenced this outcome.

Methods
The subjects of this retrospective study were pregnant women referred to our Hospital due to an abnormal Pap smear, from 2007 to 2011. We compared initial and postpartum cytologies and established three categories: progression, persistence and regression. We also evaluated the influence of age (≤25; >25).

Results
We included a total of 56 women with an abnormal cervical cytology discovered while pregnant. The mean age was 31±5.3 years. The cytologies included 23 cases of L-SIL, 6 H-SIL, 23 ASCUS and 4 ACG. Of these, 21 were referred back to their gynecologist for control, and were therefore lost to follow up.

The total regression rate was 54.3%, 40% of the lesions persisted and 5.7% progressed. The results according to initial cytology can be found in the table below. There were no significant differences in the regression rates when stratified by age ≤25 o >25 (60% vs. 53.3%;p=0.25), or initial lesion grade (57.1% for L-SIL vs. 40% for H-SIL;p=0.39)

Conclusions
Within our small sample of pregnant women with abnormal cytology we could not demonstrate age or cytology grade to be risk factors for postpartum persistence or regression of Pap smear anomalies.
Oral Presentation/Debate: CERVICAL CANCER I

CLINICAL IMPACT OF THE FDG-PET/TC IN LOCALLY ADVANCED CERVICAL CANCER

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Objectives
To evaluate the value of FDG-PET/CT for primary staging of locally advanced cervical cancer (LACC).

Methods
This prospective study included 25 women (25-78 years old; mean age = 53.3) diagnosed with LACC. All cases were squamous cell carcinoma (100%) and distribution according to International Federation of Gynecology and Obstetrics (FIGO) stage was as follows: IB2 (n=3), IIA2 (n=2), IIB(n=14), III (n=1) and IVA (n=5). All patients underwent a whole-body FDG-PET/CT for primary staging. PET positive findings were described (site, maximum diameter and SUVmax) and correlated with para-aortic lymphadenectomy (PAL) and histopathologic confirmation in case of distant metastasis.

Results
FDG-PET/CT showed positive para-aortic nodes in 6 patients: 5 TP (1 with a positive PAL and 4 with confirmed metastasis) and 1 FP with a negative PAL (inflammatory node related to infected tumor).

FDG-PET/CT was negative in para-aortic región in 19 patients ;16 TP + 3FN (lymph node metastasis <7 mm).

PET/CT showed distant metastasis in 4 patients, sited in lung, liver and mediastinal nodes.

PAL was technically feasible in 22/25 women: positive in 5 (2 TP and 3FN by PET) and negative in 17 (16 TN and 1 FP by PET). NPV was 84,2%.

The treatment was modified in 4/25 (16%) women that received chemotherapy because of detection of unsuspected distant metastasis.

Conclusions
This study suggests that PET/CT is an effective imaging technique in the initial staging of LACC. It may help to evaluate para-aortic nodal metastasis and to plan the management, especially when unsuspected distant metastasis are detected.
Oral Presentation/Debate: CERVICAL CANCER I

PRE-OPERATIVE MRI IN EARLY STAGE CERVICAL CANCER MAY PREDICT THE NEED OF ADJUVANT THERAPIES.

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Objectives
To assess whether MR can predict the need of adjuvant therapies for patients with early-stage cervical cancer candidate to surgery.

Methods
Patients who underwent pre-operative MR for early-stage (FIGO IA1-IIB) cervical cancer in 2006-2012 were retrospectively enrolled. The need of adjuvant therapy is currently based on pathological results, as maximum depth of stromal invasion, minimum thickness of uninvolved cervical stroma, presence of peritumoral vascular invasion and positive lymph nodes. Sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and accuracy (AC) of MR in measuring the abovementioned parameters, compared to pathological results as gold standard, were evaluated.

Correlation between diffusion weighted imaging (DWI), histological type and peritumoral invasion was evaluated where DWI was acquired.

Results
217 patients (mean age 46.2 ±10.7) were included. 113/217 (54%) underwent adjuvant therapies. SE, SP, PPV, PPN and AC of MR in evaluation of minimum thickness of uninvolved cervical stroma were 88%, 75%, 70%, 90% and 80%, respectively. MR was concordant with pathological results in evaluation of maximum depth of stromal invasion in 200/217 patients (92%). SE, SP, PPV, PPN and AC of MR in evaluation of lymph nodes metastases were 64%, 85%, 65%, 84% and 78%, respectively.

DWI was assessable in 51/217 patients but there was no significant correlation (p>0.05) between ADC values, histological type and peritumoral invasion.

Conclusions
MR may be accurate in predicting the minimum thickness of uninvolved cervical stroma, maximum depth of stromal invasion and positive lymph nodes. There was no correlation between DWI and the parameters assessed.
Oral Presentation/Debate: CERVICAL CANCER I

LONG-TERM DATA ON THE TREND OF HPV-RELATED BIOMARKERS POST-TREATMENT FOR CIN

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Objectives
To assess the long-term alterations in HPV related biomarkers pre- and post-treatment for CIN and to verify their role as a prediction tool for recurrent disease.

Methods
Design: Prospective observational study
Setting: University Hospital of Ioannina
Population: Women planned to undergo LLETZ for CIN
Intervention: An LBC sample was obtained prior to treatment (time 0) and was repeated at 6, 12, 18, 24, 30, 36 months after treatment. This was tested for HPV-related biomarkers.
Outcomes: We calculated trend of positivity of HPV-related biomarkers after CIN treatment. Biomarkers' Sensitivity(S), specificity (Sp), PPV and NPV were also assessed.
Analysis: We calculated expression rates for each one of the HPV-related biomarkers prior to the treatment and at follow-up visits.

Results
Of 268 women included, histology showed CIN2+ in 148 cases. Eighteen individuals underwent second treatment. HPV-DNA appeared to be positive in 32.9% at the second follow-up visit and in 36.4% of the cases 2 years post-operatively. The NASBA test was positive prior to the treatment in 45% of the cases, and 5% at the 4th follow up visit. Flow cytometric evaluation of mRNA E6&E7 appeared to be positive in 33.3% at the 24months visit. The best sensitivity for the prediction of treatment failures was performed by HPV-DNA(65.8%) with PPV=96.2%. The NASBA test appeared to have the best specificity(93.8%) in identifying women with < CIN2+ lesions.

Conclusions
CIN treatment leads to a significant reduction in positivity for all HPV-related biomarkers. It appears that this is reduced due to the treatment itself. The application of HPV-related biomarkers (single or combinations) during follow-up, could enhance early prediction of recurrent disease.
Oral Presentation/Debate: ENDOMETRIAL CANCER

LAPAROSCOPIC VERSUS OPEN HYSTERECTOMY FOR EARLY STAGE ENDOMETRIAL CANCER: RESULTS FROM THE MRC ASTEC TRIAL

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Objectives
To determine whether the outcomes from laparoscopic hysterectomy (LH) are comparable to the open approach (OH) in women treated for presumed early endometrial cancer (EC).

Methods
Study design: prospective study
Setting: multicentric
Source: MRC ASTEC trial
Period: 1998 – 2005
Population: women diagnosed with presumed early EC
Interventions: hysterectomy with an open versus laparoscopic approach with or without lymphadenectomy
Outcomes: Overall and disease-free survival, surgical outcomes, complications

Results
We included 1,408 women with a mean age of 63 [OH:1,309(93%)-LH:99(7%)]. The proportion of women undergoing systematic lymphadenectomy (LH 41% v OH 41%) and the number of nodes harvested [median(IQR): LH 13(7-18) v OH 12(7-18)] was similar between the two groups (p=0.67). The rate of conversion to laparotomy for the laparoscopic group was high (27%). There were no differences in the rate of women requiring blood transfusion (LH 4/99(4%) vs OH 65/1309(5%), p=0.72), while LH was associated with longer operating time [median(IQR): LH 105mins(60-150) vs OH 80mins(60-95), p<0.001] but shorter hospital stay (median(IQR): LH 4d(3-5) vs OH 6d(5-7), p<0.001). The rate of complications was overall low but higher for OH (LH 21% vs OH 30%, p=0.07). With a median follow-up of 37 months, 1,216 women are still alive, there were 174 recurrences [LH=6(6%) vs OH=168(13%)] and 192 deaths (LH=7(7%) vs OH=185(14%)). The unadjusted hazard ratio for overall survival for laparoscopy in relation to laparotomy was 0.56(0.26-1.18)(p-value=0.13) and the adjusted 0.69(0.32-1.49)(p=0.35).

Conclusions
The laparoscopic approach to hysterectomy for early EC appears to be a safe, requires longer operating time but is associated with shorter hospital stay and favourable morbidity profile.
Oral Presentation/Debate: ENDOMETRIAL CANCER

AN INCREASE IN LOCO-REGIONAL RECURRENCES CAUSED BY OMITTING RADIOTHERAPY MAY BE CURED IN PATIENTS WITH EARLY-STAGE ENDOMETRIAL CANCER: THE DANISH ENDOMETRIAL CANCER STUDY (DEMCA)

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Objectives
In two prospective nationwide studies, DEMCA demonstrated that postoperative radiotherapy could be omitted in low- and intermediate-risk stage I patients without loss of survival when evaluated after 5 years. In the present study, we evaluated the consequence of this decision on the long-term risk of recurrence and death.

Methods
From 1998 to 1999, 1166 patients newly diagnosed with uterine carcinoma were included. Of these, 586 were low-risk, 231 intermediate-risk, and 78 high-risk stage I. Low- and intermediate-risk patients received standard primary surgery (hysterectomy, BSO), and no postoperative radiotherapy was given. Long-term recurrence and survival rates were estimated.

Results
After 13.8 ± 0.6 years, 13%, 33%, 67% and 94% of stage I–IV patients had recurrence/progression. For stage I, 6.3% of low-risk and 21.6% of intermediate-risk patients had relapsed compared with 32.1% of high-risk. Recurrences were dominated by locoregional relapse in the low- and intermediate-risk (locoregional/non-locoregional in percent of risk group: low: 4.1%/2.2%; intermediate: 14.3%/7.4%), while non-locoregional relapses were prominent in high-risk (5.1%/26.9%). After locoregional relapse, 1.5% of low- and 4.3% of intermediate-risk experienced a second relapse, of which 63% were non-locoregional. After curative-intent treatment of vaginal recurrence in the low- and intermediate-risk patients, 100% had complete remission after the first and 74% after the first or second recurrence. The 14-year cancer-specific survival was 96% for low-risk and 85% for intermediate-risk and almost the same as those reported after 5 years (97% and 87%).

Conclusions
We conclude that omitting radiotherapy in early-stage endometrial cancer increase local recurrences without affecting long-term survival; 74% of vaginal recurrences could be cured.
Oral Presentation/Debate: ENDOMETRIAL CANCER

RISK-SCORING MODELS FOR INDIVIDUALIZED PREDICTION OF OVERALL SURVIVAL IN LOW RISK AND HIGH RISK ENDOMETRIAL CANCER

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2Department of Bioinformatics and Statistics, Mayo Clinic, Rochester, USA

Objectives

Overall survival (OS) in endometrial cancer (EC) is dependent on multiple patient-, disease-, and treatment-specific risk factors. Comprehensive risk-scoring models were developed to estimate OS in low risk (LR) and high risk (HR) EC.

Methods

Patients undergoing primary surgery for EC from 1999 through 2008 were stratified histologically according to FIGO: (i) grade 1 and 2 endometrioid EC (LR), and (ii) grade 3 including non-endometrioid EC (HR). Associations between patient-, pathological- and treatment-specific risk factors and OS were assessed using multivariable Cox regression models. Factors independently associated with OS were used to construct nomograms and risk-scoring models.

Results

Eligible patients (N=1255) included 914 LR and 341 HR. After 30 postoperative days, deaths occurred in 141 (15%) LR vs. 161 (47%) HR patients; median follow-up 5 years. In LR patients, independent factors predictive of compromised OS included age, cardiovascular disease, pulmonary dysfunction, stage, tumor diameter, pelvic lymph node status, and 30-day postoperative complications. Among HR patients, age, ASA score, stage, lymphovascular space invasion, adjuvant therapy, paraaortic nodal status and cervical stromal invasion were independent predictors of compromised OS. The risk variables in the LR and HR nomograms (Figure) generate a risk-score estimating patient-specific survival. The models had excellent calibration and discrimination (unbiased c-indices = 0.818 and 0.811)
### Conclusions
Patients with LR and HR EC can be counseled regarding their predicted OS using the proposed risk-scoring models/nomograms. This may facilitate institution of more personalized treatment algorithms, surveillance strategies and lifestyle interventions.
Oral Presentation/Debate: ENDOMETRIAL CANCER

SURVIVAL ANALYSIS OF ROBOTIC VERSUS LAPAROSCOPIC SURGICAL STAGING FOR ENDOMETRIAL CANCER: A 3-YEAR FOLLOW-UP.

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Objectives
To compare the survival of women with endometrial cancer managed by robotic and laparoscopic assisted surgery.

Methods
Retrospective study conducted at two academic centers. Primary outcomes were overall and disease free survival, and recurrence.

Results
Between 2003 and 2010, 415 met the study criteria. One hundred and eighty three women had robotic and 232 women had laparoscopic assisted surgery. Both groups were comparable in age, body mass index, comorbid conditions, histology, surgical stage, tumor grade, total nodes retrieved and adjuvant therapy.

With a median follow-up of 38 months (range 4-61 months) for the robotic and 58 months (range 4 to 118 months) for the laparoscopic group, there were no significant differences in survival (3-year survival 93.3% and 93.6% for robotic and laparoscopic group respectively), disease free survival (DFS) (3-year-DFS 83.3% and 88.4% for robotic and laparoscopic group respectively), and tumor recurrence (14.8% vs. 12.1%).

<table>
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<tr>
<th>Follow up</th>
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<th>Disease Free survival (%)</th>
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<tr>
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<td>Robotic (n=183)</td>
<td>Laparoscopy (n=232)</td>
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Conclusions
Robotic assisted surgery yields equivalent oncologic outcomes when compared to laparoscopic surgery for endometrial adenocarcinoma.
Oral Presentation/Debate: ENDOMETRIAL CANCER

CHEMOTHERAPY IMPROVES DISEASE-FREE SURVIVAL IN STAGE IIIC LOW/INTERMEDIATE-GRADE BUT NOT IN HIGH-GRADE ENDOMETRIAL CANCER

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Objectives

Treatment failures in stage IIIC endometrial cancer (EC) are predominantly due to occult extra-pelvic metastases (EPM). The impact of chemotherapy (CT) on occult EPM was investigated according to grade; G1/2EC vs G3EC (including type II EC).

Methods

All surgical-stage IIIC EC from 1/1/1999 to 12/31/2008 treated at a single institution were included. Patient-, disease- and treatment-specific risk factors were assessed for an association with disease-free survival (DFS) using Cox proportional hazards regression.

Results

107 cases were Surgically staged with 85% (n=91) having a systematic LND (≥10 pelvic and ≥5 paraaortic LN resected). Among G1/2EC cases (n=47), independent predictors of DFS included grade 2 histology (adjusted hazard ratio (HR) 0.30; 95% CI 0.10, 0.91; p=0.03) and adjuvant CT (adjusted HR 0.22; 95% CI 0.05, 0.98; p=0.048). The 5-year extra-pelvic DFS with and without adjuvant CT was 93% and 52%, respectively (p=0.01, Figure 1A). Conversely, among G3EC (n=60), the sole independent predictor of DFS was lymphovascular space involvement (HR 2.63; 95% CI 1.16, 5.97; p=0.02). Adjuvant CT did not impact occult EPM in G3EC; the 5-year extra-pelvic DFS for G3EC with and without adjuvant CT was 43% and 42%, respectively (p=0.91, Figure 1B).
Conclusions
Chemotherapy improves DFS among stage IIIC G1/2EC but does not influence DFS, notably, extra-pelvic occult disease, among women with G3EC. Prospective assessment of CT impact on DFS in G3EC is warranted. Plus, development of innovative phase I and II trials utilizing novel systemic therapies for advanced G3EC is imperative.
Oral Presentation/Debate: ENDOMETRIAL CANCER

PIK3CA MUTATIONS BUT NOT PIK3CA AMPLIFICATIONS ARE EARLY EVENTS IN THE ENDOMETRIAL CARCINOGENESIS

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³Uni Computing Uni Research AS, Computational Biology Unit, Bergen, Norway
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Objectives
Complex atypical hyperplasias (CAH) are precursor lesions for endometrial carcinomas (EC). The diagnosis has low reproducibility and concurrent carcinoma is reported in up to 40%. Biomarkers that improve diagnostic accuracy may prevent unnecessary surgery for co-morbid women and those wanting to preserve fertility.

Aims: To identify molecular alteration distinguishing CAH from primary and metastatic EC lesions.

Methods
RNA from fresh frozen lesions (8 CAH, 158 primary and 19 metastatic EC) were hybridised to Agilent Microarrays. DNA was used for sequencing. Protein expression by immunohistochemistry and copy number alterations by fluorescence in situ hybridisation were assessed in FFPE tissue (67 CAH, 522 primary and 91 metastatic EC lesions).

Results
There was a significant increase in PI3K signaling from CAH to primary EC (p<0.001), but no further increase in metastatic lesions. Activating PIK3CA mutations were found in 3 of 8 investigated CAHs, but no PIK3CA copy number changes was observed. There was no significant change in a transcriptional signature for epithelial to mesenchymal transition (EMT) from CAH to low grade primary tumours. However, this EMT signature increased significantly with higher grade, and to metastatic lesions (p<0.001). ER and PR protein loss was seen in <3% in CAH but increased significantly with increasing tumour grade to >35% in grade 3 endometrioid primary tumours (p<0.001).

Conclusions
Activating PI3K mutations are present in CAH and PI3K kinase signalling increases from CAH to EC. Epithelial to mesenchymal transition and loss of hormone receptors appear to be later events in the carcinogenesis.
AGSO President

T. Kamura

Japan

Asian Society of Gynecologic Oncology: Who we are and Where to go.

ASGO was founded in 2009 as the principal organization in Asia contributing to the study, prevention and treatment of gynecological cancer. Asian women differ from non-Asians with respect to genetic background, disease presentation, and especially, the socio-cultural environment. In addition, a large proportion of the global burden of gynecologic cancer still remains across the Asian area. For these reasons, the Asian Society of Gynecologic Oncology plays an essential role in understanding, investigating, and resolving regional health problems much like other regional societies, such as the Society of Gynecologic Oncologists (SGO) and the European Society of Gynecologic Oncology (ESGO). Over 10 Asian countries and societies have approved this aim, and have joined as members. In order to carry out our mission, the activity of ASGO consists of the following: 1) ASGO holds biennial meetings where experts from across Asia meet to discuss the very latest advances in Gynecological Oncology treatment and care, as well as hold numerous conferences throughout the calendar year. During the year between the biennial meetings, an International Symposium is held to discuss particular topics. 2) The Journal of Gynecologic Oncology (IF 1.730) is published as the official journal of ASGO. 3) ASGO supports meetings which are held in member countries by sending speakers. 4) Exchanges clinical and relevant information among sister societies (IGCS, SGO, ESGO etc.). 5) Promotes physician exchanges for training young doctors among member countries.
Society Session: FUTURE DIRECTIONS IN GYN ONCOLOGY SOCIETIES

SGO President

B. Goff

1President SGO, USA

With the passage of the Affordable Care Act and the recognition that Americans spend two to three times what other developed countries spend on health care yet lag behind these countries in leading health indicators, the SGO is facing a rapidly changing health care environment. In the US the medical community is bracing for dramatic changes in how health care is provided and new payment reforms for both providers and hospitals. As a Society that cares for women with gynecologic cancer, our focus is how to cut costs yet improve the quality of gynecologic cancer care. Through our Quality and Outcomes Committee, we have developed quality indicators and metrics to demonstrate high quality care for women with gynecologic malignancies. We are developing registries in ovarian, cervical and endometrial cancer so physicians can track and compare outcomes, both for surgery and adjuvant therapy. In addition, the SGO has funded a Research Institute to bring together investigators interested in outcomes and comparative effectiveness research and provide data for payers. Cost effective and risk adjusted quality care will ultimately be tied to physician reimbursement, but health care providers need to be actively engaged in the process. In the area of clinical trials, the National Cancer Institute is reorganizing clinical trials research to increase efficiency and productivity. The NSABP, RTOG and GOG have consolidated into NRG Oncology. This will allow for scientific synergy, pooling of resources and potential opportunities to partner with collaborative groups abroad. Another significant focus for the SGO this year is prevention. We have launched public campaigns to address the low rates of HPV vaccination in the US and the impact that obesity plays in gynecologic cancers. In addition, we have convened a prevention task force to address low rates of genetic testing for mutations that lead to increased risk of gynecologic cancers and to develop appropriate referral and management guidelines. As a Society we look for opportunities to educate women and practitioners about preventative measures that can be taken to reduce the risk of gynecologic malignancies.
When we think of a humane approach to health and wellbeing in cancer care, the word ‘holistic’ is often used. The critical implication implicit in the use of this word is that clinical care, especially at specialist level, does not take sufficient notice of the needs of the person attached to the body part under scrutiny. That person is not only a whole body, but also a body existing within the social and emotional context of a family and community. There is a focus also on the idea of ‘narrative’: that clinicians need to take account of the patient’s unique story about what brought them to the clinic and which reveals their beliefs and understanding about why they are there. Although these issues are important, they do not address the crucial setting of the consultation and the minute by minute flows and exchanges of perspective that take place within it.

Paradoxically, a philosophical medical humanities eye view of the consultation reveals the importance of objectifying the body not only of the patient but also of the clinician. Such objectification enables a focus on precision and acute clinical skills, both of which are important to the patient. This paper will explain the essential nature of this perspective, and how it may be interlaced with the interpersonal within the clinical consultation. Both perspectives are crucial to humane clinical practice and are clearly in evidence in specialist gynaecological practice.
Parallel Session: TRANSLATIONAL RESEARCH

TUMOR PROGRESSION AND CHEMORESISTANCE IN OVARIAN CARCINOMA EFFUSIONS

B. Davidson

1Pathology, Norwegian Radium Hospital Oslo University Hospital, Oslo, Norway

The formation of malignant peritoneal (ascites) and pleural effusions is a common clinical manifestation of advanced-stage ovarian carcinoma at both diagnosis and disease recurrence. Ovarian carcinoma cells in effusion specimens contain populations of cancer stem cells and this anatomic site is increasingly regarded as important in the emergence of chemotherapy resistance in OC. Our group and collaborators has in recent years reported on the expression and clinical relevance of several molecules related to stemness, including Nestin, Notch3 and HMGA2. Using proteomics, we additionally observed marked changes in the expression of clinical role of cancer-associated markers in pre-chemotherapy effusions tapped at diagnosis and post-chemotherapy disease recurrence effusions, and reported on differences in the metabolic profiles of these specimens.

Molecules shown by our group to be significantly related to response to chemotherapy in OC include the PI3K pathway signaling molecule AKT, the NF-kappaB family member RELA, the transcription factors STAT5, Notch3 and PPAR-alpha/beta/gamma, the mitotic proteins class III beta-tubulin and Aurora-B, the death receptors DR4, DR5 and Fas, the adhesion molecule beta-parvin, the metastasis-related protein S100A4, and the anti-apoptotic molecule BCL-XL. Recently, we identified a gene signature related to chemoresistance in OC effusion specimens in a TaqMan-based qRT-PCR assay.

These data represent an in-depth study of the molecular characteristics of OC cells in effusions at diagnosis and disease recurrence. Future efforts by our group are designed to validate and expand our list of candidate molecules related to chemotherapy failure at this anatomic site, with the aim of identifying targets for therapeutic intervention.
Parallel Session: HPV TESTING/TYPING

HPV TESTING IN PRIMARY SCREENING IN LOW RESOURCES SETTINGS
M. Almonte1, R. Sankaranarayanan1

1Early Detection and Prevention, International Agency for Research on Cancer, Lyon, France

Background and aims:
Cervical cancer is a major public health problem in developing countries despite its high preventability. Cervical cancer is caused by persistent infection with one of the high-risk HPV types. Given the challenges in Pap smear screening, the role of HPV testing in primary screening in developing countries is described.

Methods:
Published information is reviewed and findings are summarised.

Results:
HPV DNA testing is a highly objective and reproducible test. Its sensitivity and specificity in detecting CIN2 and CIN3 lesions varied from 66-100% and 62-96% respectively. Evidence from randomised trials indicates that cervical cancer burden can be effectively reduced by HPV screening. In a randomised-trial in South Africa assessing HPV screen-and-treat with cryotherapy, the frequency of CIN 2 or worse lesions (CIN2+) was reduced by 73% at 36 months as compared to a 'control' group; the prevalence of CIN2+ in HIV-negative women by 69% and among HIV-positive women by 80%. There was a significant 48% reduction in cervical cancer mortality following a single round of HPV testing in a randomised trial in India. Strategies incorporating HPV testing are more cost-effective than cytology, especially when widespread HPV vaccination will reduce the prevalence of cervical lesions. Studies in developed countries showed higher detection in prevalence rounds and reduced frequency of CIN2+ in subsequent screening rounds.

Conclusions:
HPV testing is an exciting option for cervical cancer prevention in developing countries provided affordable screening tests are available. Planned investments in HPV vaccination and screening will save many precious lives in coming years.
HPV SELF-SAMPLING

P. Giorgi Rossi¹, A. Pezzarossi², W.G. HTA of the methods to increase participation to screening programs³

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²HTA, Laziosanità – Agenzia di Sanità Pubblica, Rome, Italy

Introduction:
The major barrier to cervical cancer screening effectiveness is still non-participation. HPV-DNA test has been proven effective as a primary screening test. This molecular test can be performed on self-collected samples, with sensitivity not-inferior, but lower specificity, than that of clinically collected cytology. These facts suggested that the use of self-sampling devices to increase participation in screening programmes in underscreened women was justified.

We present the results of a systematic review on the effect self-sampling on screening participation.

Methods:
Population: underscreened or Non-responder 25-64yo women; Intervention: mailing self-sampling device; Control: standard or enhanced recall for Pap-test at clinic; Outcome: participation; Study design: RCT.

A PubMed search was done until 31/7/2013. Abstracts to conferences and grey literature were searched.

Results:
We found 9 studies, randomising 98072 women. Direct home mailing of the device had higher participation than standard or enhanced recall to perform Pap test at the clinic (pooled Relative Risk=2.9 95% confidence interval: 1.6-5.2). All the studies observed a positive effect but the magnitude was extremely heterogeneous (RR range 1.2 – 9.1; I²=99%).

A further study compared the participation in a population in Mexico that had never been invited before. Participation to self-sampling was lower compared to Pap-test (RR=0.85, IC95%: 0.84-0.86), but the difference was due to the women “not found at home” to whom, according to protocol, the device was not mailed.

Conclusions:
Self-sampling devices are effective in increasing participation among non-responders. Context-specific logistical, behavioural, and cultural conditions can
strongly modify the effectiveness.

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>YEAR</th>
<th>SETTING</th>
<th>RR (95% CI)</th>
<th>Events, Treatment</th>
<th>Events, Control</th>
<th>%</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giorgi Rossi</td>
<td>2011</td>
<td>Italy</td>
<td>1.40 (1.09, 1.80)</td>
<td>121/222</td>
<td>86/19</td>
<td>11.15</td>
<td></td>
</tr>
<tr>
<td>Gok</td>
<td>2010</td>
<td>Netherlands</td>
<td>1.66 (1.27, 2.16)</td>
<td>7404/6086</td>
<td>46/277</td>
<td>11.13</td>
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<tr>
<td>Gok</td>
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<td>Netherlands</td>
<td>4.73 (2.98, 7.49)</td>
<td>7870/25561</td>
<td>17/261</td>
<td>10.63</td>
<td></td>
</tr>
<tr>
<td>Franca</td>
<td>2011</td>
<td>France</td>
<td>3.66 (3.24, 4.13)</td>
<td>9399/5552</td>
<td>311/4305</td>
<td>11.13</td>
<td></td>
</tr>
<tr>
<td>Szarewski</td>
<td>2011</td>
<td>UK</td>
<td>2.25 (1.71, 2.97)</td>
<td>153/1500</td>
<td>68/1500</td>
<td>11.10</td>
<td></td>
</tr>
<tr>
<td>Vihinen</td>
<td>2011</td>
<td>Finland</td>
<td>1.22 (1.13, 1.31)</td>
<td>756/2397</td>
<td>163/6302</td>
<td>11.37</td>
<td></td>
</tr>
<tr>
<td>Wikström</td>
<td>2011</td>
<td>Sweden</td>
<td>4.27 (3.66, 4.94)</td>
<td>779/2000</td>
<td>188/2068</td>
<td>11.31</td>
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<tr>
<td>Siancho-Garnier</td>
<td>2013</td>
<td>France</td>
<td>9.09 (7.87, 10.50)</td>
<td>16139829</td>
<td>198/98</td>
<td>11.31</td>
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<tr>
<td>Dafin</td>
<td>2013</td>
<td>Sweden</td>
<td>3.50 (2.24, 5.46)</td>
<td>147/1000</td>
<td>21/500</td>
<td>10.68</td>
<td></td>
</tr>
<tr>
<td>Overall (*-squared = 99.1%, p = 0.000)</td>
<td></td>
<td></td>
<td>2.90 (1.62, 5.19)</td>
<td>1970/72347</td>
<td>2567/25725</td>
<td>100.00</td>
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</tbody>
</table>

NOTE: Weights are from random effects analysis.
Parallel Session: OVARIAN CANCER ORIGINS - LATEST INSIGHTS AND IMPLICATIONS

PATHOGENESIS OF OTHER OVARIAN CARCINOMAS (TYPE-1) AND IMPLICATIONS FOR OVARIAN CANCER CONTROL

D. Huntsman

1Canada, BC Cancer Agency / University of British Columbia, Vancouver, Canada

Whilst high-grade serous carcinomas likely arise from fallopian tube precursor lesions, clear cell and endometrioid carcinomas, the second and third most common ovarian cancer subtypes, are strongly associated with endometriosis. The association with endometriosis is supported by recent epidemiologic studies and through an assessment of the impact of tubal ligation on subtype specific ovarian cancer risk. The notion that clear cell and endometrioid carcinomas are essentially uterine cancers in the wrong place is strengthened by the common occurrence of clear cell and endometrioid ovarian carcinomas arising directly adjacent to/contiguous with endometriosis and the near identical mutational profiles to those seen in uterine carcinomas. Strides have been made in understanding the origins of these cancers, however, there are still many unanswered questions. The proclivity of ovarian endometriosis to undergo transformation and the evolution of endometriosis into either a clear cell or endometrioid ovarian carcinoma subtype are both poorly understood. Though recent advances have been made to identify transformation-associated features of endometriosis, further work will be needed to flush out a tumour progression pathway. Whilst low-grade serous carcinomas appear to share fallopian tube origin, albeit potentially from different precursor cells, the origins of mucinous carcinomas are still controversial.
Omentectomy is the surgical removal of all or part of the greater omentum. The greater omentum consists of a double sheet of peritoneum folded on itself, which descend from the stomach and commencement of the duodenum pass in front of the small intestine and reflecting on itself ascends till the transverse colon. Between its two anterior layers, below the greater curvature of the stomach, is the anastomosis between the right and left gastroepiploic vessels. In its course it distributes several gastric and omental branches. Greater omentum is one of the most common site of metastasis from ovarian cancer and for this reason omentectomy has been recommended as staging procedure for ovarian cancer or in cases of advanced endometrial cancer. Infracolic omentectomy consist in removal of great omentum up to the transverse colon. Omentum is lifted up to see its attachment to the transverse colon. The avascular area between the posterior leaf of the omentum and the colon is incised by electrocautery parallel and close to the transverse colon. The branches of the gastroepiploic vessels, are clamped or ligated and cutted. If supracolic omentum is not involved with disease, omentectomy is completed by excising omentum at the level of transverse colon. If there is gross disease, supracolic omentectomy is done separating the transverse colon from the gastrocolic ligament and securing vessels arising from gastric arcade. Afterwards the separation is continued bilaterally toward the hepatic and splenic flexures. After complete mobilization, the entire omentum (gastrocolic and infracolic) is removed.
Parallel Session: LATE BREAKING NEWS/HIGHLIGHTS

RANDOMISED DOUBLE-BLIND PHASE III TRIAL OF CEDIRANIB (AZD 2171) IN RELAPSED PLATINUM SENSITIVE OVARIAN CANCER: RESULTS OF THE ICON6 TRIAL.

F.A. Raja¹, T.J. Perren², A. Embleton³, G.J.S. Rustin⁴, G. Jayson⁵, A.M. Swart³, M. Vaughan⁶, H. Hirte⁷, D.P. Stark³, J.A. Ledermann¹, on behalf of the ICON6 Collaborators (NCRN/NCIC/ANZGOG/GEICO)

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²Department of Oncology, St James University Hospital, Leeds, United Kingdom
³Clinical Trials Unit, Medical Research Council, London, United Kingdom
⁴Department of Oncology, Mount Vernon Hospital, Northwood Middlesex, United Kingdom
⁵Department of Oncology, Christie Hospital, Manchester, United Kingdom
⁶Medical Oncology, Christchurch Hospital, Christchurch, New Zealand
⁷Medical Oncology, Hamilton Regional Cancer Center, Hamilton Ontario, Canada
⁸Medical Oncology, St James University Hospital, Leeds, United Kingdom

Objectives
Cediranib, a potent oral inhibitor of VEGFR-1,-2,-3, inhibits VEGF signalling. Evidence of single agent activity in ovarian cancer provided the basis for a phase III trial with chemotherapy and as maintenance therapy in platinum-sensitive ovarian cancer in first relapse.

Methods
ICON6 is an international three-arm, double-blind placebo-controlled randomised trial. Patients were randomised (2:3:3) to receive up to six cycles of platinum-based chemotherapy with either placebo (reference), cediranib 20mg/d during chemotherapy followed by placebo for up to 18 months (concurrent), or cediranib 20mg/d followed by maintenance cediranib (concurrent+maintenance). Primary endpoint was progression-free survival (PFS) for reference vs. concurrent+maintenance arms. Secondary endpoints were overall survival (OS), toxicity, quality of life (QoL).

Results
In total 456 eligible patients were enrolled. PFS comparing reference and concurrent+maintenance using a log-rank test gave a p-value of 0.00001 with an associated Hazard Ratio (HR) of 0.57 (95% CI 0.45-0.74). However, because of non-proportional hazards (p=0.0237 for PFS and p=0.0042 for OS) the HR can be difficult to interpret, and instead survival time was estimated using restricted means (RM) with HRs given for completeness. The RM estimates an increased time to progression of 3.2 months from 9.4 to 12.6, during 2 years. Similarly using RM, OS increased by 2.7 months from 17.6 to 20.3 (HR 0.70; log-rank test p=0.0419). Hypertension, fatigue and diarrhoea were most notable AEs. Toxicity and QoL data will be presented.

Conclusions
Cediranib given concurrently with platinum-based chemotherapy and continued as maintenance significantly improves both PFS and OS in women with recurrent ovarian cancer.
NEOADJUVANT CHEMOTHERAPY FOLLOWED BY ROBOTIC RADICAL HYSTERECTOMY IN LOCALLY ADVANCED CERVICAL CANCER: A DOUBLE INSTITUTION STUDY

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²Department of Gynecology Cervical Cancer Center, European Institute of Oncology, Milan, Italy

Objectives
Minimally invasive surgery has been performed in locally advanced cervical cancer (LACC) without adverse effect in patient’s overall prognosis and survival. The aim of this report is to evaluate the feasibility and morbidity of total robotic radical hysterectomy (TRRH) with pelvic lymphadenectomy in patients with LACC after neoadjuvant chemotherapy (NACT).

Methods
From February 2008 to April 2013 a prospective data collection of women undergoing TRRH for cervical cancer stage FIGO IB2 to IIB, after neoadjuvant chemotherapy, was conducted at “Regina Elena” National Cancer Institute of Rome and European Institute of Oncology of Milan. All patients deemed operable underwent TRRH with pelvic lymphadenectomy within 4 weeks from the last chemotherapy cycle.

Results
Median operative time was 225 minutes (range, 105 – 387 minutes). The median blood loss was 150 mL (range, 30 – 700 mL). The median number of removed pelvic lymph nodes was 23 (range, 8 – 69). Sixteen patients had an optimal response (12 PCR, 4 pPR1) to chemotherapy, 33 patients had a pPR2 and 11 patient showed stable disease. No disease progression was observed. Adjuvant therapy was administrated in 36 patients (60%). We experienced an intraoperative complication, but no conversion to laparotomy was necessary. Six patient received a blood transfusion. At the time of this report, with a median follow-up of 21.3 months, 50 patients (83%) are free from recurrence.

Conclusions
This experience demonstrates the feasibility of TRRH pelvic lymphadenectomy after NACT in LACC with good accuracy and safety.
A PHASE 3, RANDOMIZED, DOUBLE-BLIND TRIAL OF WEEKLY PACLITAXEL PLUS TREBANANIB OR PLACEBO IN WOMEN WITH RECURRENT OVARIAN CANCER: TRINOVA-1


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²Area Clinica de Oncologia Ginecológica, Fundacion Instituto Valenciano de Oncologia, Valencia, Spain
³Department of Obstetrics and Gynecology, University Hospital Leuven, Leuven, Belgium
⁴Gynecologic Oncology Unit Fondazione IRCCS, Istituto Nazionale per La Cura e lo Studio dei Tumori, Milano, Italy
⁵Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka-Shi, Japan
⁶Department of Obstetrics and Gynecology, Samsung Medical Center, Seoul, Korea
⁷Department of Medical Oncology, Hospital Universitari Vall d’Hebron, Barcelona, Spain
⁸Université Lyon-I, Centre Léon Bérard, Lyon, France
⁹Division of Gynecologic Oncology, Centre Hospitalier de l’Université de Montréal, Montreal, Canada
¹⁰Women’s Cancer Program at the Samuel Oschin Comprehensive Cancer Center, Cedars-Sinai Medical Center, Los Angeles, USA
¹¹Department of Medicine, Institut Gustave Roussy, Villejuif, France
¹²Academic Haematology and Oncology, Cabrini Hospital, Malvern, Australia
¹³Subdirección de Medicina Interna, Instituto Nacional de Cancerologia, Mexico City, Mexico
¹⁴Department of Gynecologic Oncology and Reproductive Medicine, University of Texas MD Anderson Cancer Center, Houston, USA
¹⁵Department of Obstetrics and Gynecology, Columbia University Medical Center, New York, USA
¹⁶Department of Obstetrics and Gynecology, Medical University Innsbruck, Innsbruck, Austria
¹⁷Latvian Oncology Center, Riga Eastern Clinical University Hospital, Riga, Latvia
¹⁸Department of Global Biostatistical Science, Amgen Inc., Thousand Oaks, USA
¹⁹Department of Oncology, Amgen Inc., Thousand Oaks, USA
²⁰Department of Medicine, Princess Margaret Hospital, Toronto, Canada

Objectives
Angiogenesis is a valid therapeutic target in epithelial ovarian cancer (EOC). Trebananib (formerly AMG 386; Amgen; trial sponsor) is an anti-angiogenesis peptibody that inhibits the binding of angiopoietin 1/2 to the Tie2 receptor.

Methods
TRINOVA-1 enrolled 919 women with recurrent EOC (platinum-free interval [PFI] <12 months; platinum-refractory patients were excluded). Randomization (stratified by PFI, measurable disease, region) was to paclitaxel 80 mg/m² IV QW (3 weeks on/1 week off) with either blinded placebo IV QW or trebananib 15 mg/kg IV QW.
Results
Trebananib prolonged PFS by 52% (stratified Cox model HR=0.66, P<0.001) from a median of 5.4 (95% CI 4.3–5.5) to 7.2 months (95% CI 5.8–7.4). Response rate increased from 30% to 38%. At a planned interim analysis of OS (313 deaths), there was a trend in improvement (HR=0.86, P=0.19; median 17.3 vs 19 months). The incidence of G3/4 adverse events (AE) was similar between arms. Trebananib was associated with more AE related treatment discontinuations (6% vs 17%) and increased edema events (28% vs 64%). Class-specific anti-vascular endothelial growth factor (VEGF)–associated AEs (hypertension, proteinuria, wound-healing complications, arterial thrombotic events) were not increased. Pre-specified covariates in the primary analysis are described below. Additionally, a post hoc analysis in the elderly is reported.

<table>
<thead>
<tr>
<th>Clinical Factor</th>
<th>PFS Events / Subjects (%) Paclitaxel + Placebo</th>
<th>PFS Events / Subjects (%) Paclitaxel + Trebananib</th>
<th>PFS HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>292 / 353 (80)</td>
<td>259 / 387 (67)</td>
<td>0.65</td>
</tr>
<tr>
<td>Asian</td>
<td>62 / 82 (76)</td>
<td>38 / 58 (66)</td>
<td>0.62</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>318 / 396 (80)</td>
<td>239 / 384 (67)</td>
<td>0.65</td>
</tr>
<tr>
<td>≥70</td>
<td>43 / 62 (69)</td>
<td>51 / 77 (66)</td>
<td>0.80</td>
</tr>
<tr>
<td>Line of therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>133 / 172 (77)</td>
<td>126 / 190 (66)</td>
<td>0.75</td>
</tr>
<tr>
<td>2</td>
<td>143 / 172 (83)</td>
<td>121 / 174 (70)</td>
<td>0.54</td>
</tr>
<tr>
<td>3</td>
<td>85 / 114 (75)</td>
<td>61 / 94 (65)</td>
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<td>PFI</td>
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<td>&lt;6 months</td>
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<td>178 / 235 (76)</td>
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<td>≥6 months</td>
<td>157 / 212 (74)</td>
<td>129 / 223 (58)</td>
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<td>Prior anti-angiogenic</td>
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<td>34 / 37 (92)</td>
<td>25 / 35 (71)</td>
<td>0.69</td>
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<td>No</td>
<td>327 / 421 (78)</td>
<td>285 / 426 (67)</td>
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<td>Bulky disease (&gt;5cm)</td>
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<td>Yes</td>
<td>78 / 99 (79)</td>
<td>71 / 107 (68)</td>
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<tr>
<td>No</td>
<td>262 / 334 (78)</td>
<td>225 / 328 (69)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Conclusions
Trebananib added to weekly paclitaxel significantly improved PFS in this study population. The benefit was consistent across pre-specified clinically relevant subsets. While edema was increased, class-specific anti-VEGF associated adverse events were not increased.
PELVIC LYMPHADENECTOMY IMPROVES SURVIVAL IN CERVICAL CANCER PATIENTS WITH LOW VOLUME DISEASE IN THE SENTINEL NODE, A RETROSPECTIVE MULTICENTRE COHORT STUDY


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In this study we aim to describe the value of pelvic lymph node dissection following sentinel lymph node biopsy in early stage cervical cancer. Before pelvic lymph node dissection can be abandoned in favour of performing sentinel lymph node biopsy alone, the effect of a full pelvic lymphadenectomy on survival needs to be assessed. Methods: We performed a retrospective multicentre cohort study in eight gynaecological oncology departments. In total, 645 women with FIGO stage IA to IIB cervical cancer of squamous, adeno or adenosquamous histological type who underwent sentinel lymph node biopsy followed by pelvic lymph node dissection were enrolled in this study. Radioisotope tracers and blue dye were used to localise the sentinel node, and pathologic ultrastaging was performed. Results: Among patients with low volume disease (micrometastases and isolated tumor cells) in the sentinel node the overall survival was significantly better (p=0.046) if more than 16 non sentinel lymph nodes were removed. No such significant difference in survival was detected in patients with negative or macrometastatic sentinel nodes. Conclusion: In patients with negative or macrometastatic disease in the sentinel nodes, an additional lymph node dissection did not alter survival. Conversely, our data suggest that the survival of patients with low volume disease is improved when more than 16 additional lymph nodes are removed.
Parallel Session: LATE BREAKING NEWS/HIGHLIGHTS

POPULATION BASED OUTCOMES OF EARLY STAGE OVARIAN ENDOMETRIOID CARCINOMA (OEC) IN BRITISH COLUMBIA
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Objectives
Outcomes for early stage OEC are not well characterized. The benefit of post surgical therapy remains unclear. Our aims were: 1) determine prognostic factors and 2) determine the impact of adjuvant treatment on survival in patients with early stage OEC.

Methods
Women with FIGO stage I and II OEC referred to one of the centres of the British Columbia Cancer Agency from 1984 to 2008 were included in a retrospectively abstracted computerized database. Irradiation (abdominal pelvic) with chemotherapy (3 cycles of platinum combination) was given for stage IA/B grade 2/3, stage IC any grade and stage II any grade. Patients were restaged using FIGO 1987 criteria. Univariate analysis of DFS using the Kaplan-Meier method was used. Comparisons were performed using the log-rank test.

Results
172 patients were identified. 12% had grade 3 disease. 89%, 85% and 55% of stages II, IC and IA/B received adjuvant treatment, respectively. 24%, 40% and 36% of patients received surgery, surgery with chemotherapy and surgery with chemotherapy and irradiation, respectively. 5yr DFS was 95%, 84% and 74% for stages IA/B/C rupture only, IC other (cytologic positivity/surface involvement) and II respectively. No benefit in DFS was seen in stage IA/B with adjuvant treatment. Decision tree analysis defined two poor prognostic groups with a DFS benefit from irradiation (RR 1.77, 95% CI, 0.74-4.24), 1)≥55 yrs with stage IC other 2)stage II.

Conclusions
Omission of adjuvant treatment can be considered in the majority of early stage OEC, except stage IC other and II, where irradiation may be of benefit.
Parallel Session: LATE BREAKING NEWS/HIGHLIGHTS

ICON7: FINAL OVERALL SURVIVAL RESULTS IN THE GCIG PHASE III RANDOMISED TRIAL OF BEVACIZUMAB IN NEWLY DIAGNOSED OVARIAN CANCER

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Background
ICON7 investigated safety and efficacy of adding bevacizumab to standard chemotherapy in newly diagnosed ovarian cancer. Primary analysis of progression-free survival (PFS) demonstrated benefit of bevacizumab addition. Final analysis of OS is reported here.

Methods
Women with high-risk early (FIGO stage I or IIa (grade 3 or clear cell), capped ≤10%) or more advanced (stage IIb-IV) epithelial ovarian, primary peritoneal or fallopian tube cancer were randomised (1:1) to 6 cycles of 3 weekly chemotherapy alone, or with concurrent bevacizumab (7.5mg/kg) for 5 or 6 cycles followed by 3-weekly single-agent bevacizumab for 12 additional cycles.

Results
1,528 women were randomised from seven GCIG groups. A pre-specified poor prognosis group at high risk of progression comprised 33% (502). Using the Grambsch-Thernau test, comparison of hazard functions consistently showed non-proportional hazards (PH). The Restricted Mean Survival Time (RMST) was therefore used as the primary estimate rather than the hazard ratio. Overall OS analysis: median follow-up 49 months, 714 deaths (352 control, 362 bevacizumab), median OS was 58 months with RMST improvement of 0.9 months from 44.6 to 45.5 months (log-rank p=0.85, P-H test p=0.02). In the poor prognosis group 332 died (174 control, 158 bevacizumab), with a 4.8 month RMST improvement from 34.5 to 39.3 months (log-rank p=0.03, PH test=0.007).
Conclusions
In the whole randomised population, bevacizumab in conjunction with
 carboplatin/paclitaxel did not improve survival by a clinically important amount.
 However, in a pre-specified subgroup at high risk of progression, a 4.8 month
 benefit in restricted mean survival time is observed.
Lymphoedema (LE) is defined as a chronic inflammatory disease caused by an accumulation of protein rich tissue fluid within the interstitium due to a mechanical failure of the lymph drainage system. In case of secondary LE following (the treatment of) gynecological tumors, the reason of this mechanical failure mainly lies in the damage caused by oncological surgery and/or irradiation. LE arises if the balance between the reduced transport capacity of the lymph drainage system and the lymphatic load is disturbed. Therefore, a variety of additional factors influencing this balance may contribute to the LE risk in patients with gynaecological tumors.

Although data is inconsistent, LE still appears to be the most frequent long-term complication after gynaecological tumors. LE risks within 5 years following cancer vary between approx. 20% and >50%. Patients with vulvar cancer are at greatest risk of developing LE.

LE prevention after gynaecological tumors should always begin with extensive patient counselling on possible individual LE risk factors, and means of their reduction. Furthermore, a prophylactic application of Complex Decongestive Therapy (CDT) measures may be useful in some cases, although consistent data is missing.

The standard treatment-of-choice of LE after gynaecological tumors is CDT. CDT is a tetrade consisting of manual lymphatic drainage, compression treatment, remedial decongestive exercises and skin care. According the stage of LE, CDT may be applied in two treatment phases, the “high-dosage” phase 1 of decongestion, and the “lower-dosage” phase 2 of conservation.
Parallel Session: LIFE AFTER THE CANCER

NO HEALTH WITHOUT MENTAL HEALTH: THE IMPORTANCE OF PSYCHOSOCIAL CARE IN GYNAECOLOGICAL CANCER

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Provision of psychosocial care within treatment follow-up and survivorship contexts needs to be an integral part of best practice in gynaecological oncology. Evidence on areas of need in terms of psychosocial care is presented. The benefits to patients’ quality of life, mental health and in terms of service cost reductions, are outlined.

Currently recommended service models are described. Guidelines for the integration of routine Screening for Distress as the 6th Vital Sign and integration of psychosocial care into quality comprehensive cancer care are covered.

Clinicians’ implementation of these service models and guidelines will help bring their practice in line with current and future requirements for quality comprehensive cancer care.
LESS AGGRESSIVE SURGERY IN EARLY STAGE CERVICAL CANCER: CON SIDE VIEWPOINT

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As radical hysterectomy is sometimes associated with significant adverse effect such as urinary dysfunction, less radical or non-radical surgery for early-stage cervical cancer to reduce morbidity while maintaining radicality has gotten widespread support by many gynecologic oncologists. Personally I also support less wide & conservative surgical approach. However, when we think about the case of invasive breast cancer, we will be acknowledged that in our field level I or II evidence is so scanty. In other words, there is a firm belief but no supporting evidence. Among the best known NSABP studies are protocol B-04 and B-06 which were started from 1971, more than 40 years ago! Based on the results of these trials breast surgeons nowadays rarely perform radical mastectomy which was originated from Halstedian principles of tumor growth and dissemination. Actually the concept of 'radicality', at least the terminology, in the treatment of cervical cancer was adopted from the Halsted school. They abandoned the concept and moved from radical to simple mastectomy to lumpectomy but still we are not, can't yet till we get at least one RCT supporting less aggressive surgery. Somebody may argue that almost all the current surgical management of gynecological cancer is not derived from the phase III clinical trials. However, we can't follow a detour. It will cause chaos. I would like to close with the maxim for surgeon viz, 'new surgical approaches are uniformly recommended and adopted after phase III trials demonstrate superior safety, tolerability and/or effectiveness'.
Preoperative Thrombocytosis is Associated with Advanced Stage Disease and Elevated Circulating Hepatocyte Growth Factor Levels in Women with Ovarian Carcinoma

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Objectives
Elevated thrombocyte levels have been associated with aggressive tumor biology and poor outcome in several cancers, including epithelial ovarian cancer. We have previously described the diagnostic and prognostic value of Hepatocyte Growth Factor (HGF) in ovarian epithelial cancer. HGF enhances cell proliferation, motility, and angiogenesis, and human platelets express the HGF receptor. There are few reports of possible associations between thrombocyte and circulating HGF levels. The objectives were to evaluate the prevalence and prognostic value of thrombocytosis in women with epithelial ovarian, tubal, and peritoneal cancer, and to examine the correlation between thrombocyte and serum HGF levels in women with ovarian cancer.

Methods
All women undergoing surgery for primary epithelial ovarian, tubal, and peritoneal cancer in a five-year period between 2000 and 2005 at St. Olavs Hospital in Norway were included. Thrombocytosis was defined as platelet counts ≥400 x 10⁹/l. Clinical data, blood values including platelets and HGF, and data regarding treatment and five-year follow-up were analyzed.

Results
We included 166 cases of ovarian, peritoneal, and tubal cancer. HGF was available in 48 cases. Preoperative thrombocytosis was found in 41% of the women. The women with thrombocytosis had more advanced stage disease (p=0.007), were less optimally debulked (p=0.009), had higher levels of serum Hepatocyte Growth Factor preoperatively (p=0.045), and had lower 5-year overall survival in univariate analyses (p=0.005) than the women without thrombocytosis.

Conclusions
Preoperative thrombocytosis was associated with advanced stage disease and elevated levels of serum HGF in women with ovarian carcinoma.
CXCR3 EXPRESSION IN OVARIAN HIGH GRADE SEROUS CARCINOMA: A POTENTIAL MARKER FOR TARGETED THERAPY

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**Objectives**

Ovarian cancer is the most deadly gynaecological cancer and accounts for 4% of all cancer deaths amongst women. However, at least in advanced ovarian cancer, improvements in survival through conventional treatment strategies have reached a plateau. Angiogenesis is a critical requirement for tumourigenesis and metastasis and has been associated with a worse clinical outcome in various tumours including ovarian cancer. Hence Bevacuzimab, a Vascular Endothelial Growth Factor (VEGF) inhibitor has been trialled with some success. The ultimate imbalance between pro-angiogenic and anti-angiogenic factors may have a potential role to determine the response to VEGF inhibitors. To this end, evaluation of the combined expression of pro- and anti-angiogenic markers may identify patients who are more likely to respond to targeted therapy.

**Methods**

The expression of CXCR3 in samples from 268 ovarian high grade serous carcinoma, was investigated using a monoclonal antibody targeting CXCR3 on tissue micro-array blocks, followed by semi-quantitative scoring of stain intensity.

**Results**

High CXCR3 expression was significantly associated with increased overall and progression-free survival. Significant association with survival was maintained with Cox regression analysis. The combined expression of CXCR3 and VEGF demonstrated a potentially more influential role of CXCR3 in relation to survival than VEGF.

**Conclusions**

The emergence in the current study of a potentially new anti-angiogenic marker (CXCR3) in ovarian cancer posed the question whether the expression of CXCR3 may interfere with the efficacy of VEGF inhibitors.
e-Poster Orals: OVARIAN CANCER

PROGNOSIS PREDICTION MODEL FOR FIGO STAGE I MUCINOUS EPITHELIAL OVARIAN CARCINOMA

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Objectives
As a distinctive disease entity, mucinous epithelial ovarian carcinoma (mEOC) has different aspects of initial presentation, clinical course and response to therapy from those of serous EOC. This study is to develop a progression-free survival (PFS) prediction model for patients with FIGO stage I mEOCs.

Methods
Using the Asan Medical Center database, we identified all patients with mEOC who had surgery at our institution between 1990 and 2012. Disease-specific mortality was estimated using the Kaplan-Meier method. Significant factors on multivariate analysis were included in the Cox proportional hazards regression model, which identified factors utilized in the prediction model. The concordance index (CI) was used as an accuracy measure, with bootstrapping to correct for optimistic bias. Calibration plots were constructed.

Results
One-hundred ninety five patients were identified and 164 patients, who confirmed to be FIGO stage I, were included in this study. In the median follow-up of 65.8 months, 20 patients (13.4\%) recurred and 11 patients (7.4\%) died from the cancer. The most predictive prediction model was constructed using three variables: the level of initial CA-125, bilaterality of the tumor and additional pathologic finding such as microinvasion, intraepithelial carcinoma, or extensive invasion. This prediction model was internally validated using bootstrapping and shown to have CI of 0.68 (95\% CI 0.5654-0.7972).
Conclusions
With this prediction model, it is possible to distinguish patients who will probably have aggressive clinical course from those who will not among patients with FIGO stage I. We recommend adjuvant chemotherapy to patients who are expected to have poor prognosis even in FIGO stage I.
A CURRENT PERSPECTIVE ON THE PATHOLOGICAL ASSESSMENT OF ADULT-TYPE GRANULOSA CELL TUMORS OF THE OVARY.
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³Institute of Pathology, University of Heidelberg Medical School, Heidelberg, Germany
⁴Institute of Pathology, A2 2, Mannheim, Germany

Objectives
The diagnosis of adult-type granulosa cell tumors of the ovary (aGCT) is based on histomorphology aided by immunohistochemical stains for sex cord markers. Recently, molecular analysis for the somatic 402 C/G missense point mutation in the Forkhead box protein L2 (FOXL2) has emerged as a potential diagnostic test for aGCT. We have investigated the impact of FOXL2 mutation testing in a large cohort of aGCT diagnosed by conventional histology and immunohistochemistry.

Methods
FFPE-tissue cores from a cohort of 52 ovarian tumors previously diagnosed as aGCT by expert gynecopathologists were immunohistologically analyzed for inhibin, calretinin, CD10, CD56, CD99, CD117, synaptophysin, chromogranin, WT1, EMA, PR, ER, MelanA, p53, pan-keratin, and FOXL2. FOXL2 mutation status was determined by Sanger sequencing and high sensitivity digital TaqMan allelic discrimination assay. Histomorphology was reassessed by two expert gynecopathologists.

Results
FOXL2 mutation analyses could be successfully performed in 46 cases, of which 40 were positive for the 402C/G mutation, confirming a diagnosis of aGCT. In the remaining 6 cases one case was confirmed on review as a FOXL2 wild-type aGCT, whereas in the other cases diagnoses of juvenile GCT, endometrioid carcinoma with sex cord-like differentiation, steroid cell tumor, cellular fibroma with minor sex cord differentiation and sex cord stromal tumor, not otherwise specified were made.

Conclusions
In cases where a diagnosis of adult-type granulosa cell tumor is a consideration and unequivocal diagnosis is not possible based on routine immunostains, FOXL2 mutation testing can help to confirm the diagnosis. It is particularly relevant for accurate subclassification within the group of sex cord-stromal tumors.
SINGLE DOSE OF TRANEXAMIC ACID REDUCES BLOOD LOSS AND TRANSFUSIONS IN SURGERY FOR ADVANCED OVARIAN CANCER

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²Dept of Clinical and Experimental Medicine, Department of Orthopedics, Linköping, Sweden
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⁴Department of Obstetrics & Gynecology, Department of Obstetrics & Gynecology, Kalmar, Sweden
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Objectives
Radical debulking ovarian cancer surgery is an extensive intervention often leading to an intraoperative bleeding exceeding 1000 ml. About 50% of women undergoing such surgery require blood transfusion. The aims of this study were to determine whether a single dose of tranexamic acid (TXA) given intravenously immediately preoperatively in surgery for presumed advanced ovarian cancer reduces perioperative blood loss and blood transfusions.

Methods
100 women with presumed advanced ovarian cancer scheduled for radical debulking surgery were enrolled in a randomised double-blind, placebo controlled Swedish multicentre study between March 2008 and May 2012. 50 were allocated to receive TXA and 50 to receive placebo. 48 and 45, respectively, completed the trial and were analysed. The volume of TXA (15 mg/kg body weight, 100 mg/ml tranexamic acid) or the same volume of placebo (0.9% NaCl) was added to a 100 ml saline solution plastic bag. The study medication was given immediately before the start of surgery. Data were analysed by means of multivariate statistics adjusted for confounding factors.

Results
The total blood loss volume and RBC transfusion rate were statistically significantly lower in the TXA group compared with the placebo group. Mean total blood loss was 608 ml±666 ml and 835 ml±648 ml, respectively (p=0.039; Fisher’s PLSD p=0.045). 14 (29.2%) and 19 (42.2%), respectively received RBC transfusions (adjusted OR 0.38; upper 95% CI: 0.97; p=0.034).

Conclusions
A single dose of TXA given immediately before surgery reduces blood loss and transfusion rates significantly in surgery for advanced ovarian cancer.
Does the Risk of Malignancy Algorithm Have a Role in Triaging Symptomatic Women for Further Investigation? Results of a Pilot ‘Real World’ Study.

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Objectives

The Risk of Malignancy Algorithm (ROMA™) incorporating Human Epididymis Protein 4 (HE4) and CA125 ovarian cancer (OC) tumour-markers is used for differential diagnosis of adnexal masses. Evidence suggests ROMA performs at least as well as the ultrasound-dependent Risk of Malignancy Index, with better discrimination in premenopausal women. We wanted to assess ROMA™ as a potential first-line test in primary care to triage women to hospital.

Methods

HE4 was measured prospectively using standard clinical laboratory immunoassay in a consecutive series of 125 patients with symptoms and/or signs suggestive of OC, in whom CA125 had been requested by the assessing primary care physician (22%), gynaecologist (68%), or other hospital specialist (10%). Performance characteristics of the ROMA™ were compared with CA125 (cut-off 35 u/ml).

Results

77 (62%) women were premenopausal and 48 (38%) postmenopausal. Six (5%) were subsequently diagnosed with OC, five (4%) with non-ovarian cancers (2 endometrial, 1 colorectal, 1 stomach, 1 lung), and two with borderline ovarian carcinoma (2%). Performance characteristics with 95% confidence intervals are shown below:

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125 for OC only</td>
<td>83 (36-99)</td>
<td>73 (64-81)</td>
<td>14 (5-30)</td>
<td>99 (93-100)</td>
</tr>
<tr>
<td>ROMA™ for OC only</td>
<td>83 (36-99)</td>
<td>80 (71-86)</td>
<td>17 (7-36)</td>
<td>99 (94-100)</td>
</tr>
<tr>
<td>CA125 for all cancers</td>
<td>62 (32-85)</td>
<td>74 (65-82)</td>
<td>22 (10-39)</td>
<td>94 (87-98)</td>
</tr>
<tr>
<td>ROMA™ for all cancers</td>
<td>77 (46-94)</td>
<td>83 (75-89)</td>
<td>34 (19-54)</td>
<td>97 (90-99)</td>
</tr>
</tbody>
</table>

Conclusions

Although in this small pilot study differences were not significant, ROMA™ appeared to perform at least as well as CA125 for OC diagnosis, and outperformed CA125 for detection of all malignancies; one in three women with an abnormal ROMA™ result had malignancy/borderline OC requiring hospital referral. Only 3% with malignancy/borderline OC tested negative. This suggests a potential role for ROMA™ in triage of symptomatic women from primary to secondary care for investigation of possible malignancy.
e-Poster Orals: OVARIAN CANCER

PHARMACOLOGIC INHIBITION OF C-JUN N-TERMINAL KINASE (JNK) SIGNALING PATHWAY INHIBITS PROLIFERATION, BLOCKS CELL CYCLE PROGRESSION AND INDUCES APOPTOSIS OF HUMAN GRANULOSA CELL TUMOR

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Objectives

We aimed to investigate the role of c-Jun N-terminal kinase (JNK) signaling pathway in human GCT.

Methods

Human GCT line COV 434 and two different pharmacologic JNK inhibitors SP600125 and AS601245 were used. Cell proliferation was monitored real-time (xCelligence). JNK activation was assessed with phospho c-Jun expression Serine 10 in WB. Cell cycle was analyzed with flow cytometry, apoptosis with YO-PRO-1 staining.

Results

The cells exhibited density dependent growth curves (Table-1A). When they were treated with the inhibitors at the indicated doses at log phase. Cell proliferation was halted by both inhibitors in a dose-dependent manner (Table-1B). Furthermore, the cells accumulated at G2 phase when JNK pathway was interrupted with AS601245 (57%) and SP600125 (39%) during G2/M transition compared to control cells (10%) proceeding through G2/M phase regularly (p<0.001). Compared to 3.5% of control cells, 14% and 30% of the cells underwent apoptosis when treated with 50 µM SP600125 and AS601245, respectively. At 100 µM dose the apoptotic fraction increased 68% and 76%, respectively (p<0.01).

<table>
<thead>
<tr>
<th>TABLE-1A</th>
<th>Groups (the cell number/we l)</th>
<th>A (40X10³)</th>
<th>B (20X10³)</th>
<th>C (10X10³)</th>
<th>D (5X10³)</th>
<th>E (2500)</th>
<th>F (1250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to enter log phase (h)</td>
<td>16</td>
<td>34</td>
<td>51</td>
<td>85</td>
<td>Not reached at 120h</td>
<td>Not reached at 120h</td>
<td></td>
</tr>
<tr>
<td>Mean cell index±SD</td>
<td>3.12±1.7</td>
<td>1.5±1.1</td>
<td>0.78±0.6</td>
<td>0.32±0.03</td>
<td>0.096±0.08</td>
<td>0.03±0.01</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE-1B</th>
<th>CONTR OL</th>
<th>JNK</th>
</tr>
</thead>
<tbody>
<tr>
<td>(12.5µm)</td>
<td>(25µm)</td>
<td>(50µm)</td>
</tr>
</tbody>
</table>
Conclusions
Targeting JNK signaling pathway may provide a therapeutic benefit in the treatment of granulosa cell tumors for which no curative therapy exist beyond surgery.

Funded by Scientific and Technological Research Council of Turkey (TUBITAK) 109S164 to Ozgur Oktem.
A COMPARATIVE STUDY BETWEEN PRIMARY TUMORS, ASCITES AND METASTASES REVEALS A NEW GENE EXPRESSION PROFILE ASSOCIATED WITH OVARIAN CANCER DISSEMINATION

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Objectives
Epithelial ovarian cancer (OC) is the most lethal gynecological malignancy and the fifth cause of cancer deaths in women in the Western world. Largely asymptomatic, OC is frequently (75-80%) detected at late stage. Five-year survival rate for women with advanced stage disease is less than 20%, while the cure rate is almost 90% when are diagnosed at early stages. Epithelial OC metastasizes by direct extension from the ovary seeding the cells into the peritoneal cavity and to neighboring organs. Our aim is to study the OC dissemination comparing human paired ovarian primary tumors, ascites and metastases.

Methods
Fresh ovarian primary tumor, ascites and peritoneal metastases from patients suffering advanced serous OC were collected from surgery room and processed for further analysis. Formalin-fixed, paraffin-embedded (FFPE) tissues were collected from Pathology Department for immunohistochemical analysis. Discovery phase: We determined the global gene expression profile by microarray analysis from 5-paired fresh samples. Validation phase: We analyzed mRNA, by RTqPCR, and protein, by Western blot, from 10 unpaired fresh samples. We further evaluated protein expression by immunohistochemistry from 10-paired tumor and metastasis FFPE-samples.

Results
FABP4, INHBA and GREM1 were significantly overexpressed in metastases compared to primary tumors. INHBA and FABP4 were validated at RNA and protein level, whereas GREM1 only at RNA level.

Conclusions
The present study highlights the role of previously unknown candidates in OC dissemination that might be used as tumor biomarkers, to clinically monitor the progression of the disease, or as target therapies, to block the OC dissemination.
BORDELINE AND LOW-GRADE SEROUS OVARIAN CARCINOMA: ANALYSIS OF THE CLINICAL BEHAVIOR IN 151 PATIENTS
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Objectives
Investigate borderline serous ovarian tumors (BSOT) and low-grade serous ovarian carcinoma (LGSOC).

Methods
Retrospective study.

Results
Median age at diagnosis in 127 BSOT was 44 years, with stage I, II and III in 67\%, 9\% and 24\%. With a median follow-up of 5.8 years, an overall survival rate of 97\% and no disease-related-deaths were noted. After 5 and 10 years, 91\% and 83\% of the patients were relapse-free (RF). Univariate analyses identified a micropapillary pattern (5\% vs 21\%; p-value:0.0092) and peritoneal implants as predictors for recurrence. 5-year RF survival was highest in those without implants compared with desmoplastic implants and invasive implants (97\%, 77\%, 75\%, respectively; p-value:<0.001). 14\% of the DNA-aneuploid and 8\% diploid patients relapsed (NS=not significant).

In 24 LGSOC median age at diagnosis was 56 years, with stage I, II, III and IV in 4\%, 13\%, 70\% and 13\%. Seven (29\%) disease-related-deaths were observed during a median follow-up of 4.3 years. 5 and 10-years disease-related survival was 73\% and 61\%. Univariate analyses identified residual disease after surgery (RD) as a prognostic factor for survival (75\% survival without vs 50\% with RD:p-value:0.0342). Disease-related survival for stage I/II and III/IV was 75\% and 68\%(NS). Only 1 out of 4 patients with RD attained partial remission after first-line chemotherapy. All were progressive on second-line chemotherapy.

Conclusions
BSOT have an excellent prognosis, but a micropapillary pattern and peritoneal implants are predictors for relapse. In LGSOC, no RD proved to be prognostic for survival. A limited effect of chemotherapy was noted.
DOES CHEMOTHERAPY CAUSE HYPERCOAGULABILITY IN OVARIAN CANCER PATIENTS

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Objectives
Ovarian cancer is the 4\textsuperscript{th} leading cause of death from cancer. Thromboembolism is the second leading cause of death in cancer patients. Surgical debulking and chemotherapy, both carry an inherent risk of thromboembolism. The aim of this study was to investigate the effect of chemotherapy on plasma procoagulant activity.

Methods
Procoagulant activity was measured using Calibrated Automated Thrombogram assay (CAT) in patients with ovarian cancer. In the first part of the study, we compared the procoagulant activity in patients who had neoadjuvant chemotherapy (n=16) with patients admitted for surgery for benign ovarian tumours (n=37) and primary ovarian cancer chemotherapy naive (n=23). In the second part, we measured the procoagulant activity in a group of 14 patients before the start of chemotherapy, at the end of the third cycle and after the end of chemotherapy.

Results
ETP levels were very similar in the three groups before surgery. However, the neoadjuvant group showed a statistically significant (P = 0.05) increased in resistance of ETP to the inhibitory actions of APC compared with the other two group. In the serial study, chemotherapy caused increased resistance to APC, the resistance was statistically significant after the third cycle (P = 0.01) and after the end of chemotherapy (P = 0.004).

Conclusions
The results of this study show that chemotherapy does not directly affect thrombin production but does reduce the effectiveness of the natural anticoagulant APC hence increasing hypercoagulability. This may explain the high incidence of thrombosis during chemotherapy in cancer patients. Further studies are needed to ascertain the precise mechanisms involved.
ACCURACY AND REPRODUCIBILITY OF THE PERITONEAL CANCER INDEX IN ADVANCED OVARIAN CANCER IN LAPAROSCOPY AND LAPAROTOMY.

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Objectives
In advanced stage ovarian cancer (ASOC) the quality of the cytoreductive surgery, which is the main prognosis, is correlated with the extension of the disease and so with the Peritoneal Cancer Index (PCI). The reliability of this scoring index between different surgeons in laparoscopy and laparotomy has not yet been studied in this disease.

The aim of this prospective study were to evaluate the accuracy of the PCI between laparoscopy and laparotomy and to evaluate the reproducibility of this index between 2 observers in ASOC.

Methods
Between April 2010 and October 2011, for each of the 29 patients undergoing complete cytoreductive surgery, one senior surgeon and one junior surgeon evaluated the PCI score at 3 times the same day: during laparoscopy and during laparotomy at the beginning and at the end. A concordance analysis was conducted with Bland and Altman's method and estimated by intraclass correlation coefficients.

Results
There was a high concordance of the PCI score between junior and senior surgeons in laparoscopy and laparotomy: the mean differences were not significantly different from zero (p<0.05) and 95% limits of agreements were +/- 3.5 and +/- 3.0 respectively. Laparoscopic underestimated the PCI score of 2 points approximately compared to the beginning of the laparotomy: mean biases were -2.0 (95%CI -2.8, -1.2) for the senior surgeon and -2.2 (95%CI -3.1, 1.3) for the junior.

Conclusions
The PCI score is reproducible and reliable, to evaluate the peritoneal spread in ASOC.
CLINICAL SIGNIFICANCE OF LYMPHOVASCULAR SPACE INVASION IN UTERINE SEROUS CARCINOMA

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Objectives
Uterine serous carcinoma (USC) is responsible for a larger proportion of uterine cancer related deaths. Vascular space invasion has been identified as a prognostic factor. The aim study was to analyze the clinical significance of extensive, low or absence of lymphovascular space invasion (LVSI) in USC patients.

Methods
After IRB approval, 236 USC from the pathology databases of 4 large institutions were included. H&E slides were retrieved and reviewed by a gynecologic pathologist at each participating institution after reviewing 50 cases as a group to be consistent in the diagnosis. LVSI information was available for 151 patients. Patients were divided into three groups based on LVSI extent. Extensive LVSI (E-LVSI) was defined as ≥ 3 vessel involvement; Low LVSI (L-LVSI) was defined as less than 3 vessel involvement and the last group was absent LVSI (A-LVSI).

Results

<table>
<thead>
<tr>
<th></th>
<th>A-LVSI (65)</th>
<th>L-LVSI (55)</th>
<th>E-LVSI (31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ LN</td>
<td>15.4%</td>
<td>27.3%</td>
<td>83.9%</td>
</tr>
<tr>
<td>+ Washing</td>
<td>18.8%</td>
<td>24%</td>
<td>37%</td>
</tr>
<tr>
<td>Myometrial Invasion</td>
<td>58%</td>
<td>85%</td>
<td>100%</td>
</tr>
<tr>
<td>Cervical Invasion</td>
<td>23%</td>
<td>43%</td>
<td>66%</td>
</tr>
<tr>
<td>Lower Uterine Segment Invasion</td>
<td>34%</td>
<td>55%</td>
<td>77%</td>
</tr>
<tr>
<td>Stage III &amp; IV</td>
<td>31%</td>
<td>40%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*p<0.05

Out of these 151 patients, 65 had A-LVSI, 55 had L-LVSI, and 31 had E-LVSI. Please see table for the association between LVSI and LN involvement, washing, myometrial invasion, cervical invasion, lower uterine segment involvement (LUS), and stage. Analyzing only stage I and stage II disease (n=68) for survival and recurrence, demonstrated a median survival of 177 months, 155 months and 34 months in the A-LVSI, L-LVSI and E-LVSI groups.

Conclusions
In this study, the extent LVSI was associated with multiple pathologic factors and had significant clinical implications in terms of survival and disease recurrence in early stage disease suggesting careful attention must be paid not only to the presence of LVSI but its extent in USC.
e-Poster Orals: ENDOMETRIAL CANCER

USING TAMPONS FOR EARLY DETECTION OF ENDOMETRIAL CANCER
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Objectives
We preliminarily evaluated a novel detection method for EC combining minimally-invasive specimen collection with methylation analysis.

Methods
Women undergoing hysterectomy for EC (n=37, including 29 (78%) grade 1) or benign indications (n=29) underwent biospecimen collection—preoperative intravaginal tampon (vaginal pool), Tao brush (endometrial cytology), surgical specimen (histology). Pyrosequencing was performed to determine the mean relative methylation differential between EC and benign endometrium (BE). Genes were selected from 2 sources: 1) published literature in gynecologic cancers (RASSF1A, HSP2A, HOXA9, CDH13, HAAO, GTF2A1) and 2) global profiling of 180 ECs using the Illumina GoldenGate platform (ASCL2, HTR1B, NPY, HS3ST2, MME, ADCYAP1, CDH13). Methylation differences were assessed using Wilcoxon rank-sum and area under the curve (AUC) via logistic regression models.

Results
105 CpG sites were evaluated; 72 (69%) and 67 (66%) sites had significantly higher methylation % in women with EC vs BE via Tao brush and tampon, respectively; 56 sites (53%) hypermethylated in both biospecimens. The best discriminator in tampon samples was ASCL2 (CpG site 1, p<0.0001, AUC=0.84 (Figure 1); CpG site 2, p<0.0001, AUC=0.85). Other genes with an AUC above 0.80 were CDH13 (3 sites), HOXA9 (3 sites), HTR1B (1 site), RASSF1A (1 site).

Conclusions
Several hypermethylated CpGs in EC are also relatively hypermethylated in endometrial brushings and vaginal pool collected by tampon from women with EC vs. BE. This is compelling proof of principle evidence that detection of EC can be performed using minimally-invasive methods. Additional biomarker discovery, refined collection methods and assessment of multi-loci models are being investigated to develop an early detection tool for EC.
e-Poster Orals: ENDOMETRIAL CANCER

CLINICO-PATHOLOGICAL CHARACTERISTICS OF ENDOMETRIAL CANCER IN LYNCH SYNDROME

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Objectives
Poor data exist on clinico-pathological description of endometrial cancer (EC) in Lynch syndrome (LS) compared with sporadic ones. To evaluate the clinico-pathological findings of Lynch-related EC to establish histological criteria to discriminate familial and sporadic ECs and to decide the optimal management of patients.

Methods
Retrospective study describing the characteristics of a cohort of patients with EC and LS in three hospitals from 1984 to 2013.

Results
We studied 33 cases. The median age at diagnosis was 48 years (31-66). Twenty-six patients had an identified mutation (11 MLH1, 7 MSH2, 7 MSH6, 1 PMS2). In 74.4 % of cases, EC was the first Lynch-related tumor to occur and colonic cancer occurred first in 18.6 % of cases. No patient developed ovarian cancer. Median BMI was 22 (15-27). Sixty-eight per cent had endometrioid adenocarcinoma. Tumor grade was grade 1 in 45 % of patients, grade 2 in 30 % and grade 3 in 25 % of cases. Thirty-one per cent of patients had lymphovascular space involvement (LVSI). The FIGO stages were as follows: stage IA: 50 %, stage IB: 25 %, stage II: 3.6 % and stage III: 14.6 %. With a median follow-up of 3 years (1-28), recurrence never occurred and 3 patients died of other related cancer.

Conclusions
Endometrial cancer in LS is characterized by early age at onset and low or intermediate pathologic grade. Other data on histology and survival do not differ from sporadic cancers. Conservative treatments could be considered in patient with good prognosis tumour.
e-Poster Orals: ENDOMETRIAL CANCER

WILMS’ TUMOR GENE 1 (WT1) DENDRITIC CELL IMMUNOTHERAPY IN PATIENTS WITH UTERINE TUMORS: A PHASE I/II CLINICAL TRIAL

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\textsuperscript{4}Pathology, University Hospitals Leuven, Leuven, Belgium
\textsuperscript{5}Laboratory of Experimental Haematology Vaccine and Infectious Disease Institute, University Hospitals Antwerp, Antwerp, Belgium
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Objectives
Classical treatment modalities are limited in advanced stages of uterine carcinoma and in all stages of uterine sarcoma. Consequently, the aggressiveness of these cancers leads to a poor prognosis. New treatment modalities are needed.

Methods
Six patients with uterine cancer were included in a phase I/II trial to be treated with autologous mature DCs loaded with WT1 RNA (DCm-WT1-RNA) in order to elicit a WT1-specific T cell response. Patients received one vaccine every week during four weeks and were then boosted with vaccines once every month, if clinical response was established after the first four vaccines. Local application of Imiquimod cream at the injection site was used as an adjuvant. Toxicity, clinical response and immunological response were evaluated.

Results
The technique was feasible. Local redness at the injection site was noted and one patient showed an allergic local reaction to Imiquimod cream. One patient showed a transient biochemical response, two patients showed a radiological response and three patients showed an immunological response.

Conclusions
This study presents the promising results of the six first patients ever with uterine cancer that have been treated with autologous dendritic cells loaded with WT1 RNA. Immunological and clinical response correlated in 67% of patients. The technique however needs improvement to ameliorate the outcome of patients with this aggressive type of cancer.
LOW STAG2 EXPRESSION ASSOCIATES WITH LOW GRADE ENDOMETRIOID TYPE BUT NOT DNA PLOIDY IN ENDOMETRIAL CANCER

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Objectives
STAG2 is a gene encoding for a subunit of the cohesin complex, which regulates separation of sister chromatids during mitosis. Mutational inactivation of STAG2 has been linked to protein loss and aneuploidy in cancers (Solomon DA et al, Science 2011, 333:1039-43). Aneuploidy is associated with aggressive endometrial cancer (EC), but mechanisms leading to aneuploidy are poorly understood. We therefore investigated STAG2 protein expression in relation to DNA ploidy and clinicopathologic features in EC.

Methods
Paraffin-embedded tumor tissues from 526 EC patients treated from 2001 to 2011 were stained for STAG2 protein (immunohistochemistry; staining index (SI) 0-9) and related to DNA ploidy (flow cytometry) and clinical and histopathologic data. The cancer genome atlas (TCGA) EC data were also explored.

Results
No significant association between STAG2 protein expression and DNA ploidy was found. There was tendency towards better survival for patients with low STAG2 expression, 90% compared to 83% 5-year survival (p=0.18; cut-off lower quartile). STAG2 SI was associated with histologic subtype (p=0.02) and grade (p=0.001), with lower staining indices for endometrioid and grade 1 and 2 tumors. In TCGA data 8.1% of EC patients carried mutation in STAG2, with tendency towards better disease specific survival compared with patients without mutation (p=0.05).

Conclusions
Lower STAG2 protein expression in EC associates with markers of non-aggressive disease, but not with DNA ploidy. Apparently in line with this, presence of mutations also links to a more favorable clinical course. Further investigation of any potential role of STAG2 in aneuploidy development in EC is needed.
e-Poster Orals: ENDOMETRIAL CANCER

ANALGESIC REQUIREMENTS AND SURGICAL OUTCOMES IN PATIENTS WITH AND WITHOUT EPIDURAL ANALGESIA IN EARLY ENDOMETRIAL CANCER: RESULTS FROM THE RANDOMISED LACE TRIAL
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²School of Public Health, Queensland University of Technology, Brisbane, Australia
³Dept Anaesthesia, Royal Brisbane and Women's Hospital, Brisbane, Australia

Objectives
The LACE trial compared outcomes of open and laparoscopic surgery. For the aim of this study we compared post-operative analgesic requirements between the two treatment arms as well as the risk of surgical complications in patients who had a TAH with and without epidural analgesia.

Methods
Between 2005 and 2010, 760 patients were enrolled in the international, multicentre, prospective randomised LACE trial comparing TLH or TAH for stage I endometrial cancer. Postoperative analgesic requirements and pain levels were compared between the treatment arms. We also compared outcomes of patients who had a TAH through a vertical midline incision (VMI) who did or did not receive epidural analgesia.

Results
Baseline analgesic use was comparable between treatment arms. TAH patients (n=353) were more likely to receive epidural analgesia (33% vs. 0.5%, p<0.001) than TLH (n=407) patients. Although opioid use was comparable in both groups during the first 2 postoperative days, they were higher in the TAH group from 3 to 60 days after surgery (p<0.0001). Mean pain scores were significantly higher in the TAH arm at one (2.48 vs. 1.62, p<0.0001) and four weeks (0.89 vs. 0.63, p 0.01) following surgery. In patients who had a TAH through a VMI, surgical adverse events occurred in 86% of patients with and 66% without an epidural (p<0.01).

Conclusions
TLH is associated with lower post-operative opioid requirements and better pain levels than TAH. In patients requiring a TAH through a VMI epidural analgesia is associated with a higher risk of perioperative complications.
e-Poster Orals: ENDOMETRIAL CANCER

ORAL OR INTRAUTERINE DEVICE-DELIVERED PROGESTIN IN PATIENTS WITH COMPLEX ENDOMETRIAL HYPERPLASIA WITH ATYPIA OR EARLY ENDOMETRIAL ADENOCARCINOMA: AN UPDATED REVIEW

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Objectives

For women with early (grade 1, apparent stage I (G1)) endometrial adenocarcinoma (EC) or complex atypical endometrial hyperplasia (CAH), preservation of fertility may be important. In 2011, we performed a meta-analysis of studies to investigate pathological complete response (pCR) rate to oral or intrauterine (IUD) progestins. This current paper updates our 2011 review and extends it to include information on the prediction of response.

Methods

MEDLINE, Cochrane Library, ScienceDirect, DynaMed and MD Consult Australia were searched, yielding 2,662 potentially relevant citations since 2011. Of those, 3 new studies meeting the inclusion criteria were identified, including at least 10 patients with CAH (one study) or EC (two studies) who received treatment with either oral or intrauterine progestins. Studies where patients were treated for <6 months or with additional other interventions were excluded.

Results

In CAH, pCRs are 74% (60-97%) for oral and 84% (range 60-97%) for IUD. In EC pCRs to oral progestins are 76% (68-83%) and 68% (45-86%) to IUD. Persistent crowding or confluency with atypia indicates low likelihood of response.

Conclusions

Progestins are reasonably effective for the conservative treatment of EC and CAH. Information on patient and tumour factors that predict response to treatment is emerging. However, there is still a lack of clinical trial evidence, although four trials are now registered on clinical trials.gov.
HIGH CORRELATION OF MOLECULAR TUMOR ALTERATIONS IN ENDOMETRIAL CURRETAGE AND HYSTERECTOMY-SPECIMENS IN PATIENTS WITH ENDOMETRIAL CARCINOMA

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Objectives
Molecular alterations in endometrial cancer have been identified as having important prognostic significance. Few studies have investigated those alterations in pre-operative curettages. The objective of this study is to determine whether molecular analysis of the endometrial curettage accurately reflects the alterations of the subsequent hysterectomy.

Methods
Paired curettage and hysterectomy specimens of 48 patients diagnosed with endometrial carcinoma (EC), including 6 non-endometrioid carcinomas (NEEC) were analysed for immunohistochemical expression of p53, PTEN and β-catenin. Tumour DNA was isolated and analyzed for mutations in KRAS and PIK3CA (hotspot-mutations), TP53 (Sanger-sequencing) and microsatellite instability (MSI). In addition all samples were analyzed using GynCarta (panel of 155 hotspot mutations in 12 relevant genes in gynecological cancer)

Results
In EEC patients, loss of PTEN, β-catenin and p53-mutant expression was found in 43%, 7% and 12% of cases respectively. Hotspot mutations for KRAS and PIK3CA were identified in 23% and 10% of cases respectively. As expected, no mutations were found for β-catenin, KRAS and PIK3CA in the NEEC-cases whereas a p53 mutant expression pattern was present in 83% in this group. Concordance for PTEN, β-catenin, p53 expression and hotspot mutation for KRAS and PIK3CA was 79%, 92%, 79%, 100% and 100% respectively. Concordance of the GynCarta analysis will be presented.

Conclusions
The results suggest usefulness of immunohistochemical and DNA based techniques in the evaluation of molecular alterations in pre-operative endometrial curettage. The resulting molecular signature provides initial pre-operative diagnostic information for several oncogenic pathways, which may contribute to individualized treatment strategies.
LOW-GRADE ENDOMETRIAL STROMAL SARCOMA: INCIDENCE OF LYMPH NODE METASTASIS AND ADNEXAL METASTASIS

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Objectives
To evaluate the incidence of lymph node metastasis (LNM) and adnexal metastasis (AM) in newly diagnosed low-grade endometrial stromal sarcoma (LGESS).

Methods
Sixty-seven cases with diagnosis of LGESS who underwent surgery in our institution from January 1, 1995 to December 31, 2009 were retrospectively analyzed.

Results
The median age was 46 years. All patients underwent hysterectomy, 60 patients experienced bilateral salpingo-oopherectomy (BSO), and 36 patients received lymphadenectomy. Among the 6 patients with LNM, 5 had grossly positive LNs and deep myometrial invasion (DMI) with or without adnexal mass, 4 had lymph-vascular space invasion (LVSI). More patients with LNM experienced recurrence than patients without LNM (66.7% VS 6.7%, P<0.001). AM was identified in 7 of 60 cases, all except one manifested by gross adnexal tumor and occurring in patients with other gross pelvic extrauterine disease. DMI was confirmed in 6 of the 7 patients, and LVSI in 4. More patients with AM experienced recurrence, but the difference was not significant (71.4% VS 43.3%, P=0.158). Significantly more patients without BSO experienced recurrence (100% VS 40%, P=0.003).

Conclusions
The incidence of LNM in LGESS is commonly associated with gross extrauterine disease, DMI and LVSI. Since myometrial invasion and LVSI status often are not assessable before or at the time of hysterectomy, LN dissection remains a reasonable option at primary surgery. Though, the rate of AM appears to be negligible in the absence of gross adnexal and extrauterine tumor, BSO was urgently recommended in primary surgery regarding the high recurrence rate among patients sparing ovary.
CLEAR CELL ENDOMETRIAL CARCINOMA (CLINICAL AND MORPHOLOGIC FEATURES)

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Objectives
Clear Cell Endometrial Carcinoma (CCEC) is a rare endometrial malignancy comprising around 2% of endometrial adenocarcinomas. Clinical and morphological features of CCEC were analyzed.

Methods
All the data from surgical pathology files (n=3345) of N.N.Petrov Research Institute of Oncology (St-Petersburg, Russia) from 1985 to 2010 years were identified. Saint-Petersburg Population Cancer Registry data (2000-2005 years period) were analyzed (n=3224 cases of endometrial cancer patients).

Results
The incidence rate of CCEC was 2.2% (n=73, from 3345 cases of endometrial cancer during the period of 25 years). The patients with CCEC tended to be elder with atrophic endometrium. The tumor was characterized by deep myometrial invasion (42.5%), high rate of metastasis (39.1%) even in cases with superficial invasion (23.0%) versus endometrioid endometrial cancer: 6.0%, 14.2% and 9.0% respectively. The incidence rate of CCEC was 2.2% (n=73, from 3345 cases of endometrial cancer during the period of 25 years). The patients with CCEC tended to be elder with atrophic endometrium. The tumor was characterized by deep myometrial invasion (42.5%), high rate of metastasis (39.1%) even in cases with superficial invasion (23.0%) versus endometrioid endometrial cancer: 6.0%, 14.2% and 9.0% respectively. The survival rate for CCEC was poor: 3-year observed survival 62.7%, 5-year observed survival – 52.2% (Saint-Petersburg Population Cancer Registry), 70.9% (3-year survival) and 61.8% (5-year survival) according to the N.N.Petrov Research Institute of Oncology Hospital Cancer Registry data. Whereas prognosis in patients with endometrioid endometrial carcinoma is much more favorable: 3-year observed survival 79.4%, 5-year observed survival – 75.5%.

Conclusions
CCEC is an uncommon highly malignant nonendometrioid endometrial carcinoma, with poor prognosis and could be referred to the pathogenetic type II, according to clinical and pathologic behaviour.
e-Poster Orals: ENDOMETRIAL CANCER

FERTILITY-SPARING TREATMENT OF ENDOMETRIAL STROMAL SARCOMA
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Objectives
Endometrial stromal sarcoma (ESS) is a rare kind of uterine malignancy. The main treatment includes surgery with total hysterectomy and bilateral salpingo-oophorectomy. Fertility-sparing management of ESS has been demonstrated, while reports of pregnancy after such management are rare.

Methods
We report a case-series composed of four patients with ESS who desired for child-bearing.

Results
All the patients aged 28-34 years old presented with symptoms of menometrorrhagia. Ultrasound examinations demonstrated myomas (with the diameter of 4.5-8.2cm respectively). All the patients received conservative surgeries of local resection of the mass with uterine reconstruction. Then the adjuvant endocrine therapy was given to them with medroxyprogesterone (160-320mg/day) or triptorelin (3.75mg/28 days) for 6-14 months. The follow-up lasted 12-38 months. All the patients survived with no evidence of disease recurrence. One of them underwent an uncomplicated pregnancy, and received cesarean delivery of a liveborn male neonate at 39 weeks of gestation.

Conclusions
Fertility-sparing management of ESS may be a viable option for the young patients desiring future fertility.
A POTENTIAL NOVEL THERAPEUTIC TARGET FOR ENDOMETRIAL CANCER: CYSTATHIONINE BETA SYNTHASE

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Objectives
There is gradually accumulating evidence to suggest that hydrogen sulphide, and therefore its synthases cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE), play a role in tumorigenesis, cell proliferation and apoptosis. We aimed to investigate the expression pattern of the hydrogen sulphide synthesising enzymes CBS and CSE in human endometrial adenocarcinoma tissue samples with normal post-menopausal endometrium as a control.

Methods
CBS and CSE were located in samples from 20 women with endometrial adenocarcinoma and 5 post-menopausal control women using immunohistochemistry (IHC). Positive staining was analysed using a semi-quantitative 'modified quickscore'. Association with grade of cancer was tested using Kruskall-Wallis.

Results
We have confirmed the expression of both CBS and CSE for the first time in human endometrium. Staining was limited to endothelial and epithelial cells. Two distinct patterns of staining were observed for CSE - diffuse cytoplasmic staining (mostly weak) and discrete strongly stained cells (figure 1a).

Figure 1: Immunohistochemical staining of post-menopausal endometrium (a and b) and grade 3 endometrial adenocarcinoma (c). Panel a shows CSE expression, while panels b and c represent CBS staining.
CBS expression was almost exclusively cytoplasmic (figure 1b and 1c), and increased with grade of cancer (P<0.02) (figure 2).

Figure 2: CBS and CSE quickscore according to grade of endometrial cancer.

**Conclusions**
CBS showed a clear association with increased endometrial cancer grade and represents a potential novel therapeutic target for treatment.
NEGATIVE PREDICTIVE VALUE OF PET-CT NODAL STATUS IN WOMEN WITH OPERABLE CERVIX CANCER

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Objectives
Preoperative PET-CT is being incorporated into the clinical decision pathway in the management of early stage cervical cancer in order to better identify those who might be cured by surgery alone. Enhanced detection of extracervical disease reduces the number of women undergoing multimodal therapy, that is surgery followed by radiation and chemotherapy with its attendant higher morbidity. Patients with FDG avid nodes are directed towards primary chemoradiotherapy. Those without radiological evidence of metastases are considered for curative surgery. The aim of this study was to evaluate the accuracy of a negative PET-CT in lymph node assessment in early stage cervical cancer.

Methods
A retrospective review of 206 patients with cervical cancer over a four year period (2009-12) in a single institution since the introduction of PET-CT.

Results
Eighty-two patients with clinical Stage IA2-IB1 (58 squamous, 22 adeno, 2 villoglandular) carcinoma of cervix and no evidence of lymph node metastases on PET-CT underwent pelvic +/- paraaortic lymph node dissection prior to or during their primary curative surgery. Nine patients (5 squamous, 4 adeno) had positive nodes lymph nodes on histology giving a false negative rate of 11%.

Conclusions
Knowledge that the negative predictive value for the PET-CT detection of lymph node metastases is 89% is useful in the counseling of patients progressing to primary surgery for cervical cancer. It justifies the investigation of other modalities such as sentinel lymph node frozen section analysis to improve detection of metastasis in order to further reduce the number of patients being subjected to multimodal treatment.
ANALYSIS OF A CONTINUOUS SERIES OF 34 PATIENTS CANDIDATE FOR A VAGINAL RADICAL TRACHELECTOMY: SHOULD CONISATION BE SYSTEMATICALLY PERFORMED TO SELECT YOUNG PATIENTS FOR THIS PROCEDURE?

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Objectives
Radical trachelectomy (RT) is the most widely evaluated form of conservative management of young patients with early-stage (IB1) cervical cancer. Patients with nodal involvement or a tumour size > 2 cm are not eligible for such treatment. The aim of this study is to report the impact of a “staging” conisation before RT.

Methods
This is a retrospective study, carried out between 2000 and January 2012, on patients with macroscopic cervical cancer, confirmed by punch biopsies, “eligible” for RT (< 2 cm) who had undergone a “staging” conisation to confirm the tumour size and lymphovascular space involvement (LVSI) status.

Results
During the study period, RT had been envisaged for 34 patients. Six patients had this conisation before RT and had finally been deemed contraindications to RT due to the presence of a histologically-confirmed tumour > 2 cm and/or associated with multiple foci of LVSI.

Conclusions
These results suggest that if a conisation is not performed initially, it should then be included among the staging procedures to select patients for RT.
e-Poster Orals: CERVICAL CANCER

NERVE-SPARING VS. CONVENTIONAL LAPAROSCOPIC RADICAL HYSTERECTOMY: A PROSPECTIVE STUDY

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Objectives To determinate whether the introduction of nerve-sparing (NS) procedure influences surgical and survival outcomes of cervical cancer patients undergoing laparoscopic radical hysterectomy (LRH).

Methods Data of consecutive patients undergoing minimally-invasive surgery for cervical cancer between May 2004 and January 2013 were enrolled in the study.

Results 63 (65.6%) patients who had LRH were compared with 33 (34.7%) women undergoing NS-LRH. Among the NS group 19 (57.6%) patients had surgery via mini-laparoscopy (using 3-mm instruments). Baseline characteristics were similar between groups. Patients undergoing NS-LRH had shorter operative time (210 vs. 257 minutes; p=0.005) and higher number of pelvic lymph nodes yielded (29 [26-38] vs. 22 [8-49]; p<0.001) than patient in the control group. No differences in blood loss, complications and parametrial width were observed. Patients were catheterized with an indwelling Foley catheter for a median of 3.5 (2-7) and 5.5 (4-7) days in NS and non-NS groups, respectively (p=0.01). Urinary dysfunctions occurred in 1 (3%) and 12 (19%) patients who underwent NS and standard LRH, respectively (p=0.03). No differences in disease-free (p=0.16), cause-specific (p=1.0) and overall survival (p=1.0) were recorded.

Conclusions The beneficial effects (in terms of operative time and number of nodes harvested) of NS-LRH are likely determined by the expertise of the surgeon since NS approach was introduced after having acquired adequate background in conventional LRH. Our data shows that in experienced hands, minimally-invasive NS radical hysterectomy is safe and feasible. Moreover, NS reduces catheterization time and the rate of post-operative urinary dysfunction.
BIOSPECTROSCOPY OF CERVICAL CYTOLOGY VS. CONVENTIONAL SCREENING IN IDENTIFICATION OF HISTOLOGY VERIFIED CERVICAL INTRA-EPITHELIAL LESIONS

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\textsuperscript{5}Department of Cytopathology, "Attikon" Hospital University of Athens, Athens, Greece
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Objectives
Inter and intra observer variability in assessment of cervical cytology leads to discordance between categorised samples and histology. Biospectroscopy methods have been suggested as sensor-based tools to deliver objective assessments. Categorisation of biological samples based on imperfect conventional screening can reduce the apparent diagnostic accuracy of biospectroscopy. The aim of this study is to analyse the infrared spectra of cytology samples derived using biospectroscopy and compare the accuracy of biospectroscopy vs. conventional cytology to identify true atypia in light of the corresponding histology.

Methods
Within a typical clinical setting a total of $n=322$ cervical cytology specimens were collected immediately before biopsy ($n=154$). Cytology specimens were categorised according to conventional screening methods and subsequently interrogated employing attenuated total reflection Fourier-transform infrared (ATR-FTIR) spectroscopy with multivariate analysis.

Results
Based on the categorisation derived from conventional screening, infrared (IR) spectroscopy derived from cervical cytology does not appear to discriminate in a diagnostic fashion. Scores plots of IR spectra exhibit marked cross-over of spectral points between different categories. However, when histology based analysis was conducted, conventional screening was deeply flawed. By imposing the histology findings on the biospectroscopy analyses, ATR-FTIR spectroscopy was found to identify underlying disease missed by conventional screening.

Conclusions
Histology demonstrates that ATR-FTIR spectroscopy of LBC specimens identifies the presence of underlying atypia or disease missed in conventional
cytology screening. This study points to an urgent need for a future biospectroscopy study where categories are based on such histology. It will allow for the validation of this approach as a novel screening tool.
e-Poster Orals: CERVICAL CANCER

CONCURRENT CHEMORADIATION THERAPY IN CERVICAL CANCER: RADICAL AND ADJUVANT SETTING. TOXICITY AND LONG-TERM SURVIVAL IN A CENTRE OF REFERENCE FOR GYNECOLOGIC CANCER

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Objectives
Concurrent chemoradiation therapy has been the standard treatment in locally advanced cervical cancer since 1999. Adjuvant chemoradiation is considered in high-risk early-stages.

Methods
A homogeneous series of 338 patients treated between 1996 and December 2011 with concurrent chemoradiation in radical (269 pts) and adjuvant setting (69 pts), has been retrospectively analyzed.

Results
Patients median age is 54 and 49 years old in the radical and the adjuvant group respectively. Squamous cell carcinoma is the most common histology (77.4\% and 63.2\%), followed by adenocarcinoma (16.8\% and 26.5\%). After a median follow-up of 4.77 and 5.58 years for each group, 5-year overall survival rate is 77.6\% and 86.8\% respectively. The FIGO classification for disease stages and 5-year OS is summarized in Table 1.

The grade \geq 3 acute toxicity was observed in \textless 20\% of pts (mainly haematological), and in 1.2\% of pts for chronic toxicity (renal dysfunction). The toxicity was not increased in the adjuvant group.

The concordance kappa index was 0.921 between clinical and surgical staging, with only 4 discrepancies. Therefore, the adjuvant treatment was considered depending on the classical risk factors, especially stage and lymph node involvement (in the 21\% of pts).

Table 1.

<table>
<thead>
<tr>
<th>FIGO STAGE</th>
<th>Classification</th>
<th>5-year Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radical therapy%</td>
<td>Adjuvant therapy%</td>
</tr>
<tr>
<td>IA to IB1</td>
<td>1.7</td>
<td>33</td>
</tr>
<tr>
<td>IB2</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>IIA-IIB</td>
<td>49</td>
<td>29</td>
</tr>
<tr>
<td>III</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>IVA</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

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Conclusions
This long follow-up series shows a good overall survival rate with chemoradiation therapy in the radical and adjuvant setting in cervical cancer, with a low rate of acute and, especially, chronic toxicity, indicating a good quality of life for these patients.
ABDOMINAL RADICAL TRACHELECTOMY (ART) FOR CERVICAL MALIGNancies: SURGICAL, ONCOLOGICAL AND FERTILITY OUTCOMES IN 156 PATIENTS

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Objectives
As ART is becoming a favored fertility-sparing procedure, the relative contraindication of size ≥2cm has been questioned. We report our ART experience in patients with cervical malignancies describing the surgical, oncological and fertility outcomes.

Methods
We conducted a retrospective review of a prospectively maintained database of patients undergoing fertility-sparing ART for cervical malignancies at our institution from 04/2004 to 04/2013.

Results
156 patients with cervical malignancies underwent laparotomy for planned ART. Eight needed immediate completion of radical hysterectomy due to unfavorable intraoperative findings (6 cases were IB1 stage, tumor ≥2cm). Median age was 29.4 years (range, 11-44). Histology included 18 with adenocarcinoma, 122 with squamous carcinoma, 7 with adenosquamous carcinoma and 9 with cervical sarcoma. Median number of nodes evaluated was 25 (range, 12-53); Fifty patients with pathologic risk factors received adjuvant therapy. Sixty-six of 99 IB1 cases had tumor size ≥ 2 cm and 58 (87.9%) of them preserved fertility potential. One recurrence was observed at a median follow-up of 36.4 months (range, 0.5-108 months). For various reasons, only 20 patients attempted to conceive and 6 of them succeeded. Four of them delivered by cesarean section at 37-39 weeks, one miscarried and one is still expecting.

Conclusions
Although with higher rates of conversion to hysterectomy, ART provides secured oncological outcomes for selected patients whose tumors size ≥2cm. Influenced by social, familial and physical factors, only a small fraction of patients attempt to conceive after ART. This could be the most important reason our series had unfavorable obstetric outcome.
COMPLETION SURGERY AFTER CONCOMITANT CHEMORADIATION IN LOCALLY ADVANCED CERVICAL CANCER: A COMPREHENSIVE ANALYSIS OF PATTERN OF POSTOPERATIVE COMPLICATIONS

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Objectives
We provided a comprehensive analysis of rate, pattern, and severity of early and late postoperative complications in a very large, single Institution series of locally advanced cervical cancer (LACC) patients administered CT/RT plus radical surgery (RS).

Methods
362 consecutive LACC (FIGO Stage IB2-IVA) patients were submitted to RS after CT/RT at the Gynecologic Oncology Unit of the Catholic University (Rome/Campobasso). Four weeks after CT/RT, patients were evaluated for objective response, and triaged to radical hysterectomy, and pelvic ± aortic lymphadenectomy. Surgical morbidity was classified according to the Chassagne’s grading system.

Results
Most cases underwent type III-IV radical hysterectomy (N=313, 86.5%); pelvic lymphadenectomy was performed in all patients, while 116 (32.1%) patients were also submitted to aortic lymphadenectomy. Ninety-three (25.7%) patients experienced any grade postoperative complications, and 60 (16.6%) had >Grade 2 complications; Grade 3-4 complications occurred in 21 patients (5.8%). Of all early postoperative complications (N=100), 31 (31.0%) were urinary, 9 (9.0%) were gastrointestinal, and 45 (45.0%) were vascular. Of all late complications (N=31), 20 (64.5%) were urinary, 7 (22.6%) gastrointestinal, and 2 (6.4%) were vascular. Multivariate analysis showed that not complete clinical response to treatment retained an independent, unfavourable association with risk of development of postoperative morbidity, while advanced stage, and aortic lymphadenectomy showed only a borderline value.

Conclusions
Failure to achieve clinical complete response to treatment and, to a less extent, more advanced stage, and aortic lymphadenectomy, were associated with a higher risk of developing any grade as well as >Grade 2 complications.
PREVALENCE AND DISTRIBUTION OF HIGH RISK HUMAN PAPILLOMAVIRUS GENOTYPES IN CERVICAL CARCINOMA, LOW- GRADE, AND HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS IN JORDANIAN WOMEN

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²Department of Pathology and Laboratory Medicine, Jordan University of Science and technology, Irbid, Jordan
³Princess Haya Biotechnology Centre, Jordan University of Science and technology, Irbid, Jordan
⁴Department of Pediatrics infectious disease., Jordan University of Science and technology, Irbid, Jordan
⁵Department of Pathology, Jordan University, Amman, Jordan

Objectives
To assess high risk human papillomavirus (HR-HPV) prevalence and genotypes' distribution in invasive cervical cancer and its precursors in Jordanian patients.

Methods
A total of 124 different specimens of formalin-fixed, paraffin embedded samples, including 18 low-grade squamous intraepithelial lesions (LSIL), 28 high grade squamous intraepithelial lesions (HSIL), and 78 cervical cancers (CC) were included in this study. HPV detection and typing was done using HPV High Risk Typing Real-TM Kit (Sacace Biotechnologies, Italy) that enables the concomitant detection of the 12 most common HR-HPVs.

Results
Overall, HR-HPV prevalence was 87.2%, 78.6%, and 72.2% in CC, HSIL, and LSIL respectively. Genotype 16 was the most predominant in all cervical lesions, detected in 53.8%, 46.4%, and 38.9% of CC, HSIL, and LSIL. Among all HPV genotypes, HPV-16 and HPV-18 are found separately or together in 50% of LSILs, 60.7% of HSILs and 76.9% of cervical cancer specimens. HPV 31 was the second most common type detected in LSILs (22.2%) and HSILs ((21.4%). HPV 45 was the third most common type detected in cervical cancer (11.5%).

Conclusions
The prevalence and genotypes distribution patterns of HR- HPV types among patients with cervical cancer and its precursors in Jordan are similar to known international patterns. The results of this study provide baseline information on the HPV type distribution, which may guide the development of cervical cancer prevention and control programs in Jordan.
e-Poster Orals: CERVICAL CANCER

ALTERATIONS ON HPV-RELATED BIOMARKERS AFTER PROPHYLACTIC HPV VACCINATION

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⁵Department of Cytopathology, Attikon Hospital University of Athens, Athens, Greece

Objectives
To investigate whether HPV vaccination can alter HPV-related biomarkers in women referred for colposcopic evaluation.

Methods
Design: prospective observational study.
Setting: University Hospital of Ioannina.
Population: Women attending colposcopy clinic who were advised and accepted HPV vaccination, were compared with a similarly referred group without vaccination. Women requiring treatment were excluded.
Intervention: HPV vaccination (Cervarix or Gardasil). An LBC sample was obtained prior and after the completion of the vaccination regime that was tested for a number of HPV-related biomarkers including HPV typing and E6 & E7 mRNA (NASBA & flow cytometry) and p16INK4a.
Outcomes: Alterations of HPV-related biomarkers at 6m time visits after initial evaluation in both groups.
Analysis: The p-values, Relative Risk (RR), Absolute Relative Risk (ARR), NNT and 95% Confidence Intervals for each group were assessed.

Results
A total of 285 women were included. Ninety-one women were vaccinated (Group A). HPV vaccination reduced statistically significant the HPV positivity rates for 16 and 18 subtypes (p=0.013) [RR=0.25: 95%CI (0.068 to 0.914), ARR=0.5: 95%CI(0.155 to 0.695), NNT=2], in women tested DNA positive for HPV infection 16 or 18 prior to the vaccine. The same significant reduction was shown for the women tested also positive for HPV DNA & mRNA E6 & E7 expression for the particular HPV subtypes (p=0.001) [RR=0.058: 95%CI (0.004 to 0.896), ARR=0.622: 95%CI(0.308 to 0.778), NNT=1: 95%CI(3to1)].

Conclusions
HPV vaccination appears to reduce significantly the rates of positivity for 16 & 18 HPV infections and possibly could enhance HPV clearance. The above findings need to be confirmed in larger cohorts.
e-Poster Orals: CERVICAL CANCER

PELVIC LYMPH NODE DOSES FROM INTRAUTERINE BRACHYTHERAPY: IMPLICATIONS FOR INTEGRATED BOOST IMRT IN CERVICAL CANCER
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Objectives
In radiotherapy for cervical cancer, central disease receives high doses from intrauterine brachytherapy. However, sidewall boosts subsequently delivered for nodal disease have unsatisfactory dosimetry and extend total treatment time. Higher nodal doses can be delivered with integrated boost IMRT, but to aid dose selection the contribution from brachytherapy should be evaluated.

Methods
Treatment plans for lymph node positive cervical cancer treated with image-guided HDR brachytherapy using tube and ovoid applicators were retrospectively reviewed. Involved nodes were contoured and D90 measured as percentage of prescribed dose. Nodal subgroups were: common iliac (CI), high interiliac, obturator and medial external iliac (Obt), anterior/lateral EI (EIant) and internal iliac (II). To represent nodal region limits, doses at vascular junctions were recorded. Point B and lateral parametrial doses were compared with Pearson’s correlation coefficient.

Results
In total, 54 nodes in 30 patients were analysed. Mean D90 for each nodal group: CI 6% (SD:4), inter-iliac 14% (SD:7), Obt 18% (SD:6), EIant 14% (SD:4), II 13% (SD:3). Vasculature point doses were: common iliac 9%, inter-iliac apex 16%, inferior obturator region 20% anteriorly and 15% posteriorly. Applicator defined Point B dose did not significantly correlate with CT defined lateral parametrial doses: 30% vs 26% (coeff=0.37).

Conclusions
For integrated boost IMRT, the brachytherapy contribution to cumulative nodal dose can be predicted. With 7 Gy delivered to Point A, the common iliac region receives 0.4-0.6 Gy, inter-iliac and obturator 1-1.3 Gy and lateral parametrium 1.8-2 Gy per fraction. Long term data are required on optimal dose for local control of metastatic nodal disease.
The results of IB1 cervical cancer patients treated by Cf-252 neutron ICBT alone compared with ICBT combined EBRT.

L.E.I. Xin

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Objectives
To evaluate the results and ovarian function preserving of Ib1 cervical cancer patients treated by Cf-252 neutron ICBT alone compared with ICBT combined EBRT.

Methods
From 2006 to 2010, 24 patients with Ib1 cervical cancer whose age were under 35 years-old were accrued and divided into ICBT alone(ICBT group, Negative lymph nodes scanned by PET-CT) and EBRT combined ICBT (EBRT-c group) groups according to age, pathology and hemoglobin level using the matched-pair design. Both patients in ICBT and EBRT-c group were delivered ICBT with 10-12GY-equ/f, and the total does at point A were 42-44 and 40-42Gy-equ respectively. In addition, the patients in EBRT-c group were irradiated using whole pelvic fields, the total does was 46Gy. The local control(LC), overall survival(OS), disease-free survival(DFS) and late complication(LAC) rate, and serum E2,FSH were evaluated.

Results
The LC, OS, DFS, and LAC rates in ICBT group were not different from significantly those in EBRT-c group. The hormonal failure rate were 100% in EBRT-c group 6 months after radiotherapy. However, it was 25% and 50% in ICBT group 12 and 36 months after radiotherapy. (see Table1,2)

<table>
<thead>
<tr>
<th></th>
<th>ICBT</th>
<th>EBRT-c</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC</td>
<td>100%(12/12)</td>
<td>91.7%(11/12)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>OS</td>
<td>100%(12/12)</td>
<td>100%(12/12)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>DFS</td>
<td>100%(12/12)</td>
<td>91.7%(11/12)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>LAC</td>
<td>0.00%(0/12)</td>
<td>0.00%(0/12)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Recovered menses rate</td>
<td>50%(5/12)</td>
<td>0.00%(0/12)</td>
<td>0.036</td>
</tr>
<tr>
<td>E2</td>
<td>11.6±11.6</td>
<td>40.5±11.6</td>
<td>0.002</td>
</tr>
<tr>
<td>FSH</td>
<td>15.2±4.6</td>
<td>79.9±4.6</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Conclusions
The results of Ib1 cervical cancer patients treated by Cf-252 neutron ICBT alone are slightly better than those of patients treated by ICBT combined EBRT. Moreover, the ovarian function are preserved in part of patients.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Oral Presentation/Debates: TRANSLATIONAL RESEARCH

INHIBITION OF DNA-PK RECOVERS HR FUNCTION AND RESULTS IN PLATINUM RESISTANCE IN AN OVARIAN CANCER CELL LINE MODEL

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¹Northern Institute for Cancer Research, Newcastle University, Newcastle upon Tyne, United Kingdom

Objectives
The most toxic forms of DNA damage, double strand breaks, are repaired by two main pathways - homologous recombination (HR) and non homologous end joining (NHEJ). Fifty percent of ovarian cancers have defects in the HR pathway and have been shown to be hypersensitive to platinum and PARP inhibitors. Recent studies have shown that cisplatin and PARP inhibitor resistance develops through a second mutation restoring BRCA function and the NHEJ pathway has been implicated in this process.

Methods
We determined the effect of inhibition of NHEJ function on the cytotoxicity of cisplatin and the PARP inhibitor rucaparib in paired BRCA1 and BRCA2 defective and competent ovarian cancer cell lines using a clonogenics assay and the DNA-PK inhibitor NU7441. The effect of NU7441 on HR function was determined using the gamma-H2AX / RAD51 foci formation assay.

Results
We demonstrated that the inhibition of DNA-PK function results in HR pathway function recovery and increased cloning efficiency in BRCA1, but not BRCA2 defective cells. However, treatment with a DNA-PK inhibitor resulted in significant resistance to cisplatin, but not rucaparib, in both BRCA1 (p=0.037) and BRCA2 (p=0.016) defective cells.

Conclusions
This study has shown that inhibition of NHEJ pathway recovers HR function in BRCA1 defective cells. Furthermore, NHEJ pathway inhibition results in cisplatin resistance development independently of HR function. Therefore, defects in NHEJ pathway may be an important mechanism for the development of platinum resistance.
Oral Presentation/Debates: TRANSLATIONAL RESEARCH

HIGH-THROUGHPUT SOMATIC MUTATION PROFILING OF GYNAECOLOGICAL MALIGNANCIES

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⁴France/Benelux, Sequenom GmbH, Hamburg, Germany
⁵Gynaecology, Leiden University Medical Center, Leiden, Netherlands

Objectives

Somatic mutations play a role in tumour development and tumour progression, can predict prognosis, and guide targeted therapies. This study investigated the prevalence of somatic mutations in gynaecological malignancies by analysing the spectrum of 155 somatic hot-spot mutations in 12 genes that are frequently reported to be involved in carcinomas of the gynaecological tract.

Methods

A total of 559 tumours (205 cervical, 228 endometrial, 101 ovarian, and 25 vulvar carcinomas) were analysed using a novel, mass-spectrometry-based mutation panel to detect somatic mutations in BRAF, CDKN2A, CTNNB1, FBXW7, FGFR2, FGFR3, FOXL2, HRAS, KRAS, NRAS, PIK3CA, and PTEN.

Results

We detected 402 mutations in 277/559 (50%) tumours. Most mutations were detected in endometrial carcinomas (168/228, 73%), followed by ovarian (37/101, 37%), cervical (65/205, 32%), and vulvar carcinomas (5/25, 20%). PIK3CA was the most frequently mutated gene (119/559, 21%), followed by PTEN (95/559, 17%), KRAS (64/559, 11%), and CTNNB1 (45/559, 8%). Differences in somatic mutation profiles were observed between and within tumour types and tumour subtypes. The PI3K-Akt signalling pathway was most often affected and predominated in the mutation spectrum.

Conclusions

Somatic mutations were detected in 50% of the gynaecological malignancies in this series. Somatic mutation profiling can be useful in determining types and subtypes of tumours within the gynaecological tract, can reveal new insights into tumourigenesis, and may be used to predict prognosis and to help select tumour-specific targeting treatment strategies in gynaecological oncology.
Objectives

Epithelial Ovarian cancer (EOC), the most lethal gynecological disease, has survival rate virtually unchanged for the past 30 years. EOC comprises different histotypes with molecular and clinical heterogeneity, but up till now either the present platinum-based treatment or clinical trials have been performed without any patient stratification. The aim of the present study is to generate miRNA profiles characteristic of each stage I EOC histotype in order to subtype-specific biomarkers.

Methods

A collection of 257 snap-frozen stage I EOC tumor biopsies was gathered together from three tumor tissue collections and stratified into independent training (n=183) and validation sets (n=74). Microarray analysis and qRT-PCR were used to generate and validate the histotype-specific markers. A novel dedicated resampling inferential strategy was developed and applied to identify the highest reproducible results. mRNA and miRNA profiles were integrated to identify novel regulatory circuits.

Results

Robust miRNA markers for clear cell and mucinous histotypes were found. Specifically, the clear cell histotype is characterized by higher expression of miR-30a and miR-30a*, while mucinous histotype has higher levels of miR-192/194. Furthermore a mucinous-specific regulatory loop involving miR-192/194 cluster and a differential regulation of E2F3 in clear cell histotype were identified.

Conclusions

Our findings suggest that different stage I EOC histotypes exhibit divergent miRNA profiles, thus supporting the hypothesis that they are biologically distinct entities to be treated as different neoplastic diseases. In particular, the pattern of expression of some miRNAs was found specific for clear cell or for mucinous ovarian carcinomas, a finding of potential diagnostic and therapeutic importance.
Oral Presentation/Debates: TRANSLATIONAL RESEARCH

CLONAL EVOLUTION TOWARDS CHEMORESISTANCE IN OVARIAN CANCER CAPTURED BY DNA SEQUENCING

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Objectives: The objective was to identify genes involved in determining sensitivity or resistance to platinum-based chemotherapy in advanced stage high grade serous ovarian cancer.

Methods: Fresh frozen paired tumor biopsies obtained in 13 patients with ovarian carcinoma at diagnosis and recurrence were macrodissected and analyzed together with their normal germline DNA. Whole exome sequencing was performed on Illumina HiSeq2000 with an average coverage of 54.9x. Novel missense mutations and frameshift insertions and deletions were determined after subtraction of germline mutations and common variants.

Results: In all samples together we found 624 different mutations, some were shared while others were unique for the primary or the recurrent tumor.

Some recurrent tumors seem to originate from the primary dominant clone as many primary mutations are still present in the recurrence, while others seem to evolve from a subclone with loss of many primary variants and gain of new mutations. Correlation of the percentage newly acquired mutations with clinical features or disease free interval was not significant. Per sample, mutations were clustered based on alterations of mutant allele frequency and the function of each cluster of genes was determined.

Conclusions: Clonal evolution in ovarian cancer leads to different patterns of tumor adaptation. The recurrence can either share many mutations with the primary tumor or lose primary and gain new mutations. To study the impact of these findings on clinical behavior and platinum resistance, we are currently analyzing a larger cohort.
Oral Presentation/Debates: TRANSLATIONAL RESEARCH

HIGH LEVEL OF NUCLEAR HEAT-SHOCK FACTOR 1 (HSF1) ASSOCIATES WITH AGGRESSIVE DISEASE AND SUGGESTS TARGETS FOR THERAPY IN ENDOMETRIAL CARCINOMA

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4Department of Gynecology and Obstetrics, Haukeland University Hospital, Bergen, Norway

Objectives

Heat shock transcription factor 1 (HSF1) is a transcriptional regulator of cellular response to stress and drives the production of heat shock proteins (HSPs), such as the chaperones HSP27, HSP70 and HSP90. Inhibition of HSP90 has shown clinical utility in cancer. High HSF1 level has been linked to poor breast cancer survival (Santagata, PNAS 2011) but is unexplored in endometrial cancer.

Methods

Twenty-eight Complex atypical hyperplasias (CAH), 619 primary endometrial carcinomas and 176 metastatic lesions were prospectively collected and investigated for HSF1 protein expression (immunohistochemistry) in relation to established markers for aggressive disease and survival. Also, mRNA levels were assessed in fresh tissues from 8 CAH, 174 primary and 42 metastatic endometrial cancer lesions by microarray analysis in parallel to explore alterations in transcriptional signatures related to HSF1 overexpression.

Results

High expression of HSF1 protein in endometrial carcinoma is significantly correlated with non-endometrioid histology, high grade, ERα loss and poor survival (all p-values ≤0.01). Also among ERα-positive patients presumed to have good prognosis, high expression of HSF1 is correlated with poor survival (p=0.02). Protein levels increased significantly from hyperplasias to primary tumors to metastases (p<0.001).

Conclusions

We demonstrate for the first time in endometrial cancer that high expression of HSF1 is associated with poor outcome and that HSF1 levels increase from CAH to primary and metastatic endometrial carcinoma lesions. HSF1 status could add clinically relevant information in endometrial cancer and represents an exciting new target for therapy.
INFECTIVITY-ENHANCED ADENOVIRUSES FOR GENE THERAPY OF PATIENTS WITH RECURRENT OVARIAN AND OTHER SELECTED GYNECOLOGIC CANCERS

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²Obstetrics and Gynecology, University of North Carolina, Chapel Hill, USA
³Obstetrics and Gynecology, Washington University, St. Louis, USA

Objectives
Preclinical studies have validated our ability to enhance cancer cell infectivity with various Ad fiber knob modifications in order to enhance the potential therapeutic benefit of Ad-based gene therapeutics. We review the results of early phase clinical trials evaluating various infectivity-enhanced Ad gene therapeutics in patients with recurrent ovarian and other select gynecologic cancers.

Methods
Three phase I clinical trials were conducted evaluating infectivity-enhanced Ad-based gene therapeutics (Ad5.RGDTK.SSTr, Ad5.RGD.Δ24, Ad5/3.Δ24) Eligible patients were treated IP for 3 consecutive days in dose cohorts ranging from 1 x 10⁹ to 1 x 10¹² vp. Toxicity was assessed utilizing CTC grading and clinical efficacy was evaluated using RECIST criteria. Ascites, serum, and other tissue samples were obtained to evaluate gene transfer, generation of wild type virus, viral shedding, and Nab response.

Results
A total of 42 patients were treated per protocol. The most common vector-associated AEs were grade 1-2 fever, fatigue and abdominal pain. No dose limiting toxicities were noted. Of 41 patients evaluable for response by RECIST criteria, 26 (63%) patients had stable disease and 15 (37%) patients had progressive disease. Thirteen patients (32%) had a decrease in CA125. One patient with stable disease experienced complete resolution of disease and normalization of CA125 on further follow-up and has remained free of disease for 39 months. Ancillary biologic studies demonstrated dose dependent cellular transfection, limited systemic biodistribution, and a robust Nab response.

Conclusions
These trials demonstrate the feasibility/safety of infectivity-enhanced Ads for recurrent gynecologic cancer patients. Further investigation of these agents appears warranted.
**A fine selection of actual ENGOT studies open for participation**

*C. Marth¹, R. Berger¹*

¹Medical University Innsbruck, AGO-Austria, Innsbruck, Austria

ENGOT coordinates and promotes clinical trials within Europe and has developed a clinical trial portfolio covering the most important areas.

<table>
<thead>
<tr>
<th>Name</th>
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<th>Included population</th>
<th>Number of patients</th>
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Parallel Session: PATHOLOGY

BEYOND MORPHOLOGIC CLASSIFICATION- GENOMIC BASED STRATIFIED TREATMENT OPPORTUNITIES

D. Huntsman

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Personalization of cancer treatment decisions could take two forms. In the first, genomic data derived from tumors could be used independent of other information to identify treatment opportunities which transcend cancer sites. This offers some appeal as it would create treatment groups for rare genomic events of sufficient size for clinical studies. However, it does not take into account the importance of cell context in determining the relevance of mutations. Fortunately, in gynecologic cancers, the current histological classification reflects the molecular nature of these diseases, and therefore, provides a structure through which further genomic-based classification and identification for treatment opportunities can be derived. As an example, true HER2 amplification is seen in 20% of mucinous carcinomas of the ovary but is extremely rare in other subtypes of ovarian cancer. Also, another important feature but not as of yet targetable is the loss of ARID1A associated with endometriosis-derived ovarian cancers, the clear cell and endometriod subtypes, which are not seen in high grade serous ovarian cancers. Since the subtypes of ovarian carcinoma are truly distinct diseases the fact that distinct treatment opportunities are concentrated within subtypes is not surprising. Fortunately, unlike the classification of breast cancers, the higher level of molecular classification can be performed simply and accurately using histological techniques which will streamline the performance and interpretation of subsequent genomic analysis.
AN ECONOMIC ANALYSIS OF CISPLATIN ALONE VERSUS CISPLATIN DOUBLETS IN THE TREATMENT OF WOMEN WITH ADVANCED OR RECURRENT CERVICAL CANCER

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Objectives
Randomized trials have demonstrated improvements in overall survival when using platinum doublets compared to single agent platinum in the treatment of women with advanced or recurrent cervical cancer. We sought to evaluate the cost effectiveness of these regimens.

Methods
A decision model was developed based on Gynecologic Oncology Group (GOG) protocols 169 and 204. Cisplatin alone was compared to cisplatin/paclitaxel (CP), cisplatin/topotecan (CT), cisplatin/gemcitabine (GC), and cisplatin/vinorelbine (CV). Parameters included overall survival (OS), cost and complications. One way sensitivity analyses were performed.

Results
The incremental cost-effectiveness ratio (ICER) for C versus CP is $12,409/quality-adjusted life-year (QALY) gained. In the cost effective analysis, CT, GC, and VC were all dominated by CP. Sensitivity analyses demonstrate that even if the CT, GC, and VC were given without cost, CP would still be the regimen of choice.

Conclusions
In this model, CP is an acceptable alternative to cisplatin alone for the treatment of these patients with an increase in cost of only $12,049/QALY. With the fact that GOG 204 also showed statistically significantly improved survival for CP, CP should be considered the regimen of choice.
Oral Presentation/Debates: CERVICAL CANCER II

A PROSPECTIVE CLINICAL STUDY OF INTENSITY MODULATED RADIATION THERAPY VERSUS CONVENTIONAL RADIOTHERAPY IN CERVICAL CANCER PATIENTS WITH POSTOPERATIVE PELVIC RECURRENCE

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Objectives
To investigate the therapeutic response and toxicity of intensity modulated radiation therapy (IMRT) versus conventional radiotherapy (c-RT) in patients with postoperative pelvic recurrence of cervical cancer.

Methods
Between January 1999 and June 2009, 211 patients with postoperative pelvic recurrence of cervical cancer were enrolled. Patients were randomly allocated into two groups and treated with IMRT (n=103) or c-RT (n=108) at doses of 55-65 Gy and 45-55 Gy, respectively. Intracavitary brachytherapy and concurrent chemotherapy (Cisplatin 40mg/m²/W) were performed during external irradiation. Short-term and long-term effects and toxicities were compared between two groups.

Results
The mean dose delivered to the PTV was significantly higher in IMRT group than in c-RT group (61.8Gy vs.50.3Gy, P=0.029). IMRT plans yielded better dose sparing of small bowel, bladder and rectum than c-RT group (P<0.001). Moreover, the IMRT patients experienced less acute and chronic toxicities and better short-term effects (CR: 62.0% vs. 37.8%, P=0.273; PR: 27.8% vs. 25.6%, P=0.506; CR+PR: 89.9% vs. 63.4%, P=0.030) than those received c-RT. Although there was no statistical difference for 1-year overall survival (OS) between two groups (76.3% vs. 72.5%, P=0.486), significantly higher 3- and 5-year OS was observed in IMRT group (3-yr: 52.7% vs. 36.2%, P=0.040; 5-yr: 37.8% vs. 23.1%, P=0.017). Furthermore, the 5-year progression-free survival rates were significantly higher in IMRT group (32.3% vs. 21.6%, P=0.035).

Conclusions
IMRT makes better dose distribution and acceptable toxicities for patients with unresectable postoperative pelvic recurrent disease. The adjacent organs at risk (OAR) are well protected and the preliminary clinical result is encouraging.
Oral Presentation/Debates: CERVICAL CANCER II

PREOPERATIVE RISK ASSESSMENT MODEL FOR IDENTIFICATION OF LYMPH NODE METASTASIS IN EARLY CERVICAL CANCER

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²Obstetrics and Gynecology, University of Konkuk, Seoul, Korea

Objectives
To develop a preoperative risk prediction model for lymph node (LN) metastasis in early cervical cancer patients.

Methods
The medical records of 493 early cervical cancer patients who underwent hysterectomy and pelvic/para-aortic lymphadenectomy between 2009 and 2012 were reviewed. Data between 2009 and 2010 were assigned to a model development cohort (n=304), and data between 2011 and 2012 were assigned to a validation cohort (n=189). A multivariate logistic model was created from preoperative clinicopathologic, MRI, and PET/CT data, from which a predictive nomogram was developed and externally validated. A predicted probability of developing nodal metastasis of less than 5% was defined as low risk.

Results
Age, tumor size assessed by MRI, and LN metastasis assessed by PET/CT are independent predictors of nodal metastasis. The nomogram incorporating these three predictors showed good discrimination and calibration, with a concordance index of 0.878 [95% confidence interval (CI), 0.833-0.917]. The validation set showed good discrimination with a concordance index of 0.825 (95% CI, 0.736-0.895). In the model development cohort, 34% of the patients were classified as low risk and the negative predictive value (NPV) was 99.0%. In the validation cohort, 38% were classified as low risk and the NPV was 95.8%. Combining the model development and validation cohorts, the negative likelihood ratio was 0.094 (95% CI, 0.036-0.248).

Conclusions
A robust model predicting metastatic LN in early cervical cancer was developed, which may help design clinical trials and decide whether lymphadenectomy should be performed.

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Oral Presentation/Debates: CERVICAL CANCER II

LOCALLY ADVANCED CERVICAL CANCER TREATED BY IMAGE GUIDED ADAPTATIVE BRACHYTHERAPY: RETROEMBRACE OUTCOME REPORT

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Objectives
Image guided adaptative brachytherapy (IGABT) for cervical cancer allows higher doses to tumours while sparing the normal organs. Mono-institutional reports show superior results as compared to standard brachytherapy.

We aim to evaluate clinical outcome of IGABT within a multi-institutional cohort (12 institutions).

Methods
A retrospective consecutive web-based collection of data was completed (www.retroembrace.com). All patients with locally advanced cervical cancer (LACC) treated with curative intent through modern external beam radiotherapy ± concurrent chemotherapy and IGABT are included.

Results
Complete information regarding local control and vital status is available in 698 patients, FIGO staging: 122 IB (17.4 %), 46 IIA (6.6 %), 348 IIB (49.8 %), 17 IIIA (2.4 %), 133 IIIB (19 %), 22 stage IVA (3.1 %), 10 IVB (1.4 %). Median tumour width at diagnosis was 50 mm clinically, 46 mm at MRI examination.

At a median follow up of 32 months actuarial local control was 91% at 3 years and 87.5% at 5 years (23 persistent local disease, 40 local recurrences). Estimated actuarial OS at 3 years was 72.7% and 62.7% at 5 years. In 533 patients data on late toxicity assessed by CTCAE v3 was available with crude incidence of G3-5 events as: 27 GI (5%), 20 GU (4%), 15 vaginal (3%).

Conclusions
In the treatment of LACC, IGABT shows excellent local control with limited number of ≥ G3 late side effects, representing the current state of the art. We recommend it to become the standard of care. Nevertheless, systemic control requires further improvement; therefore multidisciplinary approach within prospective studies is additionally suggested.
Oral Presentation/Debates: CERVICAL CANCER II

PREDICTIVE VALUE OF NK CELL IMMUNOFENOTYPE AMONG CIN REGRESSION

S. Agramunt¹, E. Miralpeix¹, J. Genovés¹, J.M. Solé¹, E. Laso¹, M. López-Yarto¹, F. Alameda², G. Mancebo¹, M. López-Botet³, R. Carreras¹
¹Obstetrics and Gynecology, Hospital del Mar, Mataró (Barcelona), Spain
²Pathology, Hospital del Mar, Mataró (Barcelona), Spain
³Immunology, Hospital del Mar, Mataró (Barcelona), Spain

Objectives
Objective: To evaluate the predictive value of NK cell immunophenotype among CIN regression.

Methods
We have started 2 observational cohort studies that include patients with CIN1 and CIN2 respectively who accept to do an expectant management of their disease and to give a blood sample in order to check out the NK cell receptor profile.

We analyse their immunophenotype by acquiring the fluorochrome signaling of each receptor (namely NKG2A, NKG2C, NKG2A2C, NKG2D, ILT2 and KIR) by a flow cytometry system.

Results
72 patients with CIN1 and 76 with CIN2 diagnosis have been included respectively in both studies.
NKG2A was found to be significantly differently expressed among patients with CIN1 (39.5 ± 2.2) versus CIN2 (44.4 ± 1.9) (p =0.04).
For patients with CIN1 there is a clinically significant change in NKG2C expression when comparing CMV seronegative and CMV seropositive patients (21.0±5.4 vs 28.6±3.4, p=0.1), compared to patients with CIN2 (19.8±4.5 vs 23.3±3.0, p=0.2).

Conclusions
This is the first prospective study with capacity to establish causality associations between NK cell immunophenotype and CIN regression. NKG2C expression modulated by CMV infection could play a beneficial role on CIN regression.

If our hypothesis was confirmed, NK cell immunophenotype could be included in the clinical protocols in order to individualize and better estimate the risk of regression/progression of each patient, in order to avoid overtreatment and its potential risks.
Oral Presentation/Debates: CERVICAL CANCER II

FDG-PET FOR EVALUATING RESPONSE TO NEOADJUVANT CHEMOTHERAPY (NACT) IN LOCALLY ADVANCED CERVICAL CANCER (LACC)

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²Nuclear Medicine, Istituto Nazionale Tumori di Napoli, Naples, Italy
³Surgical Pathology, Istituto Nazionale Tumori di Napoli, Naples, Italy
⁴Medical Oncology, Istituto Nazionale Tumori di Napoli, Naples, Italy

Objectives
Although still investigational, NACT followed by radical surgery (RS) is an alternative option to concurrent chemoradiation for the treatment of FIGO stage IB2-IIB cervical cancer. Response to NACT is the most potent prognosticator, and FDG-PET may have a role for the early detection of non-response.

Methods
Twenty-two patients with LACC (squamous cell: 20, adeno: 2; grade 3: 21, grade 2: 1; stage IB2: 8, IIB: 14) were prospectively submitted to NACT (80mg/m² cisplatin; 25mg/m² vinorelbine; 3 courses, every 21 days). FDG-PET was performed before NACT (T0), after cycle 2 (T1), and after cycle 3 (T2). Based on clinical and pathological findings, patients were classified as responders (submitted to RS with evidence of pathological complete-partial response) and non-responders (submitted to RS with evidence of pathological no-change or not submitted to RS). FDG-PET findings are expressed as Total Lesion Glycolysis (TLG)-early (delta T0-1) and TLG-delta (delta T0-2), and as SUVmax-early (delta T0-1) and SUVmax-delta (delta T0-2).

Results
Twelve patients (55%) and ten patients (45%) were classified, respectively, as responders and non-responders. In responders and non-responders, FDG-PET findings were respectively: TLG-early 92.6 vs. 49.1, TLG-delta 92.7 vs. 3.2, SUVmax-early 60.7 vs. 23.3, SUVmax-delta 72.6 vs. -21.9 (p<0.01).

Conclusions
In our prospective series, FDG-PET was able to early detect the patients subset showing non-response to NACT, even in the presence of a clinical tumor shrinkage allowing RS. These data must be verified in a larger study sample, and the role of FDG-PET in the therapeutic algorithm of LACC is still to be defined.
Oral Presentation/Debates: BREAST/VULVA CANCER

ALL FLAT ATYPICAL ATYPIA LESIONS OF THE BREAST DIAGNOSED USING PERCUTANEOUS VACUUM-ASSISTED CORE NEEDLE BIOPSY DO NOT NEED SURGICAL EXCISION

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Objectives
The purposes of this study were to evaluate the outcome of cases of flat atypical atypia diagnosed at vacuum-assisted breast biopsy (VABB) and to determine whether the foci involved or the complete removal of mammographic calcifications are able to predict which lesions will be upgraded to malignancy and the clinical significance of the association of fea with atypical ductal hyperplasia and/or LIN and/or radial scar. If morphological parameters can predict malignancy.

Methods
2414 cases of consecutive VABB using VA 8-, 10- or 11-gauge stereotactically guided core biopsy from two french breast cancer centers were evaluated. Datas of patients with VABB-diagnosed fea who underwent either excisional surgery (%) or mammographic follow-up (≥5 years; %). Postprocedure mammograms were reviewed to determine whether all calcifications were removed. Two pathologists (FA,PM) reviewed the results of procedures performed.

Results
91 cases of flat epithelial atypia (FEA) were diagnosed, associated for 13% with atypical ductal hyperplasia (ADH), 3.3% with lobular neoplasia (LN) and 3.3% with radial scar (RS). A surgical excision was performed on 29 patients and close mammographic follow-up on 62 patients. The total underestimation rate was 7.7% (5 carcinoma diagnosed after surgical excision, 2 carcinoma diagnosed after follow-up). Three factors were significantly associated with underestimation for pure FEA: age ≥ 57, size of lesion > 10 mm and extent of lesion ≥ 4 foci.

Conclusions
FEA lesion associated with radiological microcalcifications less than 10 mm, extended to less than 4 foci among women aged less than 57 may obviate systematic surgery and a close mammographic follow-up should be sufficient.
CISPLATIN-BASED CHEMOTHERAPY FOR HIGH RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA: EP OR EMACP

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Objectives
Therapy of low risk gestational trophoblastic neoplasia (GTN) not responding to monotherapy and of primary high risk GTN consists of polychemotherapy. EMACP, a regimen consisting of etoposide (100 mg/m² d1-5), methotrexate (300mg/m² d1), cyclophosphamide (600mg/m² d1), actinomycin D (0.5mg/m² d2) and cisplatin (50mg/m² d4) has been found effective. Etoposide (100mg/m² d1-5) and cisplatin (20mg/m² d1-5) (EP) could be a good alternative treatment regimen with comparable effectiveness and a shorter total treatment time. In the present study we evaluate the safety, efficacy, and treatment time of EP.

Methods
All patients with high risk GTN who were treated with EP at our institution were included in this retrospectively analysis and compared with the results of patients treated with EMACP. Disease specific survival, duration of therapy and major toxicity are reported.

Results
Twelve and sixteen patients started treatment with respectively EP and EMACP. With a median follow-up duration of 154 months survival rates were comparable for both regimens (EP 91.7%, EMACP 93.8%; P = 0.68). Median treatment time was shorter with EP (EP 68, range 21-84 days; EMACP 98, range 28-168 days; (P = 0.01)). Respectively 56.3% and 25.0% of the patients were hospitalized for pancytopenia (P = 0.10). One patient developed an allergic reaction on EMACP. Three patients on EP had a thrombo-embolic event during treatment and one patient was hospitalized for diarrhoea.

Conclusions
The EP regimen has survival rates in the same range as EMACP with comparable toxicity, but with a shorter overall treatment time.
Oral Presentation/Debates: BREAST/VULVA CANCER

BREAST CANCER RISK IN A LARGE NATIONWIDE COHORT OF SUBFERTILE WOMEN.
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Objectives
Although approximately 100,000 women have received in-vitro fertilization (IVF) treatment in the Netherlands, the late health effects of ovulation-stimulating drugs are not yet known. The purpose of this study is to assess the risk of breast cancer after different subfertility treatments.

Methods
We evaluated breast cancer risk in a nationwide cohort study comprising 19,119 subfertile women who started IVF and 6,001 women treated with other subfertility treatments in the Netherlands between 1980 and 1995. Detailed information on exposure and confounders was collected from medical records and through questionnaires. Incidence data of breast cancer were obtained through linkage with the Netherlands Cancer Registry (1989-2009). Age-, sex- and calendar period specific standardized incidence ratios (SIRs) of breast cancer were calculated. Multivariable Cox regression analysis was used to quantify effects of treatment and cause of subfertility on breast cancer risk.

Results
After a median follow-up duration of 16.6 years, 560 breast cancers were observed. The risk of breast cancer was similar to that in the general population (SIR=0.96; 95% confidence interval [CI], 0.88-1.04) and after IVF treatment compared with other subfertility treatments (hazard ratio=1.02; 95% CI, 0.80-1.29), while adjusting for age at start and parity. The risk of breast cancer did not significantly differ for 1-2, 3-4, or 5 or more IVF cycles compared with no IVF. The risk of breast cancer did not significantly differ by cause of subfertility.

Conclusions
The risk of breast cancer following IVF treatment does not seem to be increased after long-term follow-up.
Oral Presentation/Debates: BREAST/VULVA CANCER

INFLAMMATORY BREAST CANCER: DISEASE CHARACTERISTICS AND SURVIVAL DATA OF A SINGLE-CENTRE PATIENT COHORT

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Objectives
Inflammatory breast cancer (IBC) is a rare subtype of breast cancer affecting <5% of patients with invasive breast tumours. We describe disease characteristics of IBC and its clinical outcome in a single-centre patient cohort.

Methods
Clinicopathological data of 111 patients with clinically diagnosed IBC between June 1996 and August 2012 were collected from our prospectively maintained institutional database and in-hospital medical records.

Results
Mean age at diagnosis was 58.4 years. The percentage of patients with hormone receptor negative, HER2+ and triple negative tumours were 44, 42 and 19%. 96% of patients presented with node-positive and 26% with primary metastatic disease (M1). Median overall survival (OS) was 9.1 years (CI 2.6-15.6 years) for patients with initially localized disease (M0) and 2.9 years (CI 1.9-3.9 years) for M1 patients. After a median follow-up of 3.5 years, 40/81 M0 patients had developed distant metastases. Median time-to-metastasis was 16.2 months. pCR after neoadjuvant treatment was predictive for a longer recurrence-free (RFS; p=0.008) and distant metastasis-free survival (DMFS; p=0.013). M0 patients treated with taxane containing neoadjuvant regimens had a significantly better DMFS (p=0.048) and OS (p=0.020).

Conclusions
IBC is an aggressive form of breast cancer characterized by a younger age at diagnosis, poor histopathological characteristics and early metastatic spread. Despite the progress made, survival outcomes remain poor. In M0 patients, the risk of relapse became almost negligible once 5 years of RFS were achieved. Better outcomes were observed in M0 patients treated with taxanes. pCR after neoadjuvant treatment was confirmed as a positive prognostic factor.
HORMONE CONCENTRATIONS IN POPULATIONS AT LOW AND HIGH RISK OF BREAST CANCER

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²Epidemiology and Biostatistics Program Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, USA

Objectives
To compare concentrations of several circulating hormones implicated in breast carcinogenesis between premenopausal Mongolian women and women living in the West (U.K.).

Methods
Hormone concentrations were measured in women living in Ulaanbaatar, Mongolia, and in the United Kingdom. Information on reproductive and medical history, migration status and lifestyle factors was obtained. Mean differences in hormone concentrations by country were calculated, and systematic variation according to the number of days since last menstrual period was modeled using quadratic regression splines adjusted for age and parity, and statistical significance of the difference in the overall area under the curves was assessed.

Results
With adjustment for age and parity, mean testosterone concentrations were higher (p<0.0001) and estradiol concentrations were lower (p=0.03) in the UK women than in the Mongolian women. Progesterone concentrations also were higher in the Mongolian women (p=0.03), in particular, in the follicular phase of the cycle. Mean hormone concentrations generally were similar in Mongolian women born in Ulaanbaatar compared with those born outside of Ulaanbaatar, although a significant decreasing trend in progesterone concentrations was observed by degree of westernization. Differences in mean hormones were similar in analyses restricted to parous women, or when further adjusted for BMI, height, and smoking status.

Conclusions
These data are not consistent with the hypothesis that lower premenopausal estrogen concentrations mediate the reduced breast cancer incidence in all Asian countries, but suggest that testosterone and progesterone may play a role in the protection that Asian women have compared with women living in the west.
Oral Presentation/Debates: BREAST/VULVA CANCER

ADJUVANT RADIO(CHEMO)THERAPY IN LYMPH-NODE POSITIVE VULVAR CANCER – THE AGO CARE-1 STUDY

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Objectives
This study evaluates the impact of postoperative radio(chemo)therapy (RT/CTX) in patients with lymph-node positive vulvar carcinoma compared to surgery alone.

Methods
Patients with primary squamous-cell vulvar cancer treated at 29 gynecologic cancer centers in Germany 1998-2008 were included in a centralized database and analyzed retrospectively to examine clinical outcome and relapse patterns.

Results
A total of 1,618 patients were documented with a median follow-up of 38.8 months. UICC-stage distribution was 580 (35.9%) T1b, 818 (50.6%) T2, 160 (9.9%) T3 and 31 (1.9%) T4 (1.8% missing data). 495 patients (30.6%) had lymph-node metastases (N+). Median progression-free survival (PFS) of N+ patients was 15.9 months and overall survival (OS) 46.9 months, compared to 99.1 and 208.8 months in N- patients. 254 (51.3%) N+ patients underwent adjuvant RT/CTX: 212 [83.5%] RT, 36 [14.2%] RT-CTX, 6 [2.4%] CTX). Median PFS and OS were significantly longer compared to N+ patients without adjuvant treatment [PFS: 18.5 vs. 12.0 months, p=0.0003, HR 0.63 (95% CI: 0.50-0.81); OS: 111.6 vs. 37.1 months, p=0.029, HR 0.71 (95% CI: 0.52-0.97)] and remained consistent in the multivariate analysis of all N+ patients (PFS: HR 0.57, 95% CI: 0.43-0.74; OS: HR=0.61, 95% CI: 0.43-0.86).

Conclusions
This large multicenter study in vulvar cancer shows that prognosis of node-positive patients was improved with adjuvant radiotherapy but still remains poor compared to the outcome of node-negative patients. In other squamous cell carcinomas, adjuvant chemoradiation is superior to radiotherapy alone; this approach might therefore be the best to further improve outcome in vulvar cancer.
Society Session: FRENCH SOCIETY OF GYNECOLOGIC ONCOLOGY (SFOG)

CLINICAL RESEARCH: STATE OF ART ON PROSPECTIVE RESEARCH IN FRANCE, THROUGH NATIONAL STUDIES (ONGOING PHRCs)

S. Classe¹, G. Ferron², E. Leblanc³, P. Nickers⁴, C. Haie Meder⁵, F. Narducci⁶, F. Lecuru⁷

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²Surgery, Institut Claudius Regaud, Toulouse, France
³Surgery, Centre Oscar Lambret, Lille, France
⁴Radiotherapy, Centre Oscar Lambret, Lille, France
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A selection of the main French prospective multicentric randomized trials currently ongoing in the field of gynecologic oncology

Prevention

Radical fimbriectomy (PI E Leblanc). For patients with a BRCA 1-2 mutation, or a family history of breast/ovarian cancer. Primary outcome (PO) : number of ovarian carcinoma.

Epithelial Ovarian cancer

CHIVA (PI G Ferron, Gineco): phase I trial. compare patients with Advanced ovarian cancer treated with neo-adjuvant chemotherapy and interval surgery to the same treatment + Vargatef® (Nintedanib). Vargatef® is an antiangiogenic agent with no proved increased incidence of bowel perforation. PO, DFS.

ANTALYA: A phase I trial, compare in patients with Advanced ovarian cancer, first line treatment with neo-adjuvant chemotherapy and interval surgery to the same treatment + avastin®. PO, DFS.

DESKTOP III (PI F Lecuru, Gineco): A german phase III trial. Place of surgery in the treatment of the first late relapse in patient with the AGO score. PO: OS. Several French center are involved.

CHIPOR (PI JM Classe, Unicancer): Phase III trial. Is adjunction of platinum based HIPEC in the treatment of the first relapse may improve the median overall survival. PO: OS.

Endometrial cancer

TOMOGYN (PI P Nickers). Phase III trial comparing 3D conformal radiotherapy and IMRT. PO: acute morbidity.

PORTEC 3 (PI C Haie Meder, Unicancer): Phase III trial : comparison of radiation therapy with or without chemotherapy. For patients with high-risk endometrial cancer. PO: OS.
Robotic surgery

ROBOGYN (PI F Narducci), Perioperative morbidity in gyneco-oncology according to laparoscopy versus robot-assisted laparoscopy. PO: morbidity.
Parallel Session: RECURRENT DISEASE

TREATMENT CONSIDERATIONS IN CERVICAL CANCER WITH PELVIC RECURRENCE AFTER ADJUVANT OR PRIMARY RADIOTHERAPY

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Up to 70% of cervical cancer patients undergo radiation therapy at some point of their treatment, but one-third of these recur or show persistent disease. After its introduction by Brunschwig (1948), pelvic exenteration (PE) is still the only treatment available with curative intent in recurrent cervical cancer following radiation. In these conditions, GOG studies showed poor response and survival after chemotherapy, which is to be considered a palliative option. During the last two decades, much progress has been made regarding perioperative management, surgical techniques and reconstruction, allowing a significant decrease of morbidity/mortality and survival improvement. It is most likely, however, that is a more careful patient selection to determine a better therapeutic outcome. Extrapelvic metastases are generally considered a contraindication to PE, particularly intra-peritoneal spread. Disease pelvic extent, and, therefore, complete vs incomplete resection, is the most potent survival predictor. Treatment-free interval and lymph node status seem to independently affect prognosis as well. Accurate preoperative evaluation, including FDG-PET scan and laparoscopy, is recommended to exclude, in principle, a palliative intention to treat.

<table>
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<tr>
<th>Author</th>
<th>Year</th>
<th>No. Pts</th>
<th>% Mortality</th>
<th>% 5-y OS</th>
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<td>Crozier</td>
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<td>105</td>
<td>10</td>
<td>38</td>
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<td>2006</td>
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<td>35</td>
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<td>-</td>
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<td>-</td>
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<tr>
<td>Yoo</td>
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<td>61</td>
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<td>56</td>
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<tr>
<td>Schmidt</td>
<td>2012</td>
<td>212</td>
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<td>39</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1129</strong></td>
<td></td>
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</table>
The standard surgical treatment for early-stage cervical cancer is radical hysterectomy plus systematic pelvic lymphadenectomy, showing a 5-year progression-free survival of 87%–92%. However, considering that more than 25% of these women are <40 years old and often nulliparous in developed countries, the matter of fertility-sparing surgery seems of utmost importance. Radical trachelectomy and chemo-conization proved to be effective methods to treat safely these cancers, but with some negative issues: pregnancies after trachelectomy carry a severe obstetric morbidity as about one third of them ends with first or second trimester miscarriage or premature labor, while the latter strategy implies the use of neoadjuvant chemotherapy that often discourages patients to accept such a proposal.

Simple conization, with or without lymphadenectomy could be represent a plausible treatment scheme for managing stage IA1-2 tumors in patients desiring offspring. Moreover, recent studies suggest that selected patients with stage IB1 disease undergoing radical hysterectomy could have been safely cured by simple hysterectomy and even by cervical conization. In this context, a multicentric Italian study reported that cervical conization could be suitable to treat stage IB1 lesions smaller than 15–20 mm with pathologic negative lymphnodes. The sentinel node procedure has been advocate to further reduce the invasiveness of the surgical therapy and seems promising to predict parametrial invasion. However, the association of two experimental procedures is to be regarded unsafe until the real potential and risks of each strategy will be thoroughly assessed by future clinical controlled trials in the referral centers.
Background: Borderline and non epithelial ovarian tumors often occur in young women and fertility preservation is an important issue. The aim was to evaluate the current state of art regarding fertility-sparing procedures in terms of oncological and fertility outcomes.

Methods: We analyzed the current literature about fertility-sparing surgery in borderline and non epithelial ovarian tumors.

Results: Fertility-sparing surgery is indicated in all stages ovarian borderline tumors. Conservative treatment increases the rate of recurrence without any effect on survival. The rate of recurrence is correlated with the type of treatment, with a higher rate in patients undergoing cystectomy. If a relapse in the remaining ovary occurs, further conservative management may be offered. The reported spontaneous pregnancy rate is 50%. In young women affected by stage I sex-cord stromal tumors, a fertility-sparing surgery is feasible without worsening the prognosis. In malignant ovarian germ cell tumors, conservative surgery plus adjuvant chemotherapy is the standard treatment, except for stage IA dysgerminoma and stage I immature teratoma, in which surgery alone is curative. Literature reports high number of pregnancies, but only about 25% of women became pregnant after treatment. An evaluation of reproductive potential in individual patients after treatment should be done, so that they can be counseled regarding potential fertility preservation strategies, such as oocyte cryopreservation.

Conclusions: Fertility-sparing surgery is safe in borderline ovarian cancer, in early stage sex-cord stromal tumors and in malignant germ cell ovarian tumors. The individual reproductive potential should be evaluated to identify patients needing preservation strategies.
CHEMOTHERAPY AND PRESERVATION OF OVARIAN FUNCTION
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Premature ovarian failure and infertility following chemotherapy are major concerns for young cancer patients. Worldwide, 4% of cancers are diagnosed in patients under the age of 35. The most frequently diagnosed tumors at this age are: breast, cervical cancers, melanoma, NHL and leukemia. Despite the scientific progresses, we are still not able to limit the damage of chemotherapy on extratumoral tissues with high proliferative index. Gonadal tissue is highly sensitive to chemotherapy damage with an increasing rate of follicle loss through apoptotic cell death. The risk of ovarian failure depends on multiple factors: a. age of patient; b. gonadotoxicity profile of chemotherapy; c. schedule and duration of treatment; d. concomitant approaches (eg. pelvic radiation therapy). The possibilities of preserve fertility in women exposed to chemotherapy are: in vitro fertilization plus embryo cryopreservation, unfertilized ova cryopreservation and the administration of a gonadotropin releasing hormone (GnRHa) agonist. None of this methods has been universally identified as standard approach. Also, the possible hormone dependency of the tumor (eg. germinal cancers, breast cancers that express hormone receptors) must be taken into account limiting the use of hormonal stimulation often required. Between the various available methodologies, increasing evidences (mostly in breast cancer treatment) emerge from studies involving the use of GnRH agonist (GnRHa) concomitant to adjuvant chemotherapy and from several trials that tested new parameters as markers to predict the infertility risk of patients (anti-Mullerian hormone-AMH, inhibin B and follicle count). A multidisciplinary approach is needed for fertility counseling in young patients with cancer undergoing chemotherapy.
Society Session: TURKISH ASSOCIATION OF GYN ONCOLOGY - VIDEO SESSION

Cancer control in Turkey

M. Gultekin

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Cancer has an increasing incidence in Turkey with a rate of 227 per 100,000. According to the projected data, the rise will continue until year 2030 and the expected number of patients living with cancer will increase to more than a million. However, with a logistic cancer control strategy, almost a third of these cases may be prevented. With these facts, Turkey has implemented a national control program in 2009, with a launch of Phase II by 2013. The program includes registry, prevention, screening, treatment and palliative care. This lecture will summarise the highlights of Turkish Cancer Control Activities which are active cancer registry with a 100% coverage rate, cancer preventive strategies such as tobacco, obesity, alcohol and excess salt consumption control programs, promotion of physical activity programs, Asbest and Radon control programs, electromagnetic fields control programs. New data arising from national cancer screening programs will also be shared coming from HPV based cervical screening, teleradiology based mobile breast cancer screening Project in females between 40-69 yrs of age. Also, some additional information will be given about the treatment and palliative care plans of Turkey until 2023.
STEP BY STEP RADICAL HYSTERECTOMY

M. Kose

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Main aim of the type 3 radical hysterectomy is to remove cervical cancer with negative surgical margins. Intraoperative pelvic examination and lymphatic evaluation is necessary. Hysterectomy should be performed on the basis of intraoperative findings and results of frozen section examination for suspicious lymph nodes. If there is an obvious parametrial involvement of lymphatic node involvement hysterectomy should be abandoned and radiotherapy should be planned for the patient. Surgical steps can be summarized as below; Round ligaments are ligated from the closest part to the pelvic side wall and bilateral ureters should be identified. Surgical fossas including pararectal, paravesical rectovaginal and retrovesical fossas should be developed. Bilateral uterine arteries are identified at the level of hypogastric arteries and ligated. Ovaries can be removed in postmenopausal women or should be transposed in premenopausal women. Then, vesica plica-uterinas are identified and dissected from the uterus at least 3-4 cm by sharp and blunt dissection. Bilateral ureters are dissected from the broad ligaments and dissected from the uterus as much as possible. After these steps, bilateral sacrouterine are identified and rectum should be separated from the posterior part of the vagina. Then, bilateral sacrouterine and cardinal ligaments are ligated from the closest part of the pelvic side wall. After the identification and separation of the ureters from the uterus and servical web, then anterior and lateral parametrias are resected from the pelvic side walls. Then upper 1/3 part of the vagina resected by scalpel or scissors. Vaginal cuff can be sutured by an absorbable suture.
Oral Presentation/Debates: OVARIAN CANCER I

RESULTS OF INTENSIVE ALGORITHM-BASED SCREENING IN THE UK FAMILIAL OVARIAN CANCER SCREENING STUDY (UK FOCSS PHASE 2)


1Molecular Oncology, Barts Cancer Institute, London, United Kingdom
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5Medicine, Harvard Medical School, Boston, USA
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Objectives
To establish the performance of intensive screening for familial ovarian cancer using the risk of ovarian cancer algorithm (ROCA) and transvaginal sonography (TVS).

Methods
Between 14/06/2007 and 29/03/2012, 4,531 women at an estimated ≥10% lifetime risk of OC/FTC were screened by 42 UK centres for 14,263 women screen years with 4-monthly CA125 analysed by the ROCA. TVS was annual but brought forward if ROCA results were non-normal. Women with suspicious scan and/or algorithm results were referred for possible surgical intervention. Participants were followed prospectively by centres, questionnaire and cancer registries. Data was censored 365 days after final screen, withdrawal or death.

Results
18 incident OC/FTC occurred. 6/18 were occult cancers from risk-reducing salpingo-oophorectomy (RRSO). No symptomatic interval cancers occurred. Incident sensitivity was 100% (CI 74-100%) if occult cancers were classified as true positives and 67% (41-87%) if they were classified as false negatives. Positive and Negative Predictive Values were 13% (7-22%) and 100% (99-100%) respectively. 42% incident screen-detected OC/FTC were stage I/II vs. 30% on annual screening (UK FOCSS Phase 1) (p=0.69) and 92% were completely cytoreduced on Phase 2 vs. 62% on Phase 1 (p=0.16).

Conclusions
4-monthly ROCA-based screening had high sensitivity for OC/FTC and was associated with high complete cytoreduction rates. However, it failed to detect the majority of OC/FTC at early stage. These results are encouraging but screening cannot currently be considered a safe alternative to RRSO.
Oral Presentation/Debates: OVARIAN CANCER I

PROGRESSION-FREE SURVIVAL BY GCIG CRITERIA: ANALYSIS OF THE SECONDARY ENDPOINT OF THE AGO-OVAR16 TRIAL


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Objectives
AGO-OVAR16 is a randomized, double-blind trial of pazopanib as maintenance therapy in patients with advanced epithelial ovarian cancer (AEOC).

Methods
Patients with histologically confirmed AEOC (N=940) were randomized 1:1 to receive pazopanib 800 mg once daily or placebo for up to 24 months. Primary endpoint was investigator-assessed progression-free survival (PFS) by RECIST. A secondary endpoint was PFS by Gynecologic Cancer InterGroup (GCIG) criteria.

Results
At data cutoff, by RECIST criteria there were 273 progression and 195 censoring events in the placebo arm, 237 progression and 235 censoring events in the pazopanib arm (investigator review). By GCIG criteria, there were 290 progression events in the placebo arm (213 per RECIST and 77 per CA-125) and 255 progression events in the pazopanib arm (184 per RECIST and 71 per CA-125). Using RECIST criteria, pazopanib increased PFS vs placebo by investigator review (HR=0.766; 95% CI: 0.64-0.91; P=0.0021; median 17.9 vs 12.3 months). Analyses of PFS by GCIG were consistent (HR=0.790; 95% CI: 0.67-0.93; P=0.0047; median 16.8 vs 11.9 months). The proportion of patients with CA-125 progression as the first progression event was nearly identical between the placebo and pazopanib arms (16% and 15%, respectively). The time interval from CA-125 progression to RECIST progression was also well balanced between the placebo and pazopanib arms (2.6 vs 2.8 months, respectively).

Conclusions
In patients with AEOC, maintenance therapy with pazopanib provided a significant PFS benefit. PFS prolongation was confirmed by RECIST and GCIG criteria. ClinicalTrials.gov identifier: NCT00866697.
Oral Presentation/Debates: OVARIAN CANCER I

ASSESSMENT OF SAFETY OF SURGERY IN PATIENTS WITH OVARIAN CANCER TREATED WITH CARBOPLATIN/PACLITAXEL BEVACIZUMAB IN THE ROSIA ROUTINE ONCOLOGY PRACTICE STUDY

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Objectives
The efficacy and safety of front-line bevacizumab for ovarian cancer has been established in phase III trials (GOG-0218, ICON7). ROSiA is assessing the safety of front-line bevacizumab-containing therapy in routine oncology practice in 35 countries.

Methods
Patients with FIGO stage IIb-IV/grade 3 stage I-IIa ovarian cancer without clinical signs/symptoms of gastrointestinal obstruction or history of abdominal fistula, gastrointestinal perforation or intra-abdominal abscess within the preceding 6 months received front-line bevacizumab 15 (or 7.5) mg/kg q3w plus 4-8 cycles of paclitaxel-carboplatin after definitive surgery. Single-agent bevacizumab was continued until progression or for up to 36 cycles. The primary endpoint is safety (CTCAE v4.03). We performed exploratory analyses of surgery-relevant AEs according to type and outcome of surgery in patients who had undergone surgical debulking.

Results
At data cut-off, surgical details were available for 912 patients treated in ROSiA. Baseline characteristics were broadly similar to those of the ICON7 population (median age 56 years [range 19–82], 73% serous histology, 66% stage IIIC/IV) except for a relatively low bowel resection rate (14%) and higher proportion of...
Conclusions
Compared with GOG-0218 and ICON7, surgery in ROSiA was more representative of routine clinical practice. Surgery-relevant AEs were numerically more frequent in patients with upper abdominal surgery but there was no marked difference between patients with versus without bowel resection or according to surgical outcome. Gastrointestinal disorders, including perforations, are within ranges reported in phase III trials.
Oral Presentation/Debates: OVARIAN CANCER I

CHONDROITIN SULFATES AS A NOVEL CLASS OF BIOMARKERS TO AID CLINICAL DECISION MAKING IN OVARIAN CANCER

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Objectives
New biomarkers are needed to aid clinical decision making in epithelial ovarian cancer (EOC) benefiting the outcome of these patients. Chondroitin sulfate (CS) is a class within the group of negatively charged polysaccharides, glycosaminoglycans. The polysaccharide CS consists of alternating disaccharide units of glucuronic acid and N-acetyl-D-galactosamine which are variously modified by sulfate groups. CS is mainly located in the extracellular matrix of EOC and involved in the process of carcinogenesis. Structural alterations of CS chains (i.e. sulfation pattern) seem to affect its biological properties. We recently selected a single chain antibody which strongly reacts with CS and in this study we investigate the potential of CS as a biomarker in EOC.

Methods
The specificity of a single chain antibody against CS was determined by an indirect ELISA. Paraffin embedded tissues of normal ovaries, benign ovarian cysts and ovarian carcinomas were assessed by immunohistochemistry for the expression of the CS epitope defined by the antibody (N = 148). By statistical analysis the expression pattern was correlated with clinical parameters.

Results
The antibody showed specificity against CS motifs, likely containing GlcA-GalNAc4S6S units. Expression of specific CS motifs in the stroma of the malignant tumor was significantly increased compared with benign cysts. Overexpression of CS epitopes was correlated with serous subtype, advanced FIGO stage and poor prognosis.

Conclusions
Specific CS motifs hold biomarker value for clinical decision making in patients with epithelial ovarian cancer. This new class of biomarkers may constitute diagnostic and therapeutic applications in management of ovarian cancer.
ORAL MLN8237 WITH WEEKLY PACLITAXEL IN PATIENTS WITH RECURRENT EPITHELIAL OVARIAN, FALLOPIAN TUBE, PRIMARY PERITONEAL (OC) OR BREAST CANCER (BRc): PHASE 1 RESULTS

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Objectives

AAK is a key mitotic kinase and negative prognostic marker in multiple tumor types including OC and BrC. This phase 1/2 study (NCT01091428) evaluated paclitaxel with/without the investigational AAK inhibitor, MLN8237, in patients with OC or BrC; phase 1 results are reported.

Methods

Women ≥18 years, with previously-treated metastatic/locally recurrent disease, and ECOG PS 0-1 (OC: previous platinum and 1-2 taxane treatments) were eligible. Patients received escalating doses (3+3 schema) of paclitaxel (60 or 80 mg/m², days 1,8,15) plus oral MLN8237 BID (10-50 mg; Days 1-3,8-10,15-17 in 28-day cycles). Key objectives: safety and MTD, pharmacokinetics, and preliminary antitumor activity (RECIST and/or CA125).

Results

As of February 2013, 49 patients (OC n=38; BrC n=11), median age 59 years (range 29-75), were enrolled. Seven patients experienced DLT (MLN8237/paclitaxel [mg/mg/m²]: 20/80 [n=2/6], 40/60 [n=2/15], 50/60 [n=2/3]; 30/60 [n=1/6]); most commonly neutropenia with/without fever; MTDs were 10/80 and 40/60. Thirty-eight patients (78%) had Gr≥3 drug-related adverse events (9 [18%] serious); most commonly neutropenia (61%) and leukopenia (33%). No on-study death reported. MLN8237 exposures at 40/60 were in the previously-reported bioactive range, supporting this recommended phase-2 dose. At 40/60, a small (10-19%) increase in paclitaxel AUC was observed, not of clinical concern as the AUC was still below the single-agent AUC of 80 mg/m². One patient had complete response (OC), 16 partial responses (10 OC, 6 BC), 7 CA125 responses (OC), and 14 stable disease (11 OC, 3 BC).
Conclusions
A generally well tolerated, pharmacologically active dose of paclitaxel/MLN8237 was determined, supporting continued efficacy evaluation in solid tumors.
Oral Presentation/Debates: OVARIAN CANCER I

LOW EXPRESSION OF NIBRIN PREDICTS BETTER PROGNOSIS IN PATIENTS WITH OVARIAN CANCER TREATED WITH TRABECTEDIN PLUS PEGYLATED LIPOSOMAL DOXORUBICIN (PLD)

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Objectives
A randomised phase III OVA-301 trial compared the efficacy and safety of trabectedin plus PLD vs. PLD alone in 672 patients with recurrent ovarian cancer (ROC). Herein, we have investigated the expression of nibrin (p95/NBS1) as a possible biomarker in patients with ROC.

Methods
Immunohistochemical staining with a p95 antibody (clone Y112; Abcam) was performed in 138 samples obtained at diagnosis (trabectedin plus PLD arm: n=78; PLD arm: n=60). A computerized image analysis system was used to quantify protein expression. The ratio between nuclear positive and negative cells was calculated to categorize patients into three groups: <5% positive cells: Group=0; 5%-30%: Group=1; >30%: Group=2. The PFS and ORR analysis was based on independent oncologist assessment. OS was defined from randomization to death/last contact.

Results
In the trabectedin plus PLD arm the ORR was 39.7%, and median PFS and OS were 9.7 and 26.4 months, respectively. Following an evaluation according to nibrin expression in the trabectedin plus PLD arm, the ORR was 64.3% (Group=0; n=14) vs. 34.4% (Group=1/2; n=64) (p=0.068), median PFS: 11.5 months (Group=0) vs. 7.4 months (Group=1/2) (hazard ratio [HR]: 2.29; 95% CI: 1.03-5.06; p=0.0366), median OS: not reached for Group=0 vs. 24.4 months for Group=1/2 (HR: 3.25; 95% CI: 1.39-7.62; p=0.0041). No statistically significant differences were observed among groups in the PLD arm.

Conclusions
With the limitations of these analyses, our results indicate that low protein expression of nibrin seems to be associated with a better clinical outcome in patients with ROC treated with the combination of trabectedin plus PLD.
Oral Presentation/Debates: OVARIAN CANCER I

CYTOREDUCTIVE SURGERY IN RECURRENT OVARIAN CANCER. THE DESKTOP SERIES OF THE AGO STUDY GROUP, NOGGO, MITO, MANGO, GEICO, NSGO, AGO-AUSTRIA, SGOG, CRCTU, BGOG AND GINECO


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Objectives
The role of surgery in platinum sensitive recurrent ovarian cancer is not clearly defined, especially regarding the following questions: (1) surgical aim, (2) identification of potential candidates for surgery, and (3) improvement of prognosis.

Methods
Retrospective multicentre study for identification of the surgical aim and a score to identify candidates for surgery (DESKTOP I trial). Subsequent validation of the AGO score (DESKTOP II).

Results
DESKTOP I analyzed 267 patients. Complete resection was associated with significantly longer survival compared with surgery leaving any postoperative residuals [median 45.2 vs. 19.7 months; hazard ratio (HR) 3.71; 95% confidence interval (CI) 2.27-6.05; P < .0001]. A hypothetical score for prediction of complete cytoreduction was developed. This score was deemed positive, if three factors were present: (1) complete resection at 1st surgery (2) good performance status, and (3) absence of ascites. The prospective DESKTOP II trial screened 516 patients. 51% of the patients were classified as score positive and 129 patients with positive score and first recurrence underwent surgery. The rate of complete resection was 76% thus confirming the validity of this score regarding positive prediction of resectability in more than 2 out of 3 patients.

Conclusions
Patients with recurrent ovarian cancer seem to have a benefit only from complete
resection. The AGO score is a useful tool to identify patients in whom complete resection is feasible. The third step of the DESKTOP trials (DESKTOP III) comparing chemotherapy plus surgery versus chemotherapy alone in patients with platinum sensitive relapsed ovarian cancer is ongoing.
Oral Presentation/Debates: OVARIAN CANCER I

SAFETY AND EFFICACY OF SINGLE-AGENT CHEMOTHERAPY ± BEVACIZUMAB IN ELDERLY PATIENTS WITH PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: SUBGROUP ANALYSIS OF AURELIA


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Objectives

In AURELIA, patients randomised to receive bevacizumab with their chemotherapy for platinum-resistant ovarian cancer had significantly improved progression-free survival (PFS) and response rate (RR) versus those receiving chemotherapy alone.

Methods

 Patients with platinum-resistant ovarian cancer, ≤2 prior anticancer regimens and no prior bowel obstruction received single-agent chemotherapy (investigator’s choice: paclitaxel, pegylated liposomal doxorubicin [PLD] or topotecan) alone (CT) or with bevacizumab (5 mg/kg/wk equivalent; BEV–CT) until progression, unacceptable toxicity or consent withdrawal. Post-hoc exploratory efficacy and safety analyses were performed according to age <65 versus ≥65 years.

Results

Median age was 61 years (range 25–84) in CT patients (N=182) and 62 (range 25–80) in BEV–CT patients (N=179). In the 133 patients (37%) aged ≥65 years, the chemotherapy selected before randomisation was most commonly topotecan (43%) in the CT arm and PLD (43%) in the BEV–CT arm. Baseline hypertension was more
frequent in patients ≥65 than <65 years (BEV–CT arm: 46% vs 13%, respectively) but ascites were less common (26% vs 38%). Median bevacizumab duration was 5.1 months in both age groups; median chemotherapy duration in patients ≥65 was 3.3 months (CT arm) vs 4.4 months (BEV–CT arm). Key efficacy and safety results are below.

**Conclusions**
Consistent PFS and RR benefits of bevacizumab were seen across both age categories. In this exploratory analysis of AURELIA, grade ≥3 hypertension was more common in elderly bevacizumab-treated patients and careful monitoring is recommended. Overall BEV–CT was well tolerated in a selected patient population ≥65 years, suggesting a favourable benefit:risk profile.
Oral Presentation/Debates: OVARIAN CANCER I

GAIN-OF-RESISTANCE TO CISPLATIN AND ITS CIRCUMVENTION IN OVARIAN TUMOR CELLS HARBORING WILD-TYPE P53
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Objectives
Platinum-based therapy is a cornerstone of ovarian cancer management. Although its effectiveness is dependent on wild-type p53, many resistant cancers also express wild-type p53. This is typified by the 2780CP human ovarian tumor model, which harbors wild-type p53 but is ~20-fold resistant to cisplatin vs. parental isogenic A2780 cells. However, 2780CP cells are exquisitely sensitive to oxaliplatin and the analog DAP (DACH-dichlorodiacetato-PtIV). Our objective was to examine this observation mechanistically.

Methods
Gene expression was determined in A2780 and 2780CP cells using Eppendorf DualChip microarrays.

Results
55 genes were differentially expressed (≥1.5-fold) in control untreated 2780CP cells, with 19 significantly downregulated and 36 significantly upregulated. Expressions of the 10 most upregulated genes were not altered in A2780 cells following cisplatin or DAP treatment. Of the 10 most downregulated, p21 emerged as a gene of critical interest, being induced in A2780 cells by both drugs but only by DAP in 2780CP cells. The significance of p21 in the cytotoxicity of platinum drugs, and its dependence on p53 function, was confirmed by siRNA in A2780 cells. However, in 2780CP cells, p53 siRNA increased resistance to DAP but unexpectedly restored significant sensitivity to cisplatin. That the wild-type p53 paradoxically augments cisplatin resistance was confirmed in a human ovarian tumor panel, in which the mean IC₅₀ of cisplatin for mutant p53 tumors was 2.0 μM, whereas the wild-type p53 models exhibited ~3-fold higher resistance (IC₅₀ 5.7 μM).

Conclusions
The presence of wild-type p53 induces gain-of-resistance to cisplatin but imparts sensitivity to oxaliplatin and DAP. (Supported by NIH CA160687).
Network/Task Force: CANCER IN PREGNANCY

PROGNOSIS OF 311 WOMEN WITH PRIMARY BREAST CANCER DIAGNOSED DURING PREGNANCY: RESULTS FROM AN INTERNATIONAL COLLABORATIVE STUDY.
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On behalf of the Cancer in Pregnancy Task Force

Purpose
We aimed to determine the prognosis of breast cancer diagnosed during pregnancy (BCP).

Methods
In this cohort study, a multicentric registry of BCP patients (http://www.cancerinpregnancy.org/ and GBG 29/BIG 02-03) compiled pro- and retrospectively between 2003 and 2011 was compared with patients who did not have associated pregnancies, using an age limit of 45 years. Only patients with a new diagnosis of invasive breast cancer during pregnancy were included. The main analysis was a Cox proportional hazards regression of disease-free survival (DFS) and overall survival (OS) on exposure (pregnant or not) adjusting for age, stage, grade, hormone receptor status, HER2 status, histology, type of chemotherapy, use of trastuzumab, radiotherapy and hormone therapy.

Results
The registry contained 447 women with BCP, mainly originating from Germany and Belgium, of which 311 (69.6%) were eligible for analysis. The non-pregnant group consisted of 865 women from the institutional database of the Multidisciplinary Breast Centre, University Hospitals Leuven, Belgium. Median age was 33 years for the pregnant and 41 years for the non-pregnant patients. Median follow-up was 61 months. There were no statistically significant differences noted for DFS (HR=1.34; 95% CI 0.93-1.91; p=0.14), and OS (HR=1.19; 95% CI 0.73-1.93; p=0.51).

Conclusion
The results show similar overall survival for patients diagnosed with breast cancer during pregnancy compared to non-pregnant patients. This information is important when patients are counselled and support the option to start treatment with continuation of pregnancy.
Objectives
The vitamin D axis is involved in various aspects of human breast cancer. It is composed by vitamin D, vitamin D receptor (VDR) and group component (Gc) protein that is the precursor of the Gc protein-derived macrophage activating factor (GcMAF) (Eur Nephrol. 2011;5(1):15–9). It was demonstrated that administration of GcMAF to metastatic breast cancer patients yielded good clinical results (Int J Cancer. 2008 Jan 15;122(2):461-7). Here we demonstrate that GcMAF stimulates macrophages that attach to human breast cancer cells, induce their apoptosis and phagocytise them.

Methods
Common reagents were from Sigma Aldrich. Purified, activity-tested GcMAF was from Immuno Biotech. Human breast cancer cell line MCF-7 was from the IZSLER. Macrophages (Raw 264.7) were from HPA Culture Collection. Morphology was studied by phase-contrast microscopy using an inverted microscope (Optika Microscopes).

Results
When human breast cancer cells were co-cultured with macrophages that had been previously activated by GcMAF (100 ng/ml) for 72 h, macrophages attached to cancer cells and the chromatin in the nucleus of the cancer cells appeared fragmented and disorganized as expected in cells undergoing apoptosis. The cytoplasm appeared indented as if the macrophages attached to that region were deconstructing the cytoplasmic assembly of the cancer cell. The cytoplasm of macrophages appeared vacuolized suggesting active phagocytosis.

Conclusions
These results are consistent with the observation that macrophages infiltrated experimental tumours implanted in mice after GcMAF injections, and open the way to further studies aimed at assessing the precise role and indications for GcMAF in the immunotherapy of breast cancer.
e-Poster Orals: OVARIAN AND BREAST CANCER

LOCAL ESTROGEN THERAPY AND QUALITY OF LIFE IN BREAST CANCER PATIENTS ON TREATMENT WITH AROMATASE INHIBITORS

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Objectives
The current treatment strategy in hormone receptor positive breast cancer (BC) is the use of an aromatase inhibitor (AI) which potentially induces or enhances the symptoms of atrophic vaginitis like vaginal dryness or dyspareunia. The endocrine treatment has a potential negative impact on the quality of life (QoL). We therefore evaluated pharmacokinetic, safety, efficacy, and effect on QoL of ultra-low-dose estriol-lactobacilli vaginal tablets in postmenopausal BC survivors treated with a non-steroidal AIs reporting atrophic vaginitis.

Methods
In this bicentric phase I study, women being treated with a non-steroidal AI and reporting vaginal atrophy were recruited. The objective was to evaluate safety, clinical symptoms, changes in vaginal pH, epithelium and microflora and the impact on QoL during an initial therapy with one vaginal tablet of 0.03 mg estriol (Gynoflor®) daily for 28 days and during a subsequent maintenance therapy for another 8 weeks.

Results
Vaginal pH showed statistically significant decrease from entry to the follow-up visits. Symptoms were assessed by a VAS with an 11-point estimation scale (0 = not at all, 10 = worst imaginable feeling). Vaginal dryness continuously improved from a median of 8 at entry to 4 at the end of initial therapy, and 2 at the end of maintenance therapy. At entry only 3 patients (19%) had sexual intercourse within the last 4 weeks, which increased to 7 patients (44%) at all control visits.

Conclusions
Local therapy of postmenopausal breast cancer survivors treated with a non-steroidal AI reporting atrophic vaginitis is an effective therapy with a positive impact on the quality of life.
ONE STEP TRANSPOSITION OF THE OMENTUM WITH MESHED SKIN GRAFT AND VACUUM THERAPY FOR SEVERE RADIONECROSIS AFTER BREAST CANCER TREATMENT IN ELDERLY PATIENTS

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Objectives
Severe radionecrosis is mostly a complication of radiation therapy performed in patients with breast cancer conservative treatments during the seventies and eighties. The aim of this study is to describe this technique and its results.

Methods
Patients presenting with chest wall radionecrosis, were referred to our wound care unit in 2012 and 2013. Patients with severe complication due to radionecrosis (infection, osteoitis) and patients with severe body image impairment were proposed for surgery. Patients with too severe comorbidities did not have surgery.

Operative technique
First the size of the omentum was evaluated before the radionecrosis resection. The omentum flap was harvested by laparoscopy. Second, the radionecrosis was excised in sano. The omemtum flap was placed on the defect trough a rectus abdominis incision under video control. Third, a thin skin graft was performed and the skin was extended with a meshgraft and placed on the omentum flap. Fourth, a negative pressure system (VAC®) was inserted (-75 mmHg).Post operatively, the VAC® system was changed every 3 days, and stopped after surgeon decision. Controlled wound healing was until total healing.

Results
10 patients were operated. The median age was 77 years (67-83). The interval from radiation therapy was 34 years (16-45). The operative length was 129 minutes (100-180). The hospitalization duration was 16 days (10-35). The vacuum therapy duration was 10.5 days (7-43). The thoracic healing duration was 41 days (14-180).

Conclusions
This technique appears robust, minimally invasive and efficient in these elderly weak women.
e-Poster Orals: OVARIAN AND BREAST CANCER

FEC3-D3 VS. FEC6 IN THE ADJUVANT TREATMENT OF BREAST CANCER – A RETROSPECTIVE STUDY
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Objectives
Chemotherapy with the FEC3-D3 regimen in the adjuvant treatment of breast cancer with node involvement is frequent therapeutic option, with evidence provided by the PACS01 trial. This trial compared the FEC6 and FEC3-D3 regimens in this setting, revealing better disease-free survival (DFS), overall survival (OS) and favorable tolerability in patients treated with FEC3-D3. Many authors have presented results on the efficacy and toxicity in their clinical practice. Aims: to evaluate the toxicity profile, DFS and OS treated with FEC6 and FEC3-D3 at our institution and to compare them with the results of the PACS01 trial.

Methods
Retrospective cohort study of 423 patients, 168 treated with FEC6 and 255 with FEC3-D3. Demographic and pathologic characteristics between the 2 populations were balanced.

Results
A higher incidence of neutropenia was found in patients treated with FEC6 (31vs.15.7%;p=0.01), nevertheless, grade 3 and 4 neutropenia were more frequent in patients treated with FEC3-D3 (8.3vs.5.5%;p=0.01). Anemia was more frequent in the FEC3-D3 treated group (34.1vs.28.6%;p=0.034). Grade 3 and 4 nausea was more frequent in the FEC6 group (77.4vs.38.2%;p<0.001), while patients that underwent FEC3-D3 had more asthenia (33.1vs.31.5%;p<0.001), mialgia (24.4vs.2.4%;p<0.001) and onycholysis (5.9vs.1.2%;p=0.35). DFS and OS at 48 months were higher in the FEC3-D3 group (97vs.76%;p<0.0001 and 96vs.86%;p<0.0001 respectively).

Conclusions
These results demonstrate higher DFS and OS in patients treated with FEC3-D3 as in the PACS01 trial, with a toxicity profile consistent with the trial. In the adjuvant setting it is particularly important to consider the efficacy and toxicity of different therapeutic options.
e-Poster Orals: OVARIAN AND BREAST CANCER

INTRAOPERATIVE ELECTRON RADIOTHERAPY DURING BREAST CONSERVING SURGERY OF BREAST CANCER

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Objectives
Intraoperative boost irradiation as part of breast-conserving therapy is a perfect method to adequately capture the high risk tumor relapse area. Intraoperative radiotherapy (IOERT) as a boost for breast cancer releases a high single dose of radiation to the breast tissue; therefore acute toxicity is of particular attention. We therefore analyzed the acute and late side effects and the clinical outcome after radiotherapy with 10 Gy as a boost with a minimum follow-up of 3 months.

Methods
A total of 310 + 75 patients treated with IOERT (10Gy with 5, 7 and 9 MeV electrons) with a dedicated robotic linac (NOVAC 7, New Radiant Technology, Aprilia, Italy) to the tumor bed during breast-conserving surgery as a boost followed by whole-breast radiotherapy (WBRT, 50 - 50.4 Gy; 2 - 1.8 Gy per fraction) were included in this study. All patients underwent a retrospective follow-up regarding acute and late side effects.

Results
The IOERT was well tolerated. As a side effect there was one + 4 patients with seroma. Two patients developed chronic pain. 2 patients developed a secondary wound healing 10 patients developed a grade 2 fibrosis The remaining patients did not develop any grade 3 or 4 side effects. The observed toxicity rates were not influenced by age, tubus size, electron energy or systemic therapy. 80 patients had a follow up longer than 5 years. Three of them developed distant metastasis and one patient died. The cosmetic results of their breasts were good.

Conclusions
We did not find any significant surgical and radiation complications.
e-Poster Orals: OVARIAN AND BREAST CANCER

VITAMIN D BINDING PROTEIN-DERIVED MACROPHAGE ACTIVATING FACTOR INHIBITS HUMAN BREAST CANCER CELL PROLIFERATION AND DECREASES ALPHA-N-ACETYL GALACTOSAMINIDASE IN BREAST CANCER PATIENTS

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Objectives

It was demonstrated that vitamin D binding protein-derived macrophage activating factor (GcMAF) decreases serum alpha-N-acetyl galactosaminidase (nagalase) in breast cancer patients; decrease of nagalase was associated with significant improvement of clinical conditions (Int J Cancer. 2008 Jan 15;122(2):461-7). Since nagalase is both an index of immune suppression and of tumour burden, we studied the direct effects of GcMAF on a human breast cancer cell line (MCF-7), and we compared the effects in vitro with those observed in breast cancer patients.

Methods

The effects of GcMAF on proliferation, morphology, vimentin expression and angiogenesis were studied by cell proliferation assay, phase-contrast microscopy, immunohistochemistry and western blotting, and chorioallantoic membrane assay.

Results

GcMAF inhibited human breast cancer cell proliferation and cancer cell-stimulated angiogenesis. Furthermore, GcMAF significantly reduced vimentin expression, indicating a reversal of the epithelial/mesenchymal transition, a hallmark of human breast cancer progression. These results were consistent with the preliminary observation of two breast cancer patients. The two patients (age 65 and 62) presented with elevated levels of nagalase; 1.70 and 5.60 nM/min/mg respectively (normal values below 0.65). After 8 and 17 months of weekly intravenous administration of 100 ng GcMAF respectively, nagalase levels decreased to 0.60 and 1.10, thus indicating a decrease of the tumour burden.

Conclusions

These results support the hypothesis that the effects of GcMAF in cancer patients can be ascribed to different biological properties of the molecule that, in addition to stimulating macrophages, inhibits cancer cell proliferation, migration and metastatic potential as well as tumour-induced angiogenesis.
e-Poster Orals: OVARIAN AND BREAST CANCER

SAFETY AND EFFICACY OF RAPID DESENSITIZATION IN HYPERSENSITIVITY REACTIONS TO CHEMOTHERAPY: RESULTS OF 183 TREATMENTS AT A SINGLE INSTITUTION

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Objectives
Hypersensitivity reactions (HSRs) to chemotherapy pose a difficult challenge in cancer treatment, due to its immediate life-threatening potential and the paucity of alternative agents. This scenario is especially frequent in gynecologic malignancies. Drug desensitization is the only option to administer drugs involved in HSRs.

Our aim was to study the efficacy and safety of rapid desensitization to chemotherapy in a Spanish population.

Methods
35 patients (33 female), mean age of 55.5 years, with ovarian cancer (68%), endometrial cancer (14%), cervix cancer (8%), colorectal cancer (3%), nasopharyngeal carcinoma (3%) and cancer of unknown primary site (3%), with previous HSRs to platinum compounds (97%), taxanes (17%) and/or anthracyclines (5,7%) were desensitized with Acetylsalicylic acid (300mg) and Montelukast (10mg) premedication to protect from cutaneous and respiratory reactions according to the Brigham and Women's Hospital 12-step protocol.

Additionally, in 2 patients with previous severe anaphylaxis, premedication with Omalizumab was added.

Results
Among 183 rapid desensitizations, 93% presented with mild (12%) or no reactions (88%). 86% of these mild reactions occurred in the last step of the protocol. In subsequent infusions the protocol was modified and only milder (79%) or no reactions (21%) appeared. Full target dose was completed in 98% of desensitizations. There were 3 severe reactions, which precluded the complete administration of the drug, and only in 2 patients the desensitization protocol had to be definitely abandoned.

Conclusions
The use of rapid desensitization protocols for cancer patients with HSRs to chemotherapy, allow patients to continue on treatment and thus prolong cancer survival.
SYNCHRONOUS OVARIAN AND ENDOMETRIAL CANCER - AN INTERNATIONAL MULTICENTER CASE-CONTROL STUDY.

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Objectives
To compare the prognosis of patients with synchronous endometrial and ovarian cancer (SEOC) to matched controls with either endometrial cancer (EC) or ovarian cancer (OC).

Methods
A retrospective case-control study including patients with SEOC who had been treated at five European tertiary Gynecologic Oncology Centers between 1996 and 2011 and patients with either endometrial or ovarian cancer matched for age, FIGO stage, histology, year of diagnosis, and Eastern Cooperative Oncology Group performance score.

Results
The study cohort comprised 77, 132 and 126 patients with SEOC, EC, and OC, respectively. Patient characteristics confirmed an equal distribution of matching factors, and the median follow-up did not differ (p=.44). 48.1% of the patients with SEOC showed early FIGO stage I for both EC and OC. The 5-year recurrence-free survival rates (5-YRFS) differed between SEOC and EC (76.3% vs. 86.3%; p=.047) but not the 5-year overall survival rates (5-YOS) (71.6% vs. 79.8%; p=.12). The 5-YRFS and the 5-YOS did not differ between SEOC and OC (76.3% vs. 63.8%; p=.19) and (71.6% vs. 69.3%; P=.61), respectively. Adjustment for the FIGO stages of the two components of SEOC confirmed not differing 5-YRFS and 5-YOS between SEOC and the matched controls.

Conclusions
Prognosis of patients with SEOC tended to be the same compared to matched controls with either one EC or OC. Therefore it could be considered that patients with SEOC may be eligible for clinical trials of the advanced tumor component, if no additional therapy is indicated for the other component.
GCIG ICON8 STAGE IA ANALYSIS: SAFETY AND FEASIBILITY OF TWO DOSE-FRACTIONATED CARBOPLATIN-PACLITAXEL REGIMENS FOR THE FIRST-LINE TREATMENT OF OVARIAN CANCER

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Objectives
ICON8 (NCT10356387, CRUK/10/030) is an ongoing 3-arm 3-stage randomised trial of dose-fractionated carboplatin-paclitaxel (CP) versus standard 3-weekly chemotherapy for FIGO stage IC-IV ovarian cancer.

Methods
Patients are randomised either following immediate primary surgery (IPS) or at diagnosis (planned delayed PS) to 6 cycles of CP AUC5/6 + 175mg/m² q3w; CwP AUC5/6 q3w + 80mg/m² q1w; or wCwP AUC2 + 80mg/m² q1w. Protocol-defined stage IA outcomes were treatment completion rate, dose intensity, rates of febrile neutropenia, grade 2+ neuropathy and any grade 3/4 toxicity.

Results
147 patients were included (see table). Median age 60yrs; ECOG PS 0/1 94%; high-grade serous 67%; FIGO IC:II:III:IV 7%:14%:63%:14%; IPS 56%. Per-protocol, treatment completion was lower than expected but >80% received 6 cycles platinum-based chemotherapy and higher median total paclitaxel doses were delivered (CP:1018mg/m², CwP:1253mg/m², wCwP:1276mg/m²). The most common reason for stopping early was toxicity. The difference in grade 3/4 toxicity was mainly due to uncomplicated neutropenia, CP:8%, CwP:30%, wCwP:21%. G-

<table>
<thead>
<tr>
<th></th>
<th>CP (n=48)</th>
<th>CwP (n=50)</th>
<th>wCwP (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feasibility</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6 cycles protocol-defined chemotherapy</td>
<td>84%</td>
<td>57%</td>
<td>60%</td>
</tr>
<tr>
<td>6 cycles platinum-based chemotherapy</td>
<td>95%</td>
<td>89%</td>
<td>84%</td>
</tr>
<tr>
<td>Delivered dose intensity (mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin (AUC/wk)</td>
<td>1.73</td>
<td>1.93</td>
<td>1.88</td>
</tr>
<tr>
<td>Paclitaxel (mg/m²/wk)</td>
<td>53.5</td>
<td>62.7</td>
<td>68.1</td>
</tr>
<tr>
<td><strong>Toxicity</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Any grade 3/4</td>
<td>32%</td>
<td>56%</td>
<td>46%</td>
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</table>

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Conclusions
The dose-fractionated regimens have been more difficult to deliver but acceptable dose-intensity and toxicity was observed. Neither regimen has been modified but treatment delivery may be improved by greater G-CSF use. Accrual continues with 545/1485 randomised.
ADDITIONAL INTRAPERITONEAL CISPLATIN/ETOPOSIDE TO FIRST-LINE CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER: THE INTERIM ANALYSIS OF A RANDOMIZED PHASE II STUDY
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3Department of Obstetrics and Gynecology, Suzhou Municipal Hospital, Jiangsu, China

Objectives: The purpose of this study is to evaluate the feasibility and the role of an additional intraperitoneal chemotherapy with cisplatin and etoposide in bulky Stage IIIC and IV ovarian cancer. The interim analysis is conducted when half of the patients enrolled.

Methods: Patients with stage IIIC and IV epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer who underwent optimal primary cytoreduction (<=1 cm) were randomized to receive either intraperitoneal cisplatin 50 mg/m2 and etoposide 100 mg/m2 weekly for 4 weeks followed by intravenous paclitaxel 175 mg/m2 plus carboplatin AUC 5 or docetaxel 75 mg/m2 plus carboplatin AUC 5 every 3 weeks for 6 cycles, or the intravenous regimen as in the intraperitoneal group every 3 weeks for 6 cycles.

Results: 103 patients enrolled. 83.0% (44/53) of the patients in the intraperitoneal therapy group completed 4 cycles of the assigned therapy. Grade 3 and 4 Leucopenia and anemia were more common in the intraperitoneal group (P=0.026 and P=0.030, respectively). However, there were no significant differences in other hematologic, gastrointestinal, metabolic, or neurologic toxic effects. The median follow-up was 19.0 months. The median PFS were 27.6 months and 18.5 months in intraperitoneal therapy group and intravenous therapy group (P=0.117, HR=0.637). None statistical difference was shown between the two therapy groups in cost analysis (P=0.566).

Conclusions: As compared with intravenous chemotherapy alone, the toxicities of sequential intraperitoneal and intravenous chemotherapy are higher, but acceptable. A trend of prolonged PFS is observed in intraperitoneal group, but mature data will be available in the final analysis.
MALIGNANT BOWEL OBSTRUCTION: IS SURGICAL INTERVENTION BENEFICIAL IN RECURRENT DISEASE?

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Objectives

To define factors that could aid selecting gynecologic cancers patients with malignant gastro-intestinal obstruction (MGO) who would benefit from palliative surgical procedures.

Methods

Medical records of all patients with MGO who had palliative procedure in our institute between 1994 and 2013 were reviewed. Outcome measures were survival after surgery, post-operative oral feeding and post-operative chemotherapy. Statistical analyses included Cox proportional-hazards regression models and Kaplan–Meier curves with log-rank tests.

Results

Sixty-eight palliative surgeries were performed, with ovarian (69.2%), primary peritoneal (8.8%), cervical (11.7%) and uterine (10.3%) malignancies. Procedures included colostomy (26%), ileostomy (40%), colonic stent (1.5%), gastrostomy (13.5%) and bypass/resection (19%). Post-operative mortality rate within 30 days was 14.7%. Post-operative oral feeding and chemotherapy rates were 65% and 53% respectively. Median post-op survival was 106 days (range 3-1342). In univariate analysis, good prognostic factors included higher lymphocyte count (HR 0.59, 95% CI 0.35-0.97), ascites < 2 liter (HR 2.54, 95% CI 1.42-4.56), younger age (HR 1.033, 95% CI 1.006-1.061), non-primary peritoneal tumor (HR 5.98, 95% CI 2.3-15.62), higher blood Albumin (HR 0.53, 95% CI 0.32-0.88), and bypass/resection surgery (HR 3.025, 95% CI 1.35-6.78). In multivariate analysis, only the last four were associated with better prognosis. The only significant factor for oral feeding and chemotherapy after surgery was albumin. No patient with blood albumin ≤ 2.15gr/dL survived ≥30 days post operation.

Conclusions

In selecting patients with recurrent malignancies and MGO for palliative surgery, age, primary tumor site and albumin may serve as prognostic factors. Bypass/resection surgery is associated with an improved survival.
ULTRASOUND ACCURACY IN PREDICTION OF RECTOSIGMOID INVOLVEMENT IN ADVANCED OVARIAN CANCER PATIENTS

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Objectives
Residual tumor after primary surgery is one of the most important prognostic factors in advanced ovarian cancer patients. Optimal debulking requires bowel resection in more than 30% of patients. Prediction of rectosigmoid involvement allows for planning of adequate operation time and experienced surgical team. It was the aim of the study to evaluate ability of transvaginal ultrasound to predict rectosigmoid infiltration and need for bowel resection.

Methods
Enrolled were patients with advanced pelvic tumors scheduled for cytoreductive surgery between 2010-2012. Involvement of sigmoid colon and/or rectum was evaluated by transvaginal ultrasound and results compared to intraoperative findings and final histology reports. Only patients with confirmed epithelial ovarian cancer remained for the final analysis.

Results
In total, 193 patients were included, in 77 of them rectosigmoid involvement was found intraoperatively. Bowel resection was done in 67 cases, in 10 patients only peritoneum from anterior surface of rectum was removed. Transvaginal ultrasound successfully predicted bowel involvement in 69 out of 77 cases, thus sensitivity for prediction of rectosigmoid infiltration reached 93.2% and specificity 92.1% (PPV 89.1% and NPV 95.1%). In 8 patients ultrasound failed to detect involvement of rectum, all of them with low load of disease.

Conclusions
Transvaginal ultrasound showed high accuracy in prediction of rectosigmoid colon involvement in patients with advanced ovarian cancer. Preoperative assessment of bowel involvement may allow for scheduling of appropriate operation time and surgical team.

This project was supported by the IGA MZ, the Czech republic, No. NT13070 and Charles University projects UNCE204024 and PRVOUK P27/LF1/1.
THE DIAGNOSTIC ACCURACY OF LACTATE 1.5T MAGNETIC RESONANCE SPECTROSCOPY TO DIFFERENTIATE BETWEEN BENIGN AND MALIGNANT OVARIAN MASSES.

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\textsuperscript{3}Gynaecology, Royal Women’s Hospital, Melbourne, Australia

Objectives:
Despite imaging techniques, serum tumor-markers and numerous algorithms the accuracy of pre-operative differentiation between malignant and benign ovarian masses is limited. Magnetic Resonance Spectroscopy (MRS) can be used to quantify the presence of substances of interest inside a mass. In this study we evaluate the diagnostic power of MRS in the diagnosis of ovarian masses.

Methods:
All women referred to our department (January 1st 2003 - January 1st 2007) with an ovarian mass were included. Serum-CA125, RMI, conventional 1.5T pelvic MRI and 1.5T MRS were performed. From the MR-spectrum tumor-lactate was quantified. Pathological examination of the ovarian mass was used as reference for malignancy. Receiver-Operator-Curves (ROC’s) were constructed of CA-125, RIM and the lactate concentration and respective Area-Under-Curves (AUC’s) calculated (with 95% CI). Optimal sensitivity, specificity and likelihood ratios were calculated.

Results:

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|}
\hline
Method & Sensitivity & Specificity & AUC (95% CI) \\
\hline
CA125 & 75 (71-79) & 74 (71-77) & 0.87 (0.82-0.92) \\
RMI & 74 (70-78) & 72 (69-75) & 0.89 (0.85-0.93) \\
Lactate & 71 (67-75) & 71 (68-74) & 0.89 (0.85-0.93) \\
\hline
\end{tabular}
\end{table}

[Graph: ROC Curve]
157 women could be included (mean age 48.8 years, 17-87, SE 1.33). The ROC's of CA-125, the RMI and 1.5T MRS quantified tumor-lactate are displayed (figure). The AUC's are respectively 0.76 (95% CI: 0.66-0.85), 0.77 (95% CI: 0.76-0.86) and 0.73 (95% CI: 0.64-0.82). The optimal sensitivity, specificity, LR+ and LR- are tabulated (figure).

Conclusions:
The quantification of tumor-lactate with MRS has equal diagnostic accuracy for the diagnosis of ovarian malignancy when compared to CA-125 and the RMI. Subjective assessment of the conventional MRI appears to be most accurate. MRS quantification of other molecules (e.g. choline) may have more diagnostic power.
IOTA SIMPLE ULTRASOUND-BASED RULES: WHY DO WE HAVE INCONCLUSIVE RESULTS?

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Objectives: To evaluate the morphological ultrasound features of the 'undetermined' ovarian tumors according to the IOTA (International Ovarian Tumor Analysis) Simple ultrasound-based rules (SR) and to investigate whether these rules are applied similarly by the examiners depending on the level of experience in the field of ultrasound.

Methods: It was a two-year prospective study. The ovarian tumors were evaluated with the use of IOTA SR by non-expert examiners. If the rules could not be applied the tumors were considered undetermined. In these cases two methods were applied a second step: the subjective assessment (SA, Algorithm A) or IOTA SR but performed by an expert (Algorithm B).

Results: 257 women underwent ultrasound exam. IOTA SR were applicable in 82.2% of tumors with sensitivity and specificity of 93.4% and 93.6%, respectively. Algorithm A in undetermined tumors had a sensitivity of 100% and specificity 93.8% compared to the algorithm B were sensitivity and specificity were of 79% and 88.2%, respectively (Table 1). Presence of acoustic shadows (rule B3) and lack of blood flow (rule B5) were the most common features that were inadequately assessed by a non-expert examiners.

<table>
<thead>
<tr>
<th>Diagnosis of ovarian tumors in the population of patients (n=257)</th>
<th>IOTA non-expert</th>
<th>Algorithm A</th>
<th>Algorithm B</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUROC (95% CI)</td>
<td>75.8 (68.9-82.7)</td>
<td>97.9 (96.0-99.6)</td>
<td>83.6 (77.0-89.6)</td>
</tr>
<tr>
<td>ACC (95% CI)</td>
<td>77.3 (74.8-90.0)</td>
<td>97.9 (95.1-99.5)</td>
<td>84.9 (79.4-90.3)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>78.4 (71.3-86.1)</td>
<td>100.0 (100.0)</td>
<td>79.6 (73.0-86.0)</td>
</tr>
<tr>
<td>Specificity</td>
<td>81.3 (75.0-87.6)</td>
<td>95.8 (93.6-97.8)</td>
<td>88.0 (82.4-93.1)</td>
</tr>
<tr>
<td>PPV (95% CI)</td>
<td>67.5 (59.4-75.7)</td>
<td>99.1 (97.9-99.9)</td>
<td>79.5 (72.7-86.2)</td>
</tr>
<tr>
<td>NPV (95% CI)</td>
<td>83.3 (76.0-90.7)</td>
<td>100.0 (99.4-100.0)</td>
<td>88.2 (81.4-93.1)</td>
</tr>
</tbody>
</table>

Table 1. Clinical value of non-expert IOTA*** compared with Algorithm A and Algorithm B in ovarian cancer I/D diagnosis.

AUROC = area under the curve; 95% CI = confidence interval; I/IU=ACC-accuracy; PPV-positive predictive value; NPV-negative predictive value; *IOTA - International Ovarian Tumor Analysis; **Algorithm A - IOTA simple rules classification + subsequent subjective assessment; ***Algorithm B - IOTA simple rules classification + subsequent expert IOTA assessment; *Significant differences.
Conclusions:
Application of IOTA SR in ovarian tumors by a non-expert has a high sensitivity and specificity but only in masses with a certain diagnosis. Evaluation of the non-diagnostic tumors based on SA is a more accurate method than evaluation performed by an expert with the use of IOTA SR.
IN VITRO EXPOSURE TO CHEMOTHERAPEUTIC AGENTS INDUCE APOTOSIS, DOWNREGULATION OF HORMONAL RECEPTORS, AND UPREGULATION OF WNT4 IN HUMAN GRANULOSA CELLS

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2Genetic and Cell Biology, San Raffaele Scientific Institute, Milano, Italy

Objectives
Anti-cancer drugs reduce the primordial follicle pool and harm the ovarian vascularization, however the underlying mechanisms of ovarian damage are still unclear. The aim of this study was to analyze in vitro the molecular mechanisms responsible for the gonadotoxicity of different classes of chemotherapeutic agents on human granulosa lutein cells (GCs).

Methods
After follicular fluid collection from women undergoing ovarian hyperstimulation, GCs were isolated. The effect of different classes of chemotherapeutic agents – paclitaxel, doxorubicin and cisplatin - were evaluated on cell viability by MTT assay and on apoptosis by Bcl-2/Bax ratio and BcX-L mRNA expression. Expression of FSH-R, ER-b and WNT gene family were assessed by qRT-PCR.

Results
The percentage of viable cells upon a 30mM treatment during 48h were 22.8±4.0% for paclitaxel, 61.5±2.3% for doxorubicin, and 26.7±2.9% for cisplatin. A significant reduction of the Bcl-2/Bax ratio and of BcX-L were found in cells treated with all drugs. We observed a reduced expression of ER-b in response to doxorubicin (45.5±8.73%;p=0.02), paclitaxel (28.8±8.9;p=0.025) and cisplatin (17.4±0.3;p=0.001). Cisplatin and paclitaxel also down-regulated FSH-R expression (32.0±15.8;p=0.046; 0.63±0.21; p=0.001, respectively). Down-regulation of WNT-3 in response to doxorubicin and paclitaxel and up-regulation in response to cisplatin were found; WNT-4 was up-regulated in response to all drugs.

Conclusions
Chemotherapeutic agents might affect follicle physiology, inducing GCs apoptosis and follicular atresia through FSH-R and ER-b downregulation. Since WNT signaling pathway is essential to follicle development, these data hint for WNT-4 up-regulation as an adaptive response of GCs to damage, in order to support follicle survival.
CANCER RELATED MATERNAL MORTALITY IN THE NETHERLANDS

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Objectives
With an incidence of 1 in 1000 live births, cancer in pregnancy is rare. Since physiological pregnancy changes can mimic symptoms secondary to a malignancy, diagnosis might be delayed. The aim of this study was to assess the incidence of cancer-related maternal mortality and to evaluate delay in diagnosis and treatment in pregnancy or postpartum.

Methods
A total of 28 women that died from cancer between 2001 and 2012 were selected from the database of the Dutch Maternal Mortality Committee. Different medical specialists scored each case on delay in diagnosis and treatment and whether this was caused by patient- or doctor-related factors. An age-matched control group of non-pregnant women with similar tumours in the same tumour stage were selected from the database of the Netherlands Cancer Institute.

Results
Cancer-related maternal mortality rate in the Netherlands is 1.23 per 100,000 live births. The mean age of the study population at diagnosis was 34 year. A variety of malignancies underlie the fatalities. In 60% of the cases there was delay, especially in diagnosis (80%) and to a lesser extend in treatment (38%). The majority were doctor-related factors. 75% had a severe delay of >3 months. Survival was significantly shorter compared to controls (p <0.001).

Conclusions
This is the first study that evaluates delay in cancer-related maternal mortality. Delay in diagnosis due to doctor-related factors are common. Pregnant women with cancer may have a shorter survival time, but because of the small and diverse study population it is difficult to determine if delay had influenced prognosis.
FERTILITY AND ONCOLOGIC OUTCOME OF CONSERVATIVE SURGERY FOR OVARIAN BORDERLINE RECURRENCE AFTER CONSERVATIVE MANAGEMENT OF STAGE I SEROUS BORDERLINE OVARIAN TUMOR: ABOUT 26 CASES.

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Objectives
The aim of this study was to evaluate the impact of conservative management of recurrence after conservative treatment of stage I serous borderline ovarian tumors (SBOT).

Methods
Patients with a stage 1 serous LMPOT treated conservatively between 2000 and 2010 were retrospectively reviewed with data on the follow-up. All pathological slides of initial tumor or relapse were reviewed by the same expert pathologist.

Results
119 patients were reviewed, forty patients had relapsed and none died from ovarian disease. 26 patients had conservative procedures for recurrence. The conservative procedures for the first relapse were: unilateral cystectomy/UC (n=12; %); unilateral salpingo-oophorectomy/USO (n=10; 42%); bilateral cystectomy (n=1) and USO+CC (n=2; %) and one patient had a salpingectomy. 19 patients had only 1 conservative surgery for recurrence, 4 had two conservative surgery and 3 patients had 3 conservative management for relapse.

We obtained 11 pregnancies after conservative management of ovarian relapse: 7 after 1 relapse treated by cystectomy and 4 after 2 relapses.

Ten (40%) patients recurred after conservative management of ovarian recurrence, in whom 5 had peritoneal recurrence under the form of noninvasive implants. Two of these peritoneal recurrent patients had evolution in the form of invasive recurrence. None patient died from disease.

Conclusions
In this series, the conservative management of ovarian recurrence of stage I SBOT appeared to be a safe and useful procedure. Nevertheless, considering the high rate of successive relapse and the risk of invasive recurrence in further evolution, an oophorectomy should be propose if this recurrence observed after the achievement of the parental project.
Single Institute Retrospective Study of 75 Cases of Exenterative Surgery with Minimal Access Modalities.

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Objectives
To study the feasibility, oncological outcome and survival rates of laparoscopic and robotic exenterative surgery.

Methods
We retrospectively analysed 75 cases of exenterative surgeries done over a period of 8 years in our institute. 75 women (age 32-72 yrs) with carcinoma of cervix, vagina, ovary, rectum and bladder were treated by laparoscopic or robotic exenterative surgery. Interventions included anterior, posterior and total pelvic exenteration done laparoscopically or robotically.

Results
Out of 75 patients, anterior exenteration surgery was done in 52 (69.33%) patients, posterior exenteration in 17 (22.6%) and total exenteration in 6 (8%). Robot was used in 12 patients while the rest were done laparoscopically.
Clinical diagnosis included carcinoma of the cervix in 55 (73.3%) , rectum in 10 (13.3%) , bladder in 7 (9.3%) , ovary in 2 (26.6%) and vagina in 1 (1.3%) .
Indications for surgery were primary disease in 62 (82.6%) and secondary disease in 13 (17.3%) patients. Complications included ureteric injuries in 2 , delayed bladder recovery in 4 , anastamotic leak in 1 , wound infection in 1 and prolonged ileus in 4. Median length of hospital stay was 9 days. 1 patient of laparoscopic total exenteration required conversion to open surgery. Median follow up of 48 months showed disease recurrence of 42% and survival rates of 30%.

Conclusions
Laparoscopic and robotic surgery are feasible options for performing exenterative surgeries in advanced gynecologic malignant disease. The oncological outcomes and survival rates are comparable to open surgery with the added benefits of minimal access surgery.
e-Poster Orals: MISCELLANEOUS 1

ADJUVANT CHEMOTHERAPY IN STAGE I-II UTERINE LEIOMYOSARCOMA: A MULTICENTRIC RETROSPECTIVE STUDY OF 140 PATIENTS.

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Objectives

Almost 50-60% of patients with stage I-II uterine leiomyosarcoma (ULMS), primary treated with surgery, relapse and die for progressive disease. In this retrospective study we describe the impact of adjuvant chemotherapy in this subset of patients.

Methods

140 women treated from 1976 to 2011 were included in the study. Univariate and multivariate analysis were used to test clinical features and adjuvant treatments for the association with overall survival (OS) and disease-free survival (DFS).

Results

62 women did not receive any further treatment after surgery, 26 had radiotherapy (RT), 52 chemotherapy and 12 chemo-radiotherapy. Chemotherapy combination based on doxorubicin and ifosfamide was used in 54 cases. After a median follow-up of 63 months, 87 women (62%) relapsed, and 62 (44%) died. The vast majority who relapsed had distant recurrences (72%).

The 5 year median DFS and OS were 43% and 64% respectively. 68.7% of women treated with chemotherapy (+/- RT) vs 65.6% of patients only observed were alive at 5 years of follow up (p= 0.521). In univariate analysis no factors had a statistical impact on DFS, while number of mitosis (>20 x 10HPF), age (>60 years) and adjuvant radiotherapy were found as negative prognostic factors for OS. In multivariate analysis only mitosis and age remained significant.

Conclusions

Adjuvant chemotherapy was not associated to a survival benefits and should not be considered as standard of care for patients with stage I-II ULMS, until randomized clinical studies will give further informations.
FOLLOW-UP AND OUTCOMES OF WOMEN WITH UNTREATED CIN2 LESIONS: IS THERE A ROLE FOR THE USE OF HPV-RELATED BIOMARKERS

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Objectives
To review outcomes of women with untreated CIN2 lesions and to identify whether HPV-related biomarkers could safely predict the likelihood of regression.

Methods
Setting: Three University Hospitals; Imperial NHS Trust, London-Ioannina, Greece.
Period: 2009-2011
Population: Young women with histologically proven CIN2 lesions under close surveillance.
Interventions: Follow-up data on cytology, colposcopy and histology were retrieved. In a subgroup with CIN2 (40%), an LBC specimen was prospectively obtained prior to colposcopy and tested for HPV typing, E6 & E7 mRNA by NASBA or flow cytometry, p16INK4a and microspectroscopy.
Outcomes: Progression, persistence, regression rates at 24 months of follow-up. The sensitivity, specificity, PPV and NPV were calculated for combinations of biomarkers. The gold standard was histology.

Results
We included 102 women. Of those, 29% were eventually treated, 18% defaulted from surveillance at least once, while 71% regressed spontaneously to low-grade or normal findings at the end of the 24 months follow-up period. There were no cases of invasion. Low-grade cytology or colposcopy, young age, small lesions and HPV subtype other than 16 were related to a high likelihood of regression. HPV DNA test achieved high sensitivity, while the combination of NASBA mRNA and p16 optimal specificity; these could be integrated into a clinical algorithm.

Conclusions
A substantial proportion of CIN2 lesions in young women spontaneously regress. Some combinations of biomarkers appear to have significant accuracy in identifying misclassified lesions and in predicting lesions likely to regress. This could allow conservative management for women at low risk and avoidance of unnecessary treatment.
THE MAJORITY OF METACHRONOUS CIN1 AND CIN3 LESIONS ARE CAUSED BY DIFFERENT HPV GENOTYPES, INDICATING THAT ACTUAL PROGRESSION OF CIN1 IS A RARE EVENT

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Objectives
True progression of CIN1 is uncommon. The majority of observed progression may be explained by infection with another HPV type, or by diagnostic errors. The aim of this study was to determine the rate of true progression from a CIN1 to a CIN3 lesion, i.e. progression not due to diagnostic errors or change in HPV genotype.

Methods
Records from all patients with a CIN3 diagnosis between 1995 and 2010 were retrieved from the archives, and the frequency of an initial previous CIN1 diagnosis was assessed. Biopsies from CIN3 patients with a CIN1 diagnosis in their history were reviewed by a pathologist and HPV genotyping was performed.

Results
44 out of 1819 patients with a CIN3 diagnosis had metachronous CIN1 and CIN3 lesions. Three cases were not available for analysis and in another three cases the quality of the isolated DNA was insufficient. Eight cases showed progression due to diagnostic errors. Out of the 30 remaining patients, 19 patients had different HPV genotypes in their CIN1 and CIN3 lesion. True progression occurred in 11 cases (0.6%).

Conclusions
The presence of a CIN1 lesion in the history of patients with a CIN3 lesion is uncommon. The majority of metachronous CIN1 and CIN3 lesions are caused by different HPV genotypes, indicating that true progression is a rare event. This study raises the question whether stringent follow-up is really necessary for patients with a CIN1 lesion.
A HIGH RESOLUTION GENOMIC PICTURE OF EPITHELIAL OVARIAN CANCER: IDENTIFICATION OF PREDICTIVE AND PROGNOSTIC MARKERS BY GENOME-WIDE SNP ARRAYS.

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Objectives
Platinum resistance remains a major obstacle in the treatment of epithelial ovarian cancer (EOC), a heterogeneous disease characterized by genomic instability. We investigated copy number variations (CNVs) that impact survival or platinum response in platinum-treated EOCs.

Methods
High-resolution genome-wide SNP arrays measured CNVs in a discovery (n=127) and validation cohort (n=144) of high risk stage I or stage II-IV EOCs, treated in the University Hospitals Leuven and/or within the OVCAD project. GISTIC analysis found genomic peaks significantly overamplified or deleted. Cox regression and univariate analysis correlated the GISTIC peaks with OS, PFS and platinum response. We also analyzed 6 literature-derived candidates previously associated with chemoresistance or outcome in EOC: amplification of 19q12 (chr19:33079622-35829476 and chr19:35145875-35171137), 20q13.31-q13.32, ZNF217 and 3q29; and loss of 22q.

Results
Amplification of 14q32.33, containing AKT1 and MTA1, was significantly associated with worse OS (p=0.048), PFS (p=0.014) and platinum resistance (p=0.030) in the discovery cohort and remained significant for OS in the validation cohort (p=0.014). When pooling discovery and validation cohort together, amplification of 14q32.33 (p=0.065), 3q26.1 (p=0.014); losses of 11p11.12 (p=0.004) and 8p21.2 (p=0.031), emerged as potential prognostic markers. Amplification of 14q32.33; losses of 13q14.2 and 17q12 were also confirmed as potential predictive markers. Of the literature-derived candidates, only amplification of 3q29 correlated significantly with OS, PFS and platinum response.

Conclusions
We identified and validated in a second series that gain in 14q32.33, containing AKT1 and MTA1, is associated with worse OS and platinum resistance, suggesting that in those EOCs with 14q32.33 amplification, worse overall survival is driven by platinum resistance.
TAT-ELP AS A POTENTIAL MOLECULAR THERAPEUTIC AGENT FOR PREVENTION OF INTRAPERITONEAL DISSEMINATION IN PATIENTS WITH EPITHELIAL OVARIAN CANCER.

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Objectives
Ovarian cancer is commonly associated with widespread intra-abdominal metastasis. As the disease progresses, the cancer cells invade the liver, lungs or brain. New therapies are thought to prevent the ability of cells to metastasize to different organs in the body. The Tat-ELP polypeptide consists of the cell penetrating peptide (CPP) Tat, fused to elastin-like polypeptide (ELP). The Tat peptide is an 11 amino acid, basic peptide, which is capable of translocating different cargos across the cell membrane. It is thought to play a role in blocking the adhesion and invasion of ovarian cancer cells.

Methods
pUC19-ELP2 is synthesized, pET25B expression vectors, containing the construct is transformed into E-coli. SKOV ovarian carcinoma cells culture, and polypeptide treatment is performed. Apoptosis, Scratch Migration, and Boyden Chamber investigation Assays were carried out. BALB/c-nu/nu female mice is used as an experimental animal model.

Results
It has been demonstrated that the Tat peptide increases the cellular uptake of the ELP polypeptide by first facilitating its attachment to the outer surface of the plasma membrane, then, it is taken into the cell by endocytosis. Tat-ELP has been shown to inhibit SKOV-3 cell attachment, spreading, migration and proliferation under in vitro conditions and also prevented intraperitoneal dissemination of ovarian carcinoma cells in vivo. Tat-ELP polypeptide inhibits the adhesion and invasiveness of ovarian cancer cells and decreases the tumor mass in nude mice.

Conclusions
Tat-ELP has the potential to be used as a prophylactic treatment during or after surgical removal of primary ovarian tumors to prevent peritoneal dissemination of ovarian cancer.
INTRAABDOMINAL TUMOR MANIFESTATIONS REVEAL A DIFFERENT THERAPEUTIC RESPONSE PATTERN COMPARED TO THE AUTOLOGOUS PRIMARY OVARIAN TUMOR

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Objectives
Most primary ovarian tumors are diagnosed in an advanced stage. Tumor nodules are detectable in the abdominal cavity located in the omentum and peritoneum. Initial response rates to the standard chemotherapy combining Carboplatin with Paclitaxel (C+P) are high. Despite chemotherapy two-thirds of the patients suffer tumor progression. The aim of the present study was to analyze the heterogeneity of the different tumor locations with respect to the therapeutic response pattern.

Methods
From 20 ovarian cancer patients in an advanced stage fresh tumor samples of different locations were collected. 3D microtumors (i.e. spheroids) were directly generated from the tumor tissues and used for testing a variety of guideline recommended therapeutic options. Efficacy of the drugs was tested with the ATP assay.

Results
In nine out of 20 (45%) ovarian cancer patients all tumors independently from the abdominal location revealed a C+P sensitivity similar to the corresponding primary tumor. In contrast, 11 out of 20 (55%) patients showed strong differences in the therapeutic response pattern between primary tumor and other tumor manifestations. In six patients primary ovarian cancer was highly C+P resistant, while all other tumor locations were C+P sensitive. Contrary, five primary tumors revealed a high C+P sensitivity, although at least one intraabdominal tumor location was highly resistant. Interestingly, in these Carboplatin resistant tumors Treosulfan monotherapy was effective.

Conclusions
Analyzing therapeutic response pattern of different intraabdominal tumor locations in addition to the primary ovarian cancer has an impact on individualized cancer therapy.
Building of new hCG regression curves for gestational trophoblastic disease.

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Objectives
Until today β-hCG regression curves, created in the 80’s and not updated since, are used in the follow-up of patients with gestational trophoblastic disease (GTD). In addition, hCG regression curves during chemotherapy hardly exist. Our objective is to make regression curves after evacuation of CM and PM, and during chemotherapy for low risk GTD.

Methods
This retrospective study included 161 GTD patients from 1990 until 2012. We created 3 main groups and evaluated general characteristics. The first group consisted of complete hydatidiform moles (CM) (N=31), the second of partial molar pregnancies (PM) (N=92). The last group included the persistent GTD treated with chemotherapy (CT) (N=38), where 29 patients with a low FIGO scoring risk received MTX-monotherapy and 3 mean to high risk patients were treated with combination chemotherapy. A switch of monotherapy was needed in 6 patients. We compared the curves from the first 2 groups with the old curves of Schlaerth et al (Obstet Gynecol 1981).

Results
Mean age was 31.8, 29.4 and 29.9 years for CM, PM and CT. Concerning gravidity we calculated a median of respectively 2.9, 2.3 and 1.8 pregnancies. The regression curves of the first 2 groups were comparable to the currently used one, though with a distinct vertical shift. A total normalisation of β-hCG was seen in 84 and 89 days after the curettage for CM and PM.

- Group I: Complete hydatidiform moles (black dots represent projection of curve of Schlaerth and Morrow)

![Graph showing hCG regression curves](image-url)
Conclusions
HCG regression curves can be used in follow-up of patients diagnosed with GTD. This paper presents hCG regression curves in our region using the recent hCG assays.
Objectives
This study estimates the chance of a live offspring and evaluates the risk of persistent trophoblastic disease after termination of a twin pregnancy with complete hydatidiform mole and normal co-twin.

Methods
A nationwide retrospective study of twin pregnancies with complete hydatidiform mole and normal co-twin consecutively collected from 1998 to 2011. Data on the 90 cases was retrieved from the databases of the two national trophoblastic disease units in Charing Cross, London and in Sheffield, UK. All cases were reviewed by experts in trophoblastic pathology.

Results
Approximately every fourth (26.7%) patient received chemotherapy treatment, and all patients were cured. Continuation of the pregnancy did not increase the risk of persistent disease. Twenty-nine patients (56.9%) had a live baby in 51 pregnancies continuing past week 14.

Conclusions
The risk of persistent trophoblastic disease is only slightly higher than after a singleton complete hydatidiform mole and does not reason early termination. The chance of a live baby is well above 50%, and expectant management instead of therapeutic termination in twin pregnancies with complete mole and normal co-fetus can be pursued.
DRAINS: SUCTION DRAINAGE VERSUS NO DRAINAGE FOR GROIN WOUNDS FOLLOWING BILATERAL INGUINOFEOMRAL LYMPHADENECTOMY FOR VULVAL CANCER

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Objectives
To date no study has been conducted comparing suction drainage or no suction drainage following inguinofemoral lymphadenectomy.

Methods
A randomised-controlled study was conducted with the aim of investigating the morbidity associated with not placing a drain following bilateral inguinofermal lymphadenectomy. Patients acted as their own control with randomisation as to which groin would be allocated the drain. The patient’s groin wounds were inspected every day post operatively and a daily assessment sheet completed recording clinical details and pain scores. Primary outcome measure was wound breakdown, separation of > 25% of the incision.

Results
Twelve women were recruited from the three participating centres. The median age was 60 years (range 43-81 years). The stage distribution was stage 1B-3, stage 2-3, stage 3C-6 cases. Median hospital stay was 7 days (range 3-22 days). The median duration of drainage was 5 days (range 0-10 days). Lymphocysts occurred in of the 7 ‘no-drain’ groins compared to 4 in the ‘drain’ groins. Five patients required hospital readmission, 4 were for complications of the ‘no-drain’ groin and one of the ‘drain’ groin: drainage of lymphocyst (3 cases) and infection requiring IV antibiotics (3 cases). In 6/12 cases overall outcome (wound breakdown, infection, lymphocyst, leakage) of the ‘no-drain’ groin was better/no different from the ‘drain’ groin.

Conclusions
The results of this pilot study confirm the acceptability of this trial design and support the performance of a national multicentre study in order to determine whether suction drainage has a significant effect on post-operative healing following inguinofemoral lymphadenectomy.
SURGICAL TREATMENT OF VULVAR CARCINOMA: CAN WE NARROW THE RESECTION MARGIN?

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Background
Local recurrence of vulvar carcinoma after primary treatment is considered to be related to the width of the surgical margin. Currently, a margin of >8mm is recommended, yet available data are conflicting and often not corrected for re-excisions.

Objective
To assess the correlation between the narrowest surgical margin and recurrence rate of vulvar carcinoma at the primary tumor site, in order to evaluate the currently recommended cut-off value.

Methods
A retrospective study of all patients who were surgically treated for primary vulvar carcinoma (FIGO stage IB to IIIC) within the Comprehensive Cancer Centre South region between 2005 and 2012. Data were analysed using descriptive statistics and Kaplan-Meier analysis.

Results
A total of 116 patients were included. For 83% the tumor was radically removed, yet for 62% the surgical margin was <8mm. Only 35% of patients with an irradically removed lesion underwent a re-excision. After re-excision, the mean closest margin of all patients was 8.3mm. After a median time of 11.5 months 28 patients (24%) developed a recurrence.

There was no difference in risk of recurrence for patients with a surgical margin <8mm or ≥8mm, 26% and 24% respectively (p=.74). However, patients with a surgical margin ≥8mm showed a trend towards a better disease-specific survival (p=.11).

Conclusions
The currently recommended cut-off value of 8mm could not be supported by our data, as there was no difference in recurrence with respect to a surgical margin <8 or ≥8mm. Additional research for a safe cut-off value is needed and will follow.
TO DETERMINE THE FEASIBILITY OF PERFORMING NEOADJUVANT CHEMOTHERAPY (NCH) FOLLOWED BY RADICAL SURGERY IN PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE VULVA.

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Objectives
To determine the feasibility of performing neoadjuvant chemotherapy (NCH) followed by radical surgery in patients with locally advanced squamous cell carcinoma of the vulva.

Methods
Prospective and multicenter trial. Thirty-five patients with a diagnosis of previously untreated locally advanced squamous cell carcinoma of the vulva were given 4 schemes of cisplatin-based NCH and 1 NCH regimen with single bleomycin. Then, they underwent radical surgery of the vulva if clinical response was 50% or more. Age, NCH schemes used, toxicity, response to treatment, type of radical surgery performed, and clinical outcome were evaluated.

Results
Thirty-three patients completed the proposed schemes, and 30 were assessed for radical surgery. Finally, 27 patients underwent radical surgery (radical vulvectomy or radical local excision plus bilateral inguinofemoral lymphadenectomy). In 2 cases of persistent rectal involvement, posterior pelvic exenteration was performed. Moreover, 24 of 27 patients remain with no evidence of disease to date. Toxicity was acceptable. Median age was 62 years (range, 54-72 years). Median follow-up was 49 months (range, 4-155 months).

Conclusions
The use of NCH in selected groups may increase surgical feasibility in initially inoperable patients, thus favoring organ preservation and less extensive resections. Adverse reactions were acceptable, and vulvoperineal deleterious effects that may occur after radiotherapy were consequently avoided.
QUALITY OF LIFE AND SEXUAL FUNCTION IN PATIENTS WITH BORDERLINE TUMORS OF THE OVARY. A SUBSTUDY OF THE ARBEITSGEMEINSCHAFT GYNAEKOLOGISCHE ONKOLOGIE (AGO) STUDY GROUP ROBOT-STUDY


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Objectives
Borderline tumors of the ovary (BOT) are characterized by low malignant potential and excellent prognosis. Surgical staging, especially if bilateral salpingooophorectomy is performed, may induce long-term side-effects, especially in premenopausal women. The aim of this retrospective multicenter study was to evaluate quality of life (QoL) and sexual function in BOT patients.

Methods
This study was part of a prospective/retrospective cohort study in Germany. After surgical therapy patients from seven centres completed three questionnaires. QoL and sexual function data were correlated with treatment characteristics: surgical approach, lymph node sampling and fertility preservation.

Results
110 patients returned the questionnaires. Median follow-up was 4.0 years. The majority (77%) lived in a relationship. 49% of the women were sexually active. The main reason for sexual inactivity was 'no partner' (38%) or 'not interested' (34%). The mean global health status was 69.8 (SD 22.7) (range from 0-100, 100 implying perfect health). Mean QoL score was 73.7 (SD 23.3, range 0 to 100). Both did not differ among the treatment groups. Those patients who were sexually active had a significantly higher QoL than those who were not (78.7 vs. 67.4, p= 0.0156). The same was confirmed for the global health status: active 75.9 vs. inactive 60.9, p= 0.0013.

Conclusions
In this retrospective study, patients with a history of BOT, had a very good QoL and global health status. Women who were sexually inactive stated lack of a partner as the main reason. Patients who were sexually active had a significantly higher QoL than those who were not.
EVALUATION OF SEXUAL FUNCTIONING AND WELL-BEING IN PATIENTS AFTER TREATMENT FOR GYNECOLOGICAL CANCER

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Objectives
Quality of life (QoL) concerns for cancer patients create new challenges. Sexual activity (SA) and sexual functioning (SF) are important factors influencing QoL. In this study we analyzed SF and well-being in women with primary gynecological malignancies compared to healthy controls.

Methods
In a multicenter study 139 patients, age 18-70, with gynecological malignancies were evaluated for sexual functioning and QoL. Data was anonymously collected through validated questionnaires and compared to healthy controls (n=60) at least 12 months after completion of primary therapy.

Results
139 of 325 invited patients with gynecological cancers (42.77%) participated in the study. Main reasons for non-participation were “questions are too intimate” (31%) and “do not want to be reminded of my disease” (10%). 56.5% of ovarian cancer patients and 50.0% of cervical cancer patients were sexually active (control: 78.0%). Main reasons for sexual inactivity were, besides lack of a partner, the presence of a physical problem or low interest in sex. Sexually active patients with gynecological cancers had significantly more discomfort than healthy controls (p=0.0007). There was no difference concerning sexual activity, sexual satisfaction, QoL and general health. Cervical cancer patients had more discomfort (p=0.0441) and endometrial cancer patients less sexual satisfaction (p=0.0292) whereas ovarian cancer patients showed no significant differences to healthy controls.

Conclusions
Communication about sexuality is still difficult for many patients. After treatment for gynecological cancers patients had a good quality of life but less sexual activity compared to healthy controls. Main reasons for sexual inactivity were low interest in sex and physical problems after therapy.
e-Poster Orals: MISCELLANEOUS 2

PREVALENCE OF LYMPHCYSTS AFTER PELVIC AND PARAORTIC LYMPHADENECTOMY AND MINIINVASIVE TREATMENT WITH ULTRASOUND-GUIDED DRAINAGE

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Objectives

Pelvic lymphadenectomy is associated with significant morbidity including lymphocysts formation. Prevalence of lymphocysts is being reported in a wide range between 2-32%. Objective of this study was to assess the prevalence of asymptomatic and symptomatic lymphocysts in patients after pelvic and/or paraaortic lymphadenectomy and evaluate feasibility of ultrasound-guided drainage in the management of symptomatic cases.

Methods

Enrolled were 472 patients after pelvic only (N=247) or pelvic and paraaortic (N=225) lymphadenectomy performed in single institution between 2006-2010. All patients were followed by regular pelvic and abdominal ultrasound every 3 months.

Results

Lymphocysts were detected in 137 (29%) and 1 (0.44%) cases, however, only 27 (3.87%) of them became symptomatic (signs of inflammation in 15 cases; pain, lymphoedema, dysuria or ureter obstruction in 12 cases) and required intervention. In all symptomatic cases, ultrasound-guided drainage was performed using Fr 15 pig-tail catheter left for 2-3 days under antibiotics. Ultrasound guided drainage was successful treatment in all patients with non-inflammatory lymphocyst and in 7 with signs of inflammation (70.4%). There were no severe complications related to the drainage in the whole group.

Conclusions

Formation of lymphocyst is common finding after pelvic lymphadenectomy and rare after paraaortic lymphadenectomy. However, only in minority of patients the lymphocyst becomes symptomatic and requires intervention. Ultrasound-guided drainage with insertion of catheter is safe and efficient method for the management of symptomatic non-inflammatory lymphocysts, but fail in about half of inflammatory cases.

This work was supported by IGA MZ, the Czech republic, No. NS13070 and Charles University projects UNCE204024 and PRVOUK P27/LF1/1.
State of the Art: ENDOMETRIAL CANCER

GUIDELINES AND EVIDENCE FROM THE TRIALS ABOUT FOLLOW UP

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Background and Aim:
Recurrence rate in early-stage endometrial cancer treated patients is up to
15% and in advanced stages or aggressive histologic condition is up to 50%.
Most of recurrences occur within 3 years since diagnosis and anatomic sites of
relapse are mostly equivalently distributed between local (pelvic) and distant
(abdominal and chest). Recurrences are often symptomatic and many local
relapses are curable. The aim of this presentation is to review and summarize
available guidelines and ongoing clinical trials about follow up in endometrial
cancer treated patients.

Methods:
5 guidelines were identified through the National Guidelines Clearinghouse. 5
ongoing and 1 completed trials were identified through ClinicalTrials.gov and
through ISRCTN Register.

Results:
Available guidelines are from ACOG (2005 release, reaffirmed 2013), CCO
(2006), AGO (2009), ESMO (2011) and NCCN (2013) and all of them include
recommendations based on the opinion of experts, in the absence of any
randomized clinical trial (Evidence level IV). Guidelines agree on a more
intensive follow-up in the first 2-3 years after treatment, while some
discrepancies exist on the procedures to be carried out. Ongoing clinical trials
have been set up in Australia, Italy, Denmark, Canada, Norway and UK about
the role of intensive vs minimal follow up schedules and about the role of a
telephone or self-referral follow up.

Conclusion:
No rational is available today for any particular follow up protocol. Only
physical examination showed some utility in detecting recurrence. Ongoing
trials will be crucial to rationalize the follow-up of endometrial cancer.
Society Session: INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY (SIOG)

THE OLDER WOMAN WITH OVARIAN CANCER: NURSING NEEDS AND INTERVENTIONS.

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Ovarian cancer (OC) is the fourth most common cause of cancer death among women. It has a poor prognosis with average five year survival rate of around 30%. New data from the UK National Cancer Intelligence Network examines routes to cancer diagnosis and for OC 32% of cases are diagnosed following admission to accident and emergency. The figures are worse for women >70 and >80 years, 35% and 47% respectively. Also reports indicate that only 50% of women with advanced OC aged >65 receive optimum platinum based chemotherapy despite recognition that performance status and age do not represent the heterogenous characteristics of older women with OC.

Against this background the paper considers the factors that are shaping the delivery of care to this group of patients. It considers early symptoms and current treatments and the nurse’s role in multidimensional older person evaluation to include individual assessment of physical, psychological and sexual health. Examples of assessment tools are presented. Discussion includes ways to identify patient and carer treatment preferences and setting desired and appropriate outcomes with elderly gynaecological cancer patients. The paper explores the nurse management of specific OC disease and treatment related symptoms. It offers practical guidance and examples of care strategies in which cancer nurses work in partnership with older women with OC to support and educate them so they are equipped to self-manage their symptoms where possible and deal with the challenges posed by their illness. The management challenges of delivering individual, responsive nursing care are highlighted.
THE INFLUENCE OF CO-MORBIDITY ON MORTALITY IN OVARIAN CANCER PATIENTS

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Objectives:
Ovarian cancer is a severe disease with a peak incidence in an age group where concurrent morbidity is common. The aim was to study the influence of common comorbidity diagnoses on mortality in ovarian cancer patients.

Methods:
The study population was patients with ovarian cancer in Sweden 1993-2006 (n =11,139) and identified in the national Cancer Register. Comorbidity data was obtained from the Patient Register. Mortality was analyzed with Cox’ proportional hazards models and subgroup analyses were performed by age and tumour histology.

Results:
Almost all comorbidity diagnoses studied increased mortality in ovarian cancer patients. Thromboembolism was the most hazardous comorbidity, followed by hematologic complications. The occurrence of diabetes mellitus has a moderate impact and hypertension a low impact on mortality. For women with less aggressive tumours (medium risk epithelial tumours) having co-morbidity seemed in general, to have larger impact on mortality than among women with highly aggressive tumours.
Conclusions:
Thromboembolism, hematologic complications and infections affected mortality in women with ovarian cancer. The impact of comorbidity was mainly apparent among those with a more prosperous prognosis, such as longer time since cancer diagnosis, less aggressive tumours and younger age.
Oral Presentation/Debates: OVARIAN CANCER II

ADVERSE EVENT PROFILE BY AGE FOR VINTAFOLIDE+PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) VS PLD ALONE IN PLATINUM-RESISTANT OVARIAN CANCER

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Objectives
Vintafolide (EC145), a folic acid/desacetylvinblastine conjugate, binds with high affinity to folate receptors expressed in cancers. This subanalysis evaluated adverse event (AE) incidence by age in the PRECEDENT trial, a randomized open-label study of subjects with platinum-resistant ovarian cancer receiving vintafolide+PLD or PLD alone.

Methods
Women ≥18 years old with ECOG status 0-2 and exposure to ≤2 prior systemic cytotoxic regimens were randomized 2:1 to vintafolide (2.5 mg IV tiw, weeks 1 and 3, q28 days)+PLD (50 mg/m² IV day 1, q28 days) or PLD alone (same dose+schedule). AEs were evaluated by age (≥65 vs <65 years old).

Results
107 patients were included in safety population: 56 were ≥65 (35, vintafolide+PLD; 21, PLD alone) and 101 were <65 years (72 vintafolide+PLD; 29, PLD alone). For vintafolide+PLD, the most commonly reported drug-related AEs (≥30% in at least one subgroup) (≥65 vs <65) were anemia (48.6% vs 36.1%), neutropenia (45.7% vs 38.9%), constipation (37.1% vs 30.6%), stomatitis (40.0% vs 45.8%), nausea (22.9% vs 48.6%), fatigue (57.1% vs 44.4%), peripheral sensory neuropathy (31.4% vs 22.2%), and hand-foot syndrome (HFS, 40.0% vs 40.3%). For PLD alone, the most commonly reported drug-related AEs (≥65 vs <65) were anemia (33.3% vs 20.7%), nausea (28.6% vs 44.8%), stomatitis (38.1% vs 41.4%), fatigue (38.1% vs 31.0%), and HFS (47.6% vs 34.5%). Nausea was significantly lower in the ≥65 vs <65 group (P=0.012) for the vintafolide+PLD arm without multiplicity adjustment.

Conclusions
Rates for AEs common to both arms were generally similar regardless of age in the PRECEDENT study.
Oral Presentation/Debates: OVARIAN CANCER II

PROGRESSION-FREE SURVIVAL BY LOCAL INVESTIGATOR VERSUS INDEPENDENT CENTRAL REVIEW: COMPARATIVE ANALYSIS OF THE AGO-OVAR16 TRIAL

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Objectives:
AGO-OVAR16 is a randomized, double-blind trial of pazopanib as maintenance therapy in advanced epithelial ovarian, fallopian tube, and primary peritoneal cancer (AEOC). Analysis of progression-free survival (PFS) as the primary endpoint in AEOC trials may be confounded by the difficulty of radiologic assessment of disease and the potential for investigator bias. To confirm the robustness of the primary analysis of PFS, concordance with that based on independent central review (ICR) was evaluated.

Methods:
Patients with histologically confirmed AEOC (N=940) were randomized 1:1 to receive pazopanib 800 mg once daily or placebo for up to 24 months. Primary endpoint was investigator scan-based PFS by RECIST v1.0. Sensitivity analyses included evaluation of PFS by ICR.

Results:
Pazopanib prolonged PFS vs placebo by investigator review (HR=0.766; 95% CI: 0.64-0.91; P=0.0021; median 17.9 vs 12.3 months). Results for PFS by ICR were similar (HR=0.802; 95% CI: 0.68-0.95; P=0.0084; median 15.4 vs 11.8 months). Progression and censoring events were recorded later by investigator review in 29% of pazopanib patients and 19% of placebo patients. The overall concordance between investigator and ICR assessments was 84% in the pazopanib arm and 86% in the placebo arm.

Conclusions:
Maintenance therapy with pazopanib provided a significant benefit in AEOC by investigator assessment. PFS prolongation was confirmed by ICR. The good overall concordance between the investigator and ICR assessments, as well as the consistency in the hazard ratio, supports the reliability of investigator-assessed
AGE-DEPENDENT DIFFERENCES IN BORDERLINE OVARIAN TUMOURS (BOT) REGARDING CLINICAL CHARACTERISTICS AND OUTCOME: AN ANALYSIS OF THE ARBEITSGEMEINSCHAFT GYNAEKOLOGISCHE ONKOLOGIE (AGO) STUDY GROUP

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Objectives:
Patients in reproductive age represent approximately one third of all BOT patients which is significantly more compared to invasive ovarian cancer. Specific information regarding their clinical characteristics and prognostic factors is very limited.

Methods:
Clinical parameters of BOT patients treated between 1998 and 2008 in 24 German centers were investigated with prospective reference pathology and follow-up. Analyses were performed separately for patients ≤40 and >40 years and then compared regarding clinicopathological variables and prognosis.

Results:
A total of 950 BOT patients with a median age of 49.1 (14.1-91.5) were analysed (280 patients ≤40 years [29.5%], 670 patients >40 years [70.5%]). While younger patients more frequently underwent initial laparoscopic surgical approach (43.9% vs. 26.0%, p<0.001) and were diagnosed in higher FIGO stage (p<0.001), histological subtypes (p=0.08), surgical outcome (p=0.80) and staging quality (p=0.79) were equally distributed for both groups. Fertility-preservation was performed in 53.2% of patients ≤40 years with preservation of the primarily affected ovary in 32 of these 149 cases (21.5%). 31 pregnancies occurred following fertility-sparing surgery (20.8%). Recurrence rates were significantly higher in patients ≤40 years (17.9% vs. 3.6%, p<0.001) whereas disease-specific survival did not differ. In case of recurrence, malignant transformation was more frequently diagnosed in patients >40 years (62.5% vs. 12.0%, p<0.001). Multivariate analysis for patients ≤40 years identified FIGO stage and organ-preservation or fertility-sparing approach as independent prognostic factors regarding PFS consistent with the overall population.

Conclusions: Despite favorable overall survival, BOT patients with childbearing potential frequently experience recurrence, seemingly related to fertility-
preservation. However, in contrast to patients >40 years, rates of malignant transformation are significantly lower, justifying fertility-sparing surgery notwithstanding the higher recurrence rates in younger patients.
Oral Presentation/Debates: OVARIAN CANCER II

SURVIVAL AND TIME TO RECURRENCE IN PATIENTS WITH ADVANCED OVARIAN CANCER IN GERMANY: DATA FROM AGO QS-OVAR 2008 PROSPECTIVE COHORT

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Objectives
To describe time to recurrence (TTR), length of treatment, treatment-free intervals (TFI), and survival in a prospective cohort of women with advanced ovarian cancer.

Methods
QS-OVAR is a prospective cohort study run by the national gynecological society (AGO) of 881 newly diagnosed patients with ovarian cancer in Germany were recruited in Q3 2008 and followed annually. Study population for this analysis consisted of 700 women with advanced disease (FIGO IIB-IV) at diagnosis.

Results
The mean length of treatment was similar between primary therapy and 2nd line, but became shorter in 3rd line (108, 109, and 87 days respectively). Treatment-free intervals and length of treatment were almost equal for patients undergoing 2nd and 3rd line of therapy (109 and 139 days for 2nd line and 87 and 75 days for 3rd line). Time to recurrence shortened with each additional line of therapy (from 379 days for primary therapy to 162 days for the 3rd line). More than half (340/511) of the patients who relapsed died during the 3 years follow-up. The survival for patients with shorter TTR was worse compared to those with longer TTR (26% for TTR < 6 months vs. 91% for TTR > 12 months).

Conclusions
In an analysis of patients with recurrent ovarian cancer, shorter time to recurrence was associated with shorter survival. Further analysis of the benefit of treatment on survival beyond 2nd line of treatment is needed.
IMMUNOMODULATORY GENE VARIANTS ARE ASSOCIATED WITH EPITHELIAL OVARIAN CANCER (EOC) RISK AND HISTOPATHOLOGIC SUBTYPE

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Objectives:
Epithelial Ovarian Cancer (EOC) is a lethal gynecologic malignancy. Typically, developing cancer cells evade immune surveillance with down-regulation of HLA class I proteins and up-regulation of immunosuppressive proteins (i.e. HLA-G). As prognostic impact may be more accurately correlated to genotype rather than protein expression, we investigated variation in immunomodulatory genes and EOC risk.

Methods:
We genotyped 322 SNPs from 82 immunomodulatory genes in 14,525 EOC cases and 23,447 controls (of European ancestry) using an Illumina Infinium iSelect BeadChip as part of the Collaborative Oncological Gene-environment Study (COGS). SNP analyses were conducted in invasive cancers combined and the four main histological subtypes using unconditional logistic regression under a log-additive model, and adjusted for study site and population substructure.

Results:
The strongest evidence of an association for invasive cancers combined and the serous subtype was HLA-G rs1619379 (OR=1.08, 95%CI=1.04-1.12, P=0.0001). The most significant association for endometroid EOC was CIQB rs2182703 (OR=1.11, 95%CI=1.03-1.18, P=0.003) and five SNPs in the HLA-B/C region, the most significant of which was rs9264868 (OR=0.87, 95%CI=0.78-0.96, P=0.007). The most significant associations for mucinous subtype was ICAM3 rs281413 (OR=0.82, 95%CI=0.73-0.93, P=0.002) and four HLA-DMB gene SNPs, the most significant of which was rs4848300 (OR=0.94, 95%CI=0.85-1.04, P=0.0024) while the most significant association with clear cell carcinoma was AOAH rs11763746 (OR=1.29, 95%CI=1.12-1.47, P=0.0003). HLA-DMB rs6906846 and rs396243 were also marginally associated with clear cell EOC, (p=0.041 and p=0.040), respectively, as well as borderline EOC.

Conclusions:
These results show associations between inherited immunomodulatory genes, specifically HLA gene variants, and risk of different EOC histologic subtypes.
Maximal cytoreduction is considered by several authors the best option for cure to offer to Advanced Ovarian Cancer (AOC) patients, since Residual Tumor (RT) after primary surgery is one of the most important prognostic factor. However, a certain number of women still undergo explorative laparotomy only, followed by neoadjuvant chemotherapy. In order to preoperatively identify those patients able to achieve optimal cytoreduction (RT < 1cm), several approaches have been attempted, including assessment of Ca125 serum levels and computed tomography scan which have failed to provide a high level of accuracy so far. In this context staging laparoscopy (S-LPS) has proved a valid tool which potentially suits the surgeon better than radiology, offering a direct anatomic view of the extension of the disease. Our Institution elaborated over the years a laparoscopy-based score system to predict the chances of complete cytoreduction. The feasibility and the reproducibility of this scoring system has been recently demonstrated in an open-label prospective multicentric trial carried in trained gynecological oncology centers (Olympia-MITO 13). However, the prognostic impact of this strategy has never been evaluated. Thus, we retrospectively analyzed the survival data of AOC women undergoing S-LPS as a routinely procedure in the management of AOC over a period of 5 years at our Institution. The use of the S-LPS in a tertiary referral center does not appear to have a negative impact in terms of survival and it may be helpful to identify those patients able to achieve optimal cytoreduction, avoiding unnecessary laparotomies and surgical complications.
Oral Presentation/Debates: MISCELLANEOUS

POPULATION BASED TESTING FOR BRCA MUTATIONS IS HIGHLY COST-EFFECTIVE COMPARED TO FAMILY HISTORY BASED APPROACH: A HEALTH-ECONOMIC DECISION ANALYTICAL MODEL FROM THE GCAPPS TRIAL


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Objectives
To compare the cost of population-screening with the current approach of family-history (FH) based testing.

Methods
A decision-analytic model developed compares lifetime costs/effects of population-based screening with FH-based screening of all UK Ashkenazi-Jewish(AJ) women ≥40years for BRCA-mutations. All women in population-screening arm and only those with a strong-FH (≥10% mutation-risk) in the FH-arm undergo genetic-counselling and genetic-testing for BRCA-mutations. BRCA-carriers identified were offered risk-reducing salpingo-oophorectomy. Model probabilities were derived from the GCaPPS-trial(ISRCTN73338115) and published literature. Costs- reported at 2010 prices. Total costs/effects in terms of life-years and QALYs were estimated by weighting values for each branch by branch probability. Cancer incidence, incremental-cost-effectiveness-ratio(ICER) and population impact were calculated. Costs/outcomes were discounted at 3.5%. Deterministic- and probabilistic-sensitivity-analysis(PSA) were undertaken to evaluate model uncertainty.
Utility-scores/probabilities were varied by confidence-interval/range and costs by ±30%.

**Results**

Compared to FH-based testing, population-based screening saved 0.058 life-years and 0.062 QALYs resulting in 21 days gain in life-expectancy in AJ-women. The baseline ICER was £499/QALY, well below the NICE threshold of £20000-£30000/QALY. Population-based screening of Ashkenazi Jews lowered ovarian cancer incidence by 0.37%, leading to a reduction in 419 ovarian cancer cases in the UK at a discounted cost of £1.25 million. The model is highly sensitive to BRCA prevalence, but upper/lower utility-values/costs had little influence on overall results. At a £20,000 threshold, 92% simulations on PSA indicated that population-based screening is a cost-effective intervention compared with current NHS policy.

**Conclusions**

Population-based screening for BRCA-mutations is highly cost-effective compared to FH-based testing in AJ women ≥40 years. Changing the clinical dogma of FH-based testing in this population needs exploring.
Oral Presentation/Debates: MISCELLANEOUS

CONTINUOUS LOW-FLOW ASCITES-DRAINAGE AND SEQUENTIAL NON-INVASIVE TUMOR-CELL SAMPLING THROUGH THE URINARY BLADDER VIA THE ALFA-PUMP CLOSED SYSTEM IN PLATINUM-RESISTANT-OVARIAN-CANCER (PROC)
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Objectives
Malignant ascites in PROC is a therapeutic dilemma. The Sequana-Medical alfapump-System (AP), a remotely controlled device connecting the patients'peritoneal cavity to their urinary bladder, has been evaluated for ascites in liver cirrhosis, but not as yet for malignant ascites.

Methods
We implanted the AP in the peritoneal cavity of two heavily pretreated PROC-patients (67y and 70y) who required repetitive ascites drainages monthly. We cross correlated the electronic download of recorded volume pumped (intraperitoneally?blader) with weekly ultrasound, monthly cystoscopies and QoL-evaluation. Early morning urine for evaluation of cytology and tumor-cell molecular analysis was collected weekly.

Results
The implantation was under general anesthesia in a 60- and 35-minute procedure. The pump, draining 350ml – 500ml ascites/day successfully drained the ascites to dryness after 3 days (1st patient) and 8 days (2nd patient). The patients did not report pollakiuria or dysuria, merely an increased micturition volume. The 1st patient died of disease progression 2 months later; the 2nd patient we noticed a gradual amelioration of peripheral edemas and overall performance-status within 3 weeks after insertion and was able to commence weekly chemotherapy with paclitaxel. Histopathological analysis of the urine revealed rich malignant cell content; this was used to create FFPE-cell-blocks for molecular- pathological profiling with sequential Caris-Target-Now-analysis and full exome-sequencing.

Conclusions
This innovative approach addresses an area of unmet need for the control of malignant ascites and provides a non-invasive method of collecting tumor tissue for continuous molecular tumor characterization. A EUTROC-multicenter randomized-trial (AMAZE) is planned for evaluation of clinical and translational implications in PROC.
FEMORAL NERVE INJURY DURING ABDOMINAL SURGERY FOR GYNECOLOGICAL CANCER. INCIDENCE AND PREDICTIVE FACTORS.

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Objectives
To report incidence and predictive factors of femoral nerve injury during abdominal surgery for gynecological cancer.

Methods
Incidence of femoral nerve injury was assessed in 406 patients (ovary: 35%, cervix: 17%, uterus: 48%) retrospectively evaluated; and in 107 patients (ovary: 43%; cervix 14%; uterus : 43%) entering a prospective study. Incidence was calculated according to age (< 65; > 65 yrs), BMI (< 25, > 25 kg/m\textsuperscript{2}), surgery approach (laparotomy, laparoscopy) and duration (< 120; > 120 min), lymphadenectomy (yes/no), Bookwalter retractor (yes/no). Muscle weakness was assessed by a physiatric specialist according to the MRC classification. Duration of Bookwalter stay in surgical field and of traction of the self-retaining retractors exposing the deep pelvis were prospectively recorded.

Results
Weakness of the right quadriceps femoris was observed in 11/406 (2.7%) patients, with MRC severity 0-1 in 8. The nerve injury was significantly more frequent when lymphadenectomy (5.4% vs 1%, \(p < 0.01\)) was performed, and Bookwalter retractor was utilized (4.5% vs 0%, \(p < 0.01\)). In the prospective study grade 3 weakness of the right quadriceps femoris was observed in 1/35 Bookwalter pts (3%). The Bookwalter was utilized for a median of 122 min (range 30-285) and traction of the self-retaining pelvic retractors was applied for a median of 15 min (range 4-22).

Conclusions
Bookwalter retractor and pelvic lymphadenectomy were associated to femoral nerve injury. The lesion may be caused by the nerve compression at the right inguinal ligament due to the self-retaining retractors exposing the deep pelvis.
PREDICTING DEATH IN HOSPITAL FOR PATIENTS WITH GYNECOLOGICAL CANCER IN ENGLAND: ASSESSING IMPACT OF EMERGENCY ADMISSIONS

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Objectives
Most patients wish to die at home. This study determines the impact of unscheduled hospital admissions in the last month of life on likelihood of dying in hospital.

Methods
Data were extracted from a linked ONS and HES dataset for 71,440 patients who died of gynaecological cancer in England from January 2000 to July 2012. Regression analysis was used to predict the impact on place of death of socio-demographic indicators, and frequency and length of elective and emergency admissions in the last month of life.

Results
The validated model correctly identified 73% of hospital deaths with a sensitivity of 75% and a specificity of 72%, and area under ROC curve of 0.77. Significant variables were year of death (OR 0.93, p < 0.001), age group (OR 1.17, p < 0.001), deprivation status (OR 1.06, p < 0.001), frequency and length of elective and emergency admissions (p < 0.001). Each subsequent emergency admission in the last month of life increased the odds of death in hospital by 2.4 times (OR 2.38, p < 0.001). Hospital deaths were significantly lower in all other regions compared to London. If half of all people had one less emergency admission then 16% of hospital deaths could be avoided.

Conclusions
Inequity in end of life care exists within gynaecological cancers, with elderly patients more likely to die in hospital. Improved services are required in the community to prevent unscheduled admissions alongside better identification of the dying phase for hospitalised patients.
Oral Presentation/Debates: MISCELLANEOUS

IMPACT OF TREATMENT FOR GYNAECOLOGICAL CANCER UPON HEALTH-RELATED QUALITY OF LIFE IN ROUTINE CLINICAL PRACTICE

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Objectives
Assessing treatment for gynaecological cancer has been limited to clinical trials, cross-sectional and retrospective analyses and poorly designed prospective studies. Little is known about the short and long-term outcomes for women in routine clinical practice. We assessed the impact of treatment upon a woman’s quality of life and bowel, vaginal, urinary and sexual functioning through the clinical pathway from diagnosis and during the first year of treatment.

Methods
Longitudinal study. At baseline (pre-treatment) and then at routine follow-up every 3 months during the first year post-treatment 182 women completed the EORTC QLQ C30, SF-36, SF-6D and an electronic pelvic floor assessment questionnaire (ePAQ-PF).

Results
83 women had endometrial, 49 ovarian, 27 cervical and 23 vulval cancer. Mean age was 59.8 (SD 13.3; range=23.8-86.6). Surgery significantly affected physical functioning which appeared worse for women who had laparoscopic surgery even after adjusting for age and BMI. A comparison of surgery only versus multiple treatments revealed significantly worse role and social functioning, insomnia, diarrhea, bowel continence and bowel and vaginal quality of life after adjusting for age and BMI (p<0.05). Women with advanced stage of disease were significantly worse in multiple domains compared to those treated for early stage cancer.

Conclusions
Women with advanced stage disease and who have multiple treatments have worse outcomes over time. Within the context of routine clinical practice it is particularly important that the treatment consequences upon the bowel and vagina and upon physical and emotional health are monitored over the first year.
Oral Presentation/Debates: MISCELLANEOUS

MELANOMA RISK IN A SUBFERTILE POPULATION: RESULTS FROM A LARGE DUTCH COHORT STUDY.

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Objectives
Over the past decades the incidence of melanoma has shown a worldwide increase, which has been largely attributed to sunlight exposure. Besides sunlight exposure, also associations between hormonal factors and melanoma have been suggested based on associations with parity or exogenous hormone use. Therefore, we investigated whether subfertile women have an altered risk of melanoma.

Methods
In 1996, a nationwide cohort study (the OMEGA-cohort) was set-up to examine the risk of cancer in a subfertile population receiving ovarian stimulation for in-vitro fertilization (IVF). The cohort includes 19,119 women who received IVF and 6,001 subfertile women not treated with IVF. Detailed information on exposure and confounders was collected from medical records and through questionnaires. Cancer incidence was ascertained through linkage with the Netherlands Cancer Registry (1989-2009). Melanoma risk in the cohort was compared with the general population and between the IVF group and the non-IVF group.

Results
After a median follow-up of 16 years 93 melanomas were observed. The risk of melanoma was not increased in the IVF group compared with the non-IVF group (hazard ratio (HR) = 1.6; 95% CI: 0.7-3.4). In addition, no increased risk was found for the IVF group compared with the general population. Nulliparous women had a marginally significantly increased risk for melanoma (HR=1.6; 95% CI: 0.9-2.6) compared with parous women.

Conclusions
In a subfertile population with 31% nulliparous women we found that IVF was not associated with increased melanoma risk, while nulliparity does appear to affect melanoma risk.
Network/Task Force: EUROPEAN NETWORK OF YOUNG GYNAE ONCOLOGISTS (ENYGO) 2

NEOADJUVANT CHEMOTHERAPY FOR ADVANCED OVARIAN CANCER MIGHT BE ASSOCIATED WITH REDUCED SURVIVAL.
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Objectives:
The proportion of Danish patients with advanced ovarian cancer who is treated with neoadjuvant chemotherapy (NACT) has increased. We aimed to evaluate the impact of first-line treatment on overall survival (OS).

Methods:
Patients with stage III-IV epithelial ovarian cancer treated in a Danish referral center from December 1st 2005 to October 31st 2011 were included and followed until February 14th 2013 or death.

Results:
The table illustrates baseline and surgical data. Median OS for the 990 patients treated with primary debulking surgery (PDS) was 31.9 months, equally to the 335 patients treated with NACT+interval debulking surgery (IDS) who had a median OS of 29.4 months (p=0.099). In a multivariate analysis including age, stage, co-morbidity, ASA-score, performance status, extensive surgery and residual tumor; NACT+IDS was associated with increased risk of death (HR=1.80, CI: 1.38-2.33, p<0.0001) after two years of follow-up.

<table>
<thead>
<tr>
<th></th>
<th>PDS (n=990)</th>
<th>NACT+IDS (n=335)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>65 (56-73)</td>
<td>65 (59-71)</td>
<td>0.89</td>
</tr>
<tr>
<td>Stage IV</td>
<td>23%</td>
<td>39%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No-comorbidity</td>
<td>64%</td>
<td>64%</td>
<td>0.95</td>
</tr>
<tr>
<td>ASA-score &gt;2</td>
<td>14%</td>
<td>16%</td>
<td>0.58</td>
</tr>
<tr>
<td>Performance status &gt; 2</td>
<td>3%</td>
<td>2%</td>
<td>0.3</td>
</tr>
<tr>
<td>Residual tumor = 0 mm</td>
<td>39%</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Residual tumor 1-10 mm</td>
<td>27%</td>
<td>22%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residual tumor &gt; 10 mm</td>
<td>35%</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>Extensive surgery</td>
<td>34%</td>
<td>24%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unintended injury on ureter, urinary bladder or bowel</td>
<td>9%</td>
<td>5%</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Death <30 days of surgery

<table>
<thead>
<tr>
<th></th>
<th>P=0.059</th>
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</thead>
<tbody>
<tr>
<td>PDS</td>
<td>3.2%</td>
</tr>
<tr>
<td>NACT+IDS</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

**Conclusions:**
Patients treated with PDS and NACT+IDS had identical median OS. Patients treated with NACT+IDS had better surgical outcome, less extensive surgery and fewer per-operatively injuries. After two years, NACT+IDS was associated with increased risk of death.
Network/Task Force: EUROPEAN NETWORK OF YOUNG GYNAE ONCOLOGISTS (ENYGO) 2

A PROSPECTIVE STUDY OF FERTILITY-SPARING TREATMENT WITH MEGESTROL ACETATE FOLLOWING HYSTEROSCOPIC CURETTAGE FOR WELL-DIFFERENTIATED ENDOMETRIOID CARCINOMA AND ATYPICAL HYPERPLASIA IN YOUNG WOMEN

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Objectives
To investigate the feasibility and efficacy of curettage with hysteroscopy followed by megestrol acetate (MA) for well-differentiated endometrioid carcinoma (EC) confined to endometrium and atypical hyperplasia (AH) in young women.

Methods
Fourteen patients with EC and 12 patients with AH prospectively enrolled onto this study. All patients received at least 12 weeks oral MA (160mg/day) following thorough curettage with hysteroscopy. Response was assessed histologically every 12 weeks. The primary endpoint was the complete response rate. Adverse event, pregnancy rate and recurrence rate were secondary end points.

Results
Twenty-one (80.8\%) patients responded to treatment. The median time to response was 12 weeks. After a median follow-up of 32 months, 6 patients recurred. Significantly more patients with infertility or PCOS experienced recurrence (P=0.040, P=0.015). Eight patients attempted to conceive after complete response, 5 spontaneous conceive and 4 normal delivery were achieved. No disease-related or treatment-related death was observed.

Conclusions
Fertility-sparing treatment with MA following entirely hysteroscopic curettage is effective with the least toxicities for rigorously selected young women with well-differentiated EC confined to endometrium or AH, however, close follow-up is needed for potential consequences of improper patient selection and substantial rate of recurrence.
Network/Task Force: EUROPEAN NETWORK OF YOUNG GYNAE ONCOLOGISTS (ENYGO) 2

HYPODONTIA- ? SURROGATE MARKER OF INCREASED EPITHELIAL OVARIAN CANCER RISK

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Objectives
Epithelial Ovarian Cancer (EOC) causes significant deaths annually with no screening to enable early detection. To establish prevalence rates of absent upper lateral incisor teeth in women with EOC.

Design and Setting: Prospective, collaborative study carried out under the auspices of the Gynaecological Oncology and Orthodontics team at a tertiary referral centre for gynaecological oncology.

Materials and Methods:
Following ethics approval, case control study designed. Following diagnosis and treatment for gynaecological cancers, women reviewed in the follow up clinic. Study discussed and information provided to patients with EOC as well as women with other gynaecological cancers. Following approval, they were invited to complete a detailed questionnaire including details of family history of malignancies and hypodontia. Consent also obtained to contact their dentist to procure details of recorded absence of upper lateral incisors.

Results:
64 participants age > 50 years recruited till date. 6/64 had absent lateral incisors following extracted and were excluded. Of the remaining 58, 25/58 were controls in the study. Collected data from 4/25 (16%) controls reported one or more absent lateral incisors and 8 of 21 (38%) with EOC had one or more absent lateral incisors.

Conclusions:
The initial findings suggest an increased prevalence of absent upper lateral incisors in women with a diagnosis of EOC. The study is currently ongoing with increased sample size as well as to investigate other cohorts of women including women at high risk of EOC (BRCA gene mutation) to report true prevalence.
Functional Intra-Tumour Heterogeneity in Ovarian Cancer: What Is a Representative Tumour Sample?

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Objectives
Stratification of novel cytotoxic agents in ovarian cancer is dependent upon availability of reliable biomarkers and the ability to test clinically accessible, representative samples. Most research testing the efficacy of biomarker stratified treatment use a single tumour sample, assuming a homogeneous biomarker profile. The sensitivity and reliability of such biomarkers may however be complicated by intra-tumour heterogeneity (ITH). The aim of this study was to evaluate the extent of ITH within a series of epithelial ovarian cancers using homologous recombination (HR) repair status as a marker, given that it has been shown to predict sensitivity to PARP-inhibitors and platinum.

Methods
Primary cultures were generated from ascites and solid tumour, taken from a variety of intra-abdominal sites. Cultures were characterised using a panel of immunofluorescent-labelled antibodies. HR status was determined by Rad51 foci formation and GI50 for cisplatin calculated using a standard cytotoxicity assay.

Results
Parallel cultures from ascites and solid tumour were cultured from 17 patients; 8 of which had solid tumour sampled from multiple (2-5) intra-abdominal regions. Inter- and intra-tumour heterogeneity was seen in characterisation, growthrate, HR status and cytotoxicity. Biomarker status and cisplatin sensitivity in the ascitic sample was representative of the whole tumour in only 10/17 samples.

Conclusions
The success of future clinical practice stratifying cytotoxic agents according to biomarkers is dependent upon the ability to test representative tumour. Accepting that ITH exists suggests that despite initial response, resistant subpopulations may survive, proliferate and result in relapse. Repeated testing from multiple regions is needed if novel agents are to be used in combination or succession.
Network/Task Force: EUROPEAN NETWORK OF YOUNG GYNAE ONCOLOGISTS (ENYGO) 2

NEUROTOXICITY IN OVARIAN CANCER PATIENTS ON GYNECOLOGIC ONCOLOGY GROUP (GOG) 218: THOSE AT RISK AND THE EFFECT OF SUBSTITUTION WITH DOCETAXEL

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Objectives
To describe characteristics associated with neurotoxicity (NT) in advanced ovarian cancer patients treated on GOG 218 and to examine the effect of substituting docetaxel for paclitaxel in patients with NT.

Methods
The development of NT was defined as CTC grade (G) ≥1. The NT improvement is defined as declined NT grade from previous cycle. The association between substitution with docetaxel and NT improvement was explored with generalized estimating equations adjusting for the treatment cycle and NT grading at previous cycle.

Results
Of 1864 eligible patients, 1329 (71%) developed G ≥1 NT during the study. Nearly half appeared within the first two cycles of chemotherapy with 31% experiencing G≥2. Older patients or those with worse quality of life (QOL) scores at baseline (p<0.05) were more likely to experience worse NT. 47/106 patients started with docetaxel at cycle one due to reaction to paclitaxel (n=32), fear of NT (n=4), other reasons (n=11) whereas 59/106 patients switched to docetaxel during cycle 2-6 due to NT (n=32), reaction to paclitaxel (n=19), and other reasons (n=8). Although the protocol instructed otherwise, the majority continued paclitaxel despite G ≥2 NT symptoms. There was no evidence that substitution with docetaxel improved NT (OR 1.57; 95% CI: 0.98-2.54; p>0.05). Of the 59 patients who switched to docetaxel, only 7 (12%) patients discontinued taxane prior to chemotherapy completion. A roughly equal chance of worsening NT was reported on paclitaxel (6%) as on docetaxel (5%).

Conclusions
Age and worse QOL at baseline are associated with chemotherapy-induced NT. Substitution of docetaxel does not improve NT symptoms, as examined in GOG 218.
RADICAL SURGERY IN PATIENTS WITH RESIDUAL DISEASE AFTER (CHEMO)RADIATION FOR CERVICAL CANCER

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Objectives
Routine hysterectomy after (chemo)radiation for cervical cancer showed not to improve survival. Aim of this study was to determine the possible impact of routinely scheduled biopsies and more radical surgery for residual central disease in cervical cancer after (chemo)radiation on locoregional survival.

Methods
Data were analyzed of a consecutive series of cervical cancer patients (FIGO stage IB1-IVA) treated with (chemo)radiation between 1994-2011. Patients underwent gynecologic examination with biopsies 8-10 weeks after treatment. Since 2001 larger biopsies by electric loop excision were taken and more radical surgery (type III hysterectomy or exenteration) was performed for central residual disease.

Results
Primary (chemo)radiation was given to 491 cervical cancer patients, 345 patients had a post treatment biopsy. Viable tumor cells were identified in 84 patients of which 61 were eligible for salvage surgery. Residual disease after (chemo)radiation was a poor prognostic factor (HR 3.5; 95%CI: 2.1-5.7, p<0.001). After 2001 larger biopsies were more frequently taken (29% vs. 76%, p<0.001). In those without viable tumor cells, locoregional recurrence after 2001 decreased from 21% to 10% (p=0.01). After 2001 more patients underwent more radical surgery (46% vs. 90%) (p<0.001). Locoregional recurrence after surgery before 2001 occurred in 6/13 (46%) patients, comparable to 19/48 (40%) (p=0.67) after 2001. More radical surgery was not associated with improved disease specific survival (HR 1.21; 95%CI: 0.49-3.01; p=0.68), but did result in significantly more severe morbidity.

Conclusions
More radical surgery in patients with central residual disease after (chemo)radiation does not improve survival and should not be recommended.
PATIENT-DERIVED XENOGRAFT MODELS OF ENDOMETRIAL CANCER: ESTABLISHMENT, VALIDATION AND PRECLINICAL DRUG EVALUATION
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Objectives
Development of new treatment strategies for endometrial cancer (EC) may be hampered by the lack of representative pre-clinical in vivo models. Patient-derived tumor xenograft (PDTX) models appear to have better retention of the characteristics of the source tumors. We here present preliminary data on the establishment and characterization of PDTX models for EC.

Methods
We established PDTXs of different subtypes of EC. Tumor samples were implanted s.c. in NOD-SCID mice (F1). When ~1000 mm³, tumors were retransplanted in NOD-SCID and/or nude mice. Validation and comparison with the patient’s tumor was performed by histological and genetic analyses.

Results
For engraftment, a success rate of ~50% was obtained. In particular, 18 PDTX models, of different histological subtypes, were initiated, of which 7 were successful (i.e. tumor growth in F1-F2). Five PDTX models were categorized as ‘failed’ (no tumor growth observed after 8 months). Six other PDTX models were only recently initiated. Tumor growth rate in F1 was generally slower than in the subsequent generations. Histological analyses showed that tumor morphology (H&E), proliferation (Ki-67), hormone receptor status (ER, PR) and PTEN status remained similar in F1-F2-F3 as compared to the patient’s tumor. Hotspot mutation profiling showed that mutations in the original tumor were also observed in xenografts and no additional mutations in xenografts were identified. Finally, we successfully evaluated the in vivo responsiveness to standard chemotherapy and a PI3K – mTOR inhibitor, BEZ-235, in these models.

Conclusions
We show first evidence for the establishment of EC PDTX models that can be used for future preclinical drug evaluation.
Locally advanced cervical cancer continues to constitute a therapeutic dilemma. Treatment options may vary broadly within national and international guidelines and often rely on physician’s preference and experience. Especially when young women with active childbearing wish are affected, and where fertility sparing surgical techniques such as radical trachelectomy cannot be an option at initial presentation of the disease, increasingly more treating physicians follow the approach of neoadjuvant chemotherapy for downstaging of the disease and subsequent local tumor resection. Even in older women the neoadjuvant approach seems feasible to avoid pelvic radiotherapy and so the potential long- and short term toxicity. Even though prospective randomized evidence so far has failed to demonstrate any significant prolongation of overall survival, PFS seems to be significantly in favour of the neoadjuvant approach in selected cases, while other advantages, such as avoidance of radiotherapy induced toxicity or even organ preserving surgery in younger women may offer additional benefits.
Sunrise Session: COLOPSCOPY WORKSHOP

EUROPEAN GUIDELINES FOR TREATMENT OF CIN

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During the last decades the management of Cervical Intraepithelial Neoplasia (CIN) has been directed towards more conservative treatment. Today, it is clear that in the spectrum of cervical pathology the line between premalignant and benign lesion can be drawn between CIN 1 and CIN 2 & CIN 3. These two grades of CIN are described as high grade squamous epithelial lesions (H-SIL), to differentiate them from low grade lesions and HPV induced changes (HPV/L-SIL).

L-SIL affects high proportion of women, has low risk of progression and high potential for regression. Most L-SIL reflect the expression of HPV infection rather than a true neoplasia. Thus, treatment is unnecessary in many patients with L-SIL, because their lesion will regress spontaneously.

Women with H-SIL have significant risk of progression to invasive cancer and should be treated. The expectant management of H-SIL with repeat cytology and colposcopy is not acceptable, except for pregnant patients and very young patients with CIN 2. The follow up of these cases is based on colposcopy.

There is no obviously superior conservative technique for treating CIN. The techniques of local destruction are easy to perform and require local or no anesthesia. However, detection of invasive cancer after treatment with destructive techniques, limits the value of these methods. Excision is preferred because of better histopathological assessment. It is necessary in unsatisfactory examination, in the presence of large lesions, in non-correlating cytology & colposcopy and in recurrent disease. Excision should remove tissue to a depth of greater than 7 mm.
Sunrise Session: COLOPSCOPY WORKSHOP

CHALLENGES IN MANAGEMENT OF LOW-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS

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The management of low-grade squamous intraepithelial lesions (LSIL) has changed significantly over the past years. It continues to be ambiguous, is constantly being improved by evidence-based studies, and involves ablation and excision. The observational monitoring without destructive interventions is justified also. The management depends on several factors. In young age women the probability for clearance of disease is high, in older women it more often changes to a more severe diagnosis. Many results support the safety of conservative approach in management of adolescent and young women with LSIL cytology.

LSIL is a relatively common diagnosis found in cervical cytology screening, so knowledge of the correct way to manage LSIL is important. Studies suggest that testing for high risk human papillomavirus (HR-HPV-test) can improve risk stratification in women with minor cytological abnormalities. There data that detection of HR-HPV in women with LSIL may allow clinicians to further triage women for advanced clinical management. However other studies suggest that the risk among HPV-negative women with abnormal cytology was still high enough to warrant immediate colposcopy referral and the high HPV positivity of LSIL at even the oldest ages suggests the lack of cost-effectiveness of HPV triage of LSIL for clinicians.

A woman with persistent ASCUS/LSIL positive cytology should be referred for colposcopy. A colposcopically identified lesion should be biopsied by 2 or more biopsy specimens. Management should be provided according to the histology result. The preferred option for biopsy-proven CIN 1 in women less than 30 years old is observation with repeat assessment at 12 months with cytology testing. (Colposcopy at 12 months is an acceptable option.) In the case of a patient older than 30-35 years the ablation is recommended (TZ 1 and 2 types) or excision (TZ 3 type).

Therefore, practice recommendations for management of women with LSIL should be balanced, taking local circumstances into account.
Sunrise Session; REPRODUCTIVE TECHNOLOGY IN FERTILITY SPARING MANAGEMENT

OVARIAN STIMULATION AND GAMETE CRYOPRESERVATION

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Treatment of malignancy may necessitate surgical resection of reproductive organs or administration of gonadotoxic chemotherapy or radiation therapy. In young women this often leads to infertility, which is a major quality of life concern.

Until a few years ago, practically no effective fertility protection therapies were available. Thanks to recent progress in reproductive medicine, there is now a broad spectrum of therapy options for women who may want children some time in the future and who have to undergo cytotoxic therapy. The specific protective therapy to be used depends on the time remaining until the onset of cytotoxic therapy.

An already established method is ovarian stimulation to extract, fertilise and cryopreserve mature oocytes.

More recently, it has also become a clinical standard practice to freeze unfertilized mature oocytes, which is particularly important for young women who do live in a stable partnership.

Both techniques require a time window for ovarian stimulation of about two weeks before cytotoxic therapy can be initiated.

This lecture will discuss already established methods for preserving fertility in young women receiving potentially gonadotoxic treatment.
Sunrise Session: REPRODUCTIVE TECHNOLOGY IN FERTILITY SPARING MANAGEMENT

OVARIAN TISSUE CRYOPRESERVATION
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Girls and women suffering from cancer requiring gonadotoxic treatment may as a side effect become infertile. When the ovaries are depleted of follicles menstrual cycles ceases and it is not possible to become pregnant.

Cryopreservation of ovarian tissue prior to treatment and cryopreserving the tissue can maintain a viable pool of follicles. When the women have been cured and is considered fit, the thawed ovarian tissue may be transplanted.

In Denmark one laboratory freezes all tissue in collaboration with three fertility clinics round the country. The ovarian tissue is excised at the local hospital and transported to the freezing facility. Transplantation will performed at the local hospital. Totally more than 650 (>100 younger than 18 years) patients have been included.

In Denmark 33 women have received ovarian tissue 44 times (1 woman 3 times and 8 women twice). All women regained ovarian function for longer or shorter periods and none experienced relapse due to the transplantation. The longevity of the tissue depends on the age of the woman and the amount of tissue transplanted, but is often several years. Recently, one child has had ovarian tissue transplanted for natural induction of puberty.

Nine women have been pregnant; three women have delivered six healthy babies. The presentation will review our experiences and results with transplantation of cryopreserved ovarian tissue.
Fellows' Workshop: IMAGING TECHNIQUES & INTERPRETATION IN GYNAECOLOGICAL ONCOLOGY: CT & USS

CT CHEST, ABDOMEN AND PELVIS: PRINCIPLES, CLINICAL APPLICATION AND INTERPRETATION IN GYNAECOLOGICAL ONCOLOGY

C. Brunell

The Fellows Workshop is a radiological workshop, aimed at non radiological clinicians with an interest in Gynaecological Oncology Imaging. The workshop has three parts:
1. Introduction to the basic physics of Computerised Tomography (CT) including, attenuation, CT number, windowing, image reconstruction, use of contrast agents and other aspects of image optimisation.
2. Applications of CT scanning, relevant to Gynaecological Oncology, will be detailed and discussed.
3. Guidance will be given on developing a structured approach to image viewing and image interpretation based on normal CT appearances and the mechanisms of tumour spread common to most gynaecological cancers. The work shop will conclude with several case studies for interpretation and a reminder of the risks of radiation exposure.
THE ROLE OF THE EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER GYNECOLOGIC CANCER GROUP (EORTC GCG) IN THE CURRENT EUROPEAN RESEARCH LANDSCAPE.

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The EORTC GCG continue to be an internationally open academic body for those institutions and investigators across Europe willing to develop academic research in gynaecologic cancers in a multidisciplinary and independent research environment.

Resources and facilities:
The EORTC, a unique pan European clinical research infrastructure whose network comprises over 300 hospitals in over 30 countries, was founded in 1962 with the objectives of improving the standard of care in cancer [D. Lacombe, et al. EJC 2012 ; 10 (1)(Suppl) 2-12].

Current research:
The EORTC GCG is dealing with establishing clinically useful predictive and prognostic factors and identifying subgroups of patients based on genomic patterns and activated pathways. These objectives can only be reached with transversal cooperation within the EORTC framework as well as international cooperation [A. Casado, et al. EJC 2012; 10 (1) (Suppl): 66-75]. An example of this collaboration is the International Rare Cancers Initiative (IRCI) [E. Shash, et al ecancermedicalscience 2013; 7; 321]. TR investigations for all gynecologic cancers, innovative immunotherapy approaches, mechanisms of resistance, survivorship issues and the elderly are in the agenda of the EORTC GCG.

Current challenges and priorities:
As health care costs are constantly rising and governments are reforming their healthcare systems there is an urgent need to reshape the European clinical research landscape to optimize the research and development process. The real benefit of drugs needs to be assessed independently. Meaningful data for reimbursement strategies will be a major goal of future clinical trials [S. Burock, et al. EJC 2013; 49 (13) 2777-2783].
Despite the fall in incidence of cervical cancer in countries with a screening programme, a large proportion of patients have locally advanced disease at presentation. Since 1999 concurrent chemoradiotherapy represents the standard of care for locally advanced cervical cancer (LACC). As a significant number of patients doesn't achieve pelvic control and eventually die from the disease, different therapeutic approaches such as neoadjuvant chemotherapy (NACHT) followed by surgery have been developed. A recent Cochrane review concluded that, whilst both overall and progression free survival were improved with NACHT, the evidence is based on only a small number of trials, and further research is warranted. The scientific community is waiting for the results of the randomized clinical trial carried out by the EORTC (55994), which should demonstrate whether or not NACHT followed by surgery displays a better oncological outcome compared with chemoradiotherapy for patients with stage IB2-IIB cervical cancer. The study is ongoing and the inclusion of 625 patients is expected in spring 2014. In the multimodality treatment era, NACHT before chemoradiotherapy or adjuvant chemotherapy after chemoradiotherapy has been advocated for the treatment of LACC. Fewer molecular targeted agents have been evaluated in cervical cancer in comparison with other common tumors. Promising target is the vascular endothelial growth factor (VEGF) signaling pathway, which plays critical roles in tumor growth and angiogenesis, such as epidermal growth factor receptor (EGFR) and PI3/Akt/m-TOR pathways. Future trials are going to combine targeted agents with the best arm of EORTC 55994, NACHT followed by surgery or chemoradiotherapy.
Parallel Session: HEREDITARY SYNDROMES

IMAGING PRE-INVASIVE TUBAL LESIONS IN HIGH RISK POPULATIONS

J. McAlpine

Autofluorescence imaging is a relatively new modality, which enables real time, high resolution imaging of epithelial tissue. Cancerous or even precancerous changes in the epithelium lead to loss of normal tissue autofluorescence (AF). Coupled to handheld devices or endoscopic tools direct fluorescence visualization (FV) has been described in many anatomic locations including the fallopian tubes. Change to the pattern of tissue AF may be secondary to breakdown of the collagen matrix, tissue remodeling, or increased metabolism, all of which can occur during the process of malignant transformation. These changes can be compared to normal adjacent epithelium and are being explored as means of early diagnosis in fallopian tube (FT) cancers/ovarian/primary peritoneal cancers. We will review the challenges in the implementation of AF FT screening, success in other cancers, and other imaging technologies including early attempts in targeted fluorescent localization.
Parallel Session: IMAGING

ENDOMETRIAL CANCER: PREOPERATIVE ULTRASOUND ASSESSMENT TO TAILOR SURGERY

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Endometrial cancer is often diagnosed at an early stage where the prognosis is very good. However, women with ‘High risk’ cancer have a worse prognosis, and these women might benefit from more extensive surgery with lymphadenectomy. Today, there is no consensus to use imaging to assess tumor extension, in fact many institutions use only preoperative grade to identify high risk cases. 70-75% will be low risk based on endometrial biopsy - of these 45% will be high risk according to final histology and will thus need additional surgery and/or radio-chemo therapy.

Ultrasound can improve preoperative identification of women with high risk cancer that might benefit from more extensive surgery. By combining grade with ultrasound assessment one can improve the correct classification of patients (as high or low risk) by up to 29%. Subjective assessment of myometrial and cervical invasion is as good as any measurement technique. Sonographic features associated with high risk cancer are; mixed/hypoechoic echogenicity, multiple global vessels, and high color score. Overestimation of myometrial invasion using ultrasound is often related to bulky exophytic tumors, and underestimation to infiltrative diffuse growing tumors.
LOSS OF ARID1A CONFERS RESISTANCE TO MULTIPLE TARGETED CANCER DRUGS THROUGH ACTIVATION OF AKT SIGNALING

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Background
Inhibition of signaling pathways that are activated by oncogenic mutations in cancer can elicit significant responses in the clinic. However, many recurring mutations in patient tumors have not yet been linked to specific signaling pathways, precluding the selection of targeted therapies in such cases. As one example, inactivating mutations in the SWI/SNF component ARID1A are frequent across multiple cancer lineages, but it remains unclear how the tumor benefits from ARID1A loss.

Material and Methods
Functional genetic screens provide a powerful tool to identify genes that act in specific signaling pathways. We have described previously the generation of several large shRNA collections in retroviral vectors as well as a technology to rapidly screen such libraries, named "shRNA bar code screening". We have used these shRNA libraries to identify biomarkers of response to targeted cancer drugs in breast cancer, neuroblastoma and lung cancer.

Results
We report here the identification of ARID1A as a frequent hit in large-scale shRNA screens with ARID1A knockdown conferring resistance to agents targeting the HER2/PI3K/mTOR signaling cascade in breast cancer. Our data identify ARID1A as a modulator of response to HER2/PI3K/mTOR targeting drugs via activation of AKT via ANXA1 induced Ca2+ signaling. We find that the AKT inhibitor MK2206 or the CAMKK inhibitor STO609 restores sensitivity of ARID1A knockdown breast cancer cells to both the mTOR kinase inhibitor AZD8055 and trastuzumab.

Conclusions
Our findings provide a molecular basis for the selection of ARID1A mutations in human cancer. Importantly, our data imply that patients with ARID1A mutant tumors may benefit from including inhibitors targeting AKT in the treatment regimen.
Parallel Session: MANAGEMENT OF HIGH RISK PATIENT

CANCER DURING PREGNANCY: THE OBSTETRICAL POINT OF VIEW

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Cancer is diagnosed in 1 in 1000 to 2000 pregnancies. The complex medical, ethical and psychological issues arising in pregnant women with cancer demand care from a multidisciplinary team. Since curing the mother is the priority, the proposed treatment should adhere the standard treatment for non-pregnant patients. Slight modifications to the standard treatment can be suggested in pregnancy considering fetal health.

As the fetus is most vulnerable to radiation or teratogens, exposure should be avoided as much as possible during pregnancy. Before the onset of treatment, an ultrasound assessment of the fetal anatomy should be performed. After cervical surgery, serial cervical length measurements to assess for cervical incompetence are advisable. A subgroup of patients receiving chemotherapy seems to be at increased risk for IUGR and preterm contractions, so a regular fetal monitoring for growth and fetal wellbeing is required.

A term delivery should be aimed for. If chemotherapy treatment is ongoing, delivery should be planned with a 2-3 week interval to avoid spontaneous labour occurring at the nadir of neutropenia.

Vaginal birth is preferred, despite in women with cervical cancer (fatal recurrences in the episiotomy), vulvar cancer or pelvine metastases. The placenta should be examined for metastatic disease.

As the postpartum period and malignancy are both risk factors for venous thromboembolism, prophylaxis should be consideration after an operative delivery. Breastfeeding can be allowed, despite in patients with chemotherapy administered in the last weeks before the delivery or postpartum.
Parallel Session: MANAGEMENT OF HIGH RISK PATIENT

VULVAR CANCER WITH POSITIVE NODES OF THE GROIN – PELVIC LYMPHADENECTOMY, ADJUVANT RADIOTHERAPY OR RADIOCHEMOTHERAPY?

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Lymph-node metastases to the groin are the most important prognostic factor in vulvar cancer. Even though outcome is already impaired with only one affected node, parameters determining adjuvant therapy remain subject of discussion. The Gynecologic Oncology Group study GOG 37 investigated the value of pelvic lymphadenectomy compared to irradiation of groins and pelvis after vulvectomy and inguino-femoral lymphadenectomy and observed a survival benefit for patients with 2 or more positive groin nodes in the irradiation group. Even after more than 20 years, discussion on the study design and interpretation of these results is on-going. Reasons for the reservation to implement the results of GOG 37 are a higher pelvic recurrence rate observed in the radiation group as well as the fact that no adjuvant radiotherapy to the groins was applied in the surgery group despite positive groin nodes, potentially accounting for the high rate of groin recurrences in this group with consecutive poorer outcome. Given these results and the fact that vulvar cancer is affecting a considerable number of frail, elderly patients with significant comorbidities, making radiotherapy sometimes difficult to apply, there might even be an argument for surgical assessment of the pelvic nodes in patients with positive groin nodes and omission of pelvic radiation in case of negative pelvic nodes Although not supported by high-level evidence. Another possible strategy in treatment of node-positive patients might be an intensified adjuvant therapy in analogy to other squamous cell cancers applying chemoradiation instead of radiotherapy alone.
Parallel Session: MANAGEMENT OF HIGH RISK PATIENT

MANAGEMENT OF GYNECOLOGIC SOFT TISSUE SARCOMA AFTER COMPLETE RESECTION

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Uterine sarcomas and more generally gynecologic sarcoma are rare malignancies accounting for 8-10\% of all gynecologic malignancies, but are significantly aggressive. Gynecologic/uterine sarcomas include leiomyosarcoma (LMS, 65\%), endometrial stromal sarcoma (ESS, 20\%), high-grade undifferentiated sarcoma (HGUS, 5\%) adenosarcoma (5\%) and other (5\%). Prognosis of gynecologic sarcoma is poor, with a five-year survival rate as low as 30\% excluding low grade endometrial stromal sarcomas and adenosarcoma. Tumor stage is the strongest prognostic factor for all uterine sarcomas, with 5-year survival of about 50\% for stage I and 10\% for more advanced stages. Hysterectomy and bilateral salpingo-oophorectomy is the cornerstone of treatment for early-stage (I or II) disease. The ovary can be preserved in premenopausal women with early-stage LMS and ESS, and routine lymphadenectomy is not necessary unless enlarged lymph nodes are present. Surgical resection when feasible may also be appropriate for patients presenting with advanced-stage tumors. Uterine sarcomas are rare and, consequently, data supporting the use of adjuvant radiotherapy consist of few randomized studies and multiple single-institution retrospective reports. Over the last decades, adjuvant treatment has changed from radiation therapy to chemotherapy, without any change in survival. Chemotherapy regimens with efficacy in treating uterine sarcoma include gemcitabine-docetaxel, doxorubicin and ifosfamide. Trabectedin is indicated for patients with advanced soft tissue sarcoma after failure of treatment with anthracyclines and ifosfamide. Based on the relative rarity of these tumors, management of these patients should be centralized and must be performed by a multidisciplinary team including gynecologic oncologist, pathologist, medical oncologist and radiation oncologist.
A COMPARISON OF FIRST-LINE TREATMENT WITH GEMCITABINE PLUS DOCETAXEL VERSUS GEMCITABINE PLUS VINORELBINE IN WOMEN WITH METASTATIC BREAST CANCER

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Objectives
Two regimen associated Gemcitabine + Docetaxel (G+D) or Gemcitabine + Vinorelbine (G+V) were compared in efficacy and/or toxicity in patients with metastatic breast cancer (MBC).

Methods
Patients with MBC, that relapsed after one adjuvant/neoadjuvant regimen containing an anthracycline that was completed for at least 12 months, were to be randomized equally to: 1/ D 75 mg/m² on day 1 + G 1250 mg/m² on days 1/8 q3W, 2/ G 1250 mg/m² on days 1/8 + V 60 mg/m² on days 1 & 8 q1 then 80 mg/m² on days 1 & 8 q3W. Primary endpoint was time to progression (TTP). Secondary endpoints were overall survival (OS), overall response rate (ORR) and toxicity (T).

Results
63 patients (31 in the arm G+D, 32 in the arm G+V) were enrolled in the study and randomized, from January 2010 to June 2012. The number of cycles was 8.

The median age was 57 years old in the arm G+D and 58,5 years old in the arm G+V.

All patients achieved the treatment with median TTP of 7 months in the arm G+D and 6.5 months in the arm G+V. 23 % of patients progressed in the arm G+D and 30 % in the arm G+V. The ORR was compared in each arm. Toxicity was more observed in the arm G+D.

Conclusions
No substantial differences between treatments were observed in safety and efficacy. However, the arm G+V is associated with lower grade toxicity in neutropenia. These results should be interpreted with caution due to early termination of the study.
Poster Presentations: Breast Cancer

THE TUMOR SUPPRESSOR ERP29 C.*293A>G AND THE DNA TRANSCRIPTION FACTOR IKBKAP P.CYS1072SER POLYMORPHISMS ALTER BREAST CANCER RISK

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Objectives

ERP29, a tumor suppressor gene, and IKBKAP, a gene of transcriptional process, were related with the onset of tumors. The influence of ERP29 c.*293A>G and IKBKAP p.Cys1072Ser polymorphisms in breast cancer (BC) risk has never been performed before and was the aim of this study.

Methods

ERP29 c.*293A>G and IKBKAP p.Cys1072Ser genotypes of 742 BC patients and 742 healthy women were obtained in genomic DNA by real-time polymerase chain reaction.

Results

The frequency of ERP29 c.*293AG+GG genotype was higher in patients than in controls (36.6% versus 30.7%, P=0.03). Carriers of G allele were under a 1.33-fold (95%CI: 1.03-1.72) increased risk for BC. ERP29 c.*293AG+GG (62.5% versus 32.4%, P<0.0001) and IKBKAP p. 1072SerSer (50.0% versus 34.4%, P=0.002) genotypes were more frequent in non-Caucasian than in Caucasian patients. ERP29 c.*293AG+GG genotype was also more frequent in non-Caucasian patients than in controls (62.5% versus 30.7%, P=0.01). Carriers of G allele were under a 2.31-fold (95%CI: 1.22-4.39) increased risk for BC. The frequency of ERP29 c.*293AG+GG genotype in underweight and normal patients was higher than that found in pre-obese and obese ones (43.9% versus 33.0%, P=0.005), and also than in controls (43.9% versus 30.7%, P=0.003). Underweight and carriers of G allele were under a 1.64-fold (95%CI: 1.19-2.27) increased risk for BC. IKBKAP p. 1072SerSer genotype was more common among women who breastfed compared to those who did not (6.5% versus 2.3%, P=0.03).

Conclusions

Our data suggest, for the first time, that ERP29 c.*293A>G and IKBKAP p.Cys1072Ser polymorphisms alter the risk and clinical features of BC.
CHAC1 EXPRESSION IN BREAST CANCER

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Objectives

The unfolded protein response (UPR) pathway is activated in many human solid tumors. CHAC1 (cation transport regulator-like protein 1) has been identified as UPR component but its role in cancer has not yet been characterized. Thus, we investigated its mRNA expression and function in breast cancer.

Methods

We studied the prognostic role of CHAC1 mRNA expression and its two known transcript-variants 1 and 2 in 116 breast tissues using quantitative real-time reverse transcriptase-PCR. Furthermore we conducted functional studies using siRNA-mediated knockdown and plasmid-mediated overexpression of CHAC1 in breast cancer cells. Microarray-based gene expression profiling was conducted in CHAC1 overexpressing cell lines.

Results

High grade or hormone-receptor negative tumors exhibited higher CHAC1 mRNA expression levels (P=0.004, or P<0.001, respectively). In multivariate survival analyses, high expression of CHAC1 emerged as an independent prognostic factor for poor survival [transcript variant 1: RR(death) 6.7 (2.4-18.9), P<0.001; RR(relapse) 6.7 (2.1-21.3), P=0.001; transcript variant 2: RR(death) 4.9 (2.0-12.4), P<0.001, RR(relapse) 8.0 (2.4-26.8); P<0.001]; total CHAC1: RR(death), 3.0 (1.3–7.1) P=0.012, RR(relapse) 4.8 (1.6–14.6), P=0.005]. Functional studies revealed that CHAC1-knockdown suppressed breast cancer cell migration and proliferation, whereas ectopic overexpression yielded opposite effects. Several differentially expressed genes have been identified in CHAC1 overexpressing breast cancer cell lines.

Conclusions

The data collected in our studies might contribute to a better understanding of the impact of higher CHAC1 levels in tumor tissue of breast cancer patients. Our findings suggest that CHAC1 expression could be an independent prognostic indicator.
PROTEIN EXPRESSION OF ADIPONECTIN AND ADIPORECEPTORS IN BENIGN BREAST LESIONS, DUCTAL CARCINOMA IN SITU AND INVASIVE BREAST CANCER


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Objectives
Obesity is responsible for 30-50% increase in postmenopause breast cancer. A possible explanation for this might be an association of adipokines secreted by adipose tissue with breast cancer. The objective was to compare the immunohistochemical expression of adiponectin (APN) and its receptors type 1 and 2 (AdipoR1/R2) in invasive ductal carcinoma (IDC), ductal carcinoma in situ (DCIS) and benign breast lesions (BE).

Methods
Tissue Microarray (TMA) slides were prepared from 69 IDC, 73 DCIS and 81 BE treated at CAISM/UNICAMP from 2008 to 2011. Markers expression was evaluated in tumor/epithelial tissue and the immunohistochemical interpretation was performed by the intensity of marker expression and percentage of stained cells. The statistical analysis was made by the chi-square, Mann-Whitney, Kruskal-Wallis tests and Spearman correlation.

Results
APN was expressed in 65%, 48% and 12% of IDC, DCIS and BE, respectively; AdipoR1 was expressed in 98%, 94% and 71% of IDC, DCIS and BE, respectively. All IDC and DCIS cases expressed AdipoR2 versus 81% of BE. The mean score of APN expression was higher in IDC but the difference was significant between IDC and BE and between DCIS and BE. Regarding AdipoR1/R2, both were more highly expressed in IDC than in DCIS and BE. In IDC there was no correlation between APN expression and AdipoR1/R2 expression. In DCIS and BE, the APN expression was positively correlated with AdipoR1/R2 expression.

Conclusions
Differences in protein marker expression observed in different breast diagnoses, suggest that these markers participate in the etiologic mechanism of these conditions.
Poster Presentations: Breast Cancer

FABP4 PROTEIN EXPRESSION IN WOMEN WITH BREAST CANCER, DUCTAL CARCINOMA IN SITU AND BENIGN BREAST LESIONS – ASSOCIATION WITH OBESITY

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Objectives
Fatty acid binding protein (FABP4) is one of the most abundant intracellular binding proteins present in mature adipocytes. High concentrations of FABP4 are found in obese individuals, who are at high risk for developing several types of cancer, including breast cancer. The objective was to assess FABP4 protein expression in breast epithelial and adipose tissue in women with breast cancer (BC), ductal carcinoma in situ (DCIS) and benign breast lesions (BE).

Methods
Paraffin-embedded blocks from 223 women (69 BC, 73 DCIS and 81 BE) treated at CAISM/Unicamp from 2008 to 2011 were included and Tissue Microarray (TMA) slides were prepared. FABP4 expression was assessed in the tumor/epithelial tissue, proximal fat (PF) and distant fat (DF) tissue in BC, DCIS and BE. To evaluate the correlation between marker expression at different sites and clinical/histological parameters, the Chi-square, Fisher exact, Mann-Whitney, Kruskal-Wallis tests and Spearman correlation were used. Values of p<0.05 were considered significant.

Results
FABP4 protein expression was observed in epithelial tissue in 90% of BC, 40% of DCIS and 28% in BE. In PF and DF, FABP4 was more highly expressed in patients with BE than in patients with BC. All cases expressed this marker moderately or intensely in the peri-epithelial and distant adipose tissue. FABP4 expression demonstrated a positive correlation with BMI in BC, although this association did not occur in DCIS and BE.

Conclusions
Our results indicate that there is a direct correlation between FABP4 protein expression, breast cancer and obesity.
Poster Presentations: Breast Cancer

BREAST CANCER CELL INFILTRATION OF THE VASCULAR BED IN THE PERIPHERY OF THE TUMOR IS NOT ASSOCIATED WITH APOPTOTIC MARKERS

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Objectives
Vascular bed infiltration in the periphery of the breast cancer is considered a marker of increased metastatic potential. The aim of this study is to examine the association of vascular bed infiltration with the expression of apoptotic markers p53 and BCL2 in a cohort of breast cancer patients.

Methods
We studied 306 patients with invasive ductal carcinoma of the breast. The expression of the p53 and BCL2 was documented immunohistochemically with the streptavidin-biotin method in thick paraffin tissue sections treated with the appropriate monoclonal antibodies against the antigens p53 and BCL2. The infiltration of the vascular bed from cancer cells or cancer emboli was assessed with optical microscopy.

Results
The mean age of our patients was 56±14.5 years. 55.2% of our patients showed positive cancer cell infiltration of the vascular bed. However, the metastatic infiltration of blood vessels in the periphery of the tumor showed no correlation with the expression of bcl-2 (43.8% of tumors with metastatic vascular infiltration was BCL2 positive versus 56.7% BCL2 negative p=0.223). Similarly the cancerous infiltration of the vessels in the periphery of the tumor was not associated with the expression of p53 as the 47.1% of the positive to vascular infiltration tumors was p53 negative versus 45.5% p53 positive (p=0.873). Moreover the age of patients examined was not associated with BCL2 or p53 expression.

Conclusions
The ability of breast cancer cells to infiltrate the vascular bed in the periphery of the tumor is not associated with the expression of proapoptotic marker BCL2 or antiapoptotic marker p53.
Poster Presentations: Breast Cancer

EGFR EXPRESSION IS ASSOCIATED WITH HIGH PROLIFERATION AND INFILTRATION OF THE VASCULAR BED IN THE PERIPHERY OF THE BREAST CANCER LESION

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Objectives
Positive EGFR expression in invasive ductal carcinoma has been associated with unfavourable clinical course. Moreover Peritumoral vascular invasion may signal an increased metastatic potential of the breast cancer cells. The aim of this study was to investigate the expression of EGFR and its correlation with Ki67 as a marker of proliferation and vascular infiltration as a marker of invasiveness in an unselected cohort of greek patients with breast cancer.

Methods
This study comprised of 306 cases of breast cancer. Tumor blocks from each specimen was evaluated with immunohistochemical staining for the evaluation of EGFR and Ki-67. Ki67 index was evaluated as qualitative variable, separating our cohort into two groups of patients (with increased and decreased cellular proliferation index) using as the threshold value the positive immunostaining of the 25% of the cancer cells. Infiltration of the vascular bed in tumors periphery was assessed with optical microscopy examining for cancer cells or cancer embolus in the blood vessels.

Results
The mean age of our patients was 56±14.5 years. Tumors stained positive for EGFR had a higher rate of cancer cell infiltration of the vascular bed in the periphery of the tumor (72.7% compared to 38.8%, p<0.01) and a higher index of cell proliferation (84.2% in compared to 50.4%, p<0.01) in relation to the EGFR-negative tumors. There was no correlation of the EGFR expression with the age of our patients.

Conclusions
These data indicate that EGFR is a prognostic factor of worse clinical outcome and that the EGFR positive phenotype is associated with increase proliferation and invasiveness.
Abstracts from 18th International Meeting of the European Society of Gynaeological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

**Poster Presentations: Breast Cancer**

**IMMEDIATE RECONSTRUCTION AFTER MASTECTOMY IN PREGNANT PATIENTS WITH BREAST CANCER.**

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**Objectives**

Breast reconstruction after mastectomy is currently considered an essential component in managing breast cancer patients, particularly those diagnosed at a young age. However, no studies have been published on the feasibility of immediate breast reconstruction in patients diagnosed and operated during the course of gestation, as there is no consensus about this procedure in pregnant patients.

**Methods**

We retrospectively identified breast cancer patients who were subjected to mastectomy and immediate breast reconstruction during pregnancy at the European Institute of Oncology between 2002 and 2012. Patient demographics, gestational age at surgery, tumor stage, adjuvant treatment, details of the surgical procedures, surgical outcomes and fetal outcomes were analyzed.

**Results**

A total of 78 patients with breast cancer diagnosed during pregnancy were subjected to a surgical procedure during the course of gestation. 22 patients had mastectomy, of whom 13 were subjected to immediate breast reconstruction. 12 out of 13 patients had a two-stage procedure with tissue expander insertion. Median gestational age at surgery was 16 weeks. No major surgical complications were encountered. Only one patient elected to have an abortion, otherwise, no spontaneous abortions or pregnancy complications were reported. Median gestational age at delivery was 35 weeks (range: 32-40 weeks). No major congenital malformations were reported.

**Conclusions**

This is the first study of immediate breast reconstruction in pregnant breast cancer patients. Tissue expander insertion appears to ensure a short operative time, does not seem to be associated with considerable morbidity to the patient or the fetus, and hence should not be discouraged.
SECRETORY LEUKOCYTE PROTEASE INHIBITOR EXPRESSION DISRUPTS EPITHELIAL CADHERIN ADHERENT COMPLEX, INDUCES B-CATENIN RE-LOCALIZATION AND TRIGGERS APOPTOSIS IN BREAST TUMOR CELLS

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Objectives
Epithelial cadherin (Ecad) is a transmembrane glycoprotein involved in cell-cell adhesion through its extracellular domain, whereas the intracellular domain strengthens binding via interactions with B-catenin and the actin cytoskeleton. Ecad protects mammary epithelial cells from apoptosis and its loss has been well documented during breast tumor progression. Secreted serine-protease inhibitors, such as SLPI (Secretory Leukocyte Protease Inhibitor), have both anti- and pro-tumorigenic activities. Particularly in breast cancer, low and high levels of SLPI have been detected and related to tumor regression and progression. Using an in vivo model, SLPI expression was reported to decrease mammary tumor growth and to induce apoptosis-related changes. Notwithstanding its relevance, there are no reports on how changes in SLPI expression in tumor cells affect Ecad and other members of the adherent complex. Aim: To evaluate the effect of SLPI upon Ecad expression and proteins related to it in human (MCF-7) and murine (F3II) breast cancer in vitro models.

Methods
mRNA: standard/real-time PCR, protein: WIB/immunocytochemistry.

Results
SLPI expression was associated to decreased mRNA/protein Ecad levels. Moreover, it caused disruption of the Ecad-B-catenin complex, changing the balance of pro- and anti-apoptotic proteins (Bax/Bcl2), and eventually leading to apoptosis (TUNEL). This process was, at least in part, mediated by nuclear B-catenin and changes in protein expression associated to its re-localization (cMyc, cyclin D1).

Conclusions
The pro-apoptotic B-catenin effect induced by SLPI expression may have great impact in breast cancer treatment, given the potential therapeutic use of SLPI in this disease and the relevance of Ecad functionality in breast tumor progression.
OBJECTIVES
To identify variables that predict pathologic complete response (pCR) following neo-adjuvant chemotherapy (NACT) for primary invasive breast cancer, with special interest for BMI.

METHODS
A retrospective study of 267 breast cancer cases from the UZ-Leuven multidisciplinary breast cancer database who, between 01-01-2000 and 31-12-2011, received NACT. We investigated different definitions of pCR (pCR1=ypT0N0, pCR2=pCR1+ypTisN0). Potential variables that predict pCR after NACT were analyzed in univariate and multivariate model: age, BMI, multifocality, cTNM stage, histology, tumor grade, ER-, PR-, HER2-status and breast cancer phenotype.

RESULTS
pCR1 and pCR2 was achieved in 45 (16,9%) and 65 (24,3%) cases respectively. Significant predictive variables for pCR1 and pCR2 were: high tumor grade, negative ER- and PR-status, positive HER2-status and breast cancer phenotype (P<0,001). For pCR2, histology and BMI were additional predictors in univariate model: age, BMI, multifocality, cTNM stage, histology, tumor grade, ER-, PR-, HER2-status and breast cancer phenotype.

CONCLUSIONS
Following NACT, breast cancer phenotype is the best predictor for pCR. Patients with a TNBC, HER2-like and luminal HER2 tumor were most likely to achieve pCR. BMI seems to play a role in ER-negative breast cancers but its predictive role for pCR2 in univariate model was not confirmed in a multivariate model. Larger datasets and more research are probably needed to further clarify BMI’s role for pCR in ER-negative breast cancer.
Breast Cancer in Turkey

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Objectives:
Breast cancer is the leading cause of cancer for women among worldwide. Our aim with this study is to summarize the characteristics of breast cancer in Turkey.

Methods:
Turkish cancer registry is a well organized registry system working since 2002. The data stream to be provided from 12 cancer registry centres nationwide. The data is comprising of more than 25% of the whole population.

Results:
The incidence of breast cancer in Turkish women is 40 per 100,000 in 2008. The median age at diagnosis is 52. 48% of the cases got diagnosed at stage I while 38% of them was at stage II. The stage distribution is shown in the table below.

<table>
<thead>
<tr>
<th>stage</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>I</td>
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</tr>
<tr>
<td>II</td>
<td>38,1</td>
</tr>
<tr>
<td>III</td>
<td>5,1</td>
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<td>IV</td>
<td>8,9</td>
</tr>
<tr>
<td>total</td>
<td>100</td>
</tr>
</tbody>
</table>

Although age standardized rates (picture below) are similar to European data, nearly half of the patients are younger than 50 years of age in Turkey (picture2).

ASR(100,000)

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Conclusions:
Breast cancer is the most common cancer among women in Turkey like it is in the rest of the world. 86% of cases is getting diagnosed at early stages. The number of young breast cancer patients is relatively high in Turkey.
Poster Presentations: Cervical Cancer

EVALUATION OF PREOPERATIVE POSITRON EMISSION TOMOGRAPHY WITH COMPUTERED TOMOGRAPHY IN DETECTION OF LYMPH NODE METASTASIS IN CERVICAL CANCER BULKY TUMORS

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Objectives
Bulky tumors of cervical cancer (CC) have high risk of recurrence in which combination of therapeutic approaches increases the morbidity. The aim of the study was to analyze the usefulness and accuracy of preoperative positron emission tomography combined with computed tomography (PET/CT) in detection of regional lymph node metastases in patients with bulky tumors of CC.

Methods
In the time period from November 2008 to October 2012 seventeen patients with CC stage IB2-IIA2 were enrolled into the study. All patients underwent preoperative PET/CT scan, a dose-dense neoadjuvant chemotherapy followed by radical surgery. The detection of lymph node (LN) metastases by PET/CT was compared with the results of histological evaluation.

Results
Histological analysis found LN metastases in six patients (35.3%). The overall patient-specific sensitivity, specificity, positive predictive value, negative predictive value and accuracy of PET/CT were 83.3 %, 81.8 %, 71.4 %, 90.0 % and 82.4 % respectively. This means that 29.4% patients would be underdiagnosed without PET/CT evaluation.

Conclusions
Preoperative PET/CT evaluation with high specificity and positive predictive value may be useful tool for identifying patients with macrometastases which could profit rather from primary chemo – radiotherapy, or extended-field radiation therapy in case of positive para-aortic LN, rather than radical surgery. Such correction in treatment modality may decrease the morbidity and increase quality of life.
CLASS II VERSUS CLASS III RADICAL HYSTERECTOMY IN EARLY CERVICAL CANCER: AN OBSERVATIONAL STUDY IN A TERTIARY CENTER

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Objectives
The purpose of this observational study was to evaluate disease free survival (DFS), overall survival (OS), and local recurrence rate (LRR) in patients submitted to Class II RH compared with Class III RH in FIGO early cervical cancer (ECC).

Methods
We investigated 127 patients with CC admitted to the National Cancer Institute of Milan from June 2001 to October 2011 treated with Class II RH, and compared them with 202 patients operated with Class III RH between March 1980 and March 2004. A total of 329 patients were collected.

Results
Median follow-up time was 91 months (95%CI: 79-103). Five-year OS and DFS estimates were 89.5% and 85.6%, respectively. Five-year OS estimates were 86.8% and 95.2% for Class III and Class II, respectively (p= 0.0156). Five-year DFS estimates were 82.9% and 91.2% for Class III and Class II respectively (p=0.0677). The Hazard Ratio estimates of effect of surgical treatment (Class III RH versus Class II RH) for OS and DFS were 5.87 (95%CI: 1.56-22.07), and 4.64 (95%CI: 1.74-12.42), respectively, when adjusting for confounding variables. Overall recurrence rate was 12.8%, and 16.3% for Class III and 7.1% for Class II and respectively.

Conclusions
The present data confirm the results of previous randomized studies. The class II RH should be considered the standard of care in patients with ECC candidate to surgical treatment.
AUDIT OF ADJUVANT CISPLATIN +/- VAGINAL BRACHYTHERAPY FOLLOWING RADICAL HYSTERECTOMY AND NODAL DISSECTION FOR CERVICAL CANCER.

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3Gynaecological Oncology, Northampton General Hospital, Glasgow, United Kingdom

Objectives
We present a series of post operative cervical cancer patients who did not meet the Gynae Oncology Group criteria with 2 or more risk factors to then require adjuvant chemoradiation. However these patients were felt to have some risk of relapse and were offered adjuvant cisplatin with a proportion also receiving vaginal brachytherapy. Our aim was to audit these patients, obtain demographic, stage, risk factors and outcomes relating to both survival, relapse rate and toxicity.

Methods
We accessed personal databases, Chemocare, Aria, Clinical Portal and patient notes to obtain the information required as listed in the aims. This was then entered in to an excel spread sheet for analysis.

Results
A total of 15 patients found. All patients were stage 1b with the main risk factor being lymphovascular space Invasion, however, in some patients Grade 3 or a combination of both was the reason for discussion of adjuvant treatment. All patients had no long term toxicity from treatment and all are still alive with no relapses.

Conclusions
Although the numbers are small and the adjuvant treatment was given in patients who are not traditionally categorised high risk they were felt to be of some risk of relapse. Adjuvant treatment was discussed with each patient making it clear this was not standard practice. Our data would suggest the treatment was well tolerated with no grade 3 toxicity and as yet we have had no relapses, of course it could be argued that these patients may not have relapsed regardless. Only a large randomised trial can answer this question.
Poster Presentations: Cervical Cancer

IMAGE-BASED HIGH-DOSE-RATE INTERSTITIAL BRACHYTHERAPY FOR UNFAVORABLE GYNECOLOGICAL CANCER: PREDICTIVE FACTORS AND CLINICAL OUTCOME

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Objectives
To determine the role of interstitial high dose-rate brachytherapy (HDR ITB) in the management of high risk gynecological cancer

Methods
Sixty-two patients with cervical (n=24), endometrial (n=22) and vulvovaginal tumors (n=16) were treated with HDR-ITB for recurrent tumor after prior radiation (n=14); Primary cervical cancer unsuitable for intracavitary brachytherapy (n=13); recurrent cervical cancer after prior hysterectomy (n=4); primary endometrial cancer with extensive extrauterine disease (n=3); recurrent endometrial cancer after hysterectomy (n=14); primary or recurrent vulvovaginal cancer (n=14). Unirradiated cases (n=48) were treated with external irradiation (or chemoradiation) and HDR ITB to planned EQD2 doses of 67.6-79.3 Gy, and previously irradiated patients received HDR ITB alone to planned EQD2 doses of 46.7 Gy.

Results
With a median follow-up of 3.7 years (range 0.2-10.0), grade =3 late events were seen in 7.1% and 16.7% of the previously irradiated and unirradiated patients, respectively. Grade =2 bladder events were related to younger age (p=0.014), recurrent status (p=0.025), and 2 cc brachytherapy bladder dose (p=0.017) in multivariate analysis. Grade =2 rectal events were associated with vaginal site (p=0.043) and 2 cc brachytherapy rectal dose (p=0.001) in multivariate analysis. Five-year locoregional control rates in previously irradiated cases and unirradiated cases were 55% and 67.5%, respectively. Locoregional control was inversely related to implant size TV150 (p=0.001) and to brachytherapy EQD2 to CTVD90 (p=0.008) in multivariate analysis. Finally, 5-year overall survival rates in previously irradiated cases and unirradiated cases were 40% and 57%, respectively.

Conclusions
HDR provides durable control with reasonable toxicity in this patient population with an unfavorable prognosis.
HIGH RISK HPV GENOTYPES AND RECURRENCE AFTER CONSERVATIVE SURGERY FOR CERVICAL INTRAEPITHELIAL NEOPLASIA
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Objectives
We investigated which HPV genotype has a risk of recurrence by pre- or post-operative HPV genotyping.

Methods
One hundred twenty five patients with CIN who underwent conization or laser vaporization in our institution between April 2007 and December 2010 were investigated. All the patients were followed-up longer than 6 months. Recurrent disease was defined as histologically confirmed CIN after treatment. HPV genotyping was performed with Genosearch HPV 31® before and 6-12 months after treatment when the Hybrid Capture 2® was positive. Persistent infection was defined as the detection of the same genotype of HPV before and after treatment. Recurrent disease with CIN3 or CIN1, 2 persisting longer than 12 months were re-treated. Written informed consent and approval of institutional review board were obtained.

Results
Median age of patients was 35 (21-51) years old. Conization and laser vaporization was performed on 35 and 90 cases, respectively. Before treatment, HPV was detected in 85.6%, and HPV types 16, 18, 31, 52, and 58 were detected in 47.2%, 4.8%, 7.2%, 13.6%, and 13.6 %, respectively. HPV DNA testing after treatment was positive in 14.4%, and persistent infection was observed in 85.7% of them. The risk of recurrent disease did not correlate with HPV genotypes or multiple HPV infection. Recurrent diseases which needed to be re-treated have persistent infection with HPV 16, 18 or 58 compared with those having persistent infection with other HPV genotypes.

Conclusions
CIN with persistent HPV infection of type 16, 18, and 58 tend to recur after conservative surgery. Therefore, for those CIN, intensive initial management would be recommended.
EXTRAPERITONEAL PARA-AORTIC LYMPHADENECTOMY: SINGLE-PORT LAPAROSCOPY VS CONVENTIONAL LAPAROSCOPY

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Objectives
The aim of our study is to compare both approaches (conventional laparoscopy (CL) versus single-port laparoscopy (SPL)) in an experimented team using extraperitoneal laparoscopic approach.

Methods
From November 2006 to July 2012, extraperitoneal PAL were performed by CL or SPL using Gelpoint device from Applied Medical. The surgical outcomes of the two groups were statistically analyzed.

Results
The study involved 69 patients, 36 underwent PAL with CL and 33 patients underwent PAL with SPL. The mean operative time was 211.2 min (range, 132-390) and 159.6 min (range, 120-255) for CL group and SPL group respectively. The mean blood loss was not significantly different between CL group (52.5 mL; range: 0-100) and SPL group (40.5 mL, range: 0-100, p=0.62). The average lymph node count was lower in the CL set (11.1, range, 4-29) compared to the SPL set (15, range, 3-19) with p=0.03. However, this difference was not confirmed in the multivariate analysis (p=0.16). The mean hospital stay was lower for the SPL group (2.2 days, range: 1-8) compared to the in the CL group (3.1 days, range: 4-29). In this case, the significant difference enhanced in the univariate analysis (p=0.02) was confirmed by the multivariate analysis (p=0.0003). There was no conversion to open and no major complications.

Conclusions
SPL for extraperitoneal PAL appears to be feasible, with equivalent surgical outcomes compared to CL. In this logical evolution of minimal invasive surgery, cosmetic interest and impact on postoperative pain have to be documented in larger series.
IMMUNOHISTOCHEMICAL ANALYSIS OF WWOX EXPRESSION AND ITS ASSOCIATION WITH ANGIOGENESIS, P53 EXPRESSION, CELL PROLIFERATION IN CERVICAL CANCER AND CLINICOPATHOLOGICAL PARAMETERS

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Objectives
The current study evaluated the expression of WWOX and its association with clinicopathological features, p53 expression, cell proliferation (Ki-67) and angiogenesis (CD31 expression) in patients with invasive cervical squamous cell carcinoma (ISCC).

Methods
We prospectively evaluated women with stage IB ISCC (n = 20) (study group) and women with uterine myoma (n = 20) (control group) who were 49.1 ± 1.7 years of age (mean ± SEM, range 27 -78 years). Patients with cervical cancer were submitted to Piver-Rutledge class III radical hysterectomy and pelvic lymphadenectomy. Patients in the control group underwent vaginal hysterectomy. Staining for WWOX, p53, Ki-67 and CD31 was evaluated according to the number of positively stained cells.

Results
WWOX expression was significantly lower in tumor when compared with its expression in benign cervix (p = 0.019) and its expression was not associated with tumor expression of p53 and Ki-67 in patients with invasive carcinoma of the cervix (p = 0.464 and p = 0.360, respectively). Tumor expression of CD31 was significantly associated with WWOX expression (p = 0.018). There was no association between WWOX expression and tumor size (p = 0.156), grade of differentiation (p = 0.914), presence of lymphatic vascular invasion (p = 0.155), parametrium involvement (p = 0.421) or pelvic lymph node metastasis (p = 0.310) in patients with ISCC.

Conclusions
In conclusion, the results suggested that WWOX may be involved in ISCC carcinogenesis and that this marker was associated with tumor angiogenesis.
PROTEIN EXPRESSION AND MUTATIONS OF PTEN IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX
L.F. Loures¹, E.B. Cândido¹, M.A.L. Seabra¹, J.N.M. Gonzaga¹, L.C. Calazans¹, L.D. Matos¹, S.A. Triginelli¹, A.L. Silva-Filho¹
¹Department of Gynecology and Obstetrics of the School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil

Objectives:
The objective of this study was to investigate protein expression and mutations in PTEN in patients with invasive cervical squamous cell carcinoma (ISCC).

Methods:
We prospectively evaluated women with stage IB ISCC of the cervix (n = 20) (study group) and women with uterine myoma (n = 20) (control group) who were 49.1 ± 1.7 years of age (mean ± SEM, range 27-78 years). Patients with cervical cancer were submitted to Piver-Rutledge class III radical hysterectomies and pelvic lymphadenectomies and the control group underwent vaginal hysterectomies. Staining for PTEN, p53, Ki-67 and CD31 was evaluated and all nine PTEN exons were sequenced.

Results:
Our study did not identify any mutations after sequencing all nine PTEN exons. The PTEN expression intensity was lower in the ISCC group than in the benign cervix samples (150.5±5.2 versus 204.2±2.6; p<0.001) (Figures 1 and 2) but was not associated with tumor expression of p53, CD31, Ki-67 or clinicopathologic features. (Table 1)

<table>
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<th>Variables</th>
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<tbody>
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<tr>
<td>G1 and G2</td>
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</tr>
<tr>
<td>G3</td>
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</tr>
<tr>
<td>No</td>
<td>150.2 ± 14.8</td>
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</tr>
<tr>
<td>Yes</td>
<td>163.2 ± 11.1</td>
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<td>No</td>
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<tr>
<td>Yes</td>
<td>152.7 ± 13.2</td>
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</table>

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Conclusions:
PTEN protein was significantly diminished in ISCC compared with the control group. These findings suggest that the loss of PTEN expression plays a role in cervical carcinogenesis.
Poster Presentations: Cervical Cancer

**MORBIDITY OF COMPLETION SURGERY IN 159 LOCALLY ADVANCED CERVICAL CANCER PATIENTS (STAGES IB2 – IVA); RESULTS OF A MULTICENTER STUDY.**

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**Objectives**
The aim of this study was to evaluate the complications of completion surgery after concurrent radiochemotherapy (CRT) in locally advanced cervical cancer.

**Methods**
This retrospective multicenter study included, from 2006 to 2012, 159 patients with a locally advanced cervical cancer. The pre-therapeutic evaluation of node involvement consisted in a PET-CT and/or a surgical stadification. All patients were treated by CRT and evaluated for response by RMI 4 to 6 weeks after the end of CRT. Completion surgery was recommended within 4 weeks of imaging. Surgical morbidity was classified according to the Chassagne grading system.

**Results**
159 patients had completion surgery consisting in a radical hysterectomy in 67.9% of the cases and an extrafascial hysterectomy in 32.1%, realised by laparoscopy in 37.7% of the cases. Residual cervical tumour was found in 45% of the patients. Transfusion concerned 11.9% of the patients with a median of 2.6 blood units transfused. Median length of hospitalization was 6.6 days. No patient was admitted in intensive care unit and there was no death due to surgery. Thirty-eight complications were observed in 33 patients. Details are presented in Table I. Fifteen patients required a new surgery. The radicality or approach of hysterectomy and the presence of residual tumor had no impact on complications. Morbidity rate was lower if surgery was realized more than 8 weeks after CRT (p=0.009).

**Table I:** Complications of completion surgery according to Chassagne grading system.

<table>
<thead>
<tr>
<th>Type and grade of complication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-operative complications</td>
<td>14</td>
<td>8.8</td>
</tr>
<tr>
<td>Grade 1</td>
<td>14</td>
<td>8.8</td>
</tr>
<tr>
<td>Short-term (&lt;1 month) post-operative complications</td>
<td>12</td>
<td>7.5</td>
</tr>
<tr>
<td>Grade 1</td>
<td>5</td>
<td>3.1</td>
</tr>
<tr>
<td>Grade 2</td>
<td>7</td>
<td>4.4</td>
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<tr>
<td>Long-term (&lt;1 month) post-operative complications</td>
<td>12</td>
<td>7.5</td>
</tr>
<tr>
<td>Grade 1</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>Grade 2</td>
<td>6</td>
<td>3.8</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3</td>
<td>1.9</td>
</tr>
</tbody>
</table>

**Conclusions**
Our study shows a relatively low rate of complications of completion surgery after CRT in locally advanced cervical cancers.
AUDIT OF IMAGE GUIDED HIGH DOSE RATE BRACHYTHERAPY FOR CERVICAL CANCER IN NORTHERN IRELAND CANCER CENTRE

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Objectives
Image Guided High Dose Rate (HDR) brachytherapy was introduced in October 2008 in the Northern Ireland Cancer Centre. An audit was carried out to compare prescribed doses to point A and organs at risk (OAR) with standards set out in the Royal College of Radiologists' document 'Implementing image guided brachytherapy for cervix cancer in the UK.'

Methods
Case notes were reviewed of all patients who received HDR brachytherapy for radically treated cervical cancer. Equivalent doses in 2Gy per fraction (EQD2) were calculated for point A and OAR.

Results
138 patients were treated with radical intent with a median age 47.4 years (23.3 - 80.4). Median follow up was 18.3 months. 134/138 had concurrent cisplatin. CT scanning was carried out after each intra-cavity insertion and used to contour OAR and to identify Point A. Median dose to point A EQD2(αβ10) was 76.10Gy (66.5 - 79.3) with 52 patients receiving less than 75Gy. Median dose to rectum was 65.5Gy (57.2 - 82.6), bowel 70.90Gy (55.5 - 79.2) and bladder 80.6Gy (55.1 - 97.8). Pelvic control rate at 3 years was 84%. Disease Free Survival (DFS) and Overall Survival (OS) at 3 years were 76% and 79% respectively. OS of pelvic node positive patients was 62% at 3 years compared to 91% in node negative patients (p=0.002). Grade 3 late toxicity was 6.5%. Repeat MRI in week 5 of radiotherapy was introduced in 2011 and performed in 63 patients, with complete response in 21 (33.3%).

Conclusions
HDR brachytherapy using CT imaging can help to achieve good local control and survival with acceptable toxicity.
Poster Presentations: Cervical Cancer

A TRIAL-BASED ECONOMIC ASSESSMENT OF BEVACIZUAMB AND CHEMOTHERAPY VERSUS CHEMOTHERAPY ALONE FOR ADVANCED CERVICAL CANCER: COST-EFFECTIVE ANALYSIS OF GYNECOLOGIC ONCOLOGY GROUP (GOG) PROTOCOL 240

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Objectives
In a recent randomized trial, bevacizumab increased survival in recurrent/metastatic/persistent cervical cancer. We aimed to assess the cost-effectiveness.

Methods
A Markov model was created using Data 4.0 (TreeAge Pro 2013). The incremental cost-effectiveness ratio (ICER) per year of life saved (YOLS) was estimated using the weight of an average woman. Medicare data for FY 2013 were used to determine the cost of treatment and associated complications.

Results
The median age of the 452 patients in GOG 240 was 47 years. The 3.7 month survival gain (HR 0.71) was not accompanied by deterioration in patient reported outcomes (PRO). Adverse events were those previously reported with bevacizumab: hypertension 2 vs 25%, fistula 0 vs 6%, thromboembolism 1 vs 8%, and bleeding 0 vs 5%. No difference was seen in febrile-neutropenia. Using the reported median number of cycles (chemotherapy, n=6; chemotherapy plus bevacizumab, n=7), the estimated added cost per patient of adding Bevacizumab was $48,330. The cost per grade 2 and 3 hypertension, were $116 and $357 respectively. The cost per grade 3 or higher thromboembolism was $3,947, and the cost of grade 3 and 4 bleeding were $333 and $1,988, respectively. The unadjusted ICER was $157,941 per YOLS.

Conclusions
The cost is primarily related to that of bevacizumab and not related to adverse events or PRO. Although likely to impact PRO, in this trial the costs associated with fistula are unknown. Investigations of dose and cheaper anti-angiogenic agents are needed. Reconciliation of incremental clinical benefits with exponentially rising costs remains problematic.

Poster Presentations: Cervical Cancer
BIOLOGICAL SIGNIFICANCE OF MICRO-RNAs IN HPV&HIV ASSOCIATED CERVICAL CANCER

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Objectives
To identify the most common Human papillomavirus (HPV) sub-types prevalent in Human immunodeficiency virus (HIV) positive patients. Further identify the differentially expressed microRNAs in patients infected with only HIV (Group-I) and both HIV and HPV (Group-II) with respect to their controls. Finally identifying the pathways regulated by these differentially expressed microRNAs using an in silico approach.

Methods
HPV genotyping using Mutiplex PCR and Luminex suspension array technology, microRNA profiling using Affymetrix platform, validation of the differentially expressed microRNAs by Real-time PCR.

Results
Genotyping results from the cervical samples of 600 HIV-patients revealed 44% of HPV positivity, 64% single and 36% multiple HPV sub-type infections. The most predominant sub-types found were HPV-16, 31 and 18. The microRNA array analysis identified 22 differentially expressed microRNAs that most accurately discriminates between Group-I and II. Further 8 microRNAs were found to be involved in various biological pathways.

Conclusions
Results from our study show that HIV disease influences the natural history of HPV by increasing the likelihood of persistent infection. Women with HIV infection have a broader range of HPV infection. Our results also suggest that patients infected with both HIV and HPV have deregulation of microRNAs involved in cell cycle, angiogenesis, apoptosis, immune response and HIV latency. We hope that the results from our study will serve to seed further investigation in understanding the exact roles of these microRNAs in HIV and HPV associated cervical carcinogenesis.
PERIOPERATIVE MORBIDITIES (AND IMPACT ON FURTHER MANAGEMENT) AFTER LAPAROCOPIC PARA-AORTIC LYMPHADENECTOMY BEFORE CHEMORADIOThERAPY IN LOCALLY ADVANCED CERVICAL CANCER: ANALYSIS OF A LARGE PROSPECTIVE MULTICENTER STUDY

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Objectives
The aim of this prospective study conducted in 3 French Comprehensive Cancer Centers was to evaluate the per and postoperative morbidities (and the impact on further management of such complications) of laparoscopic para-aortic (PA) staging surgery in locally advanced cervical cancer (LACC) before chemoradiation therapy (CRT).

Methods
A prospective multicenter series of 237 patients treated from 2004 to 2011 for LACC with negative Positron-Emission-Tomography/PET imaging of the PA area and undergoing laparoscopic PA lymphadenectomy. Peri and postoperative morbidities were collected within the 2 months after the surgery and classified using the Clavien-Dindo classification.

Results
Four (1.7%) patients had peroperative complications (one of them needing a conversion to laparotomy for sigmoid injury). Twenty-five (10.5%) postoperative morbidities were observed (9 Grade II/medical treatment and 14 grade IIIa/radiological drainage). Only 2 patients had postoperative morbidities needing a surgical procedure/grade IIIb (1 trocar hernia and 1 lymphocyst). The most frequent morbidity was lymphocyst (n=16) or retroperitoneal collection (n=2) treated medically (n=3), using a radio-guided (n=14) or surgical drainage (n=1). In only 2 cases, a delay was observed before the initiation of CRT due to morbidity.

Conclusions
The morbidities related to the surgical procedure remain “low” with only one conversion to laparotomy. The most frequent complication was lymphocysts. Only 2 patients had CRT delayed due to morbidity. So this peri and postoperative morbidity remains “acceptable” but this study was done in experienced teams.
Poster Presentations: Cervical Cancer

CYCLOOXYGENASE-2, MYCC GENE AND LYMPHOVASCULAR SPACE INVASION AS THE PROGNOSTIC PARAMETERS OF SURGICALLY TREATED CARCINOMA OF THE UTERINE CERVIX

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²Department of Pathological Oncology, Masaryk Memorial Cancer Institute, Brno, Czech Republic

Objectives
In the Czech Republic the cervical cancer incidence is about 19/100 000 women. Standardised gynaecological oncological therapeutical guidelines are based on ordinary predictive factors. This affords the appropriate space for new, especially biomolecular prognostic factors.

Methods
The aim of our study was the verification of some potentionally interesting biomarkers for the prognosis of patients who underwent surgery. From August 2005 to November 2010, 79 patients with histologically confirmed carcinoma of the uterine cervix treated at the Masaryk Memorial Cancer Institute were included to our study. Except common histopathological parameters, we detected the MYCC genes by FISH method and cyclooxygenase-2 (COX-2) with using immunohistochemical methods.

Results
Based on our results the presence of lymphovascular tumor invasion seems to be powerful parameter predicting disease-free (DFS) and overall survival of patients with cervical cancer. The presence of lymphovascular space invasion seems to be more important than lymph node metastases for clinical decision making. Patients with negative or weak COX-2 expression and the MYCC/centromere ratio below 1,2 attain significantly better DFS compared to the women with high COX-2 expression and the MYCC/centromere ratio 1,2 and higher (p=0,003). A similar result was proven for overall survival.

Conclusions
The incorporation of new biomolecular markers to standard cervical cancer prognostic factors can specify the risk of cancer spreading and predetermine the treatment and follow up in the future. The pilot project was rising by support of Experimental intention Ministry of Health FUNDIN MZ0 MOU2005 and IGA Research Grant Project NT 11089-4/2010.
HYDRONEPHROSIS AFTER SYSTEMATIC NERVE-SPARING PARA-AORTIC LYMPHADENECTOMY (NSPALD) AND NERVE-SPARING RADICAL HYSTERECTOMY (NSRH) IN PATIENTS WITH CERVICAL CANCER EARLY STAGE

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²Gynecologic Oncology Department, Main Military Clinical Hospital named after N.N. Burdenko, Moscow, Russia
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Objectives
To evaluate and compare the incidence of hydronephrosis after systematic para-aortic lymphadenectomy (PAL) and radical hysterectomy (RH) with or without nerves preservation in patients with cervical cancer Ia–Iib stage.

Methods
79 patients who underwent operation between 2006 and 2013 were included in this study. 51 patients of the first group undergoing NSPAL level 2-4 and NSRH III-IV type were compared with 28 patients of the second group undergoing PAL level 2 – 4 and RH III-IV type. All patients had urinary tract ultrasonography 1 month after operation.

Results
Patients of first and second groups were compared. There were significant differences in frequency of hydronephrosis in nerve-sparing group. So, dilatation of renal pelvis more than 20 mm was detected only in 2 patients (3.9%) of the first group and in 9 patients (32.1%) of the second group (p=0.002). 4 patients of second group with hydronephrosis had draining of kidney and no one in first group with hydronephrosis. Dilatation of renal pelvis less than 20 mm had 9 patients (17.6%) of the first group and 2 patients (7.1%) of the second group (p>0.05). Median thickness of renal pelvis dilatation was 13.64±5.4 mm in first group and 22.7±6.1 mm in second group (p=0.001).

Conclusions
The NSPAL with NSRH is associated with decreased incidence of hydronephrosis.
Poster Presentations: Cervical Cancer

OCCULT CERVICAL CANCER AFTER SIMPLE HYSTERECTOMY: SURGERY OR RADIOTHERAPY ONLY?

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Objectives
The purpose of this study is to compare safety and efficiency of radical parametrectomy vs radiotherapy without parametrectomy for patients with occult invasive cervical cancer found after simple hysterectomy.

Methods
This is a retrospective study. We compared the outcomes, follow-up and risk of recurrence between patients who had radical parametrectomy and patients who had only radiotherapy.

Results
We selected 13 patients in surgery group (SG) and 16 in radiotherapy group (RG). There was no significant difference for tumor size in the 2 groups (24.1 mm in SG vs 30.1 mm in RG). Patients in surgery group had systematically pelvic lymphadenectomy and radical parametrectomy and partial colpectomy. We noticed no major complication, no bladder or ureteral injury. 5 (38.5%) patients had adjuvant therapy. In radiotherapy group, after pelvic lymphadenectomy, 2 patients (12.5%) had only pelvic radiotherapy, 5 (31.3%) had only brachytherapy, 5 (31.3%) had pelvic radiotherapy and brachytherapy, 2 (12.5%) had concomitant chemoradiotherapy and 2 (12.5%) had concomitant chemoradiotherapy and brachytherapy. We noticed more recurrences in radiotherapy group than surgery group, 6 (37.5%) vs 1 (7.7%) but the difference wasn’t significant. We noticed too, more deaths in radiotherapy (4 deaths 25%) than surgery group (0%). The median follow-up was similar in the 2 groups with 54 months (3-98) in SG and 52 months (4-138) in RS.

Conclusions
Radical parametrectomy seems to be more successful for the control of occult cervical cancer than radiotherapy without radical parametrectomy. Nevertheless, our study have a small population and so we need more randomized prospective studies with bigger population to have better conclusions.
EFFECTIVENESS OF RADICAL SURGERY AT COMPLETION OF CHEMORADIATION THERAPY FOR LOCAL ADVANCED CERVICAL CANCER

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Objectives
Chemoradiation therapy (CRT) is the usual treatment of locally advanced cervical carcinomas (LACC). A controversy exists as to whether surgery is indicated at completion of CRT. Given the morbidity of this association, we explored the effectiveness of interval radical surgery.

Methods
Patients with IB2-IIB LACC were submitted to CRT after MRI and laparoscopic paraaortic LND. At 45 Gy of CRT, a comparative MRI measured largest tumor diameter's reduction. Radical surgery consisted in type B2 hysterectomy. In group 1, the tumor shrunk by less than 50%, a surgery was indicated. In group 2, the tumor reduced by more than 50% but cervico-vaginal brachytherapy (CVB) was not technically feasible and surgery was performed. Data were prospectively assessed.

Results
From 1998 to 2012, 233 patients fulfilled the criteria. Median follow up was 3 years. 20 patients entered group 1 and 9 patients group 2. The delay between the end of CRT and the surgery was 69 days. No intraoperative morbidity was recorded. 30 days grade 3 morbidity was 3%. Long term grade 3 complications was 6 %. Final pathological results found active tumor in 80% of group1 and 55% of group 2 (p<0,05). In the group 1 and the group 2 respectively, pelvic LND was pN1 in 25% and 0 % (p<0,05); early recurrence rate was 30 % and 11 % (p<0,05); survey was 75 % and 89 % (p<0,05).

Conclusions
Interval radical surgery is feasible with minimal early and late morbidity.

However when CRT seems inefficient enough prognosis seems poor.
MTOR OVEREXPRESSION IS ASSOCIATED WITH RADIO-RESISTANCE IN CERVICAL CANCER

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Objectives
mTOR is an important factor for cell proliferation. It is reported that overexpression of mTOR is correlated with poor prognosis in many cancers. The objective of this study is to investigate the relationship of mTOR overexpression and radio-sensitivity.

Methods
51 patients were examined about mTOR expression by immuno-histochemistry. 38 patients were treated with concurrent chemoradiotherapy, 8 patients were treated with hysterectomy and 2 patient were treated with chemotherapy as main treatment. We examined mTOR expression in cervical cancer and association with clinico pathological findings.

Results
Overexpression of mTOR was recognized in 35(69%) patients. The frequency of parametrial invasion and lymphnode metastasis in mTOR positive and negative were 26/35 (74%) versus 6/16 (38%) (p=0.012) and 18/35 (51%) versus 2/16 (13%) (p=0.008). In 38 cases treated with radiotherapy, mTOR overexpression was seen in 28 cases (74%). Averages of tumor diameter in mTOR positive and negative cases were 4.7cm and 5.0cm respectively (n.s). There were 9 local recurrences, which were all mTOR positive and treated with chemo-radiotherpy including small tumors (0, 3, 3.5cm).

Conclusions
It is suggested that mTOR overexpression promotes lymphnode and parametrial metastasis and is associated with radio-resistance. In case of mTOR overexpression, we need to consider treatment by hysterectomy or usage of mTOR inhibitor at chemo-radiation, and control of mTOR expression is important in treatment of cervical cancer.
PROGNOSTIC VALUE OF PRETREATMENT FDG UPTAKE IN CERVICAL CANCER PATIENTS TREATED WITH DEFINITIVE CHEMORADIOThERAPY

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3Department of Radiation Oncology, Sakarya University, Sakarya, Turkey

Objectives
We analyzed the correlation of 18F-fluorodeoxyglucose (FDG) uptake into primary tumors using the maximum standardized uptake value (SUVmax) and clinicopathological factors of disease.

Methods
The records of 149 patients with biopsy-proven cervical cancer treated with definitive chemoradiotherapy (ChRT) were reviewed. All patients underwent pretreatment FDG PET/CT, and post-therapy FDG PET/CT was performed within a median interval of 4.2 months (range, 3.0–11.2 months) after the completion of ChRT.

Results
The mean SUVmax in patients with lymph node metastasis was significantly higher than that in patients without metastasis (19.7±8.2 vs. 16.4±8.2, respectively; p=0.01). A significant difference existed between tumor size (<4 cm vs. ≥4 cm) and the primary tumor SUVmax (14.7±6.6 vs. 18.7±8.5, respectively; p=0.02). The relationship between primary tumor FDG uptake and survival was evaluated by the cut-off value determined by receiver operating characteristic curve analysis. The area under the curve was 0.901 (p<0.001; 95% confidence interval, 0.848–0.954), and 15.6 was determined as the SUVmax cut-off value. The 4-year actuarial overall survival (OS) and disease-free survival (DFS) for SUVmax<15.6 compared with SUVmax≥15.6 were 85% vs. 34% (p<0.001) and 80% vs. 29%, respectively (p<0.001). In multivariate analysis, age, SUVmax ≥15.6, and lymph node metastasis were independent prognostic factors of OS, and FIGO stage ≥IIB, SUVmax ≥15.6, and lymph node metastasis were significant factors for DFS.

Conclusions
The primary tumor pretreatment SUVmax is correlated with increased tumor size and lymph node involvement at diagnosis, how well the primary tumor responds to treatment, the likelihood of disease recurrence, and OS.
THE DIFFERENT IMPACTS OF OVERALL TREATMENT TIME ON PROGNOSIS IN DEFINITIVE RADIOTHERAPY OR CONCURRENT CHEMORADIOTherAPY FOR CERVICAL CANCer

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Objectives
To investigate the impact of overall treatment time (OTT) on outcomes of definitive radiotherapy (RT) or chemoradiotherapy (CCRT) for cervical cancer.

Materials and Methods:
From September 2001 to December 2010 patients with Stage I-III cervical treated by definitive RT or CCRT were included in this study. The doses of radiotherapy were homogenous by stage with or without CCRT. We analyzed the actuarial rates of cancer-specific survival (CSS), distant metastasis (DM), and local failure (LF) by using Kaplan-Meier curves. Multivariate analyses were carried out with Cox regression models.

Results
OTT> 63 days was a significant factor for CSS for stage IB¹ (p=0.025) and IIB (p=0.015) patients undergoing RT alone. OTT> 63 days was a significant factor for LF for stage IB¹ (p=0.008) and IIB (p=0.069) patients undergoing RT alone. In patients undergoing CCRT, however, OTT> 63 days was not a significant factor for CSS for stage IIB (p=0.869) and IIIB (p=0.901) patients. OTT> 63 days was not a significant factor for LF for stage IIB (p=0.923) and IIIB (p=0.450) patients. Multivariate analyses confirmed OTT effects on CSS (p<0.001) and LF (p=0.001) in RT alone patients but not CCRT patients. OTT> 63 days was not significant for DM in RT alone or CCRT.

Conclusions
We should control OTT within 63 days in cervical patients with RT alone. In CCRT patients, the necessity of strict limitation for OTT may be dependent on patient’s tolerance of CCRT.
**Poster Presentations: Cervical Cancer**

**EFFICACY OF P16 PROTEIN STAINING ON PAP SMEARS WITH ATYPICAL SQUAMOUS CELLS IN PREDICTING HIGH GRADE CERVICAL PATHOLOGY**

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**Objectives**

To evaluate the efficacy of p16 (INK4A) immunostain on cytologies with atypical squamous cell (ASC) for the detection of high-grade cervical lesions.

**Methods**

Medical records of the Pathology Department database from January 2007 to February 2009 were reviewed retrospectively to find out Pap-smears containing ASC (both ASC-US and ASC-H). All these smears were recently followed by cervical biopsies either directly from the suspicious area or colposcopy assisted. A total number of 100 conventional Pap-smears with follow-up biopsies were included in the analysis and all Pap-smear specimen was decolorized and counterstained with P16 (INK4A). Results were compared with available histopathological data.

**Results**

A total number of 21 smears were considered as positive for their immunostaining properties for p16 antibody. 8 of them were in the ASC-US group and remaining 13 were in the ASC-H group.

Clinical performance of P16 positivity to detect CIN2+ lesion (CIN 1, 2, 3 or carcinoma) in ASC cytology was:

- Sensitivity %87.5 (%95 CI:0.5291-0.9776)
- Specificity %84.7 (%95 CI:0.7606-0.9071)

Clinical performance of P16 positivity to detect CIN2+ lesion in ASC-H cytology was:

- Sensitivity % 87.5 (%95 CI:0.5291-0.9776)
- Specificity %68 (%95 CI:0.4601-0.8464)

<table>
<thead>
<tr>
<th>Histopathology of ASC-US</th>
<th>P16</th>
<th>Histopathology of ASC-H</th>
<th>P16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive (65)</td>
<td>1/65</td>
<td>Reactive (14)</td>
<td>1/14</td>
</tr>
<tr>
<td>CIN1 (8)</td>
<td>7/8</td>
<td>CIN1 (5)</td>
<td>5/5</td>
</tr>
<tr>
<td>CIN2+ (0)</td>
<td>-</td>
<td>CIN2+ (8)</td>
<td>7/8</td>
</tr>
<tr>
<td>Carcinoma (0)</td>
<td>-</td>
<td>Carcinoma (0)</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusions**

P16 (INK4A) immunocytochemical staining in conventional Pap smear specimens with ASC cytology might be useful as an adjunct test to predict CIN2+ cervical histology.
CAN ULTRASOUND PREDICT DEEP STROMAL INVASION AND LYMPH NODE INVOLVEMENT IN PATIENTS WITH EARLY STAGE CERVICAL CANCER? A PROSPECTIVE MULTICENTER STUDY ON 2D AND 3D ULTRASOUND

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Objectives
To assess the value of various objective two-dimensional (2D) and three-dimensional (3D) ultrasound parameters in comparison to subjective assessment in the prediction of deep stromal tumor invasion and lymph node involvement in early stage cervical cancer.

Methods
Prospective multi-center trial including 104 women with cervical cancer FIGO IA2-IIB scheduled for surgery, undergoing preoperative ultrasound. The predictive value of various 2D (size, colour score) and 3D ultrasound parameters (volume, vascular indices; VI, VFI, FI) were compared to subjective assessment in diagnosing deep stromal tumor invasion and lymph node involvement.

Results
Ninety nine women underwent radical surgery, in the remaining 5 only pelvic lymphadenectomy was performed due to a positive sentinel node. Women with deep stromal invasion or lymph node involvement had significantly larger tumors (diameter and volume), but there was no correlation to 3D vascular indices. Subjective evaluation of deep stromal invasion was superior (AUC 0.93, sensitivity 90.5%, specificity 97.2%) to any objective measurement, the best being maximal tumor diameter with cut-off 20.5 mm (AUC 0.83, sensitivity 90.5%, specificity 61.1%) and 3D tumor volume with cut-off 9.1 ml (AUC 0.85, sensitivity 79.4%, specificity 83.3%). Increasing maximal tumor diameter cut-off did not improve the identification of women with deep stromal invasion. Both subjective assessment (AUC 0.69, sensitivity 43%, specificity 96%) and objective measurements performed poorly in predicting lymph node involvement.

Conclusions
Subjective evaluation was better than objective measurements, to predict deep stromal invasion. Neither subjective evaluation nor objective parameters were adequate to predict lymph node involvement. Vascular indices were useless in the prediction of advanced disease.
CERVICAL CANCER CD133 POSITIVE CELLS POSSESS TUMOR INITIATING CELLS PROPERTIES

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Objectives
The tumor initiating cells (TICs) hypothesis suggests that tumors are formed from a hierarchy of mixed tumor cells while the TICs bear stem cell-like features, exhibit higher tumorigenicity and are responsible for tumor initiation and relapse. Here, we aimed to identify TICs in cervical cancer.

Methods
We examined the presence of CD133\textsuperscript{+} subpopulation in cervical cancer samples and cell lines. CD133\textsuperscript{+} cells were isolated by magnetic activated cell sorting. The tumor initiating property was examined by tumorspheres formation assays \textit{in vitro} and in SCID mice model \textit{in vivo}.

Results
CD133 was weakly expressed in cervical intraepithelial neoplasia I-III biopsies but the expression was significantly elevated in cervical squamous cell carcinoma (H-scoring, \(p<0.001\)). The tumorspheres formation rate was higher in the CD133\textsuperscript{+} cells than the CD133\textsuperscript{-} cells isolated from fresh cervical cancer biopsies (2.25\% vs 0.25\%) and the tumorspheres size was also significantly larger in the former. Besides, only the CD133\textsuperscript{+} group formed tumor in SCID mice. CD133\textsuperscript{+} subpopulation was also identified in cervical cancer cell lines HeLa, SiHa and C33A. They also displayed higher self-renewal ability than the negative counterparts. The primary tumorspheres from SiHa cells were dissociated to form secondary tumorspheres. These cells took less time to form tumorspheres of size similar to that of the primary tumorspheres (18 vs 35 days). Besides, only 100 SiHa CD133\textsuperscript{+} cells were needed to initiate tumor in SCID mice.

Conclusions
The CD133\textsuperscript{+} cells in cervical cancer possess higher tumorigenicity and our study opens up the possibility of targeting CD133\textsuperscript{+} cells in treating cervical cancer.
LYMPH NODE MAPPING AND SENTINEL NODE DETECTION IN PATIENTS WITH EARLY CERVICAL CANCER (FIGO IA2-IIA1)

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Objectives
To report our preliminary results in lymphatic mapping and value of sentinel lymph nodes (SLNs) in prediction of the pelvic lymph node status in cervical cancer.

Methods
For the detection of SLNs methylene blue is injected intracervically in the operating room prior to surgery, at 4 quadrants of the exocervix and at 4 quadrants on the level of transition of the cervix to vaginal fornices. After identification and excision of SLNs, systematic bilateral pelvic lymphadenectomy and radical hysterectomy is performed.

Results
From December 2011 to April 2013, 22 patients (median age 45) diagnosed with FIGO stage IA2–IIA1 cervical cancer were enrolled in the study (IA2=5, IB1=15, IB2=1, IIA1=1). Sixty eight percent of the patients had squamous cell carcinoma, 23% adenocarcinoma and 9% adenosquamous carcinoma. Intraoperative detection rate was 100%, and SLNs were detected bilaterally in all patients. Total number of 100 SLNs (2.27 per pelvic side), and 521 of non-SLNs (23.7 per patient) were excised. The SLNs were located at the level of common iliac vessels (18%), external iliac vessels (64%), and obturator fossa (36%). Metastatic sentinel nodes were found in 2 patients (9%). We found no positive non-SLNs in the presence of negative SLNs.

Conclusions
Sentinel node detection is a feasible procedure in cervical cancer patients and increases detection rate of lymph node metastases, thus improving nodal staging. Our preliminary results confirm high detection rate of SLNs using blue dye only. This method is less time consuming than radioisotopes detection method and it is easy to perform.
FREQUENCY OF REGRESSION AND PROGRESSION OF LGSIL IN WOMEN WITH POSITIVE HIGH-RISK HPV DNA TEST RESULT

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Objectives
Assessment of frequency of regression and progression of LGSIL in women positive for types of HPV DNA of high oncogenic potential.

Methods
Women diagnosed with low-grade cervical intraepithelial neoplasia were studied from 2008 to 2012 at the Laboratory of Cervical Pathophysiology, Gynecology and Obstetrics Clinical Hospital in Poznan. Patients were observed for a period of one year. Study design included cytology every three months and colposcopy every six months. After 12 months all patients had colposcopy, directed biopsies and liquid based cytology for molecular testing of high oncogenic HPV DNA.

Results
This study confirms the significant effect of age on both regression and progression of low-grade cervical intraepithelial neoplasia.

Conclusions
In the age group below 26 years, complete regression of LGSIL occurs significantly more frequently than in older women. Whereas in the over 36 age group, progression to HGSIL occurred more frequently during 12 months of follow-up.
Poster Presentations: Cervical Cancer

MIR-372 REGULATES ANGIOGENESIS AND VEGF EXPRESSION THROUGH NOVEL TARGET AKT1 IN CERVICAL CANCER CELLS

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Objectives
MiR-372 is an important regulator of multiple cellular processes, and its deregulation is a common event in diverse human diseases, particularly cancer. Recent studies have revealed that miR-372 functions as a tumor suppressor in cervical cancer cells. However, the mechanisms underlying the relationship between disordered miR-372 expression and angiogenesis have remained largely unknown.

Methods
Conditioned mediums were prepared after cervical cancer cell lines transfected with miR-372. Endothelial cell HUVEC proliferation assay, cell cycle assay and migration assay were conducted by MTT, flow cytometry and transwell system, respectively. VEGF mRNA levels were determined by Real-time PCR. The micro-vascular density was determined by CD31-positive vessels. Dual luciferase assay was used to assess whether AKT1 was a direct target of miR-372.

Results
Overexpression of miR-372 in cervical cancer cells resulted in the down-regulation of proliferation and migration of co-cultured endothelial cells and decreased expression of VEGF. Furthermore, using a nude mouse model, miR-372 decreased expression of VEGF and inhibited angiogenesis. Systematic bioinformatics analyses using publicly available algorithms (TargetScan, miRanda, and PicTar) showed a highly conserved binding site for miR-372 in the 3’ un-translated region of human AKT1 mRNA. Dual luciferase activity assay revealed that AKT1 is a direct target of miR-372. Activation of AKT1 signaling restored the miR-372-induced suppression of angiogenesis potential.

Conclusions
This study suggests the novel viewpoint that miR-372 suppresses angiogenesis and VEGF expression in cervical cancer cells through target of AKT1.
INTRODUCTION

Cervical cancer is one of the leading causes of cancer-related deaths in women worldwide, particularly in low- and middle-income countries. Early detection and effective treatment are crucial to improve outcomes. HPV infection is a major risk factor for cervical cancer, and understanding its distribution and type can help in the development of targeted interventions.

OBJECTIVE

This study aimed to compare the frequency and type distribution of HPV in Brazilian women with cervical lesions, specifically focusing on single and multiple infections.

METHODS

A cohort of 409 women was enrolled based on cervical HPV-induced lesions, undergoing colposcopy and cervical biopsy. HPV-DNA was amplified using the PGMY09/11 primers, and genotyping was performed with reverse line blot hybridization, using 21 high-risk and 10 low-risk HPV probes. Histologic specimens were classified into different categories.

RESULTS

The final diagnoses included CIN 1 in 82 cases (20%), CIN 2/3 in 320 (54%), squamous invasive carcinoma 3 (0.7%), in situ adenocarcinoma 13 (3.1%), and invasive adenocarcinoma 10 (2.4%). Single infections were found in 153 samples (37.4%) and multiple infections in 162 (39.6%). High-risk genotypes were most frequently detected, with HPV 16 in single infections (15.1%) and multiple infections (21.1%), HPV 31 in single infections (3.1%) and multiple infections (7.3%), and HPV 52 in single infections (2.6%) and multiple infections (6.3%). HPV 18 was isolated in only 6 cases and was more frequently found as a multiple infection. Women with CIN 2 or worse were more likely to have multiple HPV infections compared to those with glandular lesions.

CONCLUSIONS

In this series, squamous lesions were more frequently associated with multiple HPV infections than glandular lesions.
Poster Presentations: Cervical Cancer

LAPAROSCOPIC LYMPHADENECTOMY IN ADVANCED CERVICAL CANCER: PROGNOSTIC AND THERAPEUTIC VALUE

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Objectives
To analyze the prognostic and therapeutic value of laparoscopic paraaortic lymphadenectomy and selective excision of suspicious pelvic nodes in patients with locally advanced cervical cancer.

Methods
Retrospective study including 109 women treated in a single institution from 2000 to 2009. FIGO stage was Ib2 in 12 women, IIb in 58 and IIIb in 39. None had suspicious paraaortic nodes by pre-surgical imaging evaluation. All patients underwent extraperitoneal paraaortic laparoscopic lymphadenectomy with selective excision of enlarged pelvic nodes and received pelvic radiotherapy with concomitant chemotherapy. Extended lumboaortic radiation therapy was added to patients with metastatic paraaortic nodes. The mean follow-up was 43.1 ± 33.7 months.

Results
Metastatic lymph nodes were identified in 23/109 (21.1%) patients in the paraaortic area and in 24/45 (53.3%) patients who underwent selective excision of pelvic nodes. Patients with nodal metastases had increased risk of mortality than those with negative nodes, independently of the location (pelvic and/or paraaortic) of the metastases (hazard ratio: 4.07; 95%CI: 1.36-12.16 for patients with pelvic; p=0.012, and 3.73; 95%CI 1.38-10.09 for patients with paraaortic metastases; p=0.010). In the subset of women with paraaortic metastases treated by extended lumboaortic radiation therapy, neither the number of lymph nodes removed nor the number of positive nodes were associated with survival (p=0.556 and 0.195 respectively).

Conclusions
Paraaortic and pelvic lymphadenectomy provides valuable information about mortality risk in patients with locally advanced cervical cancer. The radicality of lymphadenectomy and lumboaortic radiation therapy in patients with positive paraaortic nodes does not show significant therapeutic benefits.
SURVIVIN EXPRESSION IN LOCALLY ADVANCED CERVICAL CANCER (LACC) PATIENTS ADMINISTERED NEOADJUVANT CHEMORADIATION (CT/RT): PREDICTION OF RESPONSE AND CLINICAL OUTCOME

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Objectives
We investigated the correlation between pathologic response to chemoradiation (CT/RT), and the immunohistochemically assessed expression of survivin protein in 71 locally advanced cervical cancer (LACC) patients treated with chemoradiation (CT/RT), followed by radical surgery. The prognostic role of survivin expression has been also evaluated.

Methods
Immunohistochemical analysis of survivin expression was carried out by using the polyclonal rabbit anti-survivin antibody (Novus Biological, Inc., Littleton).

Results
Survivin immunoreaction was observed in 69/71 cases (97.2%), with median survivin expression levels of 160 (0-280). Higher survivin levels were observed in patients with residual disease in the cervix ≥3mm (survivin levels=160 versus 120; p-value=0.016), and in women with metastatic lymph nodes (survivin levels=160 versus 150; p-value=0.032). In multivariate analysis, high survivin levels were confirmed as independent predictive factors of large residual disease in the cervix and metastatic lymph nodes. During a very long follow-up period of 83 months (8-175), recurrences occurred in 24 (33.8%) women, and all cases died of disease. Patents with high survivin experienced a shorter disease free survival (5-year DFS=80.8%) compared to women with low survivin levels (5-year DFS=55.3%) (p value=0.033). Only a trend was observed for overall survival (5-year OS: high survivin levels=81.0% versus low survivin levels=55.3%, p value=0.069).

Conclusions
The immunohistochemical assessment of survivin at diagnosis can represent a reliable and easily assessable tool to predict response to treatment in LACC submitted to preoperative CT/RT.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Poster Presentations: Cervical Cancer

PI3K MUTATIONS AND POOR RESPONSE TO STANDARD CHEMO-RADIOThERAPY IN CERVICAL CANCER. DATA FROM A PHASE 2B TRIAL, TO ASSESS EFFICACY AND TOLERANCE TO CETUXIMAB.


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7 Oncology, Institut F Baclesse, Caen, France
8 Oncology, Centre Godinot, Reims, France
9 Oncology, Alexis Vautrin, Nantes, France
10 Oncology, ICO, Nantes, France
11 Radiotherapy, P Calmette, Marseille, France
12 Radiotherapy, C Regaud, Toulouse, France
13 Oncogenetics, Institut Cure, Paris, France
14 Clinical Research, Institut Cure, Paris, France
15 Surgery, Institut Cure, Paris, France
16 Pathology, Institut Cure, Paris, France
17 Statistics, Institut Cure, Paris, France
18 Biomedical Research, Institut Cure, Paris, France

Objectives:
Objectives were 1° to assess tolerance and efficacy (CR and DFS) of Cetuximab in association with standard chemo radiotherapy in primary cervical cancer patients with pelvic only disease; 2° to collect fixed/frozen tumor material for biological assessments.

Methods:
78 patients from 11 French centers were randomized into standard therapy (ST) or ST combined with 6 weekly injections of Cetuximab. Response evaluation was by MRI and/or pathology. The population has been previously described (ASCO 2012). Median follow-up is >2 years.

Results:
There was no difference in demographics or treatment dose/duration between both populations. Tolerance was satisfactory according to DSMB. Durable grade 4 toxicities were more frequent in arm A (p=0.04). Following central review, a CR (by MRI or pathology) was documented for 21/31 patients in arm A and 23/35 patients in arm B. DFS was not significantly different between both treatment arms. While mutations (present in 21%; n= 45) were evenly distributed in both treatment arms, there was a strong interaction between mutational status and absence of response (p=0.01). None of the responding patients’ tumors harbored a PI3K (+/-Kras) mutation. There was a trend between the presence of mutations and a poorer DFS (p=0.086) and this appears more significant in the Cetuximab treatment arm (p=0.001). EGFR expression (IHC) did not seem to influence outcome.
Conclusions:
Our results point to PI3KCA mutations as a predictive factor for poor response and poor outcome following standard therapy and following Cetuximab. Mutational impact on response to EGFR inhibition requires further validation in larger patient groups.
Poster Presentations: Cervical Cancer

THE VALUE OF PRE-THERAPEUTIC PARA-AORTIC LYMPH-NODE DISSECTION IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER – A COMPARISON TO PET-CT

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Objectives
The aim of the present study was to investigate the results of a gynaecological cancer centre in Austria regarding the feasibility and detection rate of a surgical staging of para-aortic lymph nodes in patients with locally advanced cervical cancer compared to a radiologic staging with PET-CT.

Methods
We retrospectively collected the data of all patients with locally advanced cervical cancer who had surgical and radiologic staging of the para-aortic lymph nodes prior to chemoradiation therapy at our department within the years 2010 to 2012. We evaluated the surgical outcome and compared the histological results to the results of the PET-CT concerning the detection of para-aortic lymph node metastases.

Results
We included 30 patients into analyses. In 21 patients laparoscopic procedures, in 9 patients laparotomies were performed. No surgical related morbidity grade 2/3 occurred. The laparoscopic procedure was associated with a significantly shorter post-operative hospital stay compared to the laparotomy (respectively 4.1 vs. 8.5 days, \( p=0.001 \)). In 30% of the patients para-aortic lymph node metastases were diagnosed. The true-positive rate of PET-CT was 100%. Nevertheless, PET-CT showed a sensitivity of 66% and a negative predictive value of 85% only.

Conclusions
The para-aortic lymph node dissection prior to chemoradiation therapy in patients with locally advanced cervical cancer can be regarded as a procedure with a low morbidity rate. Compared to a radiologic staging with PET-CT alone in one third of the patients the para-aortic lymph node dissection provides additional information that has a crucial impact on further treatment.
Poster Presentations: Cervical Cancer

A PROSPECTIVE 212 CASES STUDY OF SENTINEL LYMPH NODE BIOPSY FOR ASSESSING THE PELVIC NODAL STATUS IN EARLY-STAGE CERVICAL CANCER

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Objectives
The aim of this study was to study the patterns of lymphatic spread to pelvic lymph nodes and analyze the clinical significance of sentinel lymph node technique for assessing the nodal status in early-stage cervical cancer.

Methods
Between January 2003 and January 2010, 212 patients with early-stage cervical cancer underwent sentinel node biopsy based on combined Methylthioninium chloride and 99mTc labeled sulfur colloid detection. The detection rates, accuracy, false-negative rates and limitations of sentinel lymph node biopsy were studied.

Results
The total detection rate of SLN was 96.7%(205/212). The most common site was obturator followed with external iliac area and parametrial area. SLN detection rate had been significant correlation with patient’s tumor size, invasion depth and FIGO stage. The unilateral SLN detection rate increased significantly in locally advanced patients. 63 positive SLNs were detected in 45 patients, the rate of lymph nodes metastasis in patients with unilateral SLN detection was significantly higher than that in bilateral SN detection. The sensitivity, negative predictive value and coincidence rate was 93.8%, 98.1% and 98.6% respectively. The false negative rate was 6.3%.

Conclusions
SLN biopsy is an accurate procedure to assess pelvic lymph node status in most patients with early-cervical cancer, but in locally advanced (tumor>4cm) and unilateral SLN detected patients its reliability need further evaluation. In these patients, SLN biopsy cannot substitute for systematic lymphadenectomy.
Poster Presentations: Cervical Cancer

PRODUCTION AND CONSUMPTION OF LACTATE IS RELATED TO THE HISTOLOGICAL TYPE IN UTERINE CERVIX CARCINOMAS

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Objectives
Metabolism is considered a hallmark for cancer. In uterine cervix, lactate-rich microenvironment may play a role in cancer cells selection. Monocarboxylate transporter 1 (MCT1), may be a key element defining lactate metabolism (consumption and/or production) and can be a therapeutic target. The aim of this work is to evaluate lactate metabolism in adenocarcinoma (AC) and squamous cell carcinoma (SCC) of uterine cervix.

Methods
We used AC cell line – HeLa – and SCC cell line – SiHa – in in vitro studies. MCT1 expression was evaluated in tissue arrays from AC and SCC. Cell metabolism was evaluated by nuclear magnetic resonance (NMR) in cells cultured with [¹³C]glucose and [¹³C]lactate. MCT1 mRNA and protein levels were evaluated, respectively by RQ-PCR and immunofluorescence in the presence and absence of lactate. c-Myc and STAT3 association with MCT1 promoter was achieved by chromatin immunoprecipitation (ChIP). c-Myc copy number was determined by fluorescent in-situ hybridization (FISH). In tissue arrays, MCT1 was detected by immunohistochemistry.

Results
SiHa uptakes and synthesizes aminoacids and fatty acids, equally from lactate and glucose. HeLa barely uptakes lactate and glucose is mainly converted into lactate. MCT1 is upregulated by lactate in SiHa in a c-Myc and STAT3 independent manner. HeLa exhibit c-Myc gene amplification and express low MCT1 levels, being decreased by lactate in a c-Myc dependent manner. MCT1 was expressed in 77% of SCC and 17% of AC.

Conclusions
Lactate metabolism is related to histological type – SCC consumes and AC produces. MCT1 seems to determine the ability to consume lactate in SCC therefore MCT1 can be a suitable therapeutic target.
High false negativity rate of frozen section examination of sentinel nodes in cervical cancer patients

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Objectives:
The intention of the sentinel lymph node (SN) assessment is to predict the status of all draining nodes. Metastatic involvement of the SN is one of the main prognostic factors in cervical cancer which determines the disease management. The results of intra-operative SN examination would allow for triaging the patients in one-step protocol, however, inadequate accuracy of frozen section (FS) has been shown in small cohorts.

Methods:
Study included 225 patients with cervical cancer FIGO IA2 – IIB in whom at least one SN has been detected and intra-operatively processed. The prevalence of macrometastases, micrometastases and isolated tumour cells (ITC) in the SN was evaluated and results of FS and final SN ultrastaging were compared. Parameters which could influence FS sensitivity have been analyzed.

Results:
Metastatic involvement of the SN was detected by pathologic ultrastaging in 73 cases (32.4%), macrometastases, micrometastases and ITC in 48, 17 and 8 patients, respectively. Intra-operative SN assessment correctly established the SN status only in 41 cases (56.2%). Final ultrastaging of intra-operatively negative SN confirmed macrometastasis, micrometastasis and ITC in additional 8, 18 and 8 patients, respectively. False negative rate of FS was higher in bigger tumors (>20 cm^3) and in the presence of LVSI.

Conclusions:
Frozen section examination of SN is not reliable, with high false negative rate mainly due to its limited ability to detect LVD. Two-step surgical management based on results of final ultrastaging is highly advisable if standard pathologic processing is used intra-operatively.
THE ABDOMINAL RADICAL TRACHELECTOMY SPARING THE UTERINE ARTERIES (A.R.T.- S.U.A) IN CERVICAL CANCER (CC): ONCOLOGICAL OUTCOMES & FOLLOW UP OF THIS NOVEL SURGICAL TECHNIQUE.

**Objectives**
To present the oncological outcomes in terms of overall survival (O.S) and Disease free interval (DFS) of the Abdominal Radical Trachelectomy Sparing the Uterine Arteries & Pelvic Autonomic Plexus (A.R.T.- S.U.A.-P.P.A.P.) surgical technique in cervical cancer.

**Methods**
Technique designed for FIGO stages Ia2, Ib1 CC < 2cm; the >2 and <3cm, received Platinum based neoadjuvant chemotherapy (NCH). Between 10/04 - 10/12, 21 pts. were included, by the intention to treat. The oncological outcomes, age, surgical feasibility, radicality, measured in the surgical specimen, and compared with radicality of an Historical group of C1 RH; hystological type; blood loss, uterine blood flow evaluated by color doppler ultrasound; operating time; mean hospitalization time; complications; recurrences; pregnancies and follow up were also analyzed.

**Results**
The technique was performed in 20/21 the cases. Age: 27 years (21-32). Five pts. received NCH. Radicality (surgical specimen): No differences were found in radicality with C1 RH. Blood loss: 600 ml. Operating time: 180 minutes. Bladder catheterization: 48 hs. Postmicturition residual volume: < 50 ml. Normal indices of doppler blood flow. Mean Hospitalization time: 4 days.

**Complications:** 1 case of dyspareunia + cervical poliposis. 1 case of dysmenorrhea. One pregnancy observed, ending in an abortion at the 3rd month. Recurrences: 2/20 (10%), submitted to chemorradiation (CHRt). Deaths: (2/20-10%) DFS & O.S: 90%. Follow-up: 56 months (12–100).

**Conclusions**
The ART-SUA-PPAP was feasible, and oncologically safe. It could be taken into account as treatment for the IA2-Ib1 cervical cancer. A large number of cases series, and randomized trials are needed to valid these results.
Poster Presentations: Cervical Cancer

CLINICOPATHOLOGICAL OR PROGNOSTIC IMPLICATIONS OF CERVICAL CANCER NEGATIVE FOR HYBRID CAPTURE TEST

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Objectives

Human papillomavirus (HPV) is a necessary cause of cervical cancer (CC). However, in some CCs no HPV is detected by common screening tests. We aimed to assess the characteristics of HPV-negative CC.

Methods

Among 137 patients with CC and pre-treatment HPV detection using Hybrid Capture2 (HC2) diagnosed between 1999 and 2012, tumors negative for HC2 (n=15;10.9%) were selected. Formalin-fixed paraffin-embedded tumor tissue from all cases was genotyped for HPV using different PCR assays (SPF10, GP5+/6+ and E7) which detect 39 HPV types (low and high-risk). Age, smoking habit, immunosupression, histology, FIGO staging, nodal status, p16INK4a immunostaining, recurrence and survival of HC2-negative CC were compared with HC2-positive CC (control group; n=122).

Results

PCR analysis detected HPV in 6/15 (40%) of the HC2-negative CC: HPV16 in two cases, and HPV11, HPV18, HPV45 and HPV68 in one case each. In 9 specimens no HPV was detected. HPV negativity was more frequent in adenocarcinomas than in squamous cell carcinomas. All tumors except one were p16INK4a positive. FIGO stage at diagnosis was more advanced in HC2-negative CC (Table1). No additional differences in clinicopathological characteristics or survival were found.

<table>
<thead>
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<th>HC2-negative</th>
<th>HC2-positive</th>
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<tr>
<td>n=15</td>
<td>n=122</td>
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<tr>
<td>Histology</td>
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<tr>
<td>Squamous cell carcinoma</td>
<td>53.3%</td>
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<td>Ia-Ib1</td>
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<td>Survival(months)</td>
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</tr>
</tbody>
</table>

Conclusions

Common HPV types are identified in 40% of the HC2-negative CCs. HC2 negativity is more frequent in adenocarcinomas. FIGO staging is higher in HC2-negative cases but does not seem to have prognostic implications.
RESULTS OF THE TREATMENT FOR CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) IN WOMEN AGED 65 YEARS OR MORE
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Objectives
To compare the results after the treatment of CIN lesions in women older and younger than 65y.

Methods
Retrospective and comparative study including 176 women under 65 years and 88 women older than 65y who underwent a conization between 1995 and 2012 in Hospital Vall d'Hebron. We review the epidemiologic data, treatment indications, cone biopsies results and relapses after treatment.

Results
Between 1995-2012, 2864 conizations were performed in our hospital, of which 88 (3%) were to women older than 65 years. The median follow up time was 28 months in both groups.

CIN3 was the indication for conization in 39% of the older patients and in 18% of the younger patients (p<0.01).

The postconization endocervical curettage was positive for residual CIN in 13% of the older patients, compared to 5% in the younger ones (p<0.01).

Cone biopsies in older patients diagnosed occult carcinoma in 12 cases (13.68%) and adenocarcinoma in one case (1.13%). In younger patients, occult carcinoma was detected in 9 cases (5.11%). The incidence of occult carcinoma in the older group was significantly higher (p<0.01).

Relapses as high grade lesions were detected in 7.27% of the treated patients older than 65y and only in 2.3% of the younger patients. In hysterectomized patients, vaginal recurrence as VaIN 2+ was detected in 28.5% in older patients, compared to 11% in younger patients.

Conclusions
Elderly patients have more severe cervical lesions, higher incidence of occult carcinoma in cone specimens and more recurrences of high grade lesions after the treatment.
SURVIVAL RATE OF PATIENTS WITH CERVICAL CANCER AT USE OF A COMBINATION OF CHEMICAL RADIOMODIFICATORS AND RADICAL IRRADIATION

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The aim
Find survival rate of patients with cervical cancer (CC) at use of a combination of COX-2 inhibitors (diclofenac, ketoprofen) with small doses of cytostatics (methotrexate, 5-fluorouracil) against radical radiation therapy (RT).

Material and methods
Studied the results of treatment of 120 patients with CC with FIGO stages IIA-IIIB, divided into groups:
- basic group 1 (n=40): the patients who have received RT with intratumoral introduction of diclofenac (3.0ml, through the day, ?5) and per oral reception of low doses of methotrexate (2.5mg, 1 times a day, ?25);
- basic group 2 (n=40): the patients who have received RT with intratumoral introduction of small doses of 5-Fu (250mg, through the day, ?5) and per oral reception of ketoprofen (50mg, 2 times a day, ?25);
- control group (n=40): the patients who have received RT by traditional methods, without radiomodifiers.

Results
Criteria of efficiency of treatment was three-year survival rate (overall and disease-free survival). Three-year survival rate of patients in the basic groups were 87.3±5.3% (1-group) and 88.5±7.0% (2-group), which was higher at 12.3% and 13.5% respectively than of the standard RT treatment results in the control group (75.0±6.8%), ?<0.05. Three-year recurrence-free survival rate of patients in basic groups - 70.8±10.9% (1-group) and 80.4±7.9% (2-group) was higher than the result of control group (65.0±7.5%), ?<0.05.

Conclusions
The use of a combination of chemical radiomodifiers (COX-2 inhibitors with low doses of cytostatics) against radical irradiation improved three-year survival rate of CC patients in basic group.
EFFECT OF AGE ON THE SURVIVALS OF CERVICAL CANCER PATIENTS WITH BONE METASTASIS.

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Objectives
To determine survivals of cervical cancer patients with bone metastasis relating with effect of age at the time of cervical cancer diagnosis.

Methods
A retrospective analytic study. Setting: Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. Sample: During January 1998 to December 2010, a total of 68 cervical cancer patients with bone metastasis were treated at Ramathibodi hospital. Fifty-two medical records were identified and collected, the remaining sixteen medical records were not found. Main outcome measures: Patient characteristics, clinical information, duration from cervical cancer diagnosis to bone metastasis diagnosis, survival time after bone metastasis and overall survival time.

Results
Among fifty-two cervical cancer patients with bone metastasis, there were 13 patients who were less than 45 years old, and 39 patients were 45 years old or more at the time of cervical cancer diagnosis. The younger group had less median overall survival than the elder group with statistically significant difference (21 months, 95%CI 19.93-22.06; 34 months, 95%CI 23.27-44.72, p< 0.021). However, there were comparable in the duration from cervical cancer diagnosis to bone metastasis diagnosis and the survival time after bone metastasis.

Conclusions
Young patients with bone metastasis aged less than 45 years old at the time of cervical cancer diagnosis had poorer prognosis than the elders. To improve survivals and quality of life, more intensive treatments at the time of cervical cancer diagnosis in the young patients who could tolerate the side effects should be considered.
Poster Presentations: Cervical Cancer

CHEMORADIOTHERAPY WITH GEMCITABIN AND CISPLATIN FOR LOCALLY ADVANCED CERVICAL CANCER: RESULTS OF TOXICITIES AND RESPONSE

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Purpose
To evaluate response rate, acute toxicities of concurrent chemoradiation (CCRT) for locally advanced cervical cancer.

Methods and materials
From 2011 to 2013, 27 patients with stage IIB-IIIB cervical cancer were treated by CCRT (mean age: 49 years old; Stage IIB – 15 (55,6%), IIIA – 3 (11,1%), IIIB – 9 patients (33,3%)). EBRT consisted of 44-46 Gy/22-23 fractions to the whole pelvis, by Cobalt 60 machine, followed by high dose rate brachytherapy 5,5 - 7Gy/fraction/weekly in 4 – 5 fractions. Chemotherapy with Gemcitabin 125mg/m2 and Cisplatin 40mg/m2/weekly for 4-6 cycles started on the first day of EBRT.

Results
Grade 2-3 neutropenia was 33.3%. 7 cases (26 %) had renal toxicity (grade 1 - 6 cases, grade 2 - 1 case). 18 patients (67%) had enterocolitis (grade 1- 8 cases (44,4%), grade 2 - 9 cases (50%), grade 3- 1 patient).

Mean overall treatment time was 53 days. The overall response rate was 96,2% (complete response: 77.7%; partial response: 18,5%).

All patients were followed up more than 8 months. Treatment failures developed in 5 cases (18,5%) (local recurrences: 3 cases; distant metastases: 1 case; both local recurrence and distant metastasis: 1 case).

Conclusions
Response rate for CCRT with Cisplatin and Gemcitabin is high, followed with relatively high hematologic and gastrointestinal toxicity but tolerable, not prolong overall duration of treatment.
SURVIVAL ANALYSIS OF LAPAROSCOPIC TOTAL RADICAL HYSTERECTOMY COMPARED TO OPEN RADICAL HYSTERECTOMY IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER

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Objectives:
To compare survival outcomes of laparoscopic total radical hysterectomy (LTRH) vs. open radical hysterectomy (ORH) in patients with early-stage (IA2-IB1) cervical cancer (CC).

Methods:
A single tertiary-center, retrospective analysis was conducted in a total of 68 CC patients who surgically treated with LTRH (n=22) or ORH (n=46) between January 2007 and August 2010. The primary endpoint of the study was overall survival (OS).

Results:
Median follow-up time was 42.5 months (IQR 38.40 - 55.42) for LTRH group, and 43.50 months (IQR 37.66 - 52.65) for ORH group. There were some statistically significant differences according to stage (IB1), tumour size (≥2 cm), and depth of stromal invasion (≥33%) in favour of ORH group. Despite this, the logistic regression analysis revealed no relationship between these factors and progression or death. Then we performed Kaplan-Meier analysis for survival rates in each group. In LTRH group, 3 cases recurred, and received radiotherapy for relapse. These are alive with disease (AWD). In ORH group 5 cases recurred. 2 of 5 died of disease, and 3 of 5 recurred cases are AWD. The estimated 3-year OS (100% vs. 95.4%, P=0.82) and progression-free survival (86.1% vs. 90.6%, P=0.32) did not differ between LTRH and ORH groups.

Conclusions:
LTRH was associated with similar survival outcomes compared to ORH.
GLYCAN PROFILING USING FORMALIN-FIXED, PARAFFIN-EMBEDDED TISSUES: HIPPEASTRUM HYBRID LECTIN IS A SENSITIVE BIOMARKER FOR SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX

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Objectives
Cervical cancer is an aggressive malignancy for which useful diagnostic markers are not presently available. Altered protein glycosylation is a universal feature of cancer cells. Distinctive glycan structures are associated with specific types of cancer, but little is known about the complete glycan profile of each tumor and progress has been hindered by a lack of available techniques.

Methods
In this study, a lectin microarray that contained 45 lectins with different binding preferences covering N- and O-linked glycans was coupled with evanescent field activated fluorescent detection for glycomic analysis of squamous cell carcinoma of the cervix and normal squamous cervical epithelium. Formalin-fixed, paraffin-embedded tumor and non-tumor tissues were obtained from 16 patients with cervical cancer. Sections (1.5 mm in diameter and 10 mm thick) that included both tumor and non-tumor tissues were examined to detect alterations of glycans from the lectin-binding patterns.

Results
As a result, we found that Hippeastrum hybrid lectin was the best marker for distinguishing cervical cancer from normal squamous epithelium. Histochemistry confirmed specific staining of squamous cell carcinoma by Hippeastrum hybrid lectin in the 16 tissue specimens.

Conclusions
In conclusion, this lectin microarray technique could be applied to tissue-based glycomic analysis and discovery of glycan-related biomarkers.
PROGNOSTIC FACTORS FOR CERVICAL CANCER TREATED WITH NEOADJUVANT TRANS-UTERINE ARTERIAL CHEMOTHERAPY: A SINGLE-INSTITUTION STUDY

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Objectives
This study aimed to determine the prognostic factors associated with neoadjuvant trans-uterine arterial chemotherapy (TUAC) followed by type III radical hysterectomy (RH).

Methods
Medical histories of patients with stage IB2–IIB cervical cancer who received neoadjuvant TUAC between 1996 and 2009 at our institution were retrospectively reviewed.

Results
Seventy-three patients received TUAC using cisplatin combined with intravenous nedaplatin, irinotecan, paclitaxel, or etoposide administration. Forty-seven patients (64%) had squamous cell carcinoma (SCC). The radiological response rate was 96% (95% confidence interval [CI]: 91–100%). RH was completed in 95% of enrolled patients. Examination of the surgically obtained cervical specimens showed that tumor cells were absent in 19 cases and stromal invasion was <3 mm in 7 cases. Among those 26 patients, 23 (32%) had pathologically negative pelvic lymph nodes and no recurrence during the follow-up period. The 5-year relapse-free survival (RFS) and overall survival (OS) rates were 71% and 74%, respectively. Among 21 patients with recurrence or progressive disease, the median survival time after recurrence or progression (post-progression survival, PPS) was 293 days. Although RFS, OS, and PPS seemed favorable for SCC patients, a log-rank test showed no statistically significant differences. In multivariate analysis, a tumor size of >60 mm and pathological positive lymph nodes were negative prognostic factors for OS.

Conclusions
Tumor size was a prognostic factor for cervical cancer outcomes. The pathological response was associated with prolonged disease-free survival, and the high pathological response rate using TUAC is promising for the treatment of bulky stage cervical cancer.
LOCAL RECURRENCE AFTER NERVE SPARING RADICAL HYSTERECTOMY FOR STAGE IA2 - IIA CERVICAL CARCINOMA: PROSPECTIVE COMPARISON OF 2 SURGICAL TECHNIQUES.

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Objectives
Damage to the pelvic autonomic nerves has been suggested to cause bladder, bowel and sexual dysfunction after radical hysterectomy. In 2001 we developed a nerve sparing modification of the conventional RH: the Leiden Nerve Sparing Radical Hysterectomy (LNSRH). In 2006 we adapted the LNSRH according to a new hypothesis which suggests that local tumour spread primarily occurs in tissue from the same embryologic origin: the morphogenetic-unit. With the Swift-procedure, a modification of the LNSRH, the complete morphogenetic-unit of the cervix is removed. The aim of this study is to compare short term outcome after the LNSRH and the Swift-procedure.

Methods
A prospective cohort study comparing local recurrence rate and overall survival after 2 years (LRR and 2 years OS) of women after the LNSRH (January 1st 2001 – December 31st 2005) and the Swift-procedure (January 1st 2006 – December 31st 2010) due to FIGO 1A2-IIA cervical carcinoma.

Results
119 and 92 women were included in the LNSRH and Swift-cohort respectively. Histologic sub-type, invasion depth and lymph vascular space infiltration did not differ between the cohorts. LRR was 8.4% (95% CI 4.0-14.6) vs 8.7% (95% CI 3.8-16.4) in the LNSRH and Swift cohort (p = 1.0) respectively. The 2 years OS did not differ between the LNSRH and Swift-cohorts: 89.1% (95% CI: 82.0-94.1) vs 90.4% (95% CI: 82.6-95.5) respectively (p = 0.75).

Conclusions
Removal of the complete morphogenetic unit of the cervix in nerve sparing radical hysterectomy did not improve short term oncological outcome in this comparative prospective cohort study.
NEO-ADJUVANT CHEMORADIATION FOR LOCALLY ADVANCED CERVICAL CANCER: A PROMISING REPORT ON OUTCOME.

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Objectives
To report on outcome after neo-adjuvant chemoradiation for locally advanced cervical cancer (LACC).

Methods
Forty-nine patients with LACC were treated (Figo IB2: n=3; II: n=33; III: n=9; IV: n=4). Chemotherapy = weekly cisplatin (40mg/m²). Radiation consisted of an intensity-modulated arc therapy delivered in 25 fractions. No neo-adjuvant brachytherapeutic treatment was performed. Dose prescription was 62 Gy and 60 Gy (Dmed) to the primary tumour and PET/CT-positive lymph nodes; 45 Gy (minimal dose) to the uterus, cervix, upper vaginal 1/3 to ½, parametria and pelvic lymph nodes. Para-aortic irradiation was performed if N+. Six weeks after, a hysterectomy was performed. Suspected lymph nodes were resected selectively. Radiotherapeutic and surgical feasibility and the low morbidity/toxicity rates have been published (Vandecasteele et al.; Tummers et al.).

Results
Median FU is 29 months (4-81m). Median age at diagnosis was 53y (21-81). Pathologic complete response rate is 37%. Surgical margins were free of disease in all but 2 cases (a brachytherapeutic boost was performed). Two- and 5-year local control rates are 95% and 91%. Two patients relapsed in pelvic lymph nodes (95% 2- and 5-year regional control). Two- and 5-year distant metastasis free survival is 95% and 91%. Two- and 5-year disease-specific survival are both 89%. Two- and 5-year OS are 84% and 66% (5/9 deaths were not cervical cancer related).

Conclusions
Neo-adjuvant chemoradiation using modern radiotherapy techniques leads to promising control and survival rates. Further research should be considered to confirm these data.
Poster Presentations: Cervical Cancer

LAPAROSCOPIC RADICAL Hysterectomy FOR CERVICAL CANCER – EXPERIENCE OF PRIVATE ONCOLOGIC CLINIC IN UKRAINE
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Objectives
The role of minimally invasive surgery in the management of gynecologic cancers continues to expand. Currently, laparoscopic surgery is a viable option for patients with gynecologic cancers. This work represents our experience in performing totally laparoscopic radical hysterectomy (TLRH) with pelvic lymphodissection (PLND) in patients with cervical cancer. The analysis of morbidity and short-term postoperative results was conducted.

Methods
In 2010-2013, 142 patients underwent laparoscopic radical operations for gynecologic malignancies. Among them 50 TLRH (Piver III-IV) with PLND were performed for cervical cancer. FIGO stage distribution was: I – in 35 cases (70%), II – 7 (14%), III – 8 (16%). Standard five ports technique was used. For performing PLND harmonic scalpel was applied. In 27 cases ovary preservation with transposition were performed.

Results
The mean age was 41.5 (30-62) years. The average operative time was 204 (110-415) minutes. The median hospital stay was 4.6 (2-12) days. In three patients we performed simultaneous cholecystectomy. Histological types included squamous cell carcinoma in 45 (90%) cases and adenocarcinoma – in 5 (10%). The number of lymph nodes harvested was 19.6 (7-40).
Postoperative complications were registered in 10 patients (20%): seroma – 1, lymphorrhrea – 3, vaginal stump rapture 1.5 month after operation – 1, vesicovaginal fistula – 3, necrosis of distal part of ureter – 2, injury of bladder - 1. No death occurred.

Conclusions
Benefits of TLRH for cervical cancer are lower postoperative pain, short hospital stay, better cosmetic results. High level of urinary tract complications is explained by stage of disease and necessity of radical parametrial dissection.
FEASIBILITY STUDY OF INTENSITY MODULATED RADIOTHERAPY IN CANCER CERVIX WITH INADEQUATE SURGICAL STAGING : ANALYSIS OF LOCOREGIONAL CONTROL & TOXICITIES

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Objectives
Pelvis intensity modulated radiotherapy (IMRT) is increasing used to treat postoperative cervical cancer. The present study was done to evaluate locoregional control and toxicities in patients who had inadequate surgery / staging referred for adjuvant treatment to a tertiary care center in northern India.

Methods
From March 2010 to December 2011, 14 patients of postoperative cervical cancer were treated by pelvic IMRT. Total dose to whole pelvis ranged from 45 – 50.40 Gy in 25-28 daily fractions in 5-5.5 weeks followed by HDR brachytherapy (6Gy weekly fraction x2) to vault. Chemotherapy was given based on histopathological indications. Hematological, bowel, bladder and rectal toxicities were documented during treatment and follow-up by CTCAEv.3 criteria.

Results
Median age was 46 years (range 35-66) with good performance score. Of 14 patients 60% had only simple hysterectomy while 40% had some form of pelvic lymph node sampling / dissection additionally. Follow-up ranged from 12 to 36 months. There was no grade 3 or more toxicities seen during and follow-up post treatment. Grade I / II toxicities in form of hematological – anemia, neutropenia and thrombocytopenia were seen in 14%, 14% and 7% respectively; Bowel in form of nausea and vomiting, diarrhoea and weight loss was seen in 50%, 60% and 20% respectively ; Grade I /II toxicities for Bladder in 7% cases and rectal in 14% was seen. No locoregional and distant relapse is seen till date. All patients except one are alive.

Conclusions
Pelvic IMRT in cervical cancer with inadequate surgery is feasible and does not compromise locoregional control with reduced toxicity.
Facets Associated with Recurrence After Radical Hysterectomy for Treatment of Cervical Cancer

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Objectives

Analyze factors and results associated with recurrence after radical hysterectomy for treatment of cervical cancer.

Methods

Retrospective analysis of 204 medical records of patients who underwent radical hysterectomy, detecting 12 recurrences. Focus was clinical and pathological features, primary and secondary treatment and outcomes.

Results

Total sample was 204 patients. 12 recurrences were detected. Median age was 40.7 years. Clinical stage was 2 Ia2, 7 Ib1 and 3 IIa. Hystologic type was 10 squamous and 2 adenosquamous. Pathological findings revealed 2 cases with positive margins, lymph vascular space invasion and positive lymph nodes and 3 cases with lymph vascular invasion and positive lymph nodes that were submitted to adjuvant therapy.

Recurrence treatment was surgery in 1 case, radiotherapy in 3, chemotherapy in 1 and chemotherapy plus radiotherapy in 7.

There were 2 deaths.

Conclusions

Recurrence rate was 5.8%. Pathological findings classically associated with elevated risk are: positive margins, lymph vascular space invasion, and positive lymph nodes. This patients should be referred to adjuvant therapy.

Recurrence was detected in 2 microinvasive cases, reinforcing that risk is present even in the absent of pathological risk factors.

First evidence of recurrence was clinical symptoms in 7 and colposcopy changes in 4, with mean time until recurrence of 21.5 months, supporting the importance of close follow up specially in the first 2 years.

It is important to analyze surgery indication and pathological features on surgical specimen to detect patients who deserve adjuvant therapy and careful follow up.
Poster Presentations: Cervical Cancer

THE ROLE OF MIRNAS IN HUMAN PAPILLOMA VIRUS (HPV)-ASSOCIATED SQUAMOUS CERVICAL CANCER
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Objectives
To identify key miRNAs that are differentially expressed during HPV-dependent carcinogenesis in CSCC.

Methods
miRNA expression was studied using microarrays in a HPV-16 cervical squamous carcinoma cell line (Siha) and a HPV-16 cervical epithelial immortalized cell line (Ect1/E6E7). Functional annotation (GO, pathway) was performed based on target genes of altered miRNA expression and established a miRNA–mRNA regulatory network. Real-time PCR was used to verify microarray-based miRNA differential expression in tissues and cells.

Results
61 unique miRNAs were detected differentially expressed, between Siha and Ect1/E6E7 cell lines, including 34 upregulated and 27 downregulated miRNAs ($P < 0.05$, false discovery rate (FDR) < 0.05). According to the miRNA-gene network, 20 miRNAs were important nodes in the network, with 9 and 11 genes up- and down-regulated, respectively ($P < 0.01$, false discovery rate (FDR) < 0.01). Functional annotation analysis indicated that the Neurotrophin, Wnt, MAPK, ErbB, P53 and mTOR signaling pathways were involved in the occurrence and development of cervical cancer. Further, real-time PCR results for differential miRNA expression were largely consistent with that of microarray analysis. Among these, miR-15a and miR-155 were significantly overexpressed in CIN and SCC, and miR-15a was most significantly overexpressed in both cell lines and SCC ($P < 0.01$).

Conclusions
We performed a comprehensive analysis for differential miRNA in cervical cancer cell lines, and identified a network of miRNA-mRNA. The differential expression of miRNAs, especially that of the let-7 cluster, miR-15a, miR-23b, miR-34a, miR155 and miR-424, appears to play important roles in the pathogenesis of HPV-related cervical tumorigenesis. These findings contribute to understanding the function of microRNAs in the pathogenesis and progression of cervical cancer.
Poster Presentations: Cervical Cancer

PROGNOSTIC SIGNIFICANCE OF DICER LOW EXPRESSION REGULATED BY MIR-130A IN CERVICAL CANCER

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Objectives
Dicer is crucial for the maturation of miRNAs. The aim of this study is to explore its clinical implications and post-transcriptional regulatory mechanisms of Dicer by microRNAs in cervical cancer.

Methods
Dicer mRNA and protein levels in cervical cancer was investigated by qRT-PCR and immunohistochemistry, and its relationship with survival was analyzed. By combining miRNA target prediction programs, 10 miRNAs were identified to target dicer transcripts. To test the repressive potential of miR-130a and miR-148b, synthetic mimetics were transfected into HeLa cells and dicer expression levels monitored by qPCR and Western blot analysis.

Results
Both dicer mRNA and protein expression significantly associated with distant metastasis and recurrence in cervical cancer. Patients with low mRNA and protein expression of dicer had a significantly shorter disease-free survival (57.6% vs 87.7%, P = 0.001; 63.5% vs 86.0%, P = 0.013) and overall survival (72.7% vs 94.7%, P = 0.0028; 75% vs 92%, P = 0.0223) than those with high dicer mRNA and protein expression. Low dicer expression (P = 0.02) and tumor stage (P = 0.05) remained independent predictors. The expression of the selected 10 miRNAs were all significantly higher in dicer low expressed cervical cancers compared to the dicer highly expressed tissues (P<0.05). MiR-130a and miR-148b exhibited 3-fold lower in cervical cancers than in normal tissues. Overexpression of miR130a was effectively downregulated dicer expression.

Conclusions
Dicer low expression is an important prognostic factor in cervical cancer. High expression of miR-130a attenuate Dicer expression.
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poster presentations: cervical cancer

sentinel lymph node biopsy in early stage cervical cancer at instituto valenciano de oncologia. our experience.

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objectives
Lymph node status is the most important prognostic factor in cervical cancer. Sentinel lymph node (SLN) procedures have been suggested to reduce peri-and postoperative morbidity and operative time.
The aim of this study was to analyze the detection rate, the sensitivity and the negative predictive value of sentinel lymph node procedure (SLN) using radioisotopic lymphatic mapping with technetium-99 m-labeled phytate and blue dye in patients undergoing radical hysterectomy with pelvic lymphadenectomy for treatment of early cervical cancer.

methods
Between January 2010 and July 2012, 32 patients with cervical cancer FIGO stage IA2, 1B1, 2A1 underwent sentinel lymph node detection.
The day before surgery, 99mTc-labeled phytate was injected (spinal needle 22,4 mC) into the uterine cervix, at 3, 6, 9, and 12 o’clock, at a dose of 163 MBq. Preoperative lymphoscintigraphy and intraoperative lymphatic mapping with a handheld gamma probe was carried out. Blue dye was injected at the same location intraoperatively.

results
28/32 patients were analyzed. SNs were localized with a combination of radiocolloid and blue dye in 20/28 patients (detection rate 96 %). The Sensitivity was 80% and negative predictive value 90%. There were no negative false in patients with bilateral SLN detection.

conclusions
Sentinel node mapping is feasible in patients with early cervical cancer. The rate of SN detection combining lymphoscintigraphy with gamma probe and blue dye is high (96%). High sensitivity and negative predictive value is related to a bilateral SLN identification.
USEFULNESS OF P16 INK4A/KI-67 AND L1 CAPSID PROTEIN IMMUNOSTAINING ON ASC-H AND LSIL-H OF LIQUID-BASED CYTOLOGY SPECIMENS
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Objectives
Here, we aimed to test the performance of L1 capsid protein, HPV DNA chip, p16 INK4a/Ki-67 to predict ≥CIN2 in residual liquid-based cytology specimens (LBCS).

Methods
We conducted p16 INK4a/Ki-67 and L1 protein immunostaining with 74 LBCS of LSIL, LSIL-H, ASC-H, and HSIL, 48 of which were histologically confirmed, and 66 cases were compared with the results of a human papillomavirus (HPV) chip test.

Results
Among LSIL-H and ASC-H cases, the positive p16 INK4a/Ki-67 immunostaining results were associated with ≥CIN2 by histological diagnosis, ≥CIN3 by histological diagnosis, and ≥CIN2 by follow-up (p = 0.024, p = 0.002, and p = 0.042, respectively). The negative L1 protein immunostaining results were associated with ≥CIN2 by follow-up (p = 0.020); however, they were not associated with ≥CIN3 by histological diagnosis or ≥CIN2 by histological diagnosis (p = 0.370 and p = 0.083, respectively) in LSIL-H and ASC-H cases. For predicting ≥CIN2 in LSIL-H and ASC-H, the regression tree analysis suggests the use of the combination of p16 INK4a/Ki-67 and L1 protein results, and HPV chip test sequentially. For determining ≥CIN3 in LSIL-H and ASC-H, this analysis suggested the use of combination L1 protein and p16 INK4a/Ki-67 immunostaining.

Conclusions
L1 protein immunostaining, p16 INK4a/Ki-67 immunostaining, and HPV testing of remaining LBCS with LSIL-H and ASC-H are useful objective biomarkers for predicting tissue HSIL+ status.
**Poster Presentations: Diagnostics**

**DIFFERENTIATING PRIMARY VERSUS SECONDARY OVARIAN TUMORS BY TARGET ENRICHED NEXT GENERATION SEQUENCING IN FORMALIN-FIXED PARAFFIN-EMBEDDED TUMOR TISSUE**

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**Objectives**

Differen tiating between a subset of primary and secondary ovarian tumors (metastases) still can be challenging for clinical pathologists. Despite the use of immunohistochemical markers and up to date imaging modalities, some cases remain unsolved. We hypothesized that genetic targets, that were identified based on a literature search, could be used to distinguish primary tumors from metastases.

**Methods**

In formalin-fixed paraffin-embedded tumor tissue, the complete APC and CTNNB1 genes were screened for mutations in proven colorectal metastases to the ovaries. As a control cohort proven primary endometrioid and mucinous ovarian tumors were tested.

**Results**

In total 53 colorectal metastases to the ovaries were examined for mutations in the APC gene. Using targeted next generation sequencing (NGS) the complete APC gene could be investigated. In 75% of the ovarian CRC metastases an APC mutation was identified. Most mutations were nonsense and frameshift mutations. The primary ovarian tumors showed an APC mutation only in 20% of cases (p<0.01), mostly being missense mutations.

**Conclusions**

APC mutation analysis by NGS can be used as a diagnostic marker for differentiating primary ovarian tumors versus metastases from the colorectal tract. The CTNNB1 gene was less useful in differentiating between primary and secondary tumors.
FACTORS AFFECTING PREOPERATIVE LOCAL STAGING OF ENDOMETRIAL CANCER

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Objectives
To identify the major factors for under- and overestimation of cervical and myometrial invasion in endometrial cancer preoperative staging by ultrasound imaging.

Methods
Included were all consecutive patients with histologically proven endometrial cancer referred for surgical staging between January 2009 and December 2011. Transvaginal and transabdominal ultrasound was performed in all cases and results compared to the final histology.

Results
Prospectively enrolled were 210 patients. Proportion of under-estimated invasion was comparable for myometrial and cervical assessment, 8.6% (n=18) and 10.5% (n=22), respectively. Overestimated cervical and myometrial invasion was found in 4.8% (n=10) and 15.7% (n=33). These outcomes correspond to the positive and negative predictive value for myometrial invasion assessment of 67.6% (95% CI: 67.7 – 76.6), 83.3% (95% CI: 74.9 – 89.8) and for cervical stromal invasion of 60.0% (95% CI: 38.2 – 79.2) and 88.1% (95% CI: 82.5 – 92.4). The diagnostic error of subjective assessment was related neither to BMI nor to position of uterus in the pelvis. The cervical and/or myometrial invasion was more often underestimated in well differentiated endometrial cancers of smaller size and with less perfusion. While less differentiated cancers of larger size and rich perfusion more often lead to overestimation of subjective assessment.

Conclusions
In contrast to previous studies neither BMI nor uterine position affected ultrasound subjective assessment of myometrial and cervical invasion. Accuracy of local staging was significantly influenced by tumor size, tumor blood suply, vessel architecture and histological grading. The future imaging studies should control for the above parameters.
Poster Presentations: Diagnostics

THE DIAGNOSTIC ACCURACY OF ULTRASOUND IN ASSESSMENT OF MYOMETRIAL INVASION IN ENDOMETRIAL CANCER –SUBJECTIVE ASSESSMENT VS. OBJECTIVE MEASUREMENTS

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Objectives
The aim of this study was to compare the accuracy of subjective assessment and objective measurements of myometrial invasion by ultrasound in endometrial cancer.

Methods
All consecutive patients with histologically proven endometrial cancer, who underwent ultrasound evaluation followed by surgical staging between January 2009 and December 2011, were prospectively enrolled into the study. Myometrial invasion was evaluated by subjective assessment (<50% or ≥50%) and calculated as minimal tumor free margin/normal myometrium thickness ratio or as tumor/uterine antero-posterior (AP) ratio. Both assessments were compared to the final histology.

Results
Alltogether 210 patients were prospectively included. All three tested approaches (subjective assessment and two objective calculations) were found to be statistically significant predictors of the myometrial invasion, exceeding AUC value of 0.65 and reaching final p value < 0.001. However, comparison of the methods revealed significant differences. Subjective assessment was confirmed as the most effective method to assess myometrial invasion with sensitivity 79.3%, specificity 73.2% and overall accuracy of 75.7%. Tumor/uterine AP ratio (cut-off 0.5) reached only sensitivity 56.2%, specificity 76.4% and overall accuracy of 68.1%, which was similar to minimal tumor free margin/normal myometrium thickness ratio (sensitivity 69.6%, specificity 65.9%, overall accuracy 67.3%). Subjective assessment underestimated myometrial invasion status in 8.6% (n=18) and overestimated in 15.7% (n=33) of the whole data set. These outcomes correspond to 67.6% positive predictive value (95% CI: 67.7 – 76.6) and 83.3% negative predictive value (95% CI: 74.9 – 89.8) of subjective assessment of myometrial invasion.

Conclusions
Subjective ultrasound assessment of myometrial invasion performed better than any of the objective models.

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HPV DNA AND MRNA IN PREGNANT WOMEN AND THEIR NEONATES.

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Objectives
To estimate HPV infection in pregnant women and possibilities of HPV transmission to the child.

Methods
The study was conducted in 2012 in the university clinic in Krakow, Poland. The clinical material were cells samples of uterine cervix of 107 delivering women and exfoliated cells from the mouth of the 112 infants for the presence of HR DNA HPV and mRNA E6/E7 HR HPV.

Results
In 22.4% and 4.7% of delivering women HR HPV DNA and mRNA E6/E7 HPV were found respectively. In 7.8% and 2.3% of placenta HR HPV DNA and mRNA E6/E7 HPV was found respectively. In neonates HR HPV DNA was found in 2.3% while mRNA HR HPV in 1.8%.

Conclusions
The study confirms that the incidence of HPV infection is slightly higher in pregnant women comparing to the general population. The risk of vertical transmission is relatively low. The expression of mRNA E6/E7 HR HPV is extremely low.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Poster Presentations: Diagnostics

IMMUNOHISTOCHEMICAL DETECTION OF PLZF AND H1.5 IN UTERINE LEIOMYSARCOMA AND LEIOMYOMA

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Objectives

The accurate distinction of leiomyoma from leiomyosarcoma is essential for patient management. However, the distinction can be difficult to make, particularly in tissue biopsy samples. Immunohistochemistry has been established as a useful technique to aid in the diagnosis of malignancies. The advantages of immunohistochemical studies are their ease of use and ease of interpretation. This study is the first to evaluate the utility of the promyelocytic leukemia zinc finger (PLZF) protein and the histone H1.5 protein as potential diagnostic immunohistochemical markers for distinguishing leiomyosarcoma from leiomyoma.

Methods

Tissue samples from 21 leiomyosarcomas and 26 leiomyomas were studied. Consecutive sections from routinely fixed and embedded tissue were subjected to immunohistochemical staining. The student t-test and the Fisher’s exact test were used to calculate the differences.

Results

Statistically significant differences were found in the staining indices of anti-PLZF and anti-histone H1.5 when comparing benign and malignant tumors (p<0.0001 and p<0.0001, respectively). The mean histone H1.5 staining index score in leiomyosarcomas was 158 (95%CI 125-192), compared to 28 in leiomyomas (95%CI 16-41). The mean PLZF score in leiomyosarcomas was 1.5 (95%CI 0.3-3.4) in contrast to a score of 71 in leiomyomas (95%CI 53-91). For histone H1.5 at a score ≥60, sensitivity and specificity were 90.0% and 84.6%, respectively, which suggests that histone H1.5 staining is a useful distinguishing marker. Combining the two immunostains, the sensitivity and specificity in differentiating between leiomyoma and leiomyosarcoma was calculated to be 95.0%, and 88.4%, respectively.

Conclusions

We describe immunostaining for PLZF and histone H1.5 in benign and malignant uterine smooth muscle tumors. Statistically significant differences in staining patterns were found, suggesting utility in distinguishing leiomyosarcomas from leiomyomas.

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Poster Presentations: Diagnostics

Prediction of types of ovarian tumors by laparoscopic observation
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Objectives
To determine the interobserver agreement and the overall diagnostic accuracy of evaluations of videotaped laparoscopic examination of ovarian tumors with a scoring system.

Methods
Two gynecologic oncologists and two general gynecologists scored video recordings of laparoscopic examinations of ovarian tumors. They were blinded for clinical information. The parameters included: adnex normal/abnormal, presence of adhesions, smooth surface, abnormal vessels, endometriosis, metastases, and free fluid. The clinical impression was classified as (probably) benign or (probably) malignant. Moreover, a specific diagnosis was suggested. Kappa (κ) statistics were used to determine the level of agreement between the observers. Because borderline tumors need to be staged they were included in the malignant group.

Results
41 patients were included. The histological diagnoses included 36 (88%) benign, 2 (5%) borderline, and 3 (7%) malignant tumors. The overall accuracy of the diagnosis of malignancy was 89%, the sensitivity 41%, and the specificity 96%. The interobserver agreement of the diagnosis of malignancy was moderate (κ = 0.57 [95% confidence interval 0.43 – 0.71]). The agreement was best for gross categorization, adhesions, and endometriosis (κ = 0.65 – 0.72). For most variables agreement was fair to moderate (κ = 0.21 – 0.57). Agreement was poorest for abnormal vessels and intra-abdominal metastases (κ = -0.05 – 0.18).

Conclusions
Based on video recordings, the interobserver agreement of the overall clinical impression and most diagnostic features of ovarian tumors used in this study are unsatisfactory and therefore not useful for clinical practice. More clearly defined criteria for laparoscopic evaluations should be used to improve the agreement.
INCIDENCE OF ANTI-N-METHYL-D-ASPARTATE RECEPTOR ANTIBODIES IN PATIENTS WITH OVARIAN TERATOMS

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Objectives
Only recently, in 2007, anti-N-methyl-D-aspartate receptor antibodies were detected as a cause of encephalitis in patients. When examining patients with NMDA receptor encephalitis, a high incidence of teratoma in these patients could be found. It was described in literature that removing these teratomas helps to improve neurological symptoms and leads to remission. It has been shown that the embryonic tissue in teratomas induces production of antibodies.

Methods
We included fifteen asymptomatic patients suffering from ovarian teratoma and examined the blood of them for autoantibodies against the glutamate domain of NMDA-receptors. We matched the patients to individuals with other ovarian pathologies, such as cysts or benign tumours and also to a healthy control group.

Results
15 patients suffering from teratomas had a mean tumour size of 4.5 cm (2-12 cm). 15 women with benign ovarian tumours who were matched to the group with teratomas had a mean tumour size of 5.5 cm (3-14 cm). Nor patients neither individuals in the control group presented any neurological symptoms. All tumours could be removed completely by laparoscopy. In one patient with teratoma and in one patient with benign ovarian disease neurological NMDA-receptor antibodies were found. All other blood samples were free from antibodies.

Conclusions
We could show that routine screening of asymptomatic patients for NMDA receptor antibodies is neither necessary nor useful and therefore is not indicated.
Poster Presentations: Endometrial Cancer

SERUM YKL-40 IS A SIGNIFICANT MARKER FOR DETECTION OF ENDOMETRIAL CANCER AND DEEP MYOMETRIAL INVASION
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Objectives
To investigate the significance of serum YKL-40 (human chitinase-3 like 1 protein) in detection of endometrial cancer (EC) and its association with clinicopathological findings.

Methods
This prospective study was performed at a tertiary referral center in Ankara, Turkey, after gaining approval from the institutional review board. Preoperative serum samples were collected from patients surgically treated for endometrial cancer between January 2012-January 2013. Patients with a prior history of other malignancies, hepatitis or arthritis were excluded. A control group comprising healthy women in similar age with no gynecological diseases was also included in the study. Serum YKL-40 levels were determined with enzyme-linked immunosorbent assay (ELISA) method. Association of serum YKL-40 levels with clinicopathological data was investigated with SPSS 20.0 software. P values less than 0.05 were considered statistically significant.

Results
A total of 63 women with EC and 27 controls were included in the study. Mean age in EC group was 58.7±1.1. Mean preoperative serum YKL-40 levels were significantly higher in women with EC (108.5±8.1 vs. 75.0±2.0 ng/ml, p<0.001). YKL-40 was higher in women with deep (>1/2) myometrial invasion, when compared with women with <1/2 myometrial invasion (133.5±18.1 vs. 96±7.6 ng/ml, p=0.008). YKL-40 was also higher in women with cervical tumor involvement (147.6±25.7 vs. 96.3±6.2 ng/ml, p=0.014).

Conclusions
Serum YKL-40 is a promising marker for endometrial cancer detection. It may also serve as a marker for preoperative assessment of deep myometrial invasion and cervical involvement. Prognostic implications of this marker should be evaluated in future studies.
Poster Presentations: Endometrial Cancer

ROBOTICS DECREASES THE RATE OF INTRA-OPERATIVE COMPLICATIONS IN THE SURGICAL TREATMENT OF ENDOMETRIAL CANCER


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Objectives
To compare the rate of intra-operative and post-operative complications of robotic surgery and laparoscopy in the surgical treatment of endometrial cancer, using the Clavien Dindo classification.

Methods
Retrospective study from 2002 to 2011. Patients with endometrial cancer who underwent laparoscopic or robot-assisted surgical treatment were included. We collected preoperative data, tumours characteristics, intra-operative data (route of surgery, surgical acts, complications), and postoperative data (early and late complications, length of hospital stay,). Post-operative complications were recorded according to the Clavien Dindo classification. Morbidity was compared between the two groups.

Results
146 patients were included in the study: 106 patients were operated on by laparoscopy and 40 with robot-assisted surgery. The two groups were comparable in terms of demographics and preoperative data. 11.3% of patients had an intra-operative complication with laparoscopy versus none with robotics (p=0.03). There was no difference between the two groups in term of postoperative events.

Conclusions
Robotic surgery was associated with a significant decrease of intra-operative complications.
EXPRESSION OF CASPASE 9, P53, KI67 IN UTERINE LEIOMYOSARCOMA

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Objectives
Processes of cell proliferation and apoptosis are coexisting in development of malignancies. The process of oncogenesis depends on gene mutations and uncontrolled mitotic cell division that is promoted by blocking pathways of apoptosis. The aim of the study was to assess the expression of caspase 9, p53 and Ki67 proteins in tissues of uterine leiomyosarcoma.

Methods
28 postoperative tissue samples of uterine leiomyosarcomas were selected among patients operated in our center. The expression of investigated markers were analyzed as an intensity of color immunohistochemical reaction, by designed computer program. Ten fields of view were chosen from every sample, in each field of view 100 cells were assessed using 400x magnification. The results were analyzed with appropriate statistical tools.

Results
Average 33.2% of leiomyosarcoma cells were caspase 9 positive. P53 protein was expressed on average in 30.1% of leiomyosarcoma cells. Ki67 expression was funded in 10.8 % of cells.

Conclusions
The expression level of caspase 9 and P53 protein in leiomyosarcoma tissue may suggest that deregulation of apoptosis process plays a role in tumor development. Ki 67 protein being considered as a marker of cell proliferation was expressed in >10% of tumors' cells. Expression of Ki67 shows the amount of cells in an active phase of cell cycle, that could explain rapid growth and high metastatic potential of leiomyosarcomas. Research aimed to assess expression of caspase 9, P53 and Ki 67 on bigger group of leiomyosarcomas and relations between these markers are still carrying on by our team.
Poster Presentations: Endometrial Cancer

FOLATE RECEPTOR ALPHA (FRA) EXPRESSION IN ENDOMETRIAL CANCER.

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Objectives
Folate receptor alpha (FOLR1/FRA) is expressed in a high percentage of serous ovarian, endometrial, lung and breast cancers but expression in normal tissues is restricted to the apical surfaces of a limited subset of polarized epithelial cells. Therefore, FRA is an interesting candidate for new targeted therapies. The aim of the present study was to evaluate the expression of FRA in endometrial cancer and evaluate its relationship to clinical and histopathological parameters.

Methods
Immunohistochemistry with MAb 26B3 was performed on paraffin–embedded tissues from 113 primary endometrial cancer patients. A positive result was defined as membrane staining of ≥5% of tumor cells. Further, staining was calculated using the M-score, a semi-quantitative algorithm which incorporates both intensity and percentage tumor staining.

Results
An endometrioid subtype was present in 85.8% of the cohort and FRA IHC was positive in 82.3% of the cohort. Significantly higher FRA expression was observed in high grade (G2-3) endometrial cancer patients (p=0.049). No other significant correlations were detected.

Conclusions
This study demonstrates that FRA is expressed in endometrial cancer and that a subgroup of endometrial cancer patients might benefit from FRA targeted diagnostics and therapeutics. Further multi-centre studies are warranted.
Poster Presentations: Endometrial Cancer

ESTROGEN FORMATION IN ENDOMETRIAL CANCER
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Objectives
To investigate the local formation of estrogens from androstenedione (A-dione) and estrone-sulphate in endometrial cancer (EC).

Methods
Study included 47 EC type 1 patients. Tissue samples were obtained after hysterectomies. We measured concentrations of estradiol and its precursor androstenedione (A-dione) in 10 EC samples by LIA. We next studied the expression of genes of the aromatase and sulphatase pathways of estrogen formation in 47 paired samples of cancerous and adjacent control tissue by quantitative PCR. We then evaluated the metabolism of A-dione, estrone-sulphate and estrone by incubation of tissue homogenates with 3H labeled steroids, followed by extraction and HPLC separation.

Results
A-dione and estradiol were detected in all but one cancer tissue, suggesting that A-dione can serve as a precursor and estradiol can be formed locally. There were no significant differences in expression of STS and SULT1E1, encoding sulphatase and sulphotransferase, respectively, but the mRNA ratio STS/SULT1E1 was increased in cancer. The mRNA levels of HSD17B1, encoding reductive estrogenic 17-ketosteroid reductase, and CYP19A1, encoding aromatase, were low but unchanged. A-dione was metabolized mainly to testosterone probably by AKR1C3, which was detected at the protein and cellular levels. Estrone-sulphate and estrone were metabolized to estradiol, demonstrating sulphatase and estrogenic 17-ketosteroid reductase activities in cancer.

Conclusions
Our gene expression analysis and metabolism studies show domination of androgenic 17-ketosteroid reductase activity, which converts A-dione to testosterone, over aromatase activity, which converts A-dione and testosterone to estrone and estradiol, respectively. Increased STS/SULT1E1 ratio suggests that in EC estradiol is formed from estrone-sulphate, and not from A-dione.
Poster Presentations: Endometrial Cancer

MRI, PET/CT AND ULTRASOUND IN THE PREOPERATIVE STAGING OF ENDOMETRIAL CANCER – A MULTICENTER PROSPECTIVE COMPARATIVE STUDY

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Objectives

Aim of this prospective multicenter study was to evaluate and compare the diagnostic performance of PET/CT, MRI and transvaginal two-dimensional ultrasound (2DUS) in the preoperative assessment of endometrial cancer (EC).

Methods

318 consecutive women with EC were included when referred to three Danish tertiary gynecological centers for surgical treatment. Preoperatively they were PET/CT-, MRI-, and 2DUS scanned. The imaging results were compared to final pathological findings. This study was approved by the National Committee on Health Research Ethics.

Results

For predicting myometrial invasion, we found sensitivity, specificity, PPV, NPV,
and accuracy for PET/CT to be 93%, 49%, 41%, 95% and 61%, for MRI to be 87%, 57%, 44%, 92%, and 66% and for 2DUS they were 71%, 72%, 51%, 86% and 72%. For predicting cervical invasion the values were 43%, 94%, 69%, 85% and 83% for PET/CT, 33%, 95%, 60%, 85%, and 82% for MRI, and 29%, 92%, 48%, 82% and 78% for 2DUS. Finally, for lymph node metastases 74%, 93%, 59%, 96%, and 91% for PET/CT and 59%, 93%, 40%, 97% and 90% for MRI. When comparing the diagnostic performance we found PET/CT, MRI and 2DUS comparable in predicting myometrial invasion. For cervical invasion and lymph node metastases, however, PET/CT was best.

Conclusions
None of the modalities can yet replace surgical staging. However, they all contributed to important knowledge and were, furthermore, able to upstage low-risk patients who would not have been recommended lymph node resection based on histology and grade alone.

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Poster Presentations: Endometrial Cancer

SEROUS PAPILLARY AND CARINOSARCOMAS OF THE UTERUS Have Worse Prognosis Compared to High-Grade Endometrioid Endometrial Cancer.

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Objectives
Type II endometrial carcinomas included serous and clear cell cancers. Due to its monoclonal endometrial origin, endometrial carcinosarcoma has been classified as a subtype of high-grade endometrial cancer. Recently, it is suggested that poorly differentiated (G3) endometrioid carcinomas should also be considered as a type II cancer. We evaluated and compared the clinicopathological and outcome parameters of patients with G3 endometrioid, papillary serous and carcinosarcoma of the uterus.

Methods
We conducted a retrospective chart review of all patients with uterine malignancies treated at our institution from 2000 to 2010. Clinicopathologic factors, surgical procedures, adjuvant therapy and survival outcomes were collected. Overall survival (OS) was calculated using the Kaplan-Meier method. Factors predictive of survival outcomes were compared using the log-rank test and cox regression analysis.

Results
We traced 105 patients of which 31 (29.5%) had G3 endometrioid histology, 36 (34.3%) papillary serous and 38 (36.2%) carcinosarcoma. There was no significant difference in the median age, complaint, complaint duration or surgical procedures between the 3 groups. Significantly more stage I disease was observed in the G3 endometrioid group (55.2% vs 40% vs 45.7%, p=0.045). Significantly more recurrences were observed in the papillary serous and carcinosarcoma groups compared to G3 patients (44.4%, 55.3% and 22.5% respectively, p=0.0067). OS was significantly worse for papillary serous and carcinosarcoma patients compared to the G3 group, p=0.0058. On multivariate analysis only stage and histology were independently associated with survival.

Conclusions
Although G3 endometrioid, papillary serous and carcinosarcomas originate from epithelial endometrial cells their different outcome measures suggests biologic heterogenisity.
FEASIBILITY OF EXTRAPERITONEAL LAPAROSCOPIC PARA-AORTIC LYMPHADENECTOMY FOR ENDOMETRIAL CARCINOMA

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Objectives:
Lymph node metastases are a strong predictor of poor outcome in endometrial cancer (EC). Paraaortic lymphadenectomy until left renal vein permits selecting patients who can benefit from extended field radiotherapy. The high BMI of patients with EC and the need for avoiding bowel adhesions, make the extraperitoneal access very useful for this purpose.

The aim of this study was to evaluate the feasibility of extraperitoneal laparoscopic paraaortic for EC

Design: Observational retrospective study.

Patients: 113 women diagnosed of EC underwent hysterectomy and laparoscopic lymphadenectomy between 2005 and 2012 in a tertiary referral center. 83 patients underwent extraperitoneal lymphadenectomy and the remaining 30, transperitoneal lymphadenectomy. Median age, FIGO stage and cell type were comparable in both groups. Average BMI was 28.7 in those who underwent extraperitoneal lymphadenectomy and 25.23 for transperitoneal lymphadenectomy (p-value .003)

Results:
Complication rates are shown in table 1, including 5 cases of extraperitoneal conversion to transperitoneal due to technical difficulties

<table>
<thead>
<tr>
<th></th>
<th>Extraperitoneal (n=83)</th>
<th>Transperitoneal (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>28(33.7%)</td>
<td>12(40.0%)</td>
<td>.656</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>14(16.9%)</td>
<td>8(26.7%)</td>
<td>.285</td>
</tr>
<tr>
<td>Postoperative&lt;7days</td>
<td>11(13.3%)</td>
<td>3(10%)</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative&gt;7days</td>
<td>12(14.5%)</td>
<td>4(13.3%)</td>
<td>1</td>
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The estimated blood loss, duration of surgery and length of stay were comparable in both groups (table 2). Note that the procedure includes pelvic lymphadenectomy and hysterectomy

<table>
<thead>
<tr>
<th></th>
<th>Extraperitoneal (n=83)</th>
<th>Transperitoneal (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased haemoglobin (g/dL)</td>
<td>2.7(0.5-10.2)</td>
<td>2.4(0.2-4.6)</td>
<td>.71</td>
</tr>
<tr>
<td>Median (min-max)</td>
<td>355.0(140-555)</td>
<td>327.5(130-430)</td>
<td>.099</td>
</tr>
</tbody>
</table>
Table 1: Length of hospital stay

<table>
<thead>
<tr>
<th>Length stay (days)</th>
<th>Median (min-max)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extraperitoneal</td>
<td>4 (2-31)</td>
<td>.175</td>
</tr>
<tr>
<td>Laparoscopy</td>
<td>4 (2-13)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:**
In experienced hands, extraperitoneal laparoscopy in EC is a feasible and safe procedure for the lymphatic staging, in spite of the high BMI of this kind of patients.
IMPACT OF ADJUVANT THERAPY ON GYNECOLOGICAL CARCINOSARCOMA OUTCOMES

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Objectives
Gynecological carcinosarcoma is a rare aggressive disease. The cornerstone of treatment remains debulking surgery and no clear survival benefit has been demonstrated with adjuvant radiotherapy nor chemotherapy. This study aims to determine if an aggressive multimodal therapy including adjuvant polychemotherapy used after 2000 add survival benefit.

Methods
All consecutive patients diagnosed with carcinosarcoma at Institut de Cancérologie de l'Ouest (ICO) from 1987 to 2012, were included. Two cohorts, A (before 2000), cohort B (after 2000) were individualized.

Results
Forty patients (median age 66 years) were included, 14 and 26 in cohort A and B. FIGO stage was higher for ovarian carcinosarcomas (OCs) than uterine carcinosarcomas (UCs), 75% versus 54% respectively. Optimal debulking surgery was performed in 70% of the patients in both groups, however lymphadectomy was more frequent in cohort B (69.2% versus 36%). Adjuvant radiotherapy was performed for UCs, more frequently after 2000 (42% versus 36%). Twenty seven patients received adjuvant chemotherapy, 86% of OCs and 58% of UCs and regimen were mostly platinum-based (90%). Adjuvant chemotherapy was more frequent in cohort B (80% versus 43%) and more often placitaxel/carboplatin regimen (85% versus 16%). With a median follow-up of 44.4 months, the recurrence rate was similar in the cohort A and B (43% versus 46%) as well as median overall survival, 20 months versus 22,2 months (p=0.76).

Conclusions
In our series, aggressive polychemotherapy did not bring survival improvement. Larger multi institutional studies are needed to assess the role of modern multimodal treatment in this agressive disease.
PREOPERATIVE PREDICTION OF UTERINE MORCELLATION AT THE TIME OF ROBOTIC-ASSISTED LAPAROSCOPIC HYSTERECTOMY

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²Northwest Hospital & Medical Center, Meridian Women's Health, Seattle, USA

Objectives
To identify preoperative factors associated with uterine morcellation when performing robotic-assisted laparoscopic hysterectomy.

Methods
Patients who underwent robotic hysterectomy from 2008 through 2012 were prospectively identified, and information including need for uterine morcellation, indication for hysterectomy, age, body mass index, gravidity, parity, type of deliveries, and menopausal status was recorded. Preoperative uterine dimensions were used to calculate uterine volume using the ellipsoid formula. Subjects without preoperative uterine dimensions based on imaging were excluded. Pathologic data including histology and uterine weight were noted. Recursive partitioning and logistic regression were used for a predictive classification scheme based on preoperative variables with split-points when appropriate.

Results
436 patients were identified with 136 subjects excluded due to lack of preoperative uterine dimensions and two excluded due to conversion to open procedures prior to completion of the hysterectomy. Of the 298 evaluated patients, 41% underwent hysterectomy for malignant indications. Morcellation was required in 62 (20.8%) of all hysterectomy specimens. Both univariate and multivariate logistical regression analysis determined that a preoperative uterine volume of ≥ 222 ml was the most important predictor of morcellation (OR 40.43, 95% CI 18.81-86.88, p<0.0001; and OR 39, 95% CI 16.17-94.03, p<0.0001). Parity decreased the need for morcellation (OR 0.34, CI 0.14-0.83, p=0.018).

Conclusions
Uterine volume ≥ 222 ml and nulliparity were the most important preoperative factors predicting uterine morcellation during robotic-assisted laparoscopic hysterectomy. Preoperative determination of the likelihood of removing an intact uterus vaginally is important for operative planning, especially in patients with uterine cancer.
Poster Presentations: Endometrial Cancer

TUMOR INFILTRATING LYMPHOCYTES PREDICT OUTCOME IN TYPE 2 ENDOMETRIAL CARCINOMA.
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Objectives
Cancer distinguishes itself from other diseases by recurrence and predicting who will suffer recurrence is pivotal to optimize treatment. Age, infiltration depth and tumor type determine the indication for adjuvant treatment in endometrial cancer. In colorectal carcinoma, predicting recurrence using immunologic variables is superior to classical variables. We evaluated the predictive value of tumor infiltrating lymphocytes in endometrial carcinoma.

Methods
Tissue Micro Arrays were constructed and stained for cytotoxic, memory and regulatory, T-lymphocytes and findings were related to disease course as described previously for 355 patients with endometrial cancer. The dataset was imputed for missing values for immunologic variables. Age, tumor type 1-2, FIGO stage, lymphvascular invasion, myometrial invasion and tumor infiltration by cytotoxic, regulatory and memory lymphocytes were considered as candidate predictors. Candidate predictors were selected through backward elimination and a C-index was calculated for classical and immunological variables, separately and combined. A subgroup analysis was performed for type 2 endometrial cancer.

Results
Calculated C-index is higher for FIGO stage combined with lymphvascular space involvement compared to T-cell infiltration and combination does not add to the predictive value (table 1). In type 2 cancer, immunological and classical variables have a comparable C-index. Combination seems to improve predictive value in this group (Table 2).

Conclusions
T-cell infiltration predicts recurrent disease as well as classical variables and combination may be useful to optimize treatment. Future studies should evaluate these findings in a larger cohort.
Objective:
Main objectives of this study was evaluation expression of DCC and FHIT proteins and estimation of proliferation level with Ki-67 antibody: at post operative material (tumor), nodal metastases and curettage material from endometrial cavity. Specimens of 50 patients who had underwent D&C and surgery at our department between 2001 and 2012 were available for analysis. For each patient an immunohistochemical study for DCC, FHIT expression and Ki-67 was performed in a D&C and postoperative specimen. Normal and atrophic endometrium of 39 randomly chosen patients were also stained as a control group.

Method:
Immunohistochemical staining with use specific monoclonal antibodies on 4-µm-thick sections of formalin-fixed, paraffin embedded endometrial specimens both in D&C and postoperative material.

Results:
Studied suppressor gene FHIT can participate in very early stages of endometrial cancer carcinogenesis. Lack of statistically significant coincidence between expression of studied suppressor genes FHIT, DCC and tumor advance factors orders skeptical attitude to use that markers on early stage diagnostic of endometrial cancer.

Conclusions:
1. Disposition expression of DCC gene show imperceptible role in endometrial carcinogenesis.
2. FHIT expression variation can have importance meaning at endometrial cancer development.
3. No statistically significant depending between expression of DCC, FHIT, Ki-67 and grading, clinical stage, myometrial invasion, presence of cervical infiltration has been found.
4. Lack significant correlation between DCC, FHIT and Ki-67 expression, give evidence on inappreciable impact of DCC and FHIT on endometrial cancer cell regulation.
Poster Presentations: Endometrial Cancer

EFFECT OF BLADDER FILLING ON BLADDER AND BOWEL DOSE IN HIGH DOSE RATE (HDR) VAGINAL VAULT BRACHYTHERAPY FOR ENDOMETRIAL CANCER

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Objectives
The aim of this study was to look at the effect of bladder filling on dosimetry in HDR vaginal brachytherapy (VBT).

Methods
We reviewed 3D CT plans for 28 patients treated with HDR vaginal vault brachytherapy. Patients had treatment with a single source vaginal cylinder applicator. 16 patients received VBT (22 Gy/4 f) alone and 12 patients received combination external beam radiotherapy (EBRT) (45 Gy/25 f) and VBT (8 Gy/2 f). Dose was prescribed to 5 mm from the applicator surface. The bladder, rectum, sigmoid and small bowel were contoured as the organs at risk (OAR) by a team of radiation oncologist and radiologist. We measured bladder volumes and D2cc per gray for each OAR taking into account the different fraction size.

Results
Median bladder volume was 63 cm³ (38-308). Table 1 summarises Pearson correlation between bladder volumes and D2cc per gray for each OAR. There was a significant negative correlation between bladder volume and dose to small bowel (r=-0.45, p=0.02).

<table>
<thead>
<tr>
<th></th>
<th>Bladder</th>
<th>Rectum</th>
<th>Sigmoid</th>
<th>Small bowel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson correlation, r</td>
<td>0.31</td>
<td>0.11</td>
<td>0.22</td>
<td>0.25 -0.27</td>
</tr>
<tr>
<td>p</td>
<td>0.02</td>
<td>0.11</td>
<td>0.22</td>
<td>0.16 -0.45</td>
</tr>
</tbody>
</table>

The additional dose contributed by VBT was calculated for each OAR for the patients who received combination VBT and EBRT. Rectum, sigmoid and small bowel received an additional median EQD2 dose of 7.3 Gy (5.3-9.9), 2.4 Gy (1.1-5.2) and 4.7 Gy (0-8.2) respectively.

Conclusions
Our results confirm previous reports that bladder filling reduces dose to the small bowel. This would be especially important for those patients receiving combination EBRT and VBT. Our centre has now introduced an oral fluid intake protocol to achieve bladder filling.
Poster Presentations: Endometrial Cancer

LAPAROENDOSCOPIC SINGLE-SITE VERSUS CONVENTIONAL LAPAROSCOPIC SURGICAL STAGING FOR EARLY-STAGE ENDOMETRIAL CANCER

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Objectives
To compare the feasibility, safety, and efficacy of LESS surgical staging for early-stage endometrial cancer with conventional laparoscopic surgical staging.

Methods
The prospective study group consisted of 37 consecutive patients who underwent LESS surgical staging including hysterectomy, bilateral salpingo-oophorectomy (BSO), and pelvic lymph node dissection (PLND). The historical control group consisted of 74 consecutive patients who underwent four-port laparoscopic surgical staging including hysterectomy, BSO and PLND. Surgical outcomes were compared between the two groups.

Results
No patient in the LESS or conventional laparoscopic surgery group required an additional trocar or conversion to laparotomy. There were no inter-group differences in mean age, menopause status, body mass index, and previous history of abdominal surgery. Further, there were no inter-group differences in the number of total (LESS vs. conventional, 25.9±10.6 vs. 24.6±9.0, P=0.497), pelvic (24.6±4.97 vs. 23.3±7.7, P=0.459), and para-aortic (4.9±aor vs. 6.9±7.3, P=0.494) lymph nodes retrieved; the operating time (183±th min vs. 173±th min, P=0.388); estimated blood loss (194±149 mL vs. 173±106 mL, P=0.394); number of patients requiring transfusion (5.4% vs. 8.1%, P=0.717); postoperative hospital stay (5.0±1.8 days vs. 5.1±1.8 days, P=0.911); intraoperative complications (2.7% vs. 0%, P=0.333); and postoperative complications (0% vs. 1.4%, P>0.999). The postoperative pain scores and analgesics requirements were significantly lower in the LESS surgical staging group.

Conclusions
LESS surgical staging was a feasible, safe, and efficacious procedure for surgical management of patients with early-stage endometrial cancer. It was associated with less postoperative pain and analgesics requirements and was comparable to conventional laparoscopic surgical staging in terms of perioperative outcomes.
A PANEL OF METASTASIS INDUCING PROTEINS ARE DIFFERENTIALLY EXPRESSED IN THREE ENDOMETRIAL CANCER CELL LINES

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2Biochemistry and Cell Biology, Institute of Integrative Biology, Liverpool, United Kingdom
3Musculoskeletal Biology, Institute of Ageing and Chronic Disease, Liverpool, United Kingdom

Objectives
Endometrial cancer is the most common malignancy of the female genital tract. Younger women are presenting with the disease which makes early detection difficult, resulting in later diagnosis and poorer prognosis. There is an urgent need to find new treatments for metastatic or recurrent endometrial carcinomas. We aim to characterize a panel of metastasis inducing proteins (MIPs; Anterior Gradient Protein 2, Osteopontin, S100A4 and S100P), that have been discovered in breast cancer as potential therapeutic targets/prognostic markers, in 3 endometrial cancer cell lines with a range of differentiation and invasive potential.

Methods
mRNA and/or protein levels were assessed by RT-PCR and western analyses with protein locations shown by immuno fluorescent antibody staining.

Results
All MIPs were expressed but at different sub-cellular locations in the cell lines. HEC1A, a highly invasive cell line showed higher levels of S100A4 and S100P compared with other lines (as well as strong nuclear staining), whereas Anterior Gradient Protein 2 (AGR2) expression was low. MFE280 showed the highest AGR2 expression levels, which corroborates its origins from a recurrent tumour, but showed relatively lower amounts of S100A4 and S100P.

Conclusions
We conclude that it is likely that this panel of MIPs may correlate with different aspects of metastatic potential of endometrial cancer and these 3 endometrial cancer cell lines provide a model in which to manipulate the expression if these MIPs and assess the impact on migratory and/or invasive potential.
Poster Presentations: Endometrial Cancer

EXPRESSION OF ER, PR, IGF-1R AND B-CATENIN IN ENDOMETRIAL CANCER PATIENTS TREATED WITH METFORMIN DUE TO DIABETES TYPE 2.

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⁵Department of Gynecology Obstetrics and Gynecological Oncology, Silesian Medical University Bytom, Bytom, Poland
⁶Chair and Department of Oncological Gynaecology and Gynaecology, University of Medical Sciences in Lublin, Bytom, Poland
⁷Department of Gynecology Oncology, Memorial Cancer Centre and Institute of Oncology Warsaw, Warszawa, Poland
⁸Department of Pathology, University of Medical Sciences Poznan, Poznan, Poland
⁹Clinic of Oncology Gynecological Oncology Department, University of Medical Sciences Poznan, Poznan, Poland

Objectives
Obesity and diabetes are a commonly known risk factor in endometrial cancer (EC). Epidemiological and experimental studies suggest a beneficial role of metformin in incidence and mortality of many malignancies, including EC. Estrogens, progesterone, IGF-1 and their receptors together with β-catenin in Wnt pathway regulate proliferation and differentiation of endometrial cells; changes in their expression are present in EC tissue. This study investigated the expression of these markers at the cellular level in EC patients with and without type 2 diabetes (DM2) and changes in their expression in diabetic women according to metformin treatment.

Methods
The expression of PR, ER, IGF-1R and β-catenin was IHC investigated in 86 postmenopausal women with endometrial cancer type I. Patients were divided according to the presence of diabetes and type of hypoglycemic drug used (metformin vs insulin or sulfonylurea derivatives).

Results
The study revealed increased IGF-1R expression in women with DM2 in comparison to the non-diabetic group (p=0.0012). Cancer patients with diabetes treated with metformin showed a significantly lower ER expression than the group receiving insulin (p=0.004). However, no statistically significant difference in PR, IGF-1R nor β-catenin expression was found among women using metformin or other type of hypoglycemic drug.

Conclusions
Metformin via different mechanisms has the ability to reduce insulin resistance and promote weight loss in DM2 patients, which might have favorable effect on
endometrial cancer. Our study revealed decreased ER expression in patients receiving metformin, which needs further research in order to be able to evaluate clinical significance of this phenomenon.
A PROSPECTIVE LONGITUDINAL EVALUATION OF QUALITY OF LIFE IN PATIENTS WITH ENDOMETRIAL CANCER

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²Oncology, Catholic University of the Sacred Heart, Campobasso, Italy

Objectives

The increase of endometrial cancer (EC) survivors has focused more attention on QoL issues. This is a prospective, longitudinal study covering multiple-issues of QoL over a follow-up period of 24 months from diagnosis.

Methods

One hundred thirty-two EC patients with FIGO Stage I-IIIC treated with surgery at our Institution were enrolled. Patients received EORTC QLQ-C30 and EORTC QLQ-CX24 questionnaires at baseline and 3, 6, 12 and 24 months after surgery. Anova for repeated measures was used to analyze scoring changes over time and to identify predictors of poor QoL scores.

Results

Median age was 67 years (range, 41–87 years). Most tumors (81.5%) were endometrioid histotype; 113 (85.6%) patients showed at diagnosis FIGO stage I-II and 19 (14.4%) cases FIGO stage III disease. 64 (48.5%) women received adjuvant treatments including radiotherapy, chemotherapy and chemoradiation. Recurrence/progression of disease was observed in 38 patients (28.7%). The mean scores at the baseline evaluation were comparable with the reference values (Danish and German populations). No statistically significant changes over time were observed for QLQ-C30, Body image and Sexual activity. A statistically significant improvement over time was observed for the following scores: symptoms experience (SE), lymphedema (LY) and menopausal symptoms (MS). In multivariate analysis: age≤65 years (p=0.004) and living status not alone (p=0.056) were identified as predictors of poor MS scores.

Conclusions

SE, LY, and MS were the most disabling treatment-related sequelae resulting negatively affected after 12 months from surgery. A trend toward a long-term recovery has been observed at two-year assessment.
ENDOMETRIAL ADENOCARCINOMA IN PATIENTS WITH AND WITHOUT RISK FOR LYNCH SYNDROME: CLINICAL FACTORS AND SURVIVAL IN A SAMPLE OF BRAZILIAN WOMEN

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Objectives
Lynch syndrome is associated with colorectal cancer and other extra-colonic cancers. In women, endometrial cancer is the most common cancer. The aims are to estimate the percentage of patients at risk for Lynch syndrome and to compare the survival of patients with and without risk of Lynch syndrome (groups 1 and 2).

Methods
Consecutive patients with endometrial carcinoma with endometrioid histology who underwent primary surgical treatment. The criteria used to assess the risk of Lynch syndrome were the Amsterdam II criteria, modified Bethesda guidelines, endometrial cancer before age 50 and first-degree relative with Lynch syndrome-associated tumor. The study was approved by the Research Ethics Committee of Universidade Federal de Ciencias da Saude de Porto Alegre.

Results
Twenty-eight (25.2%) of the 111 patients had clinical criteria and/or suspicion of Lynch syndrome (group 1). The survival at two and five years in group 1 (Lynch syndrome) was 95.8% and 90.5%, respectively, and in group 2 (probably sporadic cases), 87.6% and 78.9% (P=0.11).

Conclusions
The frequency of patients at-risk for Lynch syndrome was higher than expected, and the survival rate of patients with endometrial carcinoma and clinical history suggestive of Lynch syndrome was better (but not significant) than those with sporadic tumors, although no difference in staging between the groups was observed. This is the first study that presents a combined evaluation of the frequency of the Lynch syndrome phenotype and survival rates of Brazilian women with endometrial carcinoma.
ASSESSMENT OF TISSUE TRAUMA DURING SURGICAL STAGING OF ENDOMETRIAL CARCINOMA: A PILOT STUDY COMPARING ROBOTIC, LAPAROSCOPIC AND OPEN APPROACH.

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Objectives
It has been claimed that videoendoscopic procedures have the advantage of being less traumatic compared to conventional open techniques. The aim of this prospective pilot study was to determine whether endoscopic endometrial cancer staging is associated with less tissue trauma and inflammatory response than conventional open technique using a panel of laboratory parameters.

Methods
Fourteen endometrial cancer patients scheduled for robot assisted, laparoscopic or open surgical staging with hysterectomy, bilateral salpingoophorectomy, pelvic and paraaortic lymphadenectomy were so far enrolled in the study. Blood samples for assessment of tissue trauma and postoperative immune response markers (C-reactive protein, interleukin-6, citrulline, neopterin, white blood cells count) were taken preoperatively, and consecutively during the five postoperative days.

Results
There was no difference in age and body mass index between groups. The highest node yield was found in robotic group (29 versus 21 and 19). The white blood cell count, neopterin and IL-6 reached the highest levels on the first postoperative day, while CRP peaked on the second and third postoperative days. These parameters correlated with postoperative complications (abdominal wall hematoma and persistent lymphorrhea). Plasma citrulline levels postoperatively decreased to minimum levels on the second postoperative day. The parameters associated with tissue trauma were higher in patients undergoing open surgery.

Conclusions
Results of this pilot study illustrate the possibility of monitoring the extent of postoperative tissue trauma and presence of complications in patients undergoing major ono-gynecologic surgery. The recruitment of additional patients is ongoing.

This study was supported by IGA MZ CR grant NT 13566-4/2012
Poster Presentations: Endometrial Cancer

PREDICTIVE FACTORS FOR UPSTAGING LOW AND INTERMEDIATE RISK ENDOMETRIAL CARCINOMAS
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³Quality of Life and Cancer Research Unit, Besancon University Medical Centre, Besancon, France

Objectives
Preoperative low and intermediate risk endometrial carcinomas benefit from less invasive surgical treatment. However, some of these carcinomas are upstaged after primary surgery thus requiring re-interventions and/or adjuvant therapy. The aim of this study was to explore factors that could predict upstaging of these carcinomas.

Methods
Patients presenting preoperatively with low and intermediate risk endometrial carcinomas were included in this retrospective cohort study. Postoperatively, patients were divided into a “low stage” and an “upstage” group. These two groups were compared before and after surgery in terms of patient and tumour characteristics. Quality of life was evaluated using EORTC QLQ-C30 scores. Logistic regression was used to create predictive models.

Results
From 101 low-and-intermediate risk patients selected, 26 (25.7%) were upstaged after surgery. Preoperatively, no significant difference was found between the two groups in terms of age (p=0.43), body mass index (p=0.26), parity (p=0.71), hormone replacement therapy (p=0.58), high blood pressure (p=0.81), diabetes (0.06), depth of myometrial invasion on Magnetic Resonance Imaging (p=0.62), endometrioid carcinoma grade on pathology (p=0.93), and EORTC quality of life score (p=0.09). Postoperatively, while a similar rate of lymph node dissection was performed in the two groups (p=0.36), significantly more positive nodes (p=0.01) were found in the “upstage” group.

Conclusions
Nodal status is the only factor predicting upstaging low and intermediate risk endometrial cancer. Lymph node dissection is not systematically recommended in such cases as 75% of patients would not gain any benefit. However, sentinel node biopsy could probably be a good option so as to improve staging and decrease re-intervention.
EFFECTS OF TEMOZOLOMIDE COMBINED WITH BEVACIZUMAB IN PATIENTS WITH RELAPSED UTERINE SARCOMA

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2Obstetrics and Gynecology, National Hospital Organization Nishi-saitama, Tokorozawa, Japan
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4Gynecology, Ohki Memorial Kikuchi Cancer Clinic for Women, Tokorozawa, Japan

Objectives
Common treatment for patients with nonresectable relapsed uterine sarcoma is anthracycline-based combination chemotherapy, but the response is not satisfactory. We evaluated the effects of temozolomide combined with bevacizumab in patients with relapsed uterine sarcoma.

Methods
From 2009 to 2012, nine patients with relapsed uterine sarcoma were treated with weekly bevacizumab (2mg/kg; days 1, 8, and 15, q4 weeks) and temozolomide (80mg/body, daily), and treatment continued until disease progression. The response and adverse effects were evaluated using the response evaluation criteria in solid tumors (RECIST), and common terminology criteria for adverse events (CTCAE) version 3.0.

Results
In RECIST evaluation, 1 (11%) of 9 patients had complete response (CR) and 1 (11%) had partial response (PR). Four patients (44%) had stable disease (SD) for at least three months. The response rate (RR; CR+PR) and clinical benefit rate (CBR; CR+PR+SD) were 22% and 66%, respectively. The median progression-free survival was 9.8 months [range: 3-32 months]. There were no treatment-related deaths or CTCAE grade 4 toxicities, and they were tolerable and manageable.

Conclusions
Temozolomide combined with bevacizumab provided disease stabilization in some patients with relapsed uterine sarcoma with tolerable toxicities. These results suggested that this combination would offer another option in the treatment of non-resectable relapsed uterine sarcoma.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Poster Presentations: Endometrial Cancer

ENDOXIFEN INHIBITS ENDOMETRIAL CANCER CELL GROWTH IN A SIMILAR MANNER AS 4OH-TAMOXIFEN.

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Objectives
Hormonal treatment might be an option in endometrial cancer recurrence, especially in well-differentiated (obesity related) tumours. Tamoxifen has been shown to be active with response rates up to 35%. Endoxifen has been proposed as the most active metabolite of tamoxifen. Its formation might be inhibited in specific patients due to enzyme deficiencies or drug interactions, making the selective admission of this metabolite an interesting treatment option. To test the anti-carcinogenic properties of endoxifen in endometrial cancer we performed a proliferation assay in the human endometrial estrogen en progestogen responsive ECC1 PRAB72 cell line

Methods
Cells were cultured in hormone free medium with or without the addition of oestrogen 0.001 to 1 nM, medroxyprogesterone acetate, 4OH tamoxifen and/or endoxifen 0.1 to 1 nM. Cells were harvested and lysed and DNA concentrations were measured by mass spectrophotometry. In a second study the expression of the estrogen and progestogen related AREG gene and the expression of AR, ER alpha, IGF1 and MGP were tested by qPCR.

Results
The ECC1 PRAB72 cells were sensitive to estrogen stimulation. Induction of proliferation could be suppressed completely and dose dependently by addition of progesterone in physiologic concentrations. Similar suppression could be obtained by addition of 4OH Tamoxifen or Endoxifen. There was no added suppressive effect of combining progesterone with tamoxifen nor were there any differences between endoxifen and 4OH Tamoxifen suppression.

Conclusions
Because endoxifen seems as active as 4OH Tamoxifen these data do not suggest a difference in activity or a different mode of action in endometrial cancer cells.
FROZEN SECTION IN THE SURGICAL STAGING OF ENDOMETRIAL CARCINOMA AND THE FACTORS POSSIBLY AFFECTING ITS ACCURACY.

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Objectives
Systematic pelvic and para-aortic lymphadenectomy are recommended in high risk endometrial cancer cases. Some of these high risk criteria can only be obtained through a hysterectomy specimen, which means the patient could be subjected to two operative sittings. The aim of this work was to study the sensitivity and the specificity of frozen section in the surgical staging of endometrial cancer and to study the possible factors that might affect its accuracy.

Methods
This was a retrospective study done in the gynecological cancer center of Aschaffenburg City Hospital, Aschaffenburg, Germany. The study was performed on all the endometrial cancer patients operated upon in the time period from 01.01.2010 till 31.12.2011. The provisional frozen section staging was compared to the final pathology report and analyzed for sensitivity and specificity and for the factors that might be affecting its accuracy.

Results
In the study period we collected information from 79 patients. The overall sensitivity and specificity of the frozen section in determining the depth of myometrial invasion were 90.5% and 97.4% respectively (p < 0.001). Tumor histopathological type (p = 0.46), grade (p = 0.5), size (p = 0.125), presence of cervical invasion (p = 0.77) or presence of lymphovascular space invasion (p = 0.51) did not yield any statistically significant effect on the accuracy of the frozen section.

Conclusions
Frozen section remains a sensitive staging option, but can not replace the paraffin fixated pathology examination in the surgical staging of endometrial cancer, hence, a second operation might be unavoidable in some cases.
THE SIGNIFICANCE OF PARA-AORTIC LYMPH NODE EXPLORATION IN SENTINEL NODE MAPPING FOR ENDOMETRIAL CANCER

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Objectives
Sentinel node (SN) mapping for endometrial cancer is not widely performed for the difficulty in exploring SNs in wide areas including para-aortic lymph node (PAN) region. We aimed to examine the detection rate of SN, sensitivity, specificity and negative predictive value and SN localization, and aimed to clarify the significance of PAN exploration in SN mapping for endometrial cancer.

Methods
We performed SN mapping for the patients with endometrial cancer who were supposed to be stage I or II and to need to receive pelvic lymph node dissection after written informed consent under the approval of ethical committee. We principally used both radioisotope method with hysteroscopy (Tc99m, submucosal injection) and dye-guided method (ICG, subserosal injection), and then performed hysterectomy, bilateral salpingoophorectomy, and back-up lymph node dissection. Anti-cytokeratin immunostaining was performed with paraffin sections of SNs.

Results
In 62 patients, the detection rate of SN was 100%. Average number of SNs was 3.7 in pelvic lymph node and 1.8 in PAN region. Based on the final diagnosis with cytokeratin staining, sensitivity, specificity and negative predictive value were 100% (14/14), 100% (48/48), 100% (48/48), respectively. However, based on intraoperative diagnosis with frozen sections, sensitivity, specificity and negative predictive value were 62% (8/13), 100% (48/48), 91% (48/53), respectively. Among 14 cases with metastatic SN, 79% (11/14) cases showed metastasis in PAN, and 3 cases showed metastasis only in PAN.

Conclusions
This SN mapping study revealed high detection rate, sensitivity, specificity and negative predictive value, and also indicated the importance of the SN exploration in PAN region.
Poster Presentations: Endometrial Cancer

PREOPERATIVE RISK FACTORS OF RETROPERITONEAL LYMPH NODE METASTASIS IN ENDOMETRIAL CARCINOMA

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Objectives
The aim of our study was to determine risk factors associated with retroperitoneal lymph node metastasis in patients with endometrial carcinoma and to evaluate the usefulness of three-dimensional MRI (3D-MRI) in gynecologic fields.

Methods
A retrospective analysis of patients with endometrial carcinoma who underwent hysterectomy, bilateral salpingo-oophorectomy with pelvic/para-aortic lymphadenectomy at our institute between 2007 and 2011 was performed. As preoperative risk factors of lymphatic metastasis, age, serum CA125 level, histologic type and grade, volume of tumors, depth of uterine wall were determined. Volume of tumors were calculated by 3D-MRI. Receiver operating characteristics (ROC) curves were used to determine the tumor volume cut off values.

Results
A total of 59 women with endometrial cancer were identified. Multivariable analysis revealed that tumor volume was found to be independent risk factors for lymph node metastasis. We found that a tumor volume >12.79 cm³ was significant for lymph node metastasis (HR,12.7; p=0.04).

Conclusions
Our results suggest that tumor volume correlate with retroperitoneal lymph node metastasis in endometrial carcinoma and the usefulness of 3D-MRI in gynecologic fields.
Poster Presentations: Endometrial Cancer

FOXA1 LOSS IN ENDOMETRIAL CANCER IS ASSOCIATED WITH POOR PROGNOSIS AND ER ALPHA LOSS

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Objectives
Endometrial cancer incidence increases attributed to obesity associated estrogen stimulation inducing proliferation through ERα activation. The transcription factor Forkhead box A1 (FOXA1) has been suggested to be important in hormone dependent cancers as one key regulator of ERα activity in breast cancer. The aim of this study was to investigate the expression pattern for FOXA1 in endometrial cancer related to ERα status, clinical phenotype and transcriptional effects.

Methods
Protein expression levels of FOXA1 were explored by immunohistochemistry in 529 primary and 91 metastatic endometrial carcinoma lesions and related to ERα protein expression, clinical and histopathologic variables and survival. RNAs from 158 fresh tumors were analyzed using Agilent Microarrays (44k) in parallel.

Results
Loss of FOXA1 protein significantly correlated with low FOXA1 mRNA, high age, non-endometrioid histology, high grade, loss of ERα, and poor survival (all p-values <0.05). Contrasting breast cancer, expression of FOXA1 had no additional prognostic impact in ERα positive patients. FOXA1 expression was retained from primary tumors to regional lymph node metastases, but increased in distant metastases. Gene expression related to low FOXA1 levels did not overlap with expression pattern related to ERα loss.

Conclusions
Low FOXA1 expression associates with ERα loss and poor outcome in endometrial cancer, but with different transcriptional effects for FOXA1 and ERα loss in tumors.
Poster Presentations: Endometrial Cancer

ROBOTIC SINGLE SITE HYSTERECTOMY IN ENDOMETRIAL CANCER: EXPERIENCE WITH THE ®DA VINCI PLATFORM.

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Objectives
To report and evaluate our experience with Single Site robotic Da Vinci Platform performing extra-fascial hysterectomy plus bilateral salpingo-oophorectomy (RSS-H) in low-risk early endometrial cancer.

Methods
We retrospectively reviewed medical records of patients with low-risk early endometrial cancer treated in our Institution between April 2012 and March 2013. All surgical procedures were performed through a single 2.5 cm umbilical incision, with a multichannel system providing access for two single-site instruments, a 8.5 mm 3D HD endoscope, a 5/10mm accessory port and an insufflation channel.

Results
A total of 10 patients underwent RSS-H for early endometrial cancer. The Median Age at diagnosis was 59 years (range 49-75) and the median BMI was 26 (range 21-32). Stage was FIGO IA G1 in 80% patients and G2 in 20%. Pre surgical procedure (Docking time) required a median time of 11 min (range 7-20 min). The median consol time was 85 min (range 55-110 min) and the median operative time was 128 min (range 100-150 min). All the procedure were performed with standard bipolar forceps and the vaginal vault was closed using the vaginal方式进行 which required 30 min median time (robotic arms deattachment and vaginal suture). The Median blood loss was 20 mL (range 0 -50 mL), and we did no observe laparoscopic or laparotomy conversion. Neither complications occurred. The Median time to discharge was two days (range 1-3 d). Median follow-up time was 8 months (range 2-12) and no readmission occurred.

Conclusions
RSS-H is feasible and safe for the treatment of low-risk early endometrial cancer.
OVERALL SURVIVAL AND DISEASE-FREE SURVIVAL IN ENDOMETRIAL CANCER: PROGNOSTIC FACTORS IN 276 PATIENTS

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Objectives
To assess disease-free survival and overall survival of endometrial cancer and to determine independent factors affecting the prognosis.

Methods
A retrospective study of a single-center clinical series of 276 patients (mean age 64 years) with histologically confirmed cancer of the corpus uteri. Extrafascial total hysterectomy and bilateral salpingo-oophorectomy with selective pelvic/para-aortic node dissection according to risk for recurrence was the standard treatment. Actuarial overall survival and disease-free survival were estimated according to the Kaplan-Meier method. Univariate and multivariate Cox proportional hazards analyses were used to assess the prognostic significance of the different variables.

Results
The median follow-up was 45 months for disease-free survival and 46 months for overall survival. Statistically significant variables affecting disease-free survival and overall survival were age, serous-papillary and clear cell histological types, outer half myometrial invasion, advanced FIGO stage, grades G2 and G3, incomplete surgical resection, positive lymph nodes, lymphovascular space invasion, tumor remnant > 1 cm, and high risk group. In the multivariate Cox regression model, predictors of tumor recurrence included advanced FIGO stage (hazard ratio [HR] 4.90, 95% CI 2.57-9.36, P < 0.001) and grades G2 (HR = 4.79, 95% CI 1.73-13.27, P = 0.003) and G3 (HR = 7.56, 95% CI 2.75-20.73, P < 0.001). The same variables were also associated with a significantly higher risk of tumor-related mortality.

Conclusions
FIGO stage and tumor grading were independent prognostic factors of disease-free survival and overall survival in endometrial cancer patients. Outcome was also influenced by histopathologic type, myometrial and lymphovascular space invasion, lymph node involvement, age or tumor remnants after surgery.
PATHOLOGICAL DATA ON 19 CASES OF ENDOMETRIOID CARCINOMA OF THE ENDOMETRIUM IN WOMEN OF REPRODUCTIVE AGE.

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Objectives
19 cases of endometrial endometrioid carcinoma (EEC) aged 31-44, were diagnosed and evaluated in our hospital’s Pathological Department during the last 8 years, for possible age-related differences.

Methods
Specimens were divided in group A, 32-28 y.o. (n=9) and group B, 41-44 y.o. (n=10). Histopathological evaluation of H&E staining and ImmunoChemistry (ER, PR, P53, Ki-67) were performed.

Results
All group A patients had well differentiated EEC. 5 with polypoid carcinoma showed stable regression (in curettage specimens) for at least two years after treatment with progesterone agents. The other four were surgically staged: 2 with superficial myometrial invasion (≤3mm, Ø19-28 mm), and 2 with disease limited to a polyp. Cervix, lymph nodes and adnexae were disease free. All 9 specimens were +++ for ER, PR with insignificant P53 and Ki-67 expression.

All group B specimens were from surgically staged patients. 6/10 were G1, 3/10 G2 and 1/10 G3. 8/10 invaded < 50% of the myometrium (2/8 superficial myometrial invasion). 2/10 showed invasion >50%. 2/10 had cervical extension. 3/10 showed lymph node metastasis and 2/10 had ovarian involvement.

In the two cases of G1 with cervical extension and metastases, P53 and Ki-67 were over-expressed and ER/PR expression was reduced, compared to the rest of G1 specimens.

Conclusions
All patients 35-38 y.o. were evaluated as st Ia G1, whereas 41-44y.o. patients presented various stages and differentiation.

Raising the question of pushing the guideline borders for fertility preservation over the age of 39, one has to cautiously individualize the answer according to all clinical, imaging, pathological and specific immunohistochemical data.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Poster Presentations: Endometrial Cancer

RECURRENT AND SURVIVAL AMONG PATIENTS DIAGNOSED WITH TYPE 2 CARCINOMAS OF THE ENDOMETRIUM

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Objectives
Type 2 endometrial cancers (EC) account for 10 -15% of all endometrial cancers but contribute to almost half of the deaths. In order to standardise the management of type 2 EC patients within our cancer centre, a review was undertaken looking at the recurrence and survival outcomes for all patients diagnosed with serous and clear cell cancers of the endometrium.

Methods
A retrospective review was undertaken looking at the histological features, stage, type of surgery and adjuvant therapy, recurrence and survival outcomes in all patients diagnosed with serous and clear cell carcinomas of the endometrium between 2003 and 2013.

Results
51 patients were diagnosed with serous (25), clear cell (14) or mixed (12) EC. The majority of patients had stage 1 cancer (n=26). All but one patient had undergone surgery which included hysterectomy (open/laparoscopic), bilateral salpingo-oophorectomy +/- omentectomy +/- pelvic lymphadenectomy. Information regarding adjuvant treatment was not available for 11 patients. All patients with stage 3 and 4 EC received adjuvant treatment in the form of pelvic radiotherapy + chemotherapy/brachytherapy. 11/22 patients with stage 1, and 5/6 patients with stage 2 EC underwent adjuvant treatment. Recurrent disease was seen in 27% of stage 1 and 25% of stage 2 cancers. The median time to recurrence was 13 months. There were no survivors among the patients who were diagnosed with recurrent disease.

Conclusions
Type 2 EC is associated with a poorer prognosis compared to endometrioid EC of a similar stage. Treatment, both surgical and adjuvant, should be optimised to improve survival in this group of patients.
Poster Presentations: Endometrial Cancer

NEUROENDOCRINE TUMOURS OF THE UTERUS: AN ANALYSIS OF 8 CASES WITH CLINICAL CORRELATION

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Objectives
To describe the clinicopathological and immunohistochemical features of 8 cases with uterine neuroendocrine (NE) carcinoma.

Methods
A single-center retrospective analysis was performed including 276 endometrial cancer (EC) and 158 cervical cancer (CC) patients who had been treated between 2005 and 2012. 8 cases of NE carcinomas were identified.

Results
The 8 NE uterine carcinomas, 4 (1.5%) from the endometrium, and 4 (2.5%) from the cervix were determined. Of the cases with endometrial origin, 2 had small cell carcinoma (SCC), 1 had large cell NE carcinoma (LCNEC) mixed with SCC, and 1 had carcinosarcoma with SCC component. Of the cases with cervical origin, 3 had small cell NE carcinoma (SCNEC), and 1 had LCNEC. All cases with endometrial origin underwent comprehensive staging surgery. Of the patients with cervical origin, 2 had surgery, 1 had chemoradiation, and 1 had chemotherapy as primary treatment. Median follow-up time for patients with endometrial origin was 21 months (range, 14-35), and with cervical origin was 26 months (range, 10-45). Of the 4 cases with endometrial origin, 2 cases recurred (1 had bone metastasis and the other had para-aortic lymph node and renal metastasis). These are alive with disease and the others are alive with no evidence of disease (NED). Of the 4 cases with cervical origin, 1 case recurred (bladder and bone metastasis), 2 cases died within the first year of the diagnosis, and 2 cases are NED.

Conclusions
Uterine NE tumours are rare, but aggressive neoplasms. Most of the patients have a dismal prognosis.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

Poster Presentations: Endometrial Cancer

PATHOLOGIC AND CLINICAL FEATURES OF PATIENTS WITH OMENTAL METASTASIS FROM ENDOMETRIAL CANCER
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Objectives
To identify surgico-pathologic factors, survival and the factors determining survival in patients with omental metastasis from endometrial cancer.

Methods
Patients with endometrial cancer operated between 1993-2012 in our hospital and who had omental metastasis were included. Patients with either uterine sarcoma were excluded. Maximal debulking was defined as no gross residual tumor, optimal and suboptimal debulking were classified as residual tumor ≤1cm and >1cm, respectively.

Results
Omentectomy was performed in 811 patients with endometrial cancer and omental metastasis was found in 48 (5.9%) patients. Omental metastasis was macroscopic and microscopic in 60% and 40% of the patients, respectively. Total omentectomy increased the chance of detection of the microscopic metastases. During surgery, maximal and optimal debulking was achieved in 83.3% and 10.4% of these patients, respectively. 2-y disease-free survival (DFS) was 28.2% and 2-y overall survival (OS) was 40%.

Conclusions
Omental metastasis in endometrial cancer means poor prognosis and two thirds of these patients are lost in the end of the second year. Although total omentectomy increases the chance of the detection of micrometastases, its effect on survival is controversial. New treatment modalities are necessary in these patients.
Poster Presentations: Endometrial Cancer

TREATMENT AND OUTCOMES OF STAGE I UTERINE PAPILLARY SEROUS CARCINOMA IN BRITISH COLUMBIA
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Objectives
Uterine papillary serous carcinoma (UPSC) is a rare and aggressive type of endometrial cancer, often recurring even in patients with stage I disease. The objective of this study was to evaluate treatment and outcomes in Stage I UPSC in the context of a population-based study.

Methods
This was a population-based retrospective cohort study of all patients with stage I UPSC in British Columbia, Canada from 2004-2012. The British Columbia Cancer Agency (BCCA) recommends 3-4 cycles of paclitaxel and carboplatin chemotherapy followed by pelvic radiotherapy to all women with Stage I UPSC and any myometrial invasion (Stage IA MI+ and Stage IB). Those with tumor confined to the endometrium (Stage IA MI-) do not receive adjuvant therapy. Patient and disease characteristics, surgery, adjuvant therapy, recurrence rates and sites, and 5-year disease-free survival outcomes for each subgroup were evaluated.

Results
Of the 127 patients with stage I UPSC, 41 had Stage IA MI-, 56 had Stage IA MI+, and 30 had Stage IB disease. After a median follow-up of 25 months, 18 (14.2%) had recurrences, the majority being distant. The 5-year disease-free survival rates for each subgroup were 80.7%, 74.4% and 48.5%, respectively. There were no pelvic recurrences among those receiving adjuvant radiotherapy.

Conclusions
Our current protocol of observation alone for Stage IA MI- and chemoradiotherapy for Stage IA MI+ is associated with a low recurrence rate for these subgroups. Women with Stage IB disease have a high recurrence rate despite chemoradiotherapy, and likely require additional chemotherapy or targeted therapies.
**IMMUNOHISTOCHEMISTRY OF POOR PROGNOSIS ENDOMETRIOID ENDOMETRIAL CANCER ARISING FROM ATROPHIC ENDOMETRIUM**

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**Objectives**

Endometrial cancer (EC) is divided in two types. Type I: endometrioid histology arising from hyperplastic endometrium. Type II: non-endometrioid histology arising from atrophic endometrium. Recently, the existence of type III was proposed, characterized by endometrioid histology, but arising from atrophic endometrium, and with a worse prognosis than type I EC. The current study was performed to determine the immunohistochemical profile of type III EC and compare this to type I and II EC.

**Methods**

43 patients with type III EC were randomly selected from 572 patients with grade I EEC treated between January 1999 and December 2009 at the Radboud University Nijmegen Medical Centre (RUNMC), the Canisius-Wilhelmina Hospital (CWZ) and the Mayo Clinic. They were matched with 43 patients with type I EC from the same cohort. 21 patients with type II EC treated in the same period at the RUNMC and CWZ were included as well. Tissue samples were analyzed for PTEN, L1-CAM, ER, PR, P53, hMLH1, PMS2, βcat, Ecad and MIB.

**Results**

Type III EEC was characterized by significantly reduced expression of hMLH1, P53 and hMLH1 and significantly increased expression of ER and PR compared to type II EC. When compared to type I, type III EEC had a notably reduced expression of Ecad. Differences between type I and type III were not significant.

**Conclusions**

The immunohistochemical profile of type III EC is comparable to type I. Further research is necessary to explore the different clinical behavior of this type III EC.
Poster Presentations: Endometrial Cancer

PROGESTERONE RESPONSIVENESS IN PREMENOPAUSAL PATIENTS WITH GRADE 1 ENDOMETRIOID ENDOMETRIAL CANCER IS INDEPENDENT OF MOLECULAR ALTERATIONS IN WNT- AND PI3K-AKT-PATHWAYS

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Objectives
Previous studies have suggested that the mechanism of action of medroxyprogesterone (MPA) in endometrioid endometrial carcinoma (EEC) is the result of interaction with the Wnt and/or PIK3-AKT pathways. We investigate whether genetic alterations in two dominant genetic pathways in endometrioid endometrial carcinogenesis, Wnt- and PI3K/Akt-signalling, can predict responsiveness to progestin therapy for grade 1 EEC.

Methods
We analysed molecular alterations in 68 serial endometrial samples from 10 premenopausal patients with grade 1 EEC treated with high-dose MPA. In all women an endometrial curetting was taken every three months. Pathologic response was defined based on morphology. Treatment was considered to be successful after two consecutive negative curettages. Histology of all pretreatment and follow up curettages was reviewed and formalin fixed paraffin embedded tissue was used to analyse Wnt-signalling activation (β-catenin immunohistochemistry and Sanger sequencing of CTNBB1) and PI3/Akt-pathway activation (PTEN loss by immunohistochemistry and allele specific hotspot mutation analysis of KRAS (exon 1) and PIK3CA (exon 9 and 20)).

Results
The presence of simultaneous molecular alterations in Wnt- and PI3/Akt-signalling pathways was independent of resistance to MPA treatment: all 5 responders had both pathways activated. Two of the non responders showed activation of both pathways while other two of the non responders had one pathway activated. One non responder did not show any of the above mentioned molecular alterations.

Conclusions
Our results indicate that activation of the Wnt-signalling and/or PI3K-Akt pathway in grade 1 EEC does not predict response to MPA treatment.
POSSIBLE INCREASED EFFICACY OF DUAL PROGESTOGEN THERAPY FOR CONSERVATIVE TREATMENT OF ENDOMETRIAL CANCER


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4 Gynaecological Oncology, Bartshealth NHS trust, London, United Kingdom

Objectives
Endometrial cancer (EC) incidence is increasing across all age groups, leading to more requests for conservative management (CM) for fertility-preservation in younger women and avoidance of hysterectomy in older comorbid women.

Methods
All women with Grade 1/Grade1-2 EC from 2004-2012 were identified from our pathology database and electronic and hand-written medical records were searched for details of treatment/outcome in those undergoing CM.

Results

10 women underwent CM for fertility-preservation, 4 for comorbidity. Median follow-up post diagnosis was 25 months (range 5-79). 6/10 responded completely to dual-therapy with concomitant high-dose oral progestogen (P) and Mirena™ (M). 0/4 treated with P or M (but not both) had persistent or worsening disease and underwent hysterectomy (dual vs. single therapy p=0.085). Median time to complete
response was 8 months (range 4-17) and these women's median age was 32 years (range 28-67). Median age of non-responders was 36 years (range 27-78). Median time to hysterectomy was 5 months (range 2-11). To date, no responders have relapsed or had hysterectomy. No patients undergoing attempted CM have died and none were lost to follow-up.

Conclusions
CM of EC is safe for carefully selected women. Concurrent P and M may be more successful than either modality used alone. Fertility outcome in our cohort was poor, possibly reflecting their BMI, age and access to IVF. Women attempting CM need to be counseled accordingly.
Poster Presentations: Endometrial Cancer

**SALVAGE CYTOREDUCTIVE SURGERY FOR PATIENTS WITH RECURRENT ENDOMETRIAL CANCER: WHO WILL GAIN BENEFITS FROM IT?**

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**Objectives**
Recent studies suggested the survival benefits of salvage cytoreductive surgery (SCR) for patients with recurrent endometrial cancer (REC), but the surgical selection indications still undetermined.

**Methods**
Between January 1995 and May 2012, 75 patients with REC who underwent second cytoreductive surgery were reviewed from databases.

**Results**
The median recurrence interval was 18 months (3-372). Median age at recurrence was 56 years (33-76). 43 patients (57.3%) had R0 (no residual), 15 patients (20.0%) had R1 (residual 0.1-1.0cm), and 17 (22.7%) had R2 (residual >1 cm) resection. 35 patients (46.7%) had single, and 40 (53.3%) had multiple recurrence. The median survival time was 18 months, and 5-year overall survival (OS) rate were 42.0%. Residual disease >1cm and low histology grade were significantly associated with a worse OS in multivariate analysis (p=0.001 and 0.012, respectively). Age, recurrence interval, and recurrence tumor size and tumor number were associated with satisfied SCR.

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<td>Site of recurrence</td>
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Conclusions
Satisfied SCR were the strongest prognostic factor for REC. Patients with young age, tumor size < 6cm, single recurrence, and long recurrence interval were more likely to achieve satisfied SCR.
Poster Presentations: Endometrial Cancer

**SENTINEL LYMPH NODES MAPPING AND MICROMETASTASES DETECTION IN PATIENTS WITH EARLY-STAGE ENDOMETRIAL CANCER**

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**Objectives**

To assess the rate and diagnostic accuracy of the sentinel lymph node (SLN) procedure in predicting retroperitoneal lymph node status in patients with early-stage endometrial cancer.

**Methods**

All patients were randomly allocated to pericervical injection group, combination injection group and peritumor injection group. After SLN biopsy all patients underwent complete pelvic and paraaortic lymphadenectomy. All lymph nodes were histopathologically examined and SLNs were serial sectioned and examined by immunochemistry in patients with negative SLN and non-SLN by HE.

**Results**

One hundred and sixty patients enrolled between Sep 2010 and Mar 2013: 57 patients in cervical group, 53 in combination group, and 50 in peritumor group. At least one SLN was detected in 100%, 96.2%, 80% of patients of the 3 group, respectively. Significantly less SLN was detected in peritumor group (P<0.05), and less para-aortic SLN was detected in cervical group (P<0.05) The false negative rate was 2.0%, 2.3% and 0, respectively. Eighteen patients had micrometastases in SLN. No allergic reactions was recorded.

**Conclusions**

Although SLN biopsy has shown good diagnostic performance in endometrial cancer, such performance should be interpreted with caution because of false negative rate. SLN biopsy with cervical dual labelling could be a trade-off between systematic lymphadenectomy and no dissection at all in patients with endometrial cancer of low risk. For patients with intermediate or high risk endometrial cancer, peritumor injection or combination injection may be the appropriate selection.
THE PROFILE AND SIGNIFICANCE OF VEGF, VEGFR2 AND VEGFR3 EXPRESSION IN ENDOMETRIAL CARCINOMA.


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Objectives
Angiogenesis plays a key role in the progression of various tumours, including endometrial carcinomas. Several tyrosine kinase receptors, particularly vascular endothelial growth factor receptors (VEGFRs) are well-recognised to be involved in tumour angiogenesis. The aim of this study was to investigate the expressions and significance of vascular endothelial growth factor (VEGF), VEGFR2 and VEGFR3 in endometrial carcinoma.

Methods
The expressions of VEGF, VEGFR2 and VEGFR3 were studied by immunohistochemistry in formalin fixed paraffin embedded sections from 76 endometrial carcinomas. VEGFR2 and VEGFR3 expression levels were also studied by qRT-PCR in frozen tissue from 17 tumours in comparison to normal endometrium. The expression profile levels were correlated with tumour type, grade, stage, lymphovascular invasion and disease free survival.

Results
On immunohistochemistry, 63% carcinomas expressed VEGF, 55% expressed VEGFR2 and 26% expressed VEGFR3. There was a statistically significant correlation between VEGFR3 expression and tumour stage (p=0.02), and a trend towards poorer disease free survival (p=0.09) with higher expression. Using qRT-PCR, there was a 17.2-fold increase in VEGFR2 expression in endometrial carcinomas compared with normal endometrium, and a 21.9-fold increase in VEGFR3, with significant correlation between the expression levels of the two receptors (p<0.01).

Conclusions
The increased expressions of VEGFRs highlights them as potential therapeutic targets in endometrial carcinoma. To the authors’ knowledge, this is the first report showing a prognostic potential for VEGFR3 and suggests that evaluation of VEGFR3 expression in tumours may provide prognostic data, and help identify patients who would best benefit from anti-angiogenic therapeutic agents.
POSTER PRESENTATIONS:

Endometrial Cancer

METFORMIN DOES NOT IMPROVE SURVIVAL IN ENDOMETRIAL CANCER

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Objectives

Obesity and diabetes predispose to endometrial proliferation and carcinogenesis. Therefore altering metabolic processes may have a potential therapeutic role in endometrial cancer. Recent research reveal anticancer properties of metformin. The aim of this research was to verify whether metformin therapy improves survival in patients with endometrial cancer.

Methods

A group of 107 patients with endometrial cancer admitted to Department of Gynecologic Oncology in the years 2002-2010 was analyzed retrospectively. Patients were divided according to coexistent diabetes mellitus and metformin therapy. U Mann-Whitney test was used to compare clinicopathological features whereas Cox proportional hazard model was applied for survival analysis.

Results

The analysis included patients suffering from endometrial cancer without diabetes (n=39), with diabetes not receiving metformin (n=38) and with diabetes treated with metformin (n=30). Patients treated with metformin did not have improved survival [hazard ratio: 1.08, 95 % confidence interval: 0.46-2.56, p=0.85]. The coexistence of diabetes did not alter survival rate [1.13; 0.54-2.39; p=0.74]. When the analysis was restricted to the subgroup of type I endometrial cancer, both metformin intake and diabetes still did not influence the prognosis. Serum glucose level had no effect on survival rate [1.11, 0.52-2.32, p=0.79]. Neoplasms did not differ in terms of either staging [p= 0.86] or grading [p=0.92] between patients treated with and without metformin.

Conclusions

Coexistence of diabetes mellitus does not affect survival in endometrial cancer. Use of metformin does not influence either the histological type or the prognosis in endometrial cancer.
PROGNOSTIC IMPORTANCE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND ITS RECEPTORS IN THE UTERINE SARCOMA.
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2Departments of Tumor Markers, Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland
3Department of Pathomorphology, Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland
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Objectives
Vascular endothelial growth factor (VEGF) and its receptors play an important role in tumor progression; however, there is no report regarding this factor in uterine sarcoma.

Methods
29 patients with uterine sarcoma, 17 carcinosarcomas (CS), 12 undifferentiated stromal sarcoma (USS) were studied. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results
Of 29 sarcomas, 25 (87%) expressed VEGF. Expression of VEGF was significantly higher in patients with USS and CS (p=0.04) comparing to LM. When sarcomas were divided into two histological groups expression of VEGF was significantly higher for USS comparing to CS (p=0.035). VEGFR-1 was overexpressed only in 1 patient with USS. There were no differences in VEGFR-1 between sarcomas and controls (p=0.48). Significantly higher expression of VEGFR-2 was found in patients with CS and USS when compared to control group (p=0.013). No differences were found in expression of VEGFR-2 in patients with USS and CS (p=0.6). VEGF overexpression was strongly associated with survival (p=0.007).

Conclusions
VEGF and VEGFR-2 are suggested to be involved in progression of uterine sarcoma, but only VEGF expression significantly affected the survival of sarcoma patients.
Poster Presentations: Cervical Cancer

PREDICTOR FACTORS FOR PARAMETRIAL INVOLVEMENT IN CERVICAL CARCINOMA
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Objectives
The aim of this study is to identify the factors that can predict parametrial involvement in cervical carcinoma.

Methods
We retrospectively analysed 143 cervical cancer (1a2 and 1b1) patients who underwent radical hysterectomy and bilateral pelvic paraortic lymphadenectomy between the years 2007 and 2013. Tha statistical analyses are done by SPSS 16.

Results
The median age was 50 (range 25 to 80); 6 patients were stage 1a2 and 137 patients was clinical stage 1b1. 113 patients had squamous cell carcinoma (79%) and 30 had adenocarcinoma (21%). When we analysed the patients with tumor size ≤ 2 cm; 20 had negative LVSI, and none of them had parametrial or lymph nodal involvement. 28 patients had positive LVSI; 5 patients had parametrial invasion and 6 patients had pelvic lymph node metastases. As the tumor size increases the rate of LVSI (p=0.024), parametrial invasion (p=0.043) and lymph node metastases (p=0.001) increased. LVSI was statistically significant factor for parametrial and lymph nodal involvement (p=0.025 and 0.00).

<table>
<thead>
<tr>
<th>TM size</th>
<th>LVSI (+)</th>
<th>PM (+)</th>
<th>LN (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1 cm</td>
<td>7/12</td>
<td>2/12*</td>
<td>1/12*</td>
</tr>
<tr>
<td>1 &lt; TM ≤ 2</td>
<td>21/36</td>
<td>3/36*</td>
<td>5/36*</td>
</tr>
<tr>
<td>2 &lt; TM ≤ 3</td>
<td>42/55</td>
<td>15/55</td>
<td>22/55</td>
</tr>
<tr>
<td>3 &lt; TM ≤ 4</td>
<td>32/40</td>
<td>12/40</td>
<td>17/40</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>32</td>
<td>45</td>
</tr>
</tbody>
</table>

Conclusions
LVSI and tumor size seems to be predictor factors for parametrial and Lymph nodal involvement and less radical surgery may be performed for selected patients with tumor size less than 2 cm and no LVSI.

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Poster Presentations: Cervical Cancer

A COMPARATIVE STUDY OF SAFETY, EFFICACY AND COST BETWEEN OPEN AND LAPAROSCOPIC APPROACH FOR THE TREATMENT OF EARLY STAGE CERVICAL CANCER, WITHIN AN ENHANCED RECOVERY PROGRAMME.

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³Obstetrics and Gynaecology, Liverpool Women’s Hospital, Liverpool, United Kingdom

Objectives
Laparoscopic surgery for cervical cancer is replacing open surgery. Enhanced recovery programmes (ERP) have led to reduction in length of stay (LoS), in patients undergoing major surgery. This study aims to assess the safety and efficacy of laparoscopic versus open radical hysterectomy and calculate the direct costs of both within an ERP.

Methods
Cohort study of 23 laparoscopic radical hysterectomy cases matched with 23 open cases. Matching criteria were age, Body Mass Index (BMI), FIGO stage and American Society Anaesthesiologist (ASA) grade. All cases performed within an ERP. Direct hospital cost calculated for both procedures. Safety outcomes were compared with published case series. Due to limited follow-up duration, surgical excision parameters were used to compare the efficacy of the two procedures.

Results

<table>
<thead>
<tr>
<th>Safety</th>
<th>Laparoscopic</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>bladder injury</td>
<td>1 case or 4%</td>
<td>0</td>
</tr>
<tr>
<td>ureteric injury</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>bowel injury</td>
<td>1 case or 4%</td>
<td>0</td>
</tr>
<tr>
<td>ureteric/vescical fistula</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vascular injury</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>recurrence / follow up (months)</td>
<td>0 (4.6)</td>
<td>0 (14.2)</td>
</tr>
<tr>
<td>involved excision margins</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>closest excision margin (mm)</td>
<td>6.6</td>
<td>6.1</td>
</tr>
<tr>
<td>maximum cuff length (mm)</td>
<td>14.1</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety</th>
<th>Laparoscopic</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>length of stay (days)</td>
<td>2.7</td>
<td>4.56</td>
</tr>
<tr>
<td></td>
<td>£810</td>
<td>£1368</td>
</tr>
</tbody>
</table>
Conclusions
No significant difference in the measures of efficacy was identified between open and laparoscopic groups. Major complication rate is comparable to published series. The excess of 11% in direct cost for laparoscopic surgery is expected to be reduced as experience in the newly introduced procedure increases.
ROLE OF CYTOLOGY AND HPV TESTING AFTER TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives
The aim of the study was to investigate the role of human papillomavirus (HPV) testing and cytology as predictors of residual/recurrent disease after cervical conisation for high-grade cervical intraepithelial lesions (CIN 2 or 3).

Methods
44 women with CIN 2/3 lesion treated with loop electroexcision procedure for cervical conisation were included in a prospective follow-up study. Follow-up visits: 3 months after surgery when the patients were examined with colposcopy and Pap smear, and 9 months after treatment for HPV testing. Cytology, high-risk HPV presence, abnormal colposcopy finding during follow-up were correlated with histologically confirmed residual/recurrent disease.

Results
4 patients (9.8%) developed residual/recurrent disease during follow-up. Abnormal cytology at 3 months after treatment was significantly correlated with residual/recurrent disease. 3 of 10 patients with abnormal cytology at 3 months had recurrent disease versus 1 of 34 with a normal cytology. 9 months after treatment, viral typing revealed the persistence of high-risk HPV in all of these patients. Conversely, the viral follow-up of the other 40 patients without persisting/relapsing disease after treatment disclosed low-risk HPV genotypes in 2 cases, high-risk HPV in 1 cases. The risk of persistence and relapse of CIN in the group with positive margins was not statistically significant (P = 0.77), whereas it was in the group with HR-HPV positive (P = 0.000049).

Conclusions
Cytology remains the cornerstone in the early follow-up after cervical conisation for high-grade lesions of the cervix. HPV testing can increase sensitivity of cytology in predicting of residual/recurrent disease early and is therefore capable of optimising follow-up after the treatment of high-grade CIN.
TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY: A CHANGE IN PRACTICE IN A U.K. CANCER CENTER

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Objectives
To evaluate the safety, surgical and oncological outcomes of the implementation of Total Laparoscopic Radical Hysterectomy (TLRH) for the management of early stage cervical cancer.

Methods
Retrospective review of all the TLRHs performed in our unit between August 2010 and March 2013 for early stage cervical cancer (FIGO stage 1A2-1B1).

Results
In total 41 cases were identified and all but one were completed laparoscopically (97.5%). Mean age was 41.5 (23-86y) and mean BMI was 28 (18-37). Median operating time was 260min (90-390min) and average EBL was 157ml (36-500ml). The median inpatient hospital stay was 1.8 days (1-6 days). There were 3 intraoperative complications (7.3%). Two patients had obturator nerve transection (4.8%) and one a bladder injury (2.4%). Forty patients had clear para-cervical and vaginal excision margins (97.5%). Median node count was 16 (7-25) and seven patients received adjuvant chemo-radiation therapy (17%). There was one death from recurrence (2.4%). Range of follow up was 1-31 months, median 11 months.

Conclusions
TLRH appears in this series to be a safe alternative to the open surgical management of early stage cervical cancer. Complication rates were comparable to open surgery. Inpatient hospital stay and EBL were less than figures in published data for the open procedure.
Poster Presentations: Cervical Cancer

IS DIFFUSION-WEIGHTED MR IMAGING INCREASE THE SENSITIVITY OF DETECTION AND ASSESSING DEEP STROMAL AND PARAMETRIAL INVASION OF PRIMARY CERVICAL CARCINOMA?

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Objectives
Diffusion-weighted magnetic resonance imaging (DW-MRI) is used to evaluate malignant lesions. Aim is to assess the additional value of DW-MRI over T2-weighted MRI for detection and assessing deep stromal and parametrial invasion of primary cervical carcinoma.

Methods
Forty patients with cervical carcinoma and asymptomatic 40 patients with negative smear underwent DW-MRI in addition to T2-weighted MRI. First T2-weighted MR images, then combined T2-weighted and DW-MR images were independently evaluated by two abdominal radiologists. Intraclass correlation coefficient (ICC) values were also estimated.

Results
For tumor detection, the sensitivity for readers 1 and 2 were both 92.5% for T2-weighted images and 95% and 97.5% respectively for combined T2-weighted and DW-MR images. Although DW-MRI gave higher sensitivity values, the difference was not statistically significant for both readers (P=.644, P=.241 respectively)

For assessing deep stromal invasion, the sensitivity for the readers 1 and 2 were %100 and %90.9 respectively for T2-weighted and %95 and %96.96 for combined images. The difference was not significant for both readers (P=.999, P=.076 respectively).

For assessing parametrial invasion, the sensitivity for readers 1 and 2 were %87.5 and % 93.75 respectively for T2-weighted MRI and %87.5 and %93.75 for T2-weighted MRI plus DW-MRI. The difference was not significant for both readers (P=.999 for both readers).

Conclusions
Although DW-MRI did not show a significant increase in sensitivity for tumor detection and local assessment, it increased the sensitivity rates for tumor detection, and stromal invasion for reader 2. It also significantly increased the ICC value of tumor detection and deep stromal invasion (P=.001).
FROM ABDOMINAL RADICAL HYSTERECTOMY TO LAPAROSCOPIC RADICAL HYSTERECTOMY FOR EARLY STAGE CERVICAL CANCER: SURGICO-PATHOLOGICAL MEASUREMENTS

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Objectives
We analysed in prospective study resection size for laparoscopic radical hysterectomy (LPRH) compared with abdominal radical hysterectomy (ARH).

Methods
Total of 27 cases underwent LPRH and subsequently 27 patients were operated with ARH, all the operations were performed by the same surgical team. In R.Macedonia we introduced LPRH for the surgical treatment of FIGO Ia2 – II a cervical cancer (CC) in 2010. All participants had histologically confirmed CC, had required further investigations to determine their eligibility for the trial, i.e. 'imaging' technique with ultrasound or magnetic resonance. Fresh measurements of specimens were taken before fixation by the pathologist, compared with respect to number of lymph nodes retrieved, the measurement of two parametrial segments resected ,the average of vaginal cuff length (as a markers for radicality of surgery) and CC tumor size.

Results
The median age in LPRH 43 years compared to 54 years in the open group. The distribution of the histology was similar in the both groups, average CC tumor size was greater in ARH (4.2 cm), compared with LPRH (3.4 cm), the median number of lymph nodes removed was same in both groups (23/21 nodes), and length of vaginal cuff (0.6/0.8 cm). Measurements from resected parametrial tissue showed that mean length of the both sides was significantly higher with LPRH (left 3.1cm; right 3.0) v.s ARH (2;2.1 cm).

Conclusions
Our technique of LPRH is performed safety oncologically comparable to open surgery in terms of margins, lymph node clearance, parametrial and vaginal resection.
VALUE OF NORMAL COLPOSCOPY AFTER AN ABNORMAL PAP SMEAR
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Objectives
Cervical cancer is one of the leading causes of death among women in developing countries. Colposcopy is secondary screening test for this cancer used after a cytology is reported as abnormal.

This study determined value of normal colposcopy after an abnormal cervical cytology in referral patients with abnormal pap smear to Isfahan University hospital from 2011 to 2013.

Methods
We designed a diagnostic clinical trial study to review all pap smears and cervical pathology reports in patients with abnormal pap smear. The subjects included 168 women who underwent repeat pap smear, immediate colposcopy and punch biopsy of cervix. In the between. There were 152(90.5%) satisfactory colposcopy and 16(9.5%) unsatisfactory colposcopy.

Results
Among the 168 abnormal pap tests, there were 106(36.8%) ASC-US, 32(19.3%) LSIL, 24(14.5%) HSIL, 4(2.4%) ASC-H and 2(1.1%) CIS. Colposcopy results were 121 (72%) normal colposcopy, 31 (20.39%) CIN or suspicious lesion. Pathology examination of cervical biopsy confirmed 154(91.6%) normal histology of cervix and 14(8.3%) CIN or S.C.C.

In this research sensitivity of colposcopy as a diagnostic method was 78%, specificity 87%, positive predictive value (+pv) was 35.4% and negative predictive value (-pv) 97.8%, false negative 21.4%, and false positive was 12.9%.

Accuracy of colposcopy in patients with abnormal pap smear was 86% in this study.

Conclusions
Negative predictive value of colposcopy in this center is high (97/8%), but colposcopy cannot detect precancerous cervical lesions alone, It should be accompanied by cervical cytology and biopsy to have greater diagnostic value.
A STUDY OF 5532 PAPANICOLAU SMEAR DIAGNOSES IN GERALDINA QUEEN MATERNITY

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²Women Center, Geraldina Queen, Tirana, Albania
³Surgery, European Hospital, Tirana, Albania

Objectives
This study aimed to review Papanicolaou (Pap) smears in patients of Geraldina Queen Hospital in Tirana.

Methods
A cross-sectional descriptive study was carried out and a database search of patient’s reports from 2010 to 2013 at Women Center was reviewed. The abnormal Pap smear reports based on the Bethesda System were assessed.

Results
A total of 5532 Pap smear were reviewed from patients aging 20 to 79 years old. Totally 5274 (95.3%) cases had diagnosis of ‘negative’ and 258 (4.8%) smears were labeled as abnormal Pap smears. The numbers and rates of epithelial abnormalities were as the followings: Atypical squamous cell of undetermined significance (ASCUS; n=159 [61.6%]); atypical glandular cell of undetermined significance (AGUS; n=15 [5.8%]); low-grade squamous intraepithelial lesion (LSIL; n=71 [27.5%]); high-grade squamous intraepithelial lesion (HSIL; n=10 [3.8%]); and squamous cell carcinoma (SCC; n=3 [1.1%]).

Overall incidence of the cervical cancer among these samples was 0.2%.

Conclusions
The number of abnormal pap smears in this study is less than western countries, but is comparable with Middle East and Islamic regions. More prospective studies are recommended.

Keywords: Abnormal cervical cytology, Bethesda System, Pap smear, Prevalence, Tirana, Albania.
FEASIBILITY OF LAPAROSCOPIC EXTRAPERITONEAL PARAAORTIC LYMPHADENECTOMY AND PROGNOSTIC VALUE OF PARAAORTIC LYMPH NODE INVOLVEMENT IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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²Radiation oncology, Complejo Hospitalario Universitario Dr. Negrín, Las Palmas GC, Spain
³Pathology, Complejo Hospitalario Universitario Insular Materno-Infantil, Las Palmas GC, Spain

Objectives
To study the feasibility and safety of laparoscopic-extraperitoneal-paraaorticleymphadenectomy (LEPL), as well as the prognostic value of paraaortic LN involvement in patients with LACC.

Methods
64 patients underwent LEPL between March 2009-December 2012. All patients were treated with concurrent chemo-radiotherapy, tailored according to individual staging results. Data on demographics, pathology, perioperative-complications, recurrence and OS are presented.

Results
Patients' mean age was 47.8 years (28-69), 21.8% of them were <40. Mean BMI was 26.2 (19.1-36.5); 28% of patients had previously undergone laparotomy. Mean operative-time was 124.6 min (77-195); estimated operative bleeding was 63.5 ml (50-300). On average, 13.8 LN were removed (2-34); nodal involvement was found in 15.6%. Four intraoperative-complications occurred: two vascular events, which did not require conversion, a bowel and a ureteral injury. Mean hospital-stay was 1.8 days. Three lymphocysts (only one requiring drainage) and one case of renovascular hypertension were diagnosed postoperatively.

After a mean follow-up of 18.4 months, 85.9% of patients were FOD, 3.1% were AWD and 10.8% died from CC. The OS-rate was 42.2 months (SD 0.8; 95%CI 40.6-43.7) for patients with negative LN and 22.3 months (SD 4.9; 95%CI 12.6-32.1) for those with positive ones (p<0.0001). The mortality-rate was 1.9% for patients with negative nodes and 60% for patients with positive ones (p<0.0001).

Conclusions
LEPL is a feasible and safe procedure that should be offered to patients with LACC, since paraaortic LN involvement appears to be a major prognostic factor. We postulate that upon identification of paraaortic LN involvement, the disease should be considered systemic and therapeutic efforts should be established.
DNA METHYLATION ANALYSIS AS A TRIAGE TEST IN HPV POSITIVE WOMEN

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³Pathology, University Medical Center Groningen (UMCG), Groningen, Netherlands
⁴Medical Microbiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

Objectives
In the population-based screening program for cervical cancer around 30% of women do not respond. The PROHTECT 3B study invited non-responding women to self-collect a cervicovaginal specimen for hrHPV-testing. For hrHPV-positive women, additional liquid-based cytology was taken by the general practitioner and women with abnormal cytology were referred to the gynecologist. In this study DNA methylation triage testing was compared with routine cytology triage testing in hrHPV-positive women.

Methods
Liquid-based material was selected of 128 hrHPV-positive women with different cytological and histological results. Baseline self-sampling specimens obtained by Evalyn Brush (n=20) were also included. Methylation analysis was performed with QMSP for C13ORF18, EPB41L3, JAM3 and TERT.

Results
Triage testing by DNA methylation analysis for JAM3 showed the best results with a specificity of 88% and a sensitivity of 82% for CIN3+, while cytology showed a specificity of 48% and a sensitivity of 91%. In the patient group (n=40) with false-positive cytology 34 cases (85%) were negative for JAM3 and 36 (90%) for C13ORF18 methylation. The correlation of DNA methylation analysis between the liquid-based samples and Evalyn Brush self-sampling specimens was very high for all genes (p<0.001).

Conclusions
DNA methylation analysis as a triage test in hrHPV-positive women shows higher specificity results than cytology in this selected group of women. DNA methylation analysis appears also possible on the Evalyn Brush self-samplers and therefore might eliminate the need for a new scraping taken by the general practitioner thereby offering great logistic advantages. This study was financed by Dutch Cancer Society (RUG-NKB2009-4577).
Objectives
This study evaluates current surgical cervical cancer treatment in Sweden 2008-2012.

Methods
The National Register for Gynaecological Surgery (GynOP) collects operative and patient reported data.

Results
The registered primary cervical cancer patients were 249. The laparoscopic robot assisted operations registered were 64 including 62 radical hysterectomies and 2 radical trachelectomies and laparotomy was used in 185 patients including 5 radical trachelectomies and 2 cervical amputations.

The robot and laparotomy patients did not differ in age, BMI, ASA score or FIGO stage.

The mean operating time and the uterine weight did not differ. The blood loss was less in the robot (102mL) compared with the laparotomy group (495 mL) (p<0.001). Thirteen in the laparotomy group (7 %) received blood transfusion and none in the robot group. Intra-operative complications were more common in the laparotomy (13 patients) compared with the robot group (2 patients) (p=0.03). Re-admission or re-operations due to complications did not differ between the groups. The numbers of pelvic lymph nodes removed were higher in the laparotomy (median n=31) compared with the robotic group (median n=24) (p<0.001).

The postoperative hospital stay was longer in the laparotomy 6.1 days compared to the robot group 2.1 days (p=0.01). The patient reported time to normal activities of daily living (ADL) was shorter in the robot 9.7 days compared with the laparotomy patients 13.4 days (p=0.04).

Conclusions
Laparoscopic robotic assisted surgery is preferable to laparotomy for cervical cancer patients due to significantly shorter time to normal ADL, shorter hospital stay, less blood loss, and less intra-operative complications.
PROGNOSTIC VALUE OF P16 EVALUATION IN THE MANAGEMENT OF CERVICAL DYSPLASIA

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Objectives
Protein p16 as an important cell-cycle inhibitor is a promising diagnostic and prognostic factor of cervical dysplasia. In our study we evaluate the impact of p16 protein evaluation on management of cervical dysplasia.

Methods
A retrospective study was performed on 262 consecutive patients with colposcopically-directed cervical biopsy (CDB) with following excisional procedure (LEEP or cold-knife conisation). P16 expression in the specimen from CDB was independently evaluated by immunohistochemistry in all patients. Relation among CDB histology, p16 expression and final histology from excisional procedure was analysed.

Results
In our series, we identified 51 CIN I and 168 CIN II/CIN III in CDB specimens. In the CIN I group, 18 cases (35,3%) were p16 negative and 33 (64,7%) cases were p16 positive. In CIN I p16 negative group, only 3 of 18 patients (16,7%) had CIN II/CIN III in the final histology comparing to 26 of 33 patients (78,8%) in CIN I p16 positive group (statistically significant, p<0,05; Wilcoxon test). In CIN II/CIN III group, 158 (94,0%) specimen were p16 positive and 156 patients (92,9%) had also CIN II/CIN III in the final histology.

Conclusions
In our study of 262 patients with CDB we found that in group of CIN I patients, p16 evaluation had significant predictive value for final histology. In the group of patients with CIN II/CIN III, 94% specimens were p16 positive and therefore p16 evaluation had no prognostic impact on final histology.
DNA COPY NUMBER OF HPV-16 E6 ONCOGENE AS A NEGATIVE PROGNOSTIC FACTOR FOR CERVICAL CANCER

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Objectives
To explore the relationship between DNA copy number of HPV-16 E6 oncogene and cervical carcinoma, and its potential clinical significance as a prognostic factor.

Methods
Between January 2000 and December 2006, 134 consecutive HPV 16 positive patients who underwent radical hysterectomy with pelvic lymphadenectomy for FIGO stage IB1-IIA cervical cancer were retrospectively reviewed. RT-PCR method was used to identify DNA copy number of HPV-16 E6 oncogene from those tumor specimens. The association of HPV16 E6 DNA viral load with clinicopathologic characteristics and overall survivals was analyzed.

Results
Copy number of HPV-16 DNA was detected in all of 134 evaluable cases, and the results of correlation analysis indicated that HPV-16 viral load was significant related with cervical cancer patients age (P= 0.023), FIGO stage (P=0.036), and lymph node metastasis (P=0.047). Univariate analysis showed that the patient's age, HPV16 E6 DNA viral load, FIGO stage, histological grade, lymph node metastasis were the poor factors for overall survival time (P <0.05). Kaplan-meier survival analysis showed that the overall 5-year survival rates of the viral copy number range 107-109, 105-106, 103-104 of HPV16-E6 DNA were 39.4%, 44.0%, 86.3%, respectively (P <0.05). Cox regression analysis showed that lymph node metastasis (OR=9.617; 95% CI 1.598-7.719; p=0.002), HPV16 E6 DNA viral load (OR=12.403; 95% CI 1.628-5.535; p=0.001) are independent prognostic factors.

Conclusions
Our findings suggest that HPV16 E6 DNA viral load is an independent reliable prognostic factor of early-stage cervical cancer.
Poster Presentations: Cervical Cancer

TOPOTECAN IN COMBINATION WITH CISPLATIN FOR THE TREATMENT OF ADVANCE/RECURRENT CERVICAL CANCER, EXPERIENCE IN A SINGLE CENTER

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Objectives

Cervical cancer (CC) is the most common women malignancy in developing countries. Management of advance CC depends on extent, primary-treatment and performance-status(PS). The palliative chemotherapy(CT) with cisplatin-topotecan(CisTop) was the first to demonstrate improved survival compared to cisplatin, without further compromising quality-of-life. Objectives: Evaluation of response, safety, time to progression(TTP) and overall-survival(OS) in patients(pts) treated with CisTop.

Methods

Review of 60pts treated with CisTop(cisplatin 50mg/m²D1, topotecan 0,75mg/m²D1-3, 3qw), between june/2006-october/2010, in a single center. Pts included had inicial Stage-IVB or recurrent CC unsuitable for curative treatment.

Results

Median age was 51years. Inicial FIGO stage-II was more frequent(45%) and squamous carcinoma the most common histological-type(75%). Regarding the first-treatment: 68,3% underwent chemoradiotherapy(CT/RT); 3,3% had only surgery; 6,7% surgery+CT/RT; 6,7% surgery+RT; 3,3% surgery+CT; 16,7% palliative CT. Recurrence patterns were: pelvic(43.3%), distant-site(56,7%). The majority received CisTop as first-line(81.6%). Overall, 40% completed 6cycles of CisTop(without line difference, p=0.41). 94.3% had initial PS 0-1 and not changed at the end(p=0.147). 48.3% had clinical benefit (5%complete-responses, 25%partial-responses, 23.3%stable-disease). In a median follow-up of 36.5moths median TTP was 4months and median OS 36months. There was a worst OS in advanced-stages(p=0.004); no differences were found with: age(p=0.17), histology(p=0.75) and recurrence-site(p=0.5). Analysis of response, TTP and OS, according to the line(1st/others) didn’t show difference. Mild hematologic toxicity was the most common (anemia 66,9%; neutropenia 56%).

Conclusions

Our experience, being a retrospective analysis with few pts, found some differences to literature (equivalent TTP; superior OS and superior anti-cancer responses), but still confirming the clinical benefit of CisTop doublet without decrement in quality-of-life.
STEREOTACTIC BODY RADIOTHERAPY AS A BOOST IN ALTERNATIVE TO BRACHYTHERAPY : TECHNOLOGICAL INNOVATION AND APPLICATION IN CERVICAL CANCER RADIOThERAPY.

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Objectives
Hypofractionated treatment is a valid conservative alternative in exclusive or recurrent gynaecological cancer when brachytherapy is not feasible.

Methods
From June 2010 to December 2012 152 cervical cancer pts were treated with radiotherapy +/- brachytherapy boost. When brachytherapy is inadequate or not feasible, hypofractionated schedule with external beams is a very good solution (virtual brachytherapy).

Results
Normally all cervical cancer patients received Rapid arc radiotherapy: 45-50.4 Gy to the pelvis +/- para-aortic lymph nodes plus brachytherapy boost. In 10 pts (5/10 primary exclusive cervical cancer) we used hypofractionated boost to the persistence of disease with external beam radiotherapy. 14 pts with recurrent disease in the pelvis or to the node areas received an exclusive hypofractionated treatment. The dose for the hypofractionated boost schedule was 5 Gy x 3 fr = 15 Gy, EQD² = 18.8 Gy, isocenter EQD² = 83 Gy or 5 Gy x 5 fr: 20 Gy EQD² = 25 Gy. For the pts who received the hypofractionated treatment alone the doses was: 6 Gy x 5 fr = 30 Gy = EQD² = 40 Gy or 5 Gy x 5 fr = 25 Gy EQD² = 30 Gy. In this group of pts (24 pts) after a median follow-up of 8 months we observed that, all pts but one are in complete remission of disease and in absence of correlated toxicity.

Conclusions
The possibility to hypofractionate the treatment offers a new approach for a minimally invasive treatment in the management of cancer when current surgical approach and other conventional radiotherapy techniques are unsuitable.
Poster Presentations: Cervical Cancer

PREDICTING THE RECURRENT FACTORS OF CERVICAL CANCER USING C5, MARS AND RF: A COMPARISON STUDY

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Objectives
The choice of treatment for cervical cancer depends partly upon the risk of recurrence. This is usually done using clinical judgement alone, and can be difficult. The objective of the present study was to identify the significant recurrent factors for cervical cancer. In addition, we developed C5, Multivariate Adaptive Regression Splines (MARS) and Random Forest (RF) model for predicting the recurrent factors.

Methods
To find out the recurrent factors, we first constructed a risk factor set through an extensive literature review of cervical. The cervical cancer dataset provided by the Chung Shan Medical University Hospital Tumor Registry is used in this study. Each patient in the dataset contains 12 predictor variables and the dependent variable is recurrence or no. We evaluated three models and compared their results using three statistical indices: accuracy, sensitivity and specificity.

Results
The findings revealed that Pathologic Stage, Pathologic T, Cell Type and RT target Summary were the most important prognostic factors, in contrast to other similar analysis (Grisaru et al., Cancer 97:1904-1908). The average correct classification rates / area under the curve of the C5.0, MARS and RF models are 0.924 / 0.889, 0.866 / 0.838 and 0.854 / 0.919, respectively.

Conclusions
Based on the findings, the C5.0 model not only generates the better classification result, but also can be used to select important independent variables for recurrent cervical cancer. For medical interpretation, we can develop some results by which a physician caring a patient can better decide when to take the critical intervention.
Poster Presentations: Cervical Cancer

CK 7 AS A PREDICTIVE FACTOR FOR RESPONSE TO CONCOMITANT RADIO-CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER

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Objectives
The place of completion surgery after concurrent radiochemotherapy (CRC) for advanced cervical cancer remains controversial. Individual predictive factors of CRC response and survival are mandatory to adapt the treatment in case of failure and to determine a population of good responders who would not take interest in completion surgery after CRC. The aim of this study was to evaluate the ability of some biomarkers, analysed on initial cone biopsy, to predict the response to CRC.

Methods
Between 1996 and 2008, among 58 patients with advanced cervical cancer (IB2 – IV FIGO stage), for whom pre therapeutic biopsy was available, we tested several biomarkers: ALDH1, CD44, CD24, IDO, Ki67, P63, CK7, p-Stat3, Foxp3 and IDO.

Results
81% had epidermoid cancer (n=47), 15.5% adenocarcinomas (n=9) and 3.4% mixed or muco-epidermoid tumours (n= 2). Residual disease was found in 49.1% of cases (n=26). We found a significant association between PFS and residual disease on completion hysterectomy (p= 0.044, Fig 1). Univariate analysis of the different factors showed that CK7 negative was a strong predictor for the presence of residual tumour (p= 0.001) and associated with poor overall survival (Fig 2).

Conclusions
These results are encouraging and CK7 could be used as a predictive factor of CRC response. He could also be used to determine a population of good responders who would not take interest in completion surgery after CRC.
EXPRESSION OF HPV L1 CAPSID PROTEIN IN CERVICAL INTRAEPITHELIAL NEOPLASIA AND CANCER

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Objectives
The aim of the study is to investigate expression rate of human papillomavirus(HPV) L1 capsid protein and HPV DNA to predict cervical cancer and cervical intraepithelial neoplasia(CIN).

Methods
Immunocytochemical staining for HPV L1 capsid protein was carried out on 2,537 samples obtained from women performed liquid-based cytology. Results were compared with histopathology. High-risk HPV DNA was detected by Hybrid capture II(HC-II), and HPV genotypes was performed by HPV DNA chip test.

Results
HPV L1 capsid protein was positive in 54.7%(146/267) of CIN I, 54.7%(98/179) of CIN II, 31.7%(239/754) of CIN III, and 6.9%(16/233) of carcinoma. Histopathologic diagnosis revealed higher HPV L1 capsid protein expression rate in CIN I, II than CIN III or cancer(p<0.0001). HPV L1 capsid protein and HC-II were positive in 68.1%(64/94) of CIN I, 60.1%(86/143) of CIN II, 33.1%(229/691) of CIN III, 7.1%(15/210) of carcinoma. Final diagnosis revealed high-risk HC-II and higher HPV L1 capsid protein expression rate in CIN I, II than CIN III or cancer(p<0.0001). HPV L1 capsid protein and HPV 16 were positive in 48.6%(18/37), 53.1(26/49), 32.6(113/347), and 5.5%(7/127) of CIN I, CIN II, CIN III and cancer, respectively. HPV L1 capsid protein and HPV 18 were positive in 58.3%, 66.7%, 32.6%, 8.8%, respectively.

Conclusions
The expression rate of HPV L1 capsid protein and positive high-risk HC-II in liquid-based cytology specimen was decreased as the histopathologic diagnosis severe degree. Detection of HPV L1 capsid protein and HPV DNA may predict the progression of cervical lesion, and help to distinguish the cases with CIN and cancer.
IMAGE GUIDED BRACHYTHERAPY FOR CARCINOMA OF THE CERVIX: ASSESSING THE OPTIMAL NUMBER OF MRI SCANS

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Objectives
Recent evidence, including GEC-ESTRO recommendations and RCR WP report, supports the use of MRI based image-guided brachytherapy (IGBT) for cervical cancer for all fractions of brachytherapy. However, in practice this is difficult to achieve because of restricted access to the MR scanner. The purpose of this study was to determine whether it is necessary to carry out an MRI scan for each of the three fractions of brachytherapy.

Methods
All patients were planned and treated using co-registered CT/MR scans. For the purpose of this study, EQD2 doses to HR-CTV and organs at risk were calculated for CT based plans and compared to the CT/MRI based plans.

Results
Initially, we measured the difference in volumes of organs at risk (OAR) outlined on MRI and CT scan. We found that although, OAR volumes were generally larger on CT scan, statistically significant difference was only noted for rectal volume. We also calculated the total dose in 2 Gy per fraction (EQD2) for HR-CTV and organs at risk for the original MRI based plans and new CT based plans. All plans were within the dose limits suggested by the EMBRACE trial. However, treatment planned using CT outlining showed statistically higher dose to the sigmoid.

Conclusions
The proposed approach delivers adequate dose to the target volume while keeping the dose to the organs at risk within tolerance limits. However, at CCC we continue to use MRI scans for all three fractions of brachytherapy.
Objectives
To evaluate the feasibility and safety of tailoring parametrectomy in patients affected by locally advanced cervical cancer (LACC) according to specific prognostic factors preoperatively assessed.

Methods
Consecutive LACC patients were considered for the study and submitted to platinum-based neoadjuvant chemotherapy (NACT) followed by radical hysterectomy plus bilateral systematic pelvic lymphadenectomy. Lymph nodes were sent for frozen section. Node-negative patients were submitted to modified radical hysterectomy (type II / B) (Group A). Operative data and survival were compared with a historical control group of patients submitted to classical radical hysterectomy (type III-IV/C2) (Group B).

Results
78 patients were considered for this prospective study, among these 12 were excluded. The remaining 66 patients underwent NACT: 48 (79%) had a clinical response. Among the 48 responders patients, 13 (27%) were node positive and therefore excluded from the study. The remaining 35 node negative patients (Group A) were submitted to modified radical hysterectomy and data were compared with those of 86 patients of historical group (Group B) submitted to classical radical hysterectomy. The rate of bladder dysfunction was significantly lower in the group of patients who performed a less radical surgery (14% vs 72 %, p<0.0001). Five years overall survival was 92% for Group A and 94% for Group B (N.S).

Conclusions
Preoperative and intraoperative evaluation of adverse prognostic factors in patients affected by LACC is feasible to determine if a less radical surgery is applicable. Less aggressive surgery could be considere to LACC patients with favorable prognostic factors after NACT.
HOW A NOVEL PATTERN-BASED CLASSIFICATION SYSTEM OF ENDOCERVICAL ADENOCARCINOMA (SILVA SYSTEM) PREDICTS RISK OF LYMPH NODE METASTASIS AND IMPACTS CLINICAL DECISIONS - A MULTI-INSTITUTIONAL STUDY.


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Objectives
Currently, decision to perform lymphadenectomy in cases of invasive endocervical adenocarcinoma (ECA) greatly depends on depth of invasion (DOI). However, accurate assessment of this critical parameter is difficult. The recently described Silva system (Gyn Oncol 2012:125:S27-28) classifies ECA based on pattern of invasion and can predict risk of lymph node (LN) metastasis. Our objective was to determine how this system, in addition to other features, can guide therapy.

Methods
Cases of invasive ECA from 14 institutions (n=410) were evaluated and classified using the Silva system: pattern A (well-demarcated glands), B (early destructive stromal invasion), and C (diffuse destructive stromal invasion).

Results
Ages ranged from 20-83 years, tumor size from 0.5-65 mm, DOI from 0.5-40 mm. Lymph-vascular invasion (LVI) was present in 41.5% of cases (0% in A, 34% in B, 63.3% in C).

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Patients</th>
<th>Stage I</th>
<th>Stage II-IV</th>
<th>LN</th>
<th>Recurrence DOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current method</td>
<td>410 (100%)</td>
<td>372 (91%)</td>
<td>38 (9%)</td>
<td>66 (16%)</td>
<td>48 (11.7%)</td>
</tr>
<tr>
<td>Pattern A</td>
<td>86 (21%)</td>
<td>86 (100%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pattern B</td>
<td>106 (26%)</td>
<td>104 (98%)</td>
<td>2 (2%)</td>
<td>7 (6.6%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Pattern C</td>
<td>218 (53%)</td>
<td>182 (84%)</td>
<td>36 (16%)</td>
<td>59 (27%)</td>
<td>46 (21%)</td>
</tr>
</tbody>
</table>

Conclusions
Analysis of additional cases validated observations of our initial study. Pattern A had no LN metastases. Few pattern B and numerous pattern C cases had...
LN metastases (all with LVI). Conservative management, assessment of sentinel LN, and more aggressive lymphadenectomy should be further explored as potentially safe alternatives for patterns A, B, and C, respectively.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

**Poster Presentations: Cervical Cancer**

**THE AGE AND GENOTYPE-SPECIFIC PREVALENCE OF CERVICAL HPV DNA IN GIRLS AND ADOLESCENT WOMEN WITH NORMAL CERVICAL CYTOLOGY**

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**Objectives**

The leading etiologic cause for cervical cancer as the third most common malignancy in women, is represented by cervico-vaginal infection with high-risk human papilloma virus (HPV). The peak incidence of HPV infection occurs in adolescents and young women. Investigations worldwide showed that nearly 10% of women with normal cytological findings carry a detectable cervical HPV infection. Therefore, HPV can be considered as the most common known sexually transmitted agent worldwide.

In our study we set out to estimate the age and genotype-specific prevalence of cervical HPV DNA in girls and adolescent women with normal cervical cytology.

**Methods**

1070 girls and adolescent women underwent routine conventional smears (Pap tests) with normal colposcopic and cytological diagnoses. In each case HPV infection was primarily evaluated by PCR for HPV genotype determination.

**Results**

From 1070 patients investigated, 110 were HPV positive. The most prevalent genotypes among the infected samples were HPV16 (36-32.5%), HPV31 (19-17%), HPV18 (9-8.5%), and HPV52 (8-7%). The rest 35% (28 patients) falls off other undetermined types of HPV genotypes.

**Conclusions**

Today in the era of HPV vaccines, it is very important to evaluate the distribution of potentially malignant HPV genotypes by using molecular investigation for HPV genotypes thus predicting the effect of vaccines on the incidence of infection.
Poster Presentations: Cervical Cancer

PREVALENCE OF HIGH RISK HPV IN CERVICAL SMEAR OF WOMEN IN ILE-IFE
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Objectives
This study is aimed at estimating the prevalence of cervical infection with high-risk human papillomavirus (HR-HPV) in cervical smears of women in Ile – Ife. Well Women Clinic of the Obafemi Awolowo University Teaching Hospital Complex, Ile –If.?e.

Methods
This is a prospective cross-sectional observational study. Information was obtained through personal interviews using structured questionnaire. Samples were collected from 118 consenting women visiting the clinic during the study period. Conventional Pap smear was obtained and smear results were classified using Bethesda classification, 2001. HPV DNA was detected using the hybribio 21 HPV Geno array test kit. These data were analysed using simple and inferential statistic.

Results
The mean age of the participants was 42.9 years (standard deviation 10.9). A total of nine different HR-HPV types were identified with an HPV prevalence of 21.6% overall and 22.7% among women with cervical lesions. The predominant HR-HPV types were HPV 16, 53, 18 and 52. In all, 41.7% of the infections involved more than one HPV type. Unlike in most populations studied so far, HPV prevalence was high not only among young women, but also in middle and old age. It was also observed that the prevalence of HR-HPV increases with the number of pregnancies.

Conclusions
This study shows that HPV 53 is the second most common type after HPV 16. High prevalence of HR-HPV in all age group may be a distinctive feature of a population where HPV transmission continues into the middle age and cervical cancer incidence is very high.
LAPAROSCOPIC EXTRAFASCIAL HYSTERECTOMY (COMPLETION SURGERY) AFTER PRIMARY CHEMORADIATION IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER.

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Objectives

Residual disease (RD) after chemoradiation for locally advanced cervical cancer (LACC) is directly associated to local relapses. Nevertheless, the importance of completion surgery as an adjuvant procedure is controversial. The objective of this study is to evaluate feasibility and safety of laparoscopic extrafascial hysterectomy after chemoradiation.

Methods

Prospective study with patients affected by bulky LACC (FIGO-stage Ib2 up to IIb) treated initially with standard chemoradiation and underwent to surgery 12 weeks after therapy conclusion. Inclusion criteria were absence of signs for extra-pelvic or nodal involvement on initial imaging staging; complete clinical and radiological response.

Results

Between 2011 and 2013, 35 patients were operated. The mean age was 44 years (21 – 77). Histology revealed SCC in 21 cases (60%) and adenocarcinoma in 14 (40%) cases. FIGO-stage distribution was: 1b2, n=3 (8.5%); IIa, n=4 (11.5%); and IIb, n=28 (80%). The mean pretherapeutic tumor size was 5.2 (4 to 10.2) cm. Any casualty or conversion to laparotomy occurred. Estimated blood loss was 80 cc and mean operative time was 94 minutes. Hospital stay was in average 1.7 days. Significant complication occurred in 11% of the cases; two vaginal vault dehiscence, one pelvic abscess and one ureterovaginal fistula. Ten patients (28.5%) had pathologic RD and in 80% of these cases histology was adenocarcinoma. All patients had free margins. After mean follow-up of 14 months, all women have no signs of recurrence.

Conclusions

Laparoscopic extrafascial hysterectomy (completion surgery) after primary chemoradiation in patients with LACC is a viable and safe alternative to improve local tumor control at least in cases of adenocarcinoma.
AN ECONOMIC ANALYSIS OF NEW REGIMENS IN THE TREATMENT OF WOMEN WITH ADVANCED OR RECURRENT CERVICAL CANCER

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Objectives
Despite significant improvements in overall survival for women with advanced cancer with platinum based agents, more patients are receiving platinum upfront with radiation therapy. Therefore, newer combinations with and without platinum are being studied. We sought to evaluate the cost effectiveness of such therapies.

Methods
The GOG 240 schema was used to design a cost effectiveness analytic decision model. In analysis all regimens consisted of 6 cycles. Regimen 1 is cisplatin/paclitaxel (CP). Regimen 2 is CP with bevacizumab (CP+B). Regimen 3 is paclitaxel/topotecan (PT). Regimen 4 is PT with bevacizumab (PT+B). Parameters include overall survival (OS), cost, and complications. Sensitivity analyses were performed.

Results
The average cost for 6 cycles of each is as follows: CP, $21,760; CP+B, $97,606; PT, $51,770; and PT+B, $74,281. Sensitivity analysis revealed that to get an incremental cost-effectiveness ratio (ICER) for CP+B:CP of <$50,000 / quality adjusted life year (QALY) gained, the average overall survival of these patients is going to have to increase from 1.1 years with CP to 2.5 years with CP+B. To get an ICER <$50,000/QALY is would take a survival of 5.5 years for PT and 3.1 years for PT+B.

Conclusions
Unless the newer regimens tested against CP increase survival by more than two times, CP will be the most cost effective regimen. Even a 12 month increase in overall survival will not make the newer regimens cost effective.
EVALUATION OF CLINICAL AND PATHOLOGICAL RISK FACTORS MAY REDUCE THE RATE OF MULTIMODALITY TREATMENT OF EARLY CERVICAL CANCER


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4 Obstetrics and Gynecology, Soroka Medical Center, Beer Sheva, Israel
5 Obstetrics and Gynecology, Assaf Harofe Medical Center, Zrifin, Israel
6 Obstetrics and Gynecology, Shaare Zedek Medical Center, Jerusalem, Israel
7 Obstetrics and Gynecology, Meir Medical Center, Kfar Saba, Israel
8 Obstetrics and Gynecology, Wolfson Medical Center, Holon, Israel
9 Obstetrics and Gynecology, Ziv Medical Center, Safed, Israel
10 Obstetrics and Gynecology, Kaplan Medical Center, Rehovot, Israel

Objectives
To assess the rate of postoperative adjuvant treatment in patients who underwent radical hysterectomy for early cervical cancer and to suggest criteria for the triage of patients that have a high probability of multimodality treatment.

Methods
Multicenter retrospective study of 514 patients with FIGO stages IA2-IIA cervical cancer that underwent radical hysterectomy between 1999 and 2010. The patients were divided into two groups according to whether or not post-operative radiation was administered. The two groups were compared with regard to clinical and histopathological variables divided into major and minor criteria (intermediate risk factors) based on lymph nodes status, parametrial involvement, tumor size, deep stromal invasion and lymph-vascular space invasion.

Results
We identified 294 (57.2%) patients that received adjuvant post-operative radiotherapy or chemoradiation. Fifty three percent of these patients who were treated by adjuvant radiation had only intermediate risk factors. Combining the various combinations of two out of three of the following criteria, we found that 89% of patients with tumors ≥ 2cm and lymph-vascular space invasion received radiotherapy, 76% of patients with tumors ≥ 2cm and depth of invasion > 10 mm received radiotherapy, and 87% of patients with tumors depth of invasion > 10 mm and lymph-vascular space invasion received radiotherapy.

Conclusions
This study suggests that in patients with early cervical cancer clinical-pathological evaluation of tumor size and lymph-vascular space invasion should be undertaken prior to performing radical hysterectomy. This approach can serve to tailor treatment, reducing the rate of employing both radical hysterectomy and chemoradiation.
Objective

The aim of this study was to compare the results of see-and-treat procedure with the classical three-step procedure in terms of initial cytology and LEEP reports.

Methods

We searched the pathology charts of patients that had LEEP were searched retrospectively and then they were divided into 2 groups according to the presence or absence of a cervical biopsy before LEEP.

Results

There were 116 patients in the study. Of the patients with ASCUS/LSIL cytology and a positive cervical biopsy 48.4% had CIN 2-3 at LEEP, in contrast only 19% of the patients without a prior cervical biopsy had CIN 2-3 at LEEP (p=0.031); there was no statistically significant difference between the 2 procedures in patients with a HSIL and ASC-H smear result (p=0.726 and p=1.0 respectively).

Conclusions

In conclusion patients with ASC-H and HSIL cytology see-and-treat approach seems more advantageous, avoids delay in treatment, noncompliance and risk of skipping lesions at biopsy.
ASSSESSMENT OF DIFFERENT TREATMENT MODALITIES IN STAGE IB2-IIA (BULKY) CERVICAL CANCER

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Objectives
In this study, an analysis of stage IB₂-IIA (Bulky) cervical cancer is made. The efficacy of Neoadjuvant chemotherapy after radical surgery and primary radical surgery is investigated.

Methods
Medical data of 50 patients who were diagnosed with stage IB₂-IIA (Bulky) cervical cancer and treated between 2002-2009 were retrospectively assessed. In the radical surgery group, radical hysterectomy + bilateral pelvic + para-aortic lymphadenectomy was performed. In the neoadjuvant chemotherapy group, a combination of cisplatin/topotecan or paclitaxel/carboplatin was given to the patients and then radical surgery was performed. Both of the groups were evaluated individually.

Results
Radical surgery after neoadjuvant chemotherapy was performed in 21 patients. Primary radical surgery was performed in 29 patients. Median follow-up time was 36.0±14.0 months. Average of amour size before treatment was 50.2±7.6 mm. There was no difference in patients’ ages, follow-up time, tumor size (before treatment) or dissected lymph nodes between the groups. In the primary radical surgery group, statistics revealed that all parameters negatively effect survival. In the radical surgery after neoadjuvant chemotherapy group, lymphovascular space invasion and tumor size (before and after treatment) were determined to be significant factors for each of disease-free survival and overall survival. On multivariate analysis, tumor size (before treatment) was found to be an independent prognostic factor for both of disease-free survival (p=0.006) and overall survival (0.010).

Conclusions
In this study, those who had undergone radical surgery, had a better rate of survival. However, there was not significant superiority between the treatment options.
Poster Presentations: Cervical Cancer

EFFECT OF MARGIN STATUS ON RECURRENCE FOLLOWING CONIZATION IN WOMEN WITH CARCINOMA IN SITU OF CERVIX

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Objectives
Conization is being widely used for diagnosis and treatment of cervical intraepithelial neoplasia (CIN) and there is controversy as to the clinical significance of positive cone margin. We conducted this study to evaluate the clinical significance of a positive cone margin in patients with carcinoma in situ (CIS) of cervix.

Methods
We retrospectively analyzed the medical records of 228 patients with CIS of cervix treated by conization in 2011. We compared the pathologic and cytologic results according to the resection margin status of conization.

Results
Of 228 patients who were diagnosed as CIS of cervix at conization, 136 (59.6%) and 151 (66.2%) patients were diagnosed as CIS at PAP smear and punch biopsy before conization, respectively. Cold knife conization was conducted in 78.9% of patients, and the others underwent LEEP. Ninety six patients (42.1%) had margin involvement and the others were margin free at the conization specimens. PAP smear following conization showed that CINs were significantly more in the patients with positive cone margins (p=0.006), and 24.0% of them showed abnormal cytology. Of 28 patients who had positive cone margin and underwent following reconization or hysterectomy, 20 (71.4%) showed no residual CIN lesions.

Conclusions
Margin status of conization did not mean the presence or absence of CIN, but rather the higher frequency of residual CIN in specimens of abnormal subsequent cytology. In view of this fact, it is suggested that the margin status of conization can be a valuable marker for clinical management of CIS of cervix.

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Poster Presentations: Cervical Cancer

GENETIC CHARACTERISTICS OF HUMAN PAPILLOMA VIRUSES CAUSING FOR CERVICAL CANCER AMONG WOMEN IN BELARUS

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Objectives
The study included 299 cervical samples from patients with cervical cancer. For the sequence 35 samples that contain DNA of HPV-16 were selected.

Methods
PCR. Pair of primers to HPV-16 L1 gene, L1 (L): ttgcctcctgtcccagtatc; L1 (R): aatggctgaccacgacctac, synthesized on automatic synthesizer "Expedite TM 8900 Nucleic Acid Synthesis System".

Results
To specificities of genital HPV among women in Belarus include the association of cervical cancer with HPV-16, 31, 33, 35 and 18, which is reliably more often (p = 1.1x10⁹, p = 0.002, p = 0.007, p = 0.02, p = 0.007 respectively) than asymptomatic carriage. Phylogenetic analysis of identified subtype of HPV-16 endemic to the country in general epidemiological situation characterized by East Asian and European subtypes HPV-16. From the one patient with CIN3 living in a remote village district, Gomel region, was isolated unique subtype HPV-16, which is very far from the evolutionarily famous reference to viruses and is one of the ancestors HPV-16 circulating on the European continent.

Conclusions
1. HPV-16 is the dominant genotype, responsible of cervical cancer, and its frequency is 56.7% among patients in Belarus. 2. In Belarus is dominated by East Asian and European subtypes HPV-16, which can be attributed to a single evolutionary branch at the same time, the identification of subtypes HPV-16 with p-distance between samples was 0.003-0.007 may indicate multiple ancestor of HPV circulating in the country. 3. A unique subtype of HPV-16 in the Gomel region, which can be one of the first parents HPV-16 floating around on the European continent.
RADIOTHERAPY WITHOUT CISPLATIN FOR ELDERLY PATIENTS WITH CERVICAL CANCER

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Objectives
Radiochemotherapy for cervical cancer may have a high risk of acute- and late side effects, and hence be considered too toxic for many elderly patients. The purpose was to evaluate treatment-, side effects and survival after radiotherapy (RT) alone, for patients age 80+.

Methods
Twenty-five consecutive cervical cancer patients, 1. January 2000 - 31. December 2011, age 80+, receiving curative intended RT were included. Patient characteristics, toxicities and survival data were evaluated. Patients received external RT, either 46 Gy in 23 fractions (4 pelvic field conformal RT or Volumetric Modulated Arc Therapy (Rapid Arc)) or 64 Gy in 32 fractions (5-field intensity modulated RT (IMRT)). Patients were planned for PDR brachytherapy either intracavitary 17.5 Gy x 2 to point A or interstitial 30 Gy.

Results
Median age was 82 (range 80-88). Histology of primary tumors: Squamous cell carcinoma (64%), adenocarcinoma (16%), undifferentiated (4%), rare types (8%), unknown (8%). Primary FIGO stages: IIA (4%), IIB (56%), IIIA (4%), IIIB (32%), IVA (4%). Two patients experienced acute side effects of RTOG grade 3 to bladder and vagina respectively. Other two experienced late side effect grade 4 due to vesico- and/or recto-vaginal fistulas.
Six patients had a relapse of their disease (31% actuarial, Figure 1).

Conclusions
With a relapse rate of 31% and little severe toxicity, our results show that using RT without Cisplatin to 80+ years old cervical cancer patients is safe and provides a good disease control.
EVALUATION AND IMPACT OF RESIDUAL DISEASE IN LOCALLY ADVANCED CERVICAL CANCER AFTER CONCURRENT CHEMORADIATION THERAPY: RESULTS OF A MULTICENTER STUDY

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Objectives
The aim of this study was to evaluate diagnosis and impact of residual disease (RD) after concurrent chemo-radiation therapy (CRT) in locally advanced cervical cancer (FIGO IB2-IVA).

Methods
This retrospective multicenter study included, from 2006 to 2012, 159 patients treated by completion surgery after CRT. Magnetic resonance imaging (MRI) was performed 4 to 6 weeks after CRT and compared to pathological residual disease. Kaplan-Meier survival curves were plotted and univariate analysis was performed to assess association between RD and outcome.

Results
Residual disease was present in 45.3% of the patients and detected by MRI for 57.1% of them. MRI presented a 29.2% false positive rate and a 11.1% false negative rate. False negative rate was higher (21%) when RD was more than ten millimeter (p=0.04). The overall survival (OS) at 1, 3 and 5 years were respectively 93% (CI 95% [88.9%-97.3%]), 78.6% (CI 95% [71%-86.9%]) and 76.5% (CI 95% [68.2%-85.7%]). The disease free survival (DFS) at 1, 3 and 5 years were respectively 87.8% (CI 95% [82.6%-93.5%]), 73.4% (CI 95% [65.6%-82%]) and 71.1% (CI 95% [62.7%-80.1%]). Presence of RD decreased DFS when the size was over 10 mm (HR=4.84, p=0.03) whereas RD between 1 and 10 mm (HR=0.31, p=0.58) and less than 1 mm (HR=0.37, p=0.54) had no impact on DFS. OS was not changed by RD.

Conclusions
RD over 10 mm decreased DFS whereas it was associated to a worse false negative rate at MRI. Detection of RD should be improved, by metabolic imaging as PET/CT, to select patients who might benefit from completion surgery.
Poster Presentations: Cervical Cancer

CCN1 KNOCKDOWN BY SMALL INTERFERING RNA INHIBITS CELL PROLIFERATION AND INVASION OF SQUAMOUS CELL CARCINOMA CELLS

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Objectives
CCN1 (Cyr61) has been shown to regulate angiogenesis, cell proliferation, adhesion, migration, and differentiation. An increasing body of evidence indicates that abnormal expression of the CCN proteins is associated with tumorigenesis. Although it has been reported that overexpression of CCN1 is associated with the cell proliferation and migratory ability in squamous cell carcinoma (SCC), the role of CCN1 on the biological behavior of SCC has been rarely investigated. Herein, we investigated the effect of CCN1 downregulation on proliferation and migration of SCC cells in vitro. We also examined the relation between CCN1 expression and clinicopathological parameters in patients with SCC.

Methods
We generated two stable CCN1-knockdowned clone (Ca9-22_shCCN1) from the Ca9-22 SCC cell lines by lentiviral delivery. Cell proliferation and in vitro invasion and cell proliferation assays were used to investigate the effect of CCN1 downregulation on cell proliferation and migratory ability in Ca9-22_shCCN1. Immunohistochemistry was performed to evaluate the correlation between CCN1 expression and clinicopathological parameters in 59 SCC tissue samples.

Results
CCN1-knockdowned Ca9-22_shCCN1 cells showed reduced proliferative and migratory ability compared with the control vector-infected cells. Also, Ca9-22_shCCN1 cells showed reduced phosphorylated ERK expression, compared with the control vector-infected cells. Of 59 SCCs, 38 (64.4%) expressed CCN1, while 21 (35.6%) did not. Higher level of CCN1 expression significantly correlated with large tumor size (P=0.020), high clinical stage (P=0.030), positive lymph node metastasis (P=0.002).

Conclusions
These results suggest that the downregulation of CCN1 induces anti-proliferative and anti-invasive effects in SCC and that CCN1 might be a useful target molecule for the treatment of SCC.
Objectives
To compare preoperative sentinel lymph node (SLN) mapping with planar lymphoscintigraphy (LSG) to single photon emission computed tomography with computed tomography (SPECT-CT) for differences in intraoperative SLN retrieval time in surgically treated cervical cancer patients.

Methods
Retrospective cohort study of consecutively treated cervical cancer patients (09-2009 to 10-2012). One day prior to radical surgery, 220-290 MBq technetium-99m-nanocolloid was submucosaly injected divided over four cervical depots. Subsequent SLN mapping was performed by either LSG (before 03-2011) or SPECT-CT (after 03-2011). Robot assisted laparoscopic SLN identification and resection was based on blue dye combined with technetium-99m activity and followed by pelvic lymph node dissection. Timing of perioperative care, including SLN procedure times, was prospectively registered.

Results
Out of 62 cases, 33 underwent LSG and 29 SPECT-CT. No significant differences in baseline characteristics were detected between both groups. The bilateral SLN visualization rate on LSG was 75.8% versus 86.2% with SPECT-CT (p=0.299). Intraoperative bilateral SLN detection occurred in 84.8% of LSG subjects against 89.7% for SPECT-CT (p=0.573). Correlation in anatomical SLN location, between mapping and surgery, was low for LSG (Spearman’s p=0.098; p=0.449) but high in SPECT-CT (p=0.798; p<0.001). The bilateral intraoperative SLN retrieval times of LSG (75.4±33.5 minutes) and SPECT-CT (50.1±15.6 minutes) differed significantly (p=0.003) by an average of 25.4 minutes (95%CI: 9.3–41.5).

Conclusions
SPECT-CT significantly reduces the intraoperative SLN retrieval time, when compared to LSG. The superior anatomical concordance of SPECT-CT, combined with a trend towards better bilateral visualization, may partly explain the observed shortening in SLN retrieval time.
Poster Presentations: Cervical Cancer

GALECTIN-1 IS A RADIRESISTANT MARKER IN PATIENTS WITH CERVICAL CANCER

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Objectives
Galectin-1 is a galactose-binding protein. It is regulated by hypoxia that is closely related to radioreistance. Galectin-1 also has immune suppressive effect for T lymphocyte and promotes cancer invasion and angiogenesis. The aim of this study is investigate role of galectin-1 in patients with cervical cancer after definitive radiotherapy.

Methods
We reviewed paraffin embedded specimens of 102 patients with FIGO Stage I-II cervical cancer were enrolled in the study. Patients underwent curative-intent radiotherapy including pelvic irradiation and high-dose-rate intracavitary brachytherapy. Paraffin-embedded tissues were analyzed using immunohistochemistry (IHC) for galectin-1 staining. The rates of overall survival (OS), locoregional failure (LF), distant metastasis (DM) were compared between weak and strong expression of galectin-1. Kaplan-Meier method and Cox proportional hazard model were used for univariate and multivariate analyses, respectively.

Results
There were no significant differences in the demographic data between weak and strong expression of galectin-1. The 5-year LF rates were 13.7% and 57.1% in patient with weak and strong galectin-1 expression in tumor cells ($p$=0.002), respectively. The corresponding rates of OS were 89.5% and 57.1% ($p$=0.045). The corresponding rates of DM were 7.6% and 33.3% ($p$=0.061). Multivariate analysis revealed that galectin-1 overexpression was an independent factor for LF ($p$=0.002; Hazard ratio 9.419) and DM ($p$=0.022; Hazard ratio 7.902).

Conclusions
Overexpression of galectin-1 involves LF and DM in Stage I-II cervical cancer patients undergoing definitive radiotherapy. Further study of targeting galectin-1 may improve local and distant control.
PREVALENCE OF CO-INFECTIONS WITH HUMAN PAPILLOMAVIRUS AND MYCOPLASMA/UREAPLASMA SPECIES IN WOMEN WITH ABNORMAL CERVICAL CYTOLOGY

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Objectives
The purpose of this study were to seek for the prevalence of pathogens such as HPV and Mycoplasma. This study was to verify possible association between infections with mycoplasmas/ureaplasmas and the presence of HPV infections in women diagnosed with abnormal cervical cytology.

Methods
The investigation included 249 non-pregnant women diagnosed with abnormal PAP test (ASCUS, LSIL and HSIL). They were analyzed from March 2010 to February 2012 according to the severity of cervical cytology.

Results
HPV infection in HSIL group were higher than ASCUS, LSIL group. (Table 1) In HPV-positive patients, infections with mycoplasmas/ureaplasmas were more frequent (P < 0.05), particularly for ureaplasmas (Table 2). The percentage of females infected mycoplasmas/ureaplasmas significantly increased in women diagnosed with HSIL compared with LSIL or ASCUS.

<table>
<thead>
<tr>
<th></th>
<th>ASCUS/LSIL</th>
<th>HSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>192</td>
<td>57</td>
</tr>
<tr>
<td>mean age</td>
<td>43.2</td>
<td>42.9</td>
</tr>
<tr>
<td>HPV infection (%)</td>
<td>120(62.5)</td>
<td>51(89.4)</td>
</tr>
</tbody>
</table>

Table 1. HPV infection rate

<table>
<thead>
<tr>
<th></th>
<th>ASCUS/LSIL</th>
<th>HSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>120</td>
<td>51</td>
</tr>
<tr>
<td>Mycoplasma (%)</td>
<td>39(26.7)</td>
<td>28(54.9)</td>
</tr>
<tr>
<td>Ureaplasma (%)</td>
<td>73(60.8)</td>
<td>38(74.5)</td>
</tr>
</tbody>
</table>

Table 2. co-infection with mycoplasmas/ureaplasmas

Conclusions
mycoplasmas/ureaplasmas infection might be the factor of persistent infection with high risk HPV. Since the presence of mycoplasmas/ureaplasmas associates significantly with the HPV infection, genotyping of the mycoplasmas/ureaplasmas should be recommended.
Poster Presentations: Cervical Cancer

MRI IN CERVICAL CANCER STAGING
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Objectives
Cervical cancer is the only malignancy staged according to the clinical examination. Staging is crucial in planning the optimal treatment strategy. The aim was to evaluate the accuracy of clinical and MRI staging, and the choice of surgery technique according to the preoperative stage.

Methods
The study included 150 patients who underwent surgical treatment due to cervical cancer at Clinic for Gynecology and Obstetrics, Clinical Center of Serbia. Statistical tests used for calculating the correlation between clinical and MRI staging with postoperative stage and the relation between the kind of surgical treatment and postoperative stage were Mann-Whitney and Kruskal-Wallis test, and ANOVA.

Results
The mean age of patients was 47.7 ± 10.6. Clinical staging was accurate in more than 50%, while the stage was underestimated in 17% of patients. In 79% of clinical stage Ia there was not found malignant tissue. 47% of the stage IIa and 67% ≥ IIb were underestimated with clinical staging. The result after 10% of radical hysterectomies was stage lower than Ib. MRI was accurate in 58%, while the stage was underestimated in 34%.

Conclusions
In spite of the great achievements in medical technology, clinical examination and the gynecologist’s experience remain the golden standard in the preoperative staging in cervical cancer. Modern imaging methods are able to give us important additional information, but they are better for diagnosis of late cancer stages.
MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL FEATURES OF CERVICAL CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Objectives
It is important to predict tumor behavior and potential treatment response by searching pathways of cancer developing, such as an apoptosis and proliferative index of tumor.

Methods
Medical records of 23 patients of median age 42.4±4.5 with invasive squamous cell carcinoma cured in Almaty Oncology Centre were analyzed. 9 patients (39.1%) were diagnosed with FIGO stage IIA disease, 8 (34.8%) of stage IIb, and 6 (26.1%) of stage IIIA disease. Patients were treated primary NACT with cisplatin 100 mg/m² day 1 and 5-fluorouracil 750 mg/m² on days 1-4 i.v., repeated in 21 days, for 2 cycles. After chemotherapy radical hysterectomy was performed (with/without RT). All specimen were investigated morphologically (HE stain) and immunohistochemically to check the levels of p-53, bcl-2 and Ki-67 in tumor tissue.

Results
After surgery pelvic lymph nodes metastasis occurred in 7 patients (30.4%). Deep cervical stroma invasion occurred in 8 patients (34.8%) and positive LVSI were found in 13 patients (56.5%). Bcl-2 level expression was found in 5 patients (1 with stage IIA, 2 - IIb and 2 - IIIA). Increased level of p-53 indicated in 3 patients with stage IIb and 4 - IIIA. All patients had high level of Ki-67 increased accordingly from 40% in IIA till 85-100% in IIb-IIIA.

Conclusions
Research of molecular-genetic aspects of cervical cancer could be one of the important features in estimating of tumor response after treatment.
POSTER PRESENTATIONS: CERVICAL CANCER

COST-UTILITY ANALYSIS OF TREATMENTS FOR STAGE IB CERVICAL CANCER

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Objectives
To analyze the cost-utility of two common clinical practices for stage IB cervical cancer patients in provider and societal viewpoints.

Methods
A cost-utility analysis was conducted using decision tree model to examine value for money between: (1) radical hysterectomy with pelvic lymph node dissection (RHPND) with or without post-operative adjuvant therapy; and (2) concurrent chemoradiation (CCRT). All relevant literatures were identified. Probability data were extracted and meta-analysis was performed. Direct medical costs were estimated from hospital database and medical record review. Direct non-medical costs and utility parameters were interviewed from patients in order to estimate the outcome of Quality-Adjusted Life Years (QALYs).

Results
In the provider viewpoint, RHPND and CCRT produced the approximate costs of 169,000 and 167,000 THB respectively. The corresponding costs in the societal viewpoint were 209,000 and 203,000 THB. QALYs were 16.40 years for RHPND and 15.94 years for CCRT. The estimated incremental cost effectiveness ratio (ICER) of RHPND in comparison to CCRT in the provider and societal viewpoints were 3,000 THB/QALY and 14,000 THB/QALY, respectively. However, RHPND had more cost-effectiveness than CCRT in only the low risk (LR) group, because this group did not receive adjuvant treatment. At the current ceiling ratio of Thailand, RHPND provide better value for money than CCRT at the probability of 75%.

Conclusions
RHPND is the efficient treatment for stage IB cervical cancer. However, this advantage is only close related with LR patients. Therefore, patient selection is necessary before making treatment decision for the most effectiveness of all stakeholders.
EFFECTIVE ROLE OF P16/KI-67 DUAL IMMUNOSTAIN FOR CERVICAL CYTOLOGY WITH ATYPICAL SQUAMOUS CELLS, CANNOT EXCLUDE HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESION

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Objectives
To evaluate the accuracy of p16/Ki-67 dual immunostaining assay for cervical intraepithelial neoplasia (CIN) compared with high risk-Human Papillomavirus (HR-HPV) DNA testing in women with atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H) on cytology.

Methods
Data from seventy-three patients who received HPV genotyping and histologic examination for ASC-H Pap smear were collected. CINtec®PLUS kit was used on liquid-based residual material and the positivity was graded according to the number of dual-stained cells as follows; G1 (1-5), G2 (6-10), G3 (11-20) and G4 (>20). Accuracy was evaluated based on the histologic results from colposcopy-guided biopsy or cervical conization on follow-up.

Results
In 70 patients with available data, positive rate of p16/Ki-67 was associated with histologic severity as follows; 14.8% in normal histology, 66.7% in CIN1, 90% in CIN2, and 100% in CIN3. Average grade of positive p16/Ki-67 also increased from 0.2 in normal histology, 1.2 in CIN1, 2.4 in CIN2, and 2.9 in CIN3 (p <0.01). p16/Ki-67 was positive in 100% of HR-HPV-negative CIN3 and in 0% of HR-HPV-negative normal histology. For patients with CIN2 or more, p16/Ki-67 had a sensitivity of 94.6% and a specificity of 75.8%, while HR-HPV testing showed a sensitivity of 67.6% and a specificity of 66.7%.

Conclusions
p16/Ki-67 immunostaining demonstrated a better accuracy for detecting CIN 2 or more in patients with ASC-H cytology than HR-HPV DNA testing. Given the improved concordance with histologic diagnosis, the grading system of positive p16/Ki-67 can be a useful adjunct for predicting high-grade lesions in clinical practice.
Poster Presentations: Cervical Cancer

THE CONTENT AND PROGNOSTIC POTENTIAL OF SOME MOLECULAR BIOLOGICAL MARKERS IN UTERINE CERVIX CANCER PATIENTS
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³National Cancer Centre, N.N.Alexandrov National Cancer Centre of Belarus, Minsk, Belarus

Objectives
Investigating the prognostic potential of molecular biological markers HER2/neu, Ki-67, p53 and Bcl2 in uterine cervix cancer (UCC) patients.

Methods
The materials of the study were 228 immunohistochemical assays of cervical tissue samples prior to the treatment and then from the ablated organ which were performed in 36 stage IIB-IV UCC patients with poor prognosis. The patient age ranged from 25 to 65 years, with a median of 44.1±9.0. The histological tumor pattern was squamous cell carcinoma in 88.9% of the cases.

The immunohistochemical assay employed antibodies to p53 (clone DO-7, DAKO), Bcl2 (clone 124, DAKO), Ki-67 (clone MIB-1, DAKO) and HER2/neu (dilution 1:300, monoclonal) and En Vision⁺ visualization system (DAKO, Danuce). The objects of the study were the locations of stained nuclei, cytoplasm and membrane in the cell, as well as the intensity of peroxidase label and the percentage of stained cells.

Results
It was found that prior to special treatment
- 88.9% of the patients presented with p53 expression (low expression in 19.4%, moderate in 36.1%, high in 33.3%);
- 2.8% of the cases demonstrated HER2/neu expression in cervical tumor tissue samples;

Conclusions
- increased proliferative activity of Ki-67 in tumor samples occurred in 88.9%, confirming the information about activation of proliferation processes in these patients;
- 72.2% of the patients had a low level of Bcl2 in tumor tissue;
- co-expression was noted of apoptosis oncomarkers p53 (>60%) and Bcl2 (>11%).

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Poster Presentations: Cervical Cancer

LONG-TERM RESULTS OF PHOTODYNAMIC THERAPY FOR PATIENTS WITH GRADE II-III CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives
Evaluating long-term efficacy of photodynamic therapy (PDT) with Photolon for CIN patients in the follow-up period of 3 months to 6 years.

Methods
168 patients with pathological diagnosis of grade II-III CIN in the age range of 19 to 72 years were administered treatment. Photolon (Belmedpreparaty, Minsk) was used as a photosensitizer. Photolon solution was intravenously instilled at a dose of 1.0-2.5 mg/kg of body mass 3-4 hours before photoradiation – the time of maximal photosensitizer accumulation in tissues. Photoradiation was performed in a two-step mode using LD680-2000 laser unit (BIOSPEK, Moscow). At the 1st step, the vaginal area of uterine cervix was irradiated using a microlens light guide; at the 2nd, the full length of the cervical canal was treated. For this purpose, a 1.5-4.0 cm fiberoptic catheter with cylindric diffuser was used. The follow-up period ranged from 3 months to 6 years and 8 months.

Results
144 patients received a single PDT treatment. Recurrence occurred in 13 (7.7%) cases over a follow-up period of 1 year to 6 years and 8 months, including 7 cases of dysplasia (4 moderate cases and 3 severe ones). These patients were administered repeated PDT treatment. Five patients were diagnosed with microinvasive cervical cancer and one with stage IIIB cervical cancer which required special antitumor treatment.

Conclusions
Photodynamic therapy is an efficient organ-sparing technique for severe dysplasia management.
Poster Presentations: Cervical Cancer

LAPAROSCOPIC RADICAL TRACHELECTOMY IS AN ALTERNATIVE TO LAPAROTOMY WITH IMPROVED PERIOPERATIVE OUTCOMES FOR CERVICAL CANCER PATIENTS

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Objectives
Radical trachelectomy is a well-practised surgical approach for managing young women with cervical cancer wishing to preserve their fertility. The aim of this study was to compare perioperative outcomes between laparoscopic (LRT) and abdominal radical trachelectomy (ART).

Methods
We reviewed the records of all women undergoing either LRT or ART in our institution since 2004. Demographic data, clinicopathological data, as well as perioperative outcomes were collected and compared between the two procedures.

Results
Overall 27 women were identified. Twenty six had stage 1B1 and one stage IIA disease. Eleven women (40.8%) underwent LRT, while 16 (59.2%) underwent ART. Age, parity and BMI, as well as histological type, grade and presence of LVSIs were comparable between groups. The median length of the parametrial tissue removed was shorter in LRT vs. ART (p=0.022). Median blood loss and length of stay were significantly reduced in the LRT group (85ml vs. 800, p<0.001 and 4 days vs. 7, p=0.003). Operative time was longer with the laparoscopic approach (320min vs. 192.5, p<0.001). Immediate postoperative morbidity (mainly high urinary residuals) was comparable between groups; however, more late morbidity events were recorded in the laparotomy group.

Conclusions
This first comparison study between LRT and ART for fertility preservation in women with cervical cancer shows that laparoscopy performed better in terms of blood loss, length of stay and late postoperative morbidity. LRT could be the preferred option for these patients, however further studies are needed to confirm comparable survival outcomes.
NERVE SPARING ROBOTIC RADICAL HYSTERECTOMY FOR EARLY CERVICAL CANCER: OUR TECHNIQUE

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Objectives
To demonstrate the feasibility of doing a nerve sparing radical hysterectomy robotically and assess the oncological and functional outcome associated with this surgery.

Methods
Between August 2011 and January 2013, a total of 12 non-consecutive patients underwent robotic surgery for early cervical cancer surgery at our institution. Patients comprising of FIGO stage IA2 to IB1 were treated with nerve sparing robotic radical hysterectomy using a C2 (Querleu Morrow classification) type technique. The feasibility, operative time, blood loss, oncological outcome and post-operative bladder function was assessed.

Results
All the procedures were completed robotically without conversion to laparoscopy or laparotomy. The mean age of the patients was 56yrs (range 44-76). The mean BMI was 22.6 (range 18.1-26.4). The operative time was 156 minutes (range 120-250). The blood loss was 120ml (50-250). The Foley's catheter was removed on the 3rd post operative day, with full recovery of bladder function in all patients except one who required prolonged catheterisation for 3 weeks. Residual urine was 40 ml (range 30-80). Parametrial margins of 2.5-3 cms, distal vaginal margins of 2-2.5 cms and a mean nodal harvest of 24 (range 18-30) were achieved. The mean hospital stay was 3 days (range 2-6). Urodynamic studies done at six weeks in all the patients were normal. In median follow-up is 12 months there is no loco-regional recurrence. All the patients are sexually active.

Conclusions
Robotic nerve-sparing radical hysterectomy is technically feasible to perform. It is oncologically safe for early stage cervical carcinoma.
FERTILITY PRESERVATION BY PHOTODYNAMIC THERAPY IN YOUNG PATIENTS WITH EARLY STAGE CERVICAL CANCER: A PILOT STUDY

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Objectives
To evaluate the response and efficacy of photodynamic therapy (PDT) in young patients with early stage cervical cancer who want to preserve fertility.

Methods
We analyzed data from our patients with early-stage cervical cancer (stages IA-IIA) who underwent PDT with conization from 2003 to 2012 for fertility preservation. Surface photoillumination with red laser at a wavelength of 630nm was applied to the uterine cervix and endocervical canal of patients 48 hours after an intravenous injection of 2mg/kg of photosensitizer.

Results
The median age of 21 patients was 31 years old (range; 22-43) and 19 patients (90%) were nulliparous. The majority of the lesions were IA1 (48%) and IB1 (43%). In terms of histology, 81% were squamous and 10% were adenocarcinoma. 5 patients (24%) had a lesion of 2cm or more in size. There was 1 recurrence (4.7%) and no death during 52.6 months (range:6-114 months) follow-up period. Of the 13 women who attempted to get pregnant, 10 (77%) women conceived a total of 11 pregnancies. The first and second trimester miscarriages were 2 (except 1 ectopic pregnancy) and 1 respectively, and 7 (70%) of the pregnancies reached the third trimester, of which 5 delivered at term. No tumor-related death or PDT-related serious adverse effects were noted.

Conclusions
PDT combined with conization could be an effective conservative treatment method for fertility preservation in young patients with early stage cervical cancer.
IMPACT OF PATTERN OF RECURRENCE ON CLINICAL OUTCOME OF LOCALLY ADVANCED CERVICAL CANCER (LACC) PATIENTS SUBMITTED TO PRIMARY MULTIMODALITY TREATMENT

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Objectives

Recurrence of disease represents a clinical challenge in cervical cancer patients, especially when all available treatment modalities have been used in the primary setting. The aim of this study was to analyse the patterns of recurrence and their association with clinical outcome in LACC patients submitted to primary chemoradiation (CTRT) followed by radical surgery (RS).

Methods

This study was conducted on 364 LACC patients submitted to CTRT plus RS since January 1996 to July 2012. For each relapse, information on date of clinical/pathological recurrence, and pattern of disease presentation were retrieved. Post-relapse survival (PRS) was recorded from the date of recurrence to the date of death or last seen. Survival probabilities were compared by the log rank test. Cox's regression model with stepwise variable selection was used for multivariate prognostic analysis for PRS.

Results

Within a median follow-up of 42 months, 75 recurrences (20.6%) and 62 deaths (17.0%) were recorded. By analysing the sites of relapse for each patient, most of the recurrences were observed outside the irradiated field (n=42, 56%) and the most frequently observed site was metastatic (n=28, 37.3%). Among the parameters associated with PRS (persistence of macroscopic disease in the cervix after primary CTRT, aortic pathologic metastasis at RS, size of recurrence>3cm, SCC levels > 3 ng/ml at recurrence, radical surgical resection of the recurrence), only the last one retained an independent predictive role in reducing the risk of death (p=0.025).

Conclusions

The feasibility of secondary radical surgical resection positively impacts on PRS of LACC patients submitted to multimodality primary treatment.
Poster Presentations: Cervical Cancer

FERTILITY-SPARING SURGERY FOR YOUNG PATIENTS WITH BOTRYOID Rhabdomyosarcoma INVOLVING THE UTERINE CERVIX

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Objectives
Botryoid rhabdomyosarcoma of the uterine cervix, which is most often seen arising in the adolescents, is extremely rare. In the past, this tumor was best treated with pelvic exenteration and chemoradiation. The purpose of the report was to present our experience on fertility-sparing treatment for this disease, and to discuss the patient selection criteria and type of surgery for fertility-sparing treatment.

Methods
We conducted a retrospective review of a prospectively maintained database of pediatric/adolescent patients undergoing fertility-sparing surgery for cervical botryoid rhabdomyosarcoma at our institution from 08/2006 to 09/2012.

Results
We presented here ten pediatric (adolescent) patients with botryoid rhabdomyosarcoma involving the uterine cervix. Median age was 15.9 years (range, 11-25). The first patient was offered cervical conization while other nine patients underwent radical abdominal trachelectomy and pelvic lymph node biopsy. They all accepted adjuvant chemotherapy and presented with favorable outcomes at a median follow-up of 32.3 months (range, 7-81 months).

Conclusions
In properly selected cases of cervical botryoid rhabdomyosarcoma, conservative surgeries should attempt to preserve reproductive function without compromising in survival. Radical abdominal trachelectomy and pelvic lymph node biopsy have appeared to secure local disease control. Radical abdominal trachelectomy with skills preserving uterine arteries may allow sufficient blood supply to maintain uterine viability and achieve future fertility, and thus benefit those young patients.
CISPLATIN/PACLITAXEL VS CARBOPLATIN/PACLITAXEL TREATMENT IN ADVANCED CERVICAL CANCER: POOLED ANALYSIS DATA

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Objectives
Cisplatin (CDDP) + paclitaxel is the treatment of choice for stage IVB, recurrent, or persistent cervical cancer (CC). However, carboplatin (CBDCA) + paclitaxel has showed similar efficacy compared to CDDP + paclitaxel in a phase III study. This systematic review indirectly compares the efficacy of CDDP/taxane vs. CBDCA/taxane in the treatment of advanced CC.

Methods
A systematic search in PubMed, EMBASE, Web of Science and The Cochrane Library was performed to identify relevant studies. Trials that were conducted in advanced CC patients treated with CDDP/taxane and CBDCA/taxane and reporting objective response rate (RR), progression-free survival (PFS), time-to-progression (TTP) and overall survival (OS) were pooled. Data on RRs were aggregate by using Comprehensive Meta-Analysis software with a random-effects model; PFS and OS were summarized descriptively.

Results
18 (3 phase III, 8 phase II, 6 retrospective and 1 prospective) studies on 1,204 advanced CC patients treated with CDDP/taxane or CBDCA/taxane-chemotherapy were considered. The calculated median PFS, median OS and pooled objective RRs were 6.9 months, 12.8 months and 49.3% for CDDP + paclitaxel combinations and 5 months, 10 months and 49.3% for CBDCA + paclitaxel combinations. PFS, but not OS, was significantly in favour of CDDP/paclitaxel chemotherapy (T-test) in both chemonaive and pre-treated patients. Response rate was similar with both combinations in CDDP-pre-treated patients (43.9 vs 40%) and CDDP naive patients (68.3% vs 59.1%). Analysis of OS according to previous CDDP exposure was not possible due to the absence of reported data.

Conclusions
CBDCA + paclitaxel represents a viable alternative with comparable efficacy to CDDP + paclitaxel.
Poster Presentations: Cervical Cancer

SENTINEL LYMPH NODE BIOPSY IN EARLY-STAGE CERVICAL CANCER: A STUDY OF 46 CASES FROM A SINGLE INSTITUTION
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Objectives
The aim of this study is to determine the feasibility and usefulness of intraoperative lymphatic mapping and sentinel lymph node (SLN) identification in the management of early stage uterine cervical cancer in the Department of Gynecological Oncology of the Canarian University Hospital.

Methods
Intra-cervical injection of technetium-99 sulfur colloid and lymphoscintigraphy were performed preoperatively. Blue dye was injected intra-cervically immediately prior to surgery. 46 patients with histologically confirmed cervical cancer were retrospectively analyzed with respect to the histology, tumor stage and detection between 2007 and 2012.

Results
The median age of the patients was 44.58 years.

The tumor was less or equal to 2 cm in 78.2%, and larger than 2 cm in 28.8%. The most frequent stage was 1b1 (91.3%).

A total of 837 SLN were identified, with a median of 2.7 SLN per patient (range, 0–6). The majority (86%) of SLN were located at three main sites: the obturator (36%); internal iliac (28%); and external iliac (22%).

Bilateral SLNs were identified in 60% (27/45) of the patients.

SLNs were identified in 97.8% (45/46) of patients intraoperatively.

Five out of the 46 women (10.8%) had lymph node metastases, all identified in SLNs (sensitivity 100%)

Metastases were found exclusively in the SLNs in 3 out of 5 patients. 2 SLNs contained micrometastases between 0.1 and 0.5 mm.

Metastases localization in the SLN occurred in 5/5 patients for a disease detection rate of 100%.

Conclusions
SLN mapping in early-stage cervical carcinoma yields high detection rates. Ultrastaging improves micrometastasis detection.
Sexual Health After Pelvic Radiotherapy

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Objective
Sexual dysfunction is common among pelvic cancer survivors treated with radiotherapy and unmet needs may lower quality-of-life. This is a neglected area where feelings of shame and embarrassments prevail. Early interventions including medical treatment, targeted information and sexual counseling may improve sexual health.

Methods
At Sahlgrenska University Hospital, Sweden, a nurse-led cancer rehabilitation clinic is focusing on treatment for physical side-effects and sexual dysfunction after pelvic cancer. Prior to the visit survivors were asked to answer a postal questionnaire including questions on physical symptoms from pelvic organs, quality-of-life and sexual health. After the intervention survivors were asked to evaluate the intervention by filling out the questionnaire a second time.

Results
One hundred and six female cancer survivors, (58% gynecological, 42% gastrointestinal cancer) visited the clinic and filled out a questionnaire at baseline and 3 months after the visit. A majority reported reduced libido. Among those who reported having vaginal intercourse (31%), 43% reported no vaginal elasticity, 45% a short vagina, 57% insufficient vaginal lubrication, 44% superficial and 28% deep dyspareunia. After the intervention cancer survivors reported improved lubrication, less dyspareunia and a majority reported satisfaction with the sexual intervention given.

Conclusions
Pelvic radiotherapy affects sexual health and female pelvic cancer survivors report vaginal changes, pain and absence of sexual desire. In order to improve sexual health we need to treat physical symptoms and address sexual issues. Early sexual rehabilitation such as topical estrogen, vaginal dilation and sexual counseling may help pelvic cancer survivors regain physical and sexual health.
Poster Presentations: Nursing

THE VENUS CLINIC – A PSYCHO-SEXUAL HEALTH PROGRAM FOR GYNECOLOGICAL CANCER PATIENTS

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Objectives
Extensive curative treatment for gynecological cancer may lead to physical symptoms affecting daily life and sexual health. The impact on sexual function after treatment can be of physical, psychological and social origin. Unfulfilled needs for sexual care exist and there is a gap between the needs of survivors and what is being offered in reality.

Methods
In 2009 a sexual rehabilitation program at Karolinska University Hospital in Stockholm, Sweden was founded, financed by The Swedish Cancer Society. The clinic is managed by two oncology specialist nurses supervised by a gynecological oncologist.

Results
The nurses, with long experience in oncology and sexual counseling, are seeing gynecological cancer patients presenting with physical symptoms as insufficient lubrication, vaginal shortness, inelasticity as well as dyspareunia. To prevent vaginal stenosis the patients are given a vaginal dilator along with thorough information.

From a psychological aspect the disease- and treatment-induced morbidity affect sexual function with reduced libido as well as impaired self image. Some cancer survivors report having marital difficulties leading to divorce and separation. Singles state having problems meeting a new partner due to sexual dysfunction.

Since 2013 the Venus Clinic is a part of routine cancer rehabilitation care and offers sexual counseling and rehabilitation for rectal, urinary bladder and anal cancer patients.

Conclusions
By treating physical symptoms and giving the patient and her partner the opportunity to discuss sexual issues early in the course of treatment as well as post treatment, the impact of disease and treatment on sexual function can be less severe.
MOLECULAR PROFILING OF CIRCULATING TUMOR CELLS LINKS PLASTICITY TO THE METASTATIC PROCESS IN ENDOMETRIAL CANCER.
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Objectives
Endometrial carcinomas are usually diagnosed at an early stage with uterine-confined disease. However, up to 20% endometrial carcinomas debut as aggressive neoplasms such as high-grade endometrioid, serous and/or deeply invasive lesions, at substantial risk of recurrence and death. We aimed at investigating the potential of Circulating Tumor Cells (CTC) as biomarkers of disseminated disease in high-risk endometrial cancer (EC) patients. In parallel, we explored the phenotypic determinants of CTC in EC.

Methods
In the framework of the European Network for Individualized Treatment in Endometrial Cancer (ENITEC), we performed a comparative evaluation of CTC in EC with CellSearch technology and EpCam-based immunoisolation coupled to RTqPCR analysis.

Results
Peripheral blood samples from 22 high-risk EC patients, ranging from Grade 3 Stage IB to metastatic Stage IV carcinomas and recurrences, presented positivity for CTC identification by CellSearch in 25% of patients with a median number of 2 CTC per patient ranging from 1-10 CTC. In parallel, RTqPCR analysis in immunoisolated CTC demonstrated a remarkable plasticity phenotype, characterized by the expression of epithelial-to-mesenchymal markers like CTNNB1, NOTCH1, RUNX1, SNAI1, TGFβ1, ZEB1 and ZEB2,
probably linked to the ability of CTC to home and form micrometastases at distant sites. In addition, the expression of ALDH and CD44 suggest an association with stemness, and that of GDF15 and PIK3CA possible pathways to specifically target CTC in EC.

**Conclusions**
In addition to the clinical potential of characterizing CTC for diagnosis, prognostication and follow-up of patients, their molecular profiling may identify new therapeutic strategies to control metastatic dissemination in EC.
**Poster Presentations: Endometrial Cancer**

**THE VALUE OF IMAGING OF THE LUNGS IN THE DIAGNOSTIC WORK-UP OF PATIENTS WITH ENDOMETRIAL CANCER**

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**Objectives**

Imaging of the lungs is routinely performed in the diagnostic work-up for patients diagnosed with endometrial cancer. The goal of this study was to measure the incidence of lung metastases in patients with endometrial cancer, and to evaluate the clinical relevance of preoperative chest imaging in this population.

**Methods**

Retrospective cross-sectional study in four regional and one university hospital in the South-eastern part of The Netherlands. All 784 patients with epithelial endometrial cancer, diagnosed in the period 2002 till 2010 in five hospitals were eligible. There was a follow-up of at least two years.

**Results**

In 541 out of 784 patients (69.0%) thoracic imaging was performed. In eleven patients thoracic imaging was suspicious for metastases peri-operatively or during one year of follow-up. In eight patients thoracic metastases were related to their endometrial cancer, giving an overall incidence of 1.0%. All these eight patients had high risk subtypes of endometrial cancer (serous, clear cell, or poorly differentiated endometrioid), resulting in an incidence of 4.1% (8/193) for these subtypes. In none of the patients with a grade 1 or 2 endometrioid type endometrial cancer (n=541) lung metastases were identified at the time of diagnosis.

**Conclusions**

The chance of identifying thoracic metastases during the diagnostic work-up of patients with endometrial cancer is very small. Based on the presented data one can consider to omit thoracic imaging in the diagnostic work-up for patients with low-risk endometrial cancer.
REM (RISK OF ENDOMETRIAL MALIGNANCY): A PROPOSAL FOR A NEW SCORING SYSTEM TO EVALUATE RISK OF ENDOMETRIAL MALIGNANCY.
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Objectives
It is often difficult to distinguish a benign endometrial disease from a malignancy and tools to help physician to triage patients into high and low risk of endometrial cancer (EC) are needed. The purpose of this study was to obtain a predictive model to assess the Risk of Endometrial Malignancy (REM) in women with ultrasound endometrial abnormalities.

Methods
Women, between 45 and 80 years, diagnosed with ultrasound endometrial abnormalities and scheduled to have surgery were enrolled on a prospective study at Department of Gynaecologic Oncology of Campus Bio-Medico of Rome. Preoperative clinical, ultrasound and laboratory features were taken into account. Logistic regression algorithm was utilized to categorize patients into low and high risk groups for EC.

Results
A total of 675 patients were considered for the analysis: 88 with EC and 587 with benign endometrial disease. We divided the patients into two groups: training set (TS) and verification set (VS). Preoperative age, symptom, HE4 levels and ultrasound endometrial thickness were found statistically significant and were included into multivariate logistic regression model in order to determine the probability to have EC. In TS, REM reported 93.3% of sensitivity and 97.1% of specificity (PPV = 0.83, NPV = 0.98, AUC=0.957, 95%CI, 0.908 to 0.984). In VS REM reported 89.3% of sensitivity and 95.4% of specificity (PPV = 0.73, NPV = 0.98, AUC=0.919, 95%CI, 0.829 to 0.970).

Conclusions
Our data support the use of REM to triage patients into low and high risk of EC, even if an external validation of model is needed.
THE IMPACT OF POSITIVE PERITONEAL CYTOLOGY IN PREDICTING SURVIVAL IN ENDOMETRIAL CARCINOMA

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Objectives
We aimed to present the factors affecting survival and positive peritoneal cytology occurrence in endometrial cancer and to investigate whether positive peritoneal cytology has an effect on expected survival.

Methods
The patient chart information of 224 patients who had been treated at Ankara Oncology Hospital due to endometrial cancer between the years of 1996 and 2006 were retrospectively reviewed. Factors that were likely to have an effect on survival in all patients such as age, peritoneal cytology, histological type, grade, myometrial invasion, cervical invasion, tumor size, and lymphatic metastasis information were analyzed.

Results
We observed peritoneal cytology, grade, myometrial invasion, cervical stromal invasion, tumor size, and lymphatic metastasis presence to have a significant effect on the five-year survival on univariate analysis. FIGO 09 stage (p=0.002) and cytology (p=0.005) were found to be significant on Cox regression. All cases with cervical glandular involvement were alive. Cytology was positive in 20 of 224 patients (8.9%). Univariate analysis revealed a significant effect on positive peritoneal cytology according to myometrial invasion, cervical stromal invasion, tumor size, histological type and lymphatic metastasis. Among these, only cervical stromal invasion had a significant (p=0.004) effect on positive peritoneal cytology on logistic regression analysis.

Conclusions
Positive peritoneal cytology is an important prognostic factor where complete surgical staging has been performed in endometrial cancer and influences survival expectations.
Poster Presentations: Endometrial Cancer

IDENTIFICATION OF THE CORRECT ENDOGENOUS REFERENCE GENES FOR QRT-PCR ANALYSIS OF NORMAL AND MALIGNANT HUMAN ENDOMETRIAL TISSUES.

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Objectives

Although the use of endogenous reference genes for real-time qRT-PCR is often based on the assumption of their integral stability, occasionally this is not true, especially in pathological conditions. The aim of this study was to test the stability of endogenous reference genes in healthy and malignant endometrial tissues.

Methods

The stability of 32 candidate endogenous reference genes was evaluated in triplicate cDNA samples derived from mRNA extracted from normal endometrial tissues, classified as secretory and proliferative phase and the atrophic state, and from malignant endometrial tissue classified as grade 1, grade 2, grade 3, serous and carcinosarcoma. The expression of stable endogenous reference genes was calculated using the geNorm qBasePLUS, BestKeeper and NormFinder software packages. NormFinder takes into account the inter- and intra-group variability, whereas geNorm and BestKeeper does not.

Results

NormFinder and BestKeeper indicated that the most stable single endogenous reference gene was MRPL19, whilst geNorm indicated PPIA. Since better normalisation can be achieved using more than one reference gene, the combination of IP08 and PPIA was recommended by NormFinder, whilst geNorm recommended PPIA, MRPL19, PGK1, UBC and PUM1.

Conclusions

Because NormFinder compares both within and between groups, it is the software of choice. When comparing normal and malignant endometria gene expression more reliable normalisation is achieved when using a combination of genes. We therefore recommend that IP08, PPIA and MRPL19 should be used as internal reference genes in qRT-PCR studies of normal and malignant endometria.
RISK OF ENDOMETRIAL CANCER IN PATIENTS PREVIOUSLY TREATED WITH TAMOXIFEN FOR BREAST CANCER, A RETROSPECTIVE ANALYSIS.

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Objectives
Tamoxifen increases the risk of endometrial cancer. Aim of this study is to assess the risk and prognosis of endometrial cancer in patients previously treated with tamoxifen for breast cancer in our population.

Methods
Retrospective analysis of all patients with endometrial cancer previously treated for breast cancer at Clatterbridge Cancer Centre (CCC) from January 2008 to December 2011.

Results
A total of 475 patients with endometrial cancer were treated at CCC. 55 (11%) patients were previously treated for breast cancer.

Of 55 patients with previous breast cancer, 45 received tamoxifen, 5 aromatase inhibitor, 1 ER negative and in 4 patients treatment is not known. Median duration of tamoxifen treatment was 5 years (3.5 to 12). Out of 45 patients with endometrial cancer who received tamoxifen, 16 had adenocarcinoma and 29 had non adenocarcinoma on histology. Commonest histological grade was 3 in 9 (20%) patients followed by grade 2 and grade 1 in 8 (17%) and 3 (6%) patients respectively. 9 patients had carcinosarcoma and grade was not reported in 16 patients.

Most of the patients had FIGO stage 3 (n=16) followed by stage 1B (n=10), stage 2 (n=9), stage 4 (n=6) and 1A (n=2). 2 patients did not have surgery.

Overall 10% risk of endometrial cancer was observed in these patients with median survival of 22 months.

Conclusions
Our data suggested that long term Tamoxifen use increases the risk of endometrial cancer and overall survival of these patients remains poor.
HISTOLOGIC AND IMMUNOHISTOLOGIC CHARATERISTICS OF ENDOMETRIAL CLEAR CELL CARCINOMA

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Objectives
Two types of endometrial carcinoma, type I and type II, has been distinguished with clinicopathologic behavior. However, the biologic information on endometrial clear cell carcinomas (CCCs) remains limited. We analyzed the expression of various immunohistochemical markers in endometrial CCCs to explore the unique entity, if any, of pure CCCs.

Methods
Twenty nine cases of endometrial clear cell carcinoma were analyzed. We divided the CCCs into three groups, pure CCC, mixed CCC with endomerioid adenocarcinoma (EMA) and mixed CCC with serous adenocarcinoma (SCA), and compared their clinical and immunohistochemical characteristics using various markers such as ER, PR, PTEN, p53, p16, mismatch repair (MMR) gene loss, ARID1A, HER-2/neu, cyclin D1, HNF-1β and NAPSIN A.

Results
PTEN loss was 81.3% (13/16) in pure CCC, 100% (7/7) in mixed CCC with EMA, 33.3%(2/6) in mixed CCC with SCA(p=0.015). Overexpression of p53 and p16 was 37.5% (6/16), 0%(0/7), 0%(0/6) and 25%(4/16), 42.9%(3/7), 50%(3/6), respectively(p=0.039 and p=0.035). NAPSIN A was 81.3%(13/16), 41.9%(3/7) and 16.7%(1/6)(p=0.015).The immunoreactivity of HNF-1β was 100%(16/16) in pure CCCs.

Conclusions
Our data suggest that there is a third pathway of endometrial clear cell carcinogenesis and PTEN, p53, p16, HNF-1β and NAPSIN A has possibilities as a powerful distinguishing marker for pure clear cell carcinomas. Additional molecular studies of clear cell carcinomas to elucidate the carcinogenesis of CCCs are required.
COMPARISON OF LYMPHOVASCULAR SPACE FOR EARLY STAGE ENDOMETRIAL CANCER: LAPAROSCOPY VERSUS LAPAROTOMY

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Objectives
Total laparoscopy hysterectomy (TLH) appears associated with a higher incidence of vascular space involvement (VSI), that is becoming an independent prognostic factor for endometrial cancer (EC).

Methods
To better understand this phenomenon, we retrospectively studied data recorded of 256 patients with early EC who underwent, open (group A: n=174) or laparoscopic (group B: n=82) surgery, in two hospitals, respectively: University of Bari and Sacred Heart Hospital of Negrar, between 2004 and 2011. For TLH we used a uterine manipulator without balloon tip. The slides were reviewed by gynecologic pathologists blindly and the following criteria were considered for the definition of true VSI: (i) free-floating or focally attached viable tumor nests within endothelial-lined spaces with or without intraluminal red cells or lymphocytes; (ii) tumor cells with cytoplasm more eosinophilic or pale; (iii) smooth borders.

Results
The demographics and pathologic characteristics were similar between the two groups(fig1a). We found 30 cases of LVSI in the group A (17.2%) and 21 (25.6%) in the group B. Also after splitting population, according to age, grading, degree of MI and stage there were no statistically significant differences between the two groups for incidence of VSI.(fig 1b). A significant prognostic benefit in term of DFS and OS was observed for patients negative for VSI by log-rank test (fig2).

Conclusions
Laparoscopy doesn’t increase the rate of VSI, which we confirm to be a negative prognostic factor for EC.
Poster Presentations: Endometrial Cancer

A NOMOGRAM FOR PREDICTING LYMPH NODE STATUS IN PRESUMED LOW- AND INTERMEDIATE-RISK ENDOMETRIAL CANCER

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Objectives
Currently, in early stage endometrial cancer, indications for adjuvant therapies are exclusively based on uterine criteria as lymphadenectomy is no longer recommended. However, it has been recently demonstrated that 12% of women with low or intermediate risk endometrial cancer have lymph node metastases. Hence, the purpose of this study was to develop nomogram to predict lymph node status in presumed Low- and Intermediate-risk endometrial cancer by combining selected clinical and pathological risk factors.

Methods
Data from two university institutions with prospectively maintained endometrial cancer databases and from the Senti-Endo trial were pooled. A multivariate logistic regression analysis of selected prognostic features was performed, and a nomogram was constructed. The model was internally validated for discrimination and calibration by bootstrap resampling.

Results
One hundred and fifty eight women were identified. The lymph node metastasis rate was 13.9%. By multivariate regression analysis the model showed that age, grade, deep myometrial invasion and the lymphovascular space involvement significantly predicted the lymph node status. The nomogram showed good discrimination with an area under the receiver operating characteristic curve of 0.77 (95% confidence interval, 0.76 0.78) in the training set. The bootstrap-corrected concordance index was 0.76 (95% confidence interval, 0.74 0.78). The nomogram was well calibrated.

Conclusions
We developed a nomogram based on 4 easily available characteristics to predict lymph node status specifically in this subgroup of patients. This new tool may be useful both to assess individualised patient risk when deciding on primary surgical strategy and to allow for a selection of who may benefit most from systematic lymphadenectomy.
COLOR DOPPLER ULTRASONOGRAPHY IN ENDOMETRIAL CARCINOMA
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Objectives
The aim of his study is to evaluate if color and pulsed Doppler ultrasonography of uterine and endometrial vessels could differentiate endometrial carcinoma (EC) from endometrial hyperplasia (EH).

Methods
We examined 88 patients with transvaginal color and pulsed Doppler sonography before the surgical treatment. Thirty-eight of them were with diagnosed endometrial hyperplasia and 50 were with diagnosed endometrial carcinoma. Pourcelot resistance index (RI), systolic peak velocity (V max) and diastolic velocity (V min) were measured in both uterine arteries (AUTdex and AUTsin) and endometrial vessels. Endometrial thickness was also measured. Analysis of variance was used to test the significance among the groups.

Results
There are significant differences according to endometrial thickness between the patients with EC and EH. Patients with EC have statistically thicker endometrium (ANOVA=10.228, p<0.01). Parameters representing uterine arteries flow show statistical significance between the groups, according to values of resistance index, which is significantly lower in patients with EC (ANOVA= 6.929, p<0.01). Endometrial blood flow shows significantly lower resistance index in the group of patients with EC (ANOVA= 56,327, p<0.001).

Conclusions
Evaluation of endometrial vascularity using color Doppler ultrasonography could differentiate endometrial carcinoma from endometrial hyperplasia. It could be useful for the preoperative prediction regarding histological findings, depth of myometrial invasion and the presence of lymph node metastases.
LYMPHOVASCULAR SPACE INVASION IS HIGHLY ASSOCIATED WITH LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER

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Objectives
Lymphovascular space invasion (LVSI) has been evaluated as a predictor for nodal metastasis.

Methods
We retrospectively analyzed the medical records of 178 women with endometrial adenocarcinoma treated by surgical staging, between October/2008 and December/2012. We excluded the patients with lymph node negatives, but with less than 10 structures studied. Patients were divided in two groups, with and without LVSI, analyzed according age, number of lymph nodes examined, histological type, tumor grade, myometrial invasion, nodal status, and FIGO stage. A logistic regression model by stepwise method was developed to predict the risk of nodal metastasis.

Results
One hundred eighty-six women were included, 65 (34.9%) LVSI-positive, and 121 (65.1%) LVSI-negative. The number of lymph nodes examined was similar in both groups (median=20). In univariate analysis, LVSI was associated with non-endometrioid histology, grade 2 and 3 tumors, myometrial invasion >50%, nodal status, and FIGO stage. The patients age did not differ in both groups (median= 66 years and 64 years, respectively). After logistic regression, only LVSI-positive (p=0.0001) and deep of myometrial infiltration <50% (p=0.0012) fit the model of predicting nodal status. The OR (95% CI) for LVSI-positive was 5.1 (2.3-11.2) and for myometrial infiltration <50%, was 0.2 (0.06-0.5). The percentage of cases correctly classified by the model was 79.2%.

Conclusions
In the cases that the nodal status has not been assessed in endometrial adenocarcinoma, the presence of LVSI may be a reasonable surrogate in addition to deep of myometrial invasion, in determining the need for adjuvant therapy.
COMPARISON OF CLINICOPATHOLOGICAL CHARACTERISTICS BETWEEN GRADE 3 ENDOMETRIOID AND SEROUS/CLEAR CELLS ENDOMETRIAL ADENOCARCINOMA

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Objectives

High-grade endometrial carcinomas are a heterogeneous group of tumors that include grade 3 endometrioid, serous, and clear cell adenocarcinomas. There are controversies about differences in prognosis of these high-grade tumors. In this study, we present the clinicopathological features of grade 3 endometrioid compared to serous and clear cells carcinomas.

Methods

We retrospectively analyzed the medical records of 67 women with high grade endometrial adenocarcinoma treated by staging surgery between October/2008 and December/2012. Thirty-two (47.8%) patients presented grade 3 endometrioid and 35 (52.2%) serous or clear cells carcinoma. The two groups of patients were compared according age, surgical technique, body mass index, lymphovascular space invasion (LVSI), tumor size, myometrial invasion, node status, and FIGO stage using chi-square test for categorical and t-test for numerical variables.

Results

No differences in age of patients, surgical technique (laparoscopy or laparotomy), body mass index, and LVSI were observed between the two groups. Endometrioid carcinomas presented higher frequency of deep myometrial invasion (82.7% vs. 41.2%, p=0.02) and bigger tumors (5.4±3.1 cm vs. 3.8±1.9 cm, p=0.01) than serous/clear cells, although no differences in stage or lymph node metastasis were identified.

Conclusions

Our results suggest that tumor dissemination from endometrial cavity occurs earlier in serous/clear cells than in grade 3 endometrioid adenocarcinomas.
Poster Presentations: Endometrial Cancer

INFLUENCE OF RACE AND SOCIO-ECONOMIC STATUS ON ENDOMETRIAL CANCER: POPULATION DEMOGRAPHIC STUDY FROM A TERTIARY CANCER CENTRE IN THE UK
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Objectives
Worldwide, there appears to be a higher prevalence of endometrial cancer in Caucasian compared to Indo-Asian women. We studied the influence of ethnicity and socio-economic status on patients with endometrial cancer within our ethnically diverse population.

Methods
Demographic and clinical data of patients with endometrial cancer diagnosed between January 2010 and December 2011 were extracted. Socio-economic status was calculated from the Indices of Multiple Deprivation. The results were analysed against the background population demographics obtained from Office of National Statistics.

Results
280 patients were diagnosed with endometrial cancer. 85% of patients were classified as Caucasian (n=237), 11% as Indo-Asian (n=31), 2% as Black (n=5), and 2% as Other (n=7). This ethnic variation found in the endometrial cancer group does not significantly differ from the background population demographics. 36% of the Indo-asian group had type 2 cancers compared to 25% of the Caucasian group. The incidence of type I cancers seems to increase with affluence, whereas the type II cancers have a similar incidence throughout the deprivation scale.

Conclusions
This study suggests that the overall incidence of endometrial cancer in the Indo-asian population does not differ from the host population. However the incidence of type 2 cancers appears to be greater in the Indo-asian group, whilst type 1 cancer incidence appears to be higher in the affluent Caucasian group. Environmental factors may therefore, play an important role in the development of type 1 disease, whilst increased genetic susceptibility could be responsible for increased incidence of type 2 cancers in Indo-Asians. A larger study is ongoing.
METRONOMIC DOXIFLURIDINE CHEMOTHERAPY COMBINED WITH THE ANTI-ANGIOGENIC AGENT TNP-470 INHIBITS THE GROWTH OF HUMAN UTERINE CARCINOSARCOMA XENOGRAFTS

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Objectives
Uterine carcinosarcoma is a highly aggressive gynecological neoplasm that responds poorly to conventional chemotherapy and radiotherapy. Metronomic chemotherapy is accepted as a new approach for cancer treatment, and its underlying mechanism seems to involve the suppression of angiogenesis. However, the efficacy of metronomic and anti-angiogenic therapies against uterine carcinosarcoma is unknown.

Methods
The anti-angiogenic effect of doxifluridine was assessed in vitro using human umbilical vein endothelial cells (HUVEC) co-cultured with FU-MMT-1 human uterine carcinosarcoma cells. The antitumor and anti-angiogenic effects of metronomic doxifluridine (delivered via oral gavage) in combination with TNP-470 were evaluated in vivo. Tumor vascularity was assessed by contrast-enhanced color Doppler ultrasound, laser Doppler and microvessel density staining. Doxifluridine suppressed tube formation of HUVEC and vascular endothelial growth factor production by FU-MMT-1 cells.

Results
Metronomic doxifluridine alone significantly suppressed tumor growth compared with the untreated (control) group, while metronomic doxifluridine in combination with TNP-470 significantly inhibited tumor growth compared with each treatment alone. A significant reduction of intratumoral vascularity was observed in FU-MMT-1 xenografts following treatment with metronomic doxifluridine in combination with TNP-470, as compared with each treatment alone. Intestinal bleeding was only observed when the maximum tolerated dose of doxifluridine was administered in combination with TNP470.

Conclusions
Metronomic doxifluridine chemotherapy in combination with TNP-470 might be effective for uterine carcinosarcoma without marked toxicity, possibly acting via its potent anti-angiogenic effects. Clinical studies are needed to evaluate the safety and efficacy of this treatment in humans.
DNA MISMATCH REPAIR DEFICIENCY IN YOUNG PATIENTS WITH SPORADIC ENDOMETRIAL CANCER
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Objectives
To examine the frequency of DNA mismatch repair (MMR) deficiency and its associated pathological characteristics in young patients with sporadic endometrial cancers

Methods
Patients with endometrial cancers diagnosed at or before the age of 45 treated in Queen Mary Hospital, Hong Kong, between July 2001 and June 2009 were identified using departmental database. Clinical and pathological data was obtained by retrospective review of the clinical records. MMR deficiency was evaluated by immunohistochemical staining for the MMR protein - MLH1, MSH2, MSH6 and PMS2.

Results
A total of 122 cases were identified, with paraffin sections available in 65 cases. Loss of expression of MLH1, MSH2, MSH6 and PMS2 protein was found in 6 cases (9.2%), 5 cases (7.7%), 16 cases (24.6%) and 6 cases (9.2%) respectively.
Loss of expression of MLH1 protein was found to be associated with an increased incidence of pelvic lymph nodes metastasis (75% Vs 11.5%, p=0.018) and advanced stage disease (66.7% Vs 17.8%, p=0.022). Loss of expression of MSH2 protein was associated with an increased risk of lymphovascular permeation (100% Vs 30.6%, p=0.015). Loss of MSH6 protein expression was associated with a lower incidence of high grade tumour (18.2% Vs 56.8%, p=0.04).
### Comparison of pathological characteristics of tumours with normal MMR expression and loss of expression of individual MMR proteins

<table>
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<tr>
<th></th>
<th>MLH1 protein</th>
<th>MSH2 protein</th>
<th>MSH6 protein</th>
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<td></td>
<td>Normal Expression</td>
<td>Loss of Expression</td>
<td>p-value</td>
</tr>
<tr>
<td>Endometrioid histology</td>
<td>42 (93.3%)</td>
<td>6 (100%)</td>
<td>NS</td>
</tr>
<tr>
<td>High Grade tumour (G2 / G3)</td>
<td>26 (57.8%)</td>
<td>3 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>Advanced stage (FIGO Stage 3 / 4)</td>
<td>8 (17.8%)</td>
<td>4 (66.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Deep myometrial invasion</td>
<td>14 (30.4%)</td>
<td>2 (33.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Lymphovascular permeation</td>
<td>11 (30.6%)</td>
<td>2 (40%)</td>
<td>NS</td>
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<tr>
<td>Pelvic lymph nodes metastasis</td>
<td>3 (11.5%)</td>
<td>3 (75%)</td>
<td>0.018</td>
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</table>

### Conclusions
There was a high incidence of loss of MSH6 protein expression in young patients with sporadic endometrial cancers. The phenotype of the tumour with loss of MSH6 protein expression is different from tumour with loss of either MLH1 or MSH2 protein.
NID1 AND NUPR1 FUNCTION DOWNSTREAM THE ETV5 TRANSCRIPTION FACTOR TO PROMOTE ENDOMETRIAL TUMOR PROGRESSION AND DISSEMINATION

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Objectives
Our group has described the ETV5 transcription factor associated with the early steps of endometrial cancer invasion. Here, we aim to identify ETV5 downstream target genes involved in myometrial infiltration.

Methods
We have performed a gene expression analysis to compare Hec1a endometrial cancer cells against its stable population overexpressing ETV5. Statistical and literature mining were performed to select ETV5 candidate target genes. Selected genes were analysed by chromatin immunoprecipitation and promoter-regulation was confirmed by luciferase reporter assays. Cell migration and invasion assays were performed to examine the role of NID1 and NUPR1 genes in Hec1A ETV5 overexpressing cells. Tumor invasion was also analysed in an orthotopic mouse model. Finally, human endometrial tumor samples were analysed by RTqPCR and IHC to determine levels of gene and protein expression.

Results
ChIP analysis and luciferase reporter assays confirmed NID1 and NUPR1 as ETV5 transcriptional targets. Inhibition of NID1 and NUPR1 in Hec1A cells overexpressing ETV5 reduces cell migration and invasion both in vitro and in vivo. Expression of NID1 and NUPR1 in human endometrial tumor samples shows an increase of expression in the endometrial invasion front.

Conclusions
We have identified Nidogen1 (NID1) and NUPR1 as direct transcriptional targets of ETV5. Both genes mediate some of the migratory and invasive capabilities induced by ETV5 overexpression in endometrial cancer cells both in vitro and in vivo. The identification of new players in the myometrial infiltration step represents a valuable tool for the molecular classification of patients as well as for the design of rational targets.
CHARACTERIZATION OF THE MECHANISMS INVOLVED IN ENDOMETRIAL CARCINOMA INVASION THROUGH THE REGULATION OF THE IGCAMS SUPERFAMILY

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Objectives
Working on endometrial carcinoma as a model system to understand the mechanisms of tumor invasion we have identified an ETS transcription factor, ETV5, associated with myometrial infiltration in ECs through the promotion of EMT. ETV5 promotes EMT pointed to cell adhesion and actin cytoskeleton reorganization. One of the main families of this molecular cells adhesions altered was the Immunoglobulin superfamily (IgCAMs), key mediators of cell-cell and cell-matrix adhesion. We aim to determine the function of ETV5 in IgCAMs during the myometrial invasion in EC.

Methods
cDNA microarray studies, comparing Hec1a cells and its stable population overexpressing ETV5, analyzed gene expression patterns on a whole-genome scale. The differential expression of selected genes was validated by qRT-PCR, immunobloting and immunofluorescence comparing Hec1a against its stable population overexpressing ETV5. We identified that ETV5 regulates the expression of the selected genes through ChIP and luciferase-reporter assays. We performed qRT-PCR and immunohistochemistry on tissues of non invasive and invasive ECs to characterize Ig-CAMs expression and validate ETV5 regulation through Chip-on-Chip assay.

Results
ETV5 overexpression modulates the IgCAMs profile at transcriptional and protein levels binding to ICAM2, NrCAM, and ALCAM promoters both in EC cells and tissues. We have also correlated the expression of IgCAMs protein with other adhesion key factors in EC invasion, i.e. E-Cadherin and B-Catenin.

Conclusions
ETV5 promotes EMT, possibly binding to ALCAM, ICAM2 and NrCAM promoters. We identified the relevance of the IgCAM superfamily in the first steps of ECs and more specifically during myometrial invasion.
COMPARISON OF PREOPERATIVE TUMOR GRADE AND POSTOPERATIVE HYSTERECTOMY PATHOLOGIC FINDINGS IN ENDOMETRIAL CANCER PATIENTS

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Objectives
Preoperative tumor grading becomes one of the most important predictors for lymphadenectomy at primary surgery for endometrial carcinoma. However, there is an inconsistency of tumor grade between preoperative curettage and final hysterectomy specimens. The objective of this study is to compare the accuracy of tumor grade in endometrial cancer between fractional dilatation and curettage (D&C) and postoperative hysterectomy specimen findings.

Methods
In this retrospective analysis, 97 patients' histopathologic endometrial biopsy findings were compared with those of the subsequent hysterectomy specimen diagnosed with endometrioid type endometrial cancer. The comparison of tumor grades was performed on both endometrial biopsy and hysterectomy specimens, the relationship between the concordance rate of grade.

Results
In final hysterectomy specimens, 11 of 97 grade 1 patients by curettage were upgraded to grade 2; 2 of 97 grade 2 were upgraded to grade 3, with a significantly discrepant rate of 26.8 % (26/97) and an upgraded rate of 13.4 % (13/97). The concordance rates were 79.3 % in grade 1, 66.7 % in grade 2, and 73.7 % in grade 3. The accuracy of tumor grade diagnosis by endometrial biopsy was 73.2 %, and thirteen patients were downgraded after comparison of postoperative specimens.

Conclusions
We concluded that endometrial biopsy had a high accuracy in the diagnosis of endometrial cancer in grade 1 tumors (79.3%). The accuracy of tumor grade concordance rates for grade 1 and grade 3 were higher than grade 2. Overall, thirteen patients' tumor grades seemed to be decreased by preoperative endometrial biopsy.
 ASSOCIATION OF ANTI-MULLERIAN HORMON (AMH) SERUM LEVELS AND ENDOMETRIAL AMH RECEPTOR II EXPRESSION IN PATIENTS WITH ENDOMETRIAL CANCER

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Objectives
To evaluate serum levels of AMH (Anti mullerian hormone) and also immunohistochemical (IHC) staining properties of AMH rec type II (MISRTII) in normal and malignant endometrial cancer specimens.

Methods
52 patients with endometrial cancer and 42 controls with benign pathology were included. Serum samples for AMH were collected prior to surgery. Moreover, MISRTII expression with IHC were compared in hysterectomy materials for both patients with endometrial cancer and benign pathology.

Results
41 patients had endometrioid and 11 had non-endometriod histology. 34 patients had grade I and 10 had grade III tumors. AMH levels of control group and endometrial cancer patients was comparable. Interestingly AMH serum levels for EC patient with extrautrine involvement was higher than EC patients without distant involvement. Strong IHC staining rate was higher for EC patients than control group but this did not reach to a statistical significance (17 % vs % 3, p=0.072). For EC patients, IHC staining properties of AMH rec type II decreased, as the stage of the lesion worsen, but this trend did not reach statistical significance probably due to small sample size (19 % of samples with stage I tumors had strong staining while this was 12 % for stage III tumors).

Conclusions
There is no difference between control group and cancer group with respect to serum AMH levels. But for EC patients AMH levles tended to be higher in extrauterine inolvement. Also strong staining was higher and tended to decrease gradually as the stage increased.
PREOPERATIVE IDENTIFICATION OF HIGH RISK ENDOMETRIAL CANCER USING GRADE, HE4, AND CA125
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Objectives
To evaluate the clinical utility of HE4, CA125, and grade to identify endometrial cancer (EC) patients requiring postoperative therapy.

Methods
200 consecutive patients surgically treated for EC was identified. HE4 (Fujirebio Diagnostics, Inc) and CA125 were measured from stored preoperative serum. Recursive partitioning was used to create rules best discriminating between outcomes of interest. Sensitivity and specificity was calculated.

Results
Stage distribution was: 147 stage IA, 21 stage IB, 6 stage II, 22 stage III, 4 stage IV. 44 (22%) had grade 3 lesions and 27 (13.5%) were serous. Median HE4 and CA125 was significantly higher in patients with stage III/IV disease. Patients with abnormal CA125 (>35) any grade and/or abnormal HE4 (>250) grade 3 had an 83% chance of having stage III/IV disease with sensitivity of 58% and specificity of 94%; the use of CA125 alone had a sensitivity of only 38%. Patients with a normal CA125 (<35) and normal HE4 (< 120) had only 6.7% risk of deep MI and/or advanced disease. In contrast, patients with an abnormal CA125 and/or HE4 had a 47% chance of having deep MI and/or advanced disease with sensitivity of 87% and specificity of 56%; CA125 alone had only 49% sensitivity.

Conclusions
The use of serum HE4, CA125, and tumor grade identify patients at risk of requiring postoperative therapy and is far less costly and more sensitive than current imaging modalities. This may be useful for preoperative counseling, consideration of surgical approach, and for triage of patients with EC to gynecologic oncologists.
AN IMPORTANT ROLE FOR WNT/B-CATENIN REGULATORS SOX2 AND SOX9 IN ENDOMETRIAL ADENOCARCINOMA.

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Objectives

The Wnt/β-catenin pathway is implicated in many cancers including endometrial adenocarcinoma; nuclear accumulation of β-catenin denotes an active Wnt pathway and transcription of downstream proliferative proteins. Transcription factors SOX2 and SOX9 are postulated regulators of the canonical Wnt pathway. Dysregulation of these proteins has been reported in many human cancers and have been associated with carcinogenesis, progression and also tumour suppression.

We aimed to assess Wnt pathway activation in endometrial cancer by demonstrating the presence of nuclear β-catenin and evaluate the corresponding expression pattern of SOX9 and SOX2.

Methods

We examined the staining patterns of β-catenin, SOX9, and SOX2 in the pre/post-menopausal endometrium of normal women (n=20) and women with endometrial cancer (n=32) by immunohistochemistry. Percentage of positively-stained nuclei were calculated using ImageJ. Cytoplasmic staining was evaluated using a semi-quantitative Quickscore.

Results

Nuclear β-catenin was expressed in 16/32 cancer and 1/20 benign samples (p=0.003). Nuclear SOX9 expression in cancer was significantly reduced compared to post-menopausal (p=0.005) and increased relative to proliferative endometrium (p=0.005). Nuclear β-catenin was highly correlated with increased cytoplasmic SOX2 (p=0.009), and cytoplasmic β-catenin was highly associated with increasing SOX9 (p=0.001).

Conclusions

Altered expression of SOX factors are likely to have a role in endometrial carcinogenesis; down-regulation of SOX9 and up-regulation of SOX2. Loss of SOX9 from post-menopausal endometrium may promote carcinogenesis via Wnt activation, whereas SOX2 may activate Wnt pathway via nuclear β-catenin. These findings support the importance of the Wnt pathway confirming previous β-catenin data, and provide evidence of a novel role for SOX9 in endometrial cancer.
PROTEINS IMPLICATED IN METASTASIS ARE UPREGULATED IN HUMAN ENDOMETRIAL CANCER: POTENTIAL PROGNOSTIC INDICATORS AND THERAPEUTIC TARGETS.

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Objectives

A panel of ‘metastasis inducing proteins’ (MIPs) including S100P, S100A4 and AGR2 has been described in many cancers and is correlated with recurrent disease and poor patient outcome, but their expression has not been fully explored in human endometrial cancer (EC). The aim of this study was to investigate the expression profile of MIPs in human EC.

Methods

Forty type I and II ECs with 10 normal postmenopausal controls were investigated using immunohistochemistry (IHC). Nuclear and cytoplasmic S100P and S100A4 immunostaining was scored separately using an H-score, and a semi-quantitative Quickscore was used for AGR2. RT-PCR was used to verify the MIPs gene expression.

Results

MIPs were present in ECs. Nuclear S100P (p<0.0001) and S100A4 (p<0.008) expression were significantly higher in cancer cells when compared to postmenopausal control glandular epithelia. Type II endometrial cancers showed apparent higher level of nuclear S100P in comparison to type I. AGR2 expression was exclusively cytoplasmic, and was significantly increased in type I compared to control (P< 0.014). The PCR results for the three MIPs agreed with IHC.
Expression of nuclear S100P and S100A4 in menopausal control and endometrial cancer types.

**Conclusions**
Up-regulation of MIPs in ECs, particularly in aggressive/high grade cancers suggests a possible role for MIPs in tumour progression and metastasis. We propose that they may be potential therapeutic targets and prognostic indicators in ECs.
CD133+ CANCER STEM CELLS DERIVED FROM UTERINE CARCINOSARCOMA (MALIGNANT MIXED MÜLLERIAN TUMOR)
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Objectives
Cancer stem cells (CSCs) that display tumor-initiating properties have recently been identified. CD133, a surface glycoprotein linked to organ-specific stem cells, has been described as a marker of CSCs in different tumor types. However, no study reported CSCs in the uterine carcinosarcoma (malignant mixed Müllerian tumor).

Methods
We herein identify and characterize CSCs in human uterine carcinosarcoma, which is one of the most aggressive and therapy-resistant gynecological malignancies and is considered to be of mesodermal origin.

Results
The CD133+ population was increased in uterine carcinosarcoma, and this population showed biphasic properties in the primary tumor. CD133+ cells predominantly formed spheres in culture and were able to differentiate into mesenchymal lineages. CD133+ cells were more resistant to cisplatin/paclitaxel-induced cytotoxicity in comparison with CD133− cells. A real-time polymerase chain reaction analysis of the genes implicated in stem cell maintenance revealed that CD133+ cells express significantly higher levels of Oct4, Nanog, Sox2, and Bmi1 than CD133− cells. Moreover, CD133+ cells showed a high expression level of Pax2 and Wnt4, which are genes essential for Müllerian duct formation. These CD133+ cells form serially transplantable tumors in vivo and the resulting CD133+ tumors replicated the EpCAM, vimentin, and estrogen and progesterone receptor expression of the parent tumor, indicating that CSCs likely differentiated into cells comprising the uterine carcinosarcoma tissue. Moreover, strong CD133 expression in both epithelial and mesenchymal elements in primary tumor demonstrated significant prognostic value.

Conclusions
These findings suggest that CD133+ cells have the characteristics of CSCs and Müllerian mesenchymal progenitors.
Poster Presentations: Endometrial Cancer

VALUE OF PREOPERATIVE DIAGNOSIS IN EARLY ENDOMETRIAL CANCER


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Objectives
In endometrial cancer, evaluate the correlation between MRI performed preoperatively to determine myometrial infiltration, with the final result, described in pathological anatomical study of the piece, as well as histological correlation in preoperative biopsy and the final histology.

Methods
Patients diagnosed and treated surgically for endometrial neoplasia from 2003 to 2012, which underwent an MRI before surgery, and biopsy of the tumor.

Results
170 patients were treated, and 134 underwent MRI. 20.8% of these showed no infiltration, 55.9% had one surface infiltration, and the infiltration of 23.13% was over than 50%. Of the 103 patients with less than 50% infiltration or without infiltration, 7.7% finally infiltrated more than 50%.

Of the 31 patients who reported an infiltration in the MRI >50%, at 70.9% (22 patients) final infiltration was less than 50%, and was confirmed in only 29.1%.

So the MRI has a sensitivity of 50% and a specificity of 81.2%, with a PPV of 29.03 and a NPV of 92.23.

As presurgical histology, 82.8% were endometrioid, mucinous 2%, 5% serous papillary, 7% hyperplasia with atypia, and 3% hyperplasia without atypia. Of patients with type I histology on the presurgical biopsy (n=130) was confirmed in this 126 pacientes, and type II (n=8) was confirmed in 4. With a PPV 96.9 for type I and PPV 75 for type II.

Conclusions
MRI is a test with high NPV, so an infiltration below 50%, the probability to be infiltrated is very high. On the other hand, if we are informed of an infiltration greater than 50% on the MRI, we should ideally start with a hysterectomy and perform de lymphadenectomy, depending on the peroperative study, to avoid overtreatment on some patients.
IMPACT OF SURGERY ON THE EVOLUTION OF UTERINE SARCOMAS

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Objectives
It proposes a retrospective descriptive study of sarcomas, where it is intended to analyse the impact of the type of surgery on the evolution of the disease and the prognosis for these patients.

Methods
Sarcomas diagnosed and/or treated in our center from 1996 to 2012, histological type, degree of differentiation, suspected diagnosis, primary surgery, recurrence, overall survival and disease-free survival depending on the surgery.

Results
27 cases have been diagnosed. Mean age at diagnosis was 44.26 years, with a mean tumor size of 80mm. 48% of patients were scheduled for surgery due to myoma growth and only 7.4% due to ultrasound suspicion.

33.3% of cases showed an average growth of myoma of 4cm in 1.5 years. 66% of patients underwent open surgery, 25.9% laparoscopy and 7.4% hysteroscopy. Myomectomy was performed in 44.4% of patients. In 22.2% of patients piece morcellation was carried out, while the other 77.8% had an intact removal of tumor specimen.

40% of patients relapsed. 45% of recurrences were solely pelvic, 45% were distant and 5% were multiple. All patients were a morcellation was performed recurred, and the DFS according to type of surgery, morcellation vs no morcellation was 6.3 month vs 70.3 month. (p<0.002)

Conclusions
Piece morcellation when it is a sarcoma poses a clear aggravation of the prognosis of the patient, being able to be considered iatrogenic, as it decreases time of relapse.
**Poster Presentations: Endometrial Cancer**

**ADJUVANT VOLUMETRIC-MODULATED ARC THERAPY WITH SIMULTANEOUS INTEGRATED BOOST IN ENDOMETRIAL CANCER. PLANNING AND TOXICITY COMPARISON.**

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**Objectives**

To report dosimetric and acute toxicity data in prospectively enrolled high-intermediate risk endometrial cancer (HIR-EC) patients postoperatively treated by volumetric modulated arc therapy (SIB-VMAT).

**Methods**

Thirty high-intermediate risk endometrial cancer (HIR-EC) patients were postoperatively treated by volumetric modulated arc therapy (SIB-VMAT). Target coverage, dose homogeneity, and sparing of organs at risk (OARs) were compared with corresponding data retrieved from an historical control constituted by 30 matched patients treated by 3D-CRT CB from a previously published study (ADA-1 trial). All patients received 45 Gy on pelvic lymph nodes plus 10 Gy boost on the vaginal vault.

**Results**

The SIB-VMAT technique produced more inhomogeneous plans than 3D-CRT CB, but showed significantly better conformity index (CIs) for both PTVs. SIB-VMAT was associated with significant reduction in the irradiated small bowel volume compared with 3D-CRT CB for the majority of dose/volume constraints analyzed (Dmean: p=0.036; V10: p=0.021; V15: p=0.001; V20: p=0.001; V25: p=0.001; V30: p=0.002; V35: p=0.013; V40: p=0.008; V45: p=0.006). With regard to bladder, rectum and femoral heads, SIB-VMAT showed a significant sparing advantage at all dose levels with respect to 3D-CRT CB retrieved plans. Moreover, overall OARs Dmean were significantly reduced by the SIB-VMAT (p=0.001). GI toxicities were more frequent in 3D-CRT CB versus SIB-VMAT (90.0% versus 66.7%; p value=0.028).

**Conclusions**

Compared to data from an historical database of patients administered 3D-CRT CB, SIB-VMAT significantly improves the dose conformity and sparing of OARs in HIR-EC patients undergoing postoperative radiotherapy. The improvement in terms of acute toxicity justify further prospective clinical evaluation.
MMP-9 SERUM LEVELS IN ENDOMETRIAL CANCER PATIENTS
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Objectives
The purpose of this study was evaluation of the potential use of matrix metalloproteinase 9 (MMP-9) serum levels assessment with conventional tumor marker – CA 125, in improvement of endometrial cancer diagnostics.

Methods
The study was based on 77 untreated endometrial cancer patients, and 40 healthy controls. All tumors were verified histopathologically and staged according to FIGO classification. Concentrations of serum CA 125 were determined using the Abbott instruments system, MMP-9 by the ELISA of R&D. For the statistical analysis Mann-Whitney U tests, receiver-operating characteristic (ROC) curves to assess the diagnostic sensitivity and specificity of the marker results were used.

Results
The concentrations of MMP-9 were elevated in 35% endometrial cancer patients, more frequently than CA 125 (29%). As compared with controls, there were significantly higher serum levels of MMP-9 (p<0.001) in endometrial cancer patients, similarly to CA125 (p<0.0001). In the study group of the early stage endometrial cancer patients (FIGO IA-IC), elevated MMP-9 levels were observed in 38% of patients; while the concentration of CA125 were elevated in only 17%. There were no differences between the concentrations of MMP-9 depending on tumor stage and grade. The ROC analysis revealed the lower diagnostic sensitivity of MMP-9 (AUC 0.689), however AUC of CA125 was 0.781 in all study group. The significant differences between AUCs values were not approved.

Conclusions
The results suggest that determination of MMP-9 with CA 125 levels may be useful in endometrial cancer diagnostics improvement, especially in the early stage of the disease.
ROLE OF LYMPHADENECTOMY IN DISEASE-FREE AND OVERALL SURVIVAL ON LOW RISK ENDOMETRIUM CANCER PATIENTS

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Objectives
The objective of this research was to study the effect of lymphadenectomy on disease-free (DFS) and overall (OAS) survival in early stage low risk endometrium cancer patients.

Methods
257 patients treated surgically between 1994 and 2012 with endometrioid type, grade 1 or 2 endometrium cancer who had myometrial invasion <1/2 and no intraoperative evidence of macroscopic extrauterine spread were included into the study. Intraoperative pelvic lymphadenectomy was performed on 184 cases, pelvic lymphadenectomy was not performed on 73 cases.

Results

<table>
<thead>
<tr>
<th></th>
<th>w/o lymphadenectomy(n=73)</th>
<th>w lymphadnectomy(n=184)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>relaps</td>
<td>1 (1.4 %)</td>
<td>8 (4.3%)</td>
<td>0.242</td>
</tr>
<tr>
<td>exitus</td>
<td>0 (0%)</td>
<td>2 (1.1 %)</td>
<td>1.000</td>
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<tr>
<td>DFS(m)</td>
<td>97.9±48.7</td>
<td>88.8±43.2</td>
<td>0.828</td>
</tr>
<tr>
<td>OAS(m)</td>
<td>98.8±48.1</td>
<td>91.0±43.5</td>
<td>0.828</td>
</tr>
</tbody>
</table>

While there were 8 relapses at patients with lymphadenectomy group, only 1 relaps was seen in patients without lymphadenectomy group. None of the relapses was in pelvic region. There were no statistical difference in disease-free survival and overall survival between two groups. None of the patients died because of disease in patients w/o lymphadenectomy. But in patients w lymphadenectomy, two patients died because of bone and liver relapses, in 12. and 21. months respectively.

Conclusions
Omission of lymphadenectomy did not worsen disease-free and overall survival in early stage low risk endometrium cancer.
Poster Presentations: Endometrial Cancer

BEATSON WEST OF SCOTLAND CANCER CENTRE EXPERIENCE OF NEOADJUVANT CHEMOTHERAPY FOR INITIALLY INOPERABLE ENDOMETRIAL CANCER.

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Objectives
Following the report from Frederic Amant on the use of neoadjuvant chemotherapy in advanced endometrial cancer we report our experience from a UK regional Cancer Centre. The aim was to audit the tolerability and outcomes in a series of patients spanning 6 years treated with neoadjuvant chemotherapy for initially diagnosed inoperable endometrial cancer.

Methods
We used local databases to identify patients whom at initial MDT (multi disciplinary team) meeting review were felt to be inoperable by the Gynaec- oncologist in view of advanced disease but without visceral metastases. The aim was to give these patients 3-6 cycles of neoadjuvant chemotherapy with planned rediscussion at the MDT to decide if delayed primary surgery would be feasible. All pathological subtypes were considered. Survival, treatment and toxicity data and demographics on these patients has been collated and analysed

Results
We identified 27 who received neo-adjuvant chemotherapy. Initial analysis would suggest that the majority proceeded to surgery after chemotherapy. Chemotherapy was well tolerated. A significant proportion of these patients also received adjuvant treatment ranging from radiotherapy, concurrent chemoradiation and/or vault brachytherapy tailored to the post operative pathological findings.

Conclusions
Our data shows that majority of these patients are still alive and relapse free. This is a group of Stage 3/4 patients who would have received palliative treatment without the opportunity of neoadjuvant chemotherapy and delayed primary surgery. This approach, already proven in advanced ovarian cancer, has merit for further exploration in locally advanced inoperable endometrial cancer.
THE FREQUENCY AND SIGNIFICANCE OF WT-1 EXPRESSION IN SEROUS ENDOMETRIAL CARCINOMA

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Objectives
Serous endometrial carcinoma is an aggressive type of endometrial carcinoma. Wilms' tumour gene 1 (WT-1) is commonly expressed in ovarian serous carcinomas and is considered a diagnostic marker of these tumours. However, it is generally believed that WT-1 is rarely expressed by endometrial serous carcinoma.

The aim of this study was to evaluate the frequency and significance of WT-1 expression in endometrial serous carcinoma.

Methods
We studied the expression of WT-1 in formalin fixed paraffin embedded tumour sections from 77 cases of endometrial serous carcinoma. The expression was correlated to clinicopathological parameters including tumour stage, presence of lymphovascular space invasion, cervical involvement, extrauterine spread and disease free survival (DFS).

Results
Of the 77 tumours, 34 tumours showed positive expression for WT-1 (44.16%). There was a statistically significant association between the presence of WT-1 expression and DFS, where patients with tumours expressing WT-1 had a shorter DFS compared to those with no WT-1 expression (p = 0.031, median DFS 15 and 38 months respectively).

Conclusions
Our study shows that WT-1 is expressed in a considerable percentage of endometrial serous carcinomas, suggesting a role for WT-1 in the pathology of these tumours. This is of potential therapeutic significance as WT-1 is an emerging target for immunotherapy. Moreover, our results show that WT-1 has prognostic value, being predictive of DFS. As a potential prognostic marker and therapeutic target, we recommend that WT-1 expression should be included in histopathological reports of endometrial serous carcinoma.
IDENTIFYING PROGNOSTICALLY RELEVANT SUBSETS OF ENDOMETRIAL CANCER USING UNSUPERVISED CLUSTERING OF IMMUNOHISTOCHEMICAL STAINING DATA.

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Objectives
Multiple studies have suggested that biomarkers, such as ER and PR have a prognostic significance in EC. However, these biomarkers are currently not utilized as prognostic markers in clinical practice. Our aim was to assess the immunohistochemical risk profile of endometrial cancer patients by performing unsupervised clustering of eight prognostic factors.

Methods
We collected clinical, histopathological and follow-up data on 230 EC patients operated at Turku University Hospital in 2004-2007. A TMA was constructed for immunohistochemical analysis and the results were entered in an unsupervised hierarchical clustering analysis.

Results
The unsupervised clustering produced a cluster with three major subgroups of which one subgroup consisting of 47 (20.4%) cases had a substantially higher risk for relapse [OR 14.3 (CI 5.91-34.7, p<0.001)]. Thirty-six (16.5%) of the endometrioid type EC clustered in the high-risk subgroup and had a 12-fold risk of relapse compared to the patients in the non-high-risk subgroups [OR 12.2 (CI 4.72-31.6, p<0.001)]. When adjusted for FIGO stage and grade the high-risk group was significantly associated with disease-free survival [OR 8.3 (CI 2.88-23.95, p<0.001)].

Conclusions
Our results indicate that using a panel of immunohistochemical stainings could be a useful tool for risk assessment in EC.
LAPAROSCOPIC PELVIC SENTINEL LYMPHADENECTOMY WITH INDOCYANINE GREEN; EXPERIENCE WITH THE FIRST 20 PATIENTS

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Objectives
The Sentinel technology is increasingly being used in various malignancies such as breast cancer, melanoma, vulvar and cervical cancer. In endometrial cancer the sentinel method is still under research. As markers mostly radioactive isotopes (technetium99) and / or patent blue are used. The preoperative injection of radioactive isotopes is a burden for the patients and the patent blue shows a poorer detection rate of only about 80%.

With new laparoscopic optics fluorescent markers can be visualized with near infrared light. A suitable marker is indocyanin green (ICG), which is common in other diagnostic fields such as cholangiography or angiography with a good safety profile.

Methods
In 20 patients with cervical or endometrial cancer 5-10ml ICG-PULSION © were injected intracervically, then lymphatic mapping was performed with the fluorescence optic (Storz). After opening the peritoneum, the sentinel lymph nodes were located in the pelvis and excised for histological examination.

Results
In 20 patients, the ICG fluorescein technique could be applied. No allergic reactions were observed from the ICG. In 18/20 patients at least one sentinel node was detected with bilateral nodes in 16/20 cases. A median of 3.4(0-8) lymph nodes were detected as sentinel lymph nodes. 5 patients had metastasis in pelvic lymph nodes, in 4 out of these 5 the sentinel was also positive.

Conclusions
The laparoscopic ICG fluorescence technique is a new, promising technique for detecting the local spread of gynecological tumors in the pelvis with low complication rates and good detection rates. Further research on oncologic outcome is required.
Poster Presentations: Endometrial Cancer

SEMI-RADICAL Hysterectomy Do Not Necessarily Be Performed for Clinical Stage I/II Uterine Carcinoma: A Historical Control Study

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Objectives
To compare the prognosis and adverse effects between total abdominal hysterectomy (TAH) and semi-radical hysterectomy (SRH) in clinical stage I/II endometrial carcinoma.

Methods
Between 1990 and 2009, 247 patients with clinical stage I/II endometrial carcinoma underwent primary surgery at National Defense Medical College in Japan; 46 with simple hysterectomy (TAH group) and 201 patients with semi-radical hysterectomy (SRH group).

Results
There were no significant differences of age, clinical stage, surgical stage, histopathology, muscular invasion, lymph-vascular invasion, cervical involvement, peritoneal washing cytology, lymph node metastasis, adjuvant chemotherapy, and recurrent risk evaluation between two groups. The number of the patients with ovarian metastasis was higher in TAH group than in SRH group (p=0.02). There was no significant difference of progression-free survival (PFS) and overall survival (OS) between two groups (p=0.51, p=0.83). Patients in SRH group developed more severe adverse events concerning operation time, blood transfusion, and lymphedema. Also, recurrence rate in TAH group was similar with SRH group, and there were no significant differences of recurrent sites. In the multivariate analysis for RFS and OS, operative procedure was not a prognostic factor (p=0.51, p=0.73, respectively).

Conclusions
TAH was appropriate for patients with clinical stage I/II endometrial carcinoma.
Searching Additional Genetic Factors in Endometrial Cancer Among Lynch Syndrome Patients with Targeted Exome Sequencing

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Objectives

Lynch syndrome (LS) is an autosomal dominant inherited cancer disorder caused by mutations in mismatch repair (MMR) genes (MLH1, MSH2, MSH and PMS2). In addition to colorectal cancer LS carrier women have increased lifetime risk to develop among others endometrial cancer. Since cancer risks are broad and cancer sites vary in LS patients, our hypothesis is that risks are modified by additional germ line variants besides MMR gene mutations.

Methods

Based on literature and research team experience we designed a panel of 154 candidate endometrial cancer genes. This includes cognate oestrogen and progesterone receptors, co-regulators and chromatin-remodelling proteins, downstream primary and secondary targets of oestrogen and progesterone signalling, enzymes involved in steroid metabolism and known onco- and tumour suppressor genes.

A total of 150 women LS carriers are registered in our centre with available clinical information, among them 35 have been diagnosed with endometrial cancer. Their peripheral blood DNA is being subjected to targeted exome sequencing.

In a pilot of 15 samples targeted exome capture (Haloplex, Agilent) and next generation sequencing (HiSeq, Illumina) was performed.

Results

We identified 20 novel rare coding variants as putative additional genetic factors and validated with Sanger-sequencing. The pilot has been followed by a second NGS run of 20 additional samples.

Conclusions

Variants identified in the total population will be correlated with clinical features and cause-effect relationship will be investigated by co-segregation and allele inactivation on tumours. We expect that the results will be exploited to construct an improved diagnostic assay of endometrial cancer.
STAT1 PATHWAY MODULATE PROGRESSION OF SEROUS PAPILLARY ENDOMETRIAL CANCER

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Objectives
Serous papillary endometrial cancers (SPEC) are highly progressive with poor prognosis, and its oncogenic profile is known different from endometrioid endometrial cancers. It, however, still remains unclear that which pathway promotes tumor progression or what happens in the frontier of tumor progression.

Methods
To investigate SPEC-specific pathways, gene expression microarray was analyzed for 69 endometrial cancers under protocols approved by the Kyoto University Institutional Review Board, which expression was confirmed by immunohistochemical staining. Using SPAC-1L, SPEC cell line, cellular proliferation, migration, and invasion were assessed. In vivo studies were performed on NOD-SCID mice by inoculating SPAC-1L xenograft tumors.

Results
By microarray analysis, STAT1 pathway was revealed highly activated in SPECs. Immunohistochemical staining exhibited co-localization of ICAM-1 and PD-L1 at tumor frontier with CD8-T cells (p<0.001) as well as STAT1 expression in SPECs (p<0.05). Using a SPEC cell line, SPAC-1L, it was confirmed that IFN-gamma induced STAT1 expression not only to promote cellular proliferation (p<0.05), adhesion (p<0.0001), and invasion (p=0.0002), but to induce expression of cMyc, ICAM-1 and PD-L1 (p<0.05). In contrast, suppression of STAT1 attenuated induction of these genes (p<0.05) and inhibited xenograft tumor growth on NOD-SCID mice (p<0.0001).

Conclusions
These results indicate that STAT1 pathway modulates the micro-environment of SPECs to promote tumor progression.
Poster Presentations: Endometrial Cancer

ADJUVANT CHEMOTHERAPY DOES NOT PRECLUDE THE NEED FOR PELVIC +/- PARA-AORTIC LYMPHADENECTOMY IN FIGO STAGE I-IV UTERINE SEROUS CANCER

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Objectives
To determine the independent role of lymphadenectomy irrespective of stage or type of adjuvant treatment in women with uterine serous cancer (USC).

Methods
Women with USC were identified from the patient pathway manager (PPM) between January 2002 and December 2007. Age at diagnosis, surgico-pathological data, adjuvant treatment, follow-up & survival data, were collected. Cox proportional hazards regression was used to adjust for age (<65/≥65 yrs), FIGO stage and type of adjuvant treatment.

Results
Out of 92 women who were identified with a histological diagnosis of serous carcinoma, 77 had surgery. Sixty one women (79%) underwent lymphadenectomy and 28% had nodal metastases. The median follow-up (range) was 82 months (64 - 123). Adjuvant chemotherapy +/- radiotherapy was associated with significantly (p = 0.03) longer median overall survival (40 months, 95% CI 27 - 53) compared to radiotherapy alone (17 months, 95% CI 12 - 22), when lymphadenectomy was performed. In multivariate analysis, age<65 years, FIGO stage (IA, IB & II), pelvic plus para-aortic lymphadenectomy (HR = 0.32, 95% CI 0.17 - 0.63, p=0.001) and pelvic lymphadenectomy (HR = 0.34, 95% CI 0.15 - 0.79, p=0.01) were associated with improved overall survival, however, type of adjuvant treatment lost its prognostic value. In addition, lymphadenectomy was an independent predictor in FIGO stage I disease.

Conclusions
Women with USC undergoing lymphadenectomy are more likely to survive longer and the type of adjuvant treatment may not influence this benefit. The impact of adjuvant chemotherapy on the survival benefit following extensive lymph node dissection warrants further research.
VALIDATION METHOD TRAINING: THE EUROPEAN SCHOOL OF ABDOMINO-PELVIC SURGERY IN GYNECOLOGIC ONCOLOGY (ESAGON)

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Objectives
The European School of Abdomino-pelvic Surgery in Gynecologic Oncology was started to address the need for advanced post-graduate training in gynecologic oncology in Italy. Surgical training consists of participating as assistant in surgical cases, never as first surgeon, in a two year schedule. We developed a questionnaire with the specific aim to investigate whether participants have changed any specific aspects in their clinical practice.

Methods
15 doctors participated in the training and were interviewed afterwards. A 57-questions Questionnaire was mailed and administered 6 months after completion of the course. The results were analyzed with descriptive statistics.

Results
We analyzed some of the most significant items: 85.7% of participants felt more confident in managing cancer patients overall and 92.3% in managing surgical aspects. They were asked whether through observation only it was possible to learn technical aspects: 64.3% answered yes significantly and 28.7% yes slightly. 61.5% of participants claimed an increased of optimal cytoreductive surgery in their centers as a direct consequence of the course. 92.9% of participants felt that their skill about performing radical surgery was improved. Overall 71.4% were very satisfied with the school and experienced better autonomy and competence and feeling of increased appreciation, and 28.6% were adequately satisfied.

Conclusions
From our results the close involvement in a high volume gynecologic oncology department may balance the absence of experience as first surgeon. Our results support idea that this school may have an important role for advanced post-graduate training. Validation method training is fundamental to monitor the efficacy of experimental teaching approaches.
Organisation of Gynaecologic Cancer Care

COST OF POST-OPERATIVE INVESTIGATIONS FOLLOWING A GYNAECOLOGICAL ONCOLOGY SURGERY.
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Objectives
We have undertaken a study in a gynaecological oncology centre situated in a large general teaching hospital in order to assess the amount and the cost of the post gynaecological oncology surgery investigations. This has been related to the type of operation performed and a number of other factors in view of the recently introduced enhanced recovery programme in the unit.

Methods
A proforma was designed to facilitate data collection. The patients with a gynaecological oncology procedure and accessible notes were identified on the unit's theatre lists from October 2012 to March 2013. The data were collected from both the surgical note and the intra-operative anaesthetic chart.

Results
We have collected data for 40 patients of whom 25% had minimal access surgery with a mean hospital stay of 3.1 days and a mean cost of post-operative investigations of £8.85. 75% of the patients data collected had a laparotomy procedure with a mean hospital stay of 6.96 days and a mean cost of post-operative investigations of £28.67. The main type of post-operative investigations was a blood test, with the majority having a full blood count on day 2 post-operatively.

Conclusions
We have identified that the minimal access surgery in combination with the establishment of the enhanced recovery programme will reduce the volume of post-operative investigations and the related cost as well as the post-operative length of stay. However this is subjected to a number of limitations due to the nature of the underlying malignancy and intra- or post-operative complications.
Poster Presentations: Organisation of Gynaecologic Cancer Care

HEALTH CARE USE AMONG ENDOMETRIAL CANCER SURVIVORS

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Objectives
Increasing numbers of endometrial cancer survivors (ECS) place a high burden on the health care system. This study describes the number of visits to the general practitioner, medical specialist and other care services, compared with the general population, and factors associated with this health care use: age, marital status, education, BMI, comorbidity, years since diagnosis, radiotherapy.

Methods
ECS diagnosed between 1999 and 2007 with Figo stage I-II were selected from the Eindhoven Cancer Registry. A total of 742 survivors (77%) completed a questionnaire about their general and cancer-related health care use, using PROFILES registry.

Results
ECS visited their medical specialist more often (3.4 times/year) than the general population (2.8 times/year). In relation to their cancer, they visited their general practitioner once and their medical specialist twice per year. Use of additional care services was low (14%), but higher among younger survivors (33%). Younger women were more likely to make cancer-related visits to their general practitioner, while higher educated women were less likely to visit their general practitioner and more likely to make cancer-related medical specialist visits. Women with more comorbid conditions were more likely to make general and cancer-related general practitioner visits. Radiotherapy and BMI were not related to health care use.

Conclusions
ECS use more health care than women in the general population. Younger women visit their general practitioner more often in relation to their cancer and use more additional care services. Higher educated survivors were more likely to visit a medical specialist in relation to their cancer.
SURVIVORSHIP CARE PLANS TO INFORM THE PRIMARY CARE PHYSICIAN OF GYNAECOLOGICAL CANCER PATIENTS: TRIAL RESULTS AND IMPLICATIONS FOR FUTURE DEVELOPMENT

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⁵Eindhoven Cancer Registry, Comprehensive Cancer Center South, Eindhoven, Netherlands

Objectives
A Survivorship Care Plan (SCP) might enhance communication between the medical specialist and the primary care physician (PCP). The primary aim of this study was to assess the effect of a SCP on the communication between the PCP and the gynaecologist/medical oncologist. Furthermore, we evaluated PCPs' opinions regarding the SCP and explored their perceived role in the care for cancer survivors.

Methods
In the ROGY Care Randomized Controlled Trial, the PCP of endometrial and ovarian cancer patients in the intervention group received a SCP (copy of patient version) in addition to usual information. A questionnaire was returned by 266 PCPs (76%).

Results
One third of PCPs in the intervention group reported receiving a SCP. PCPs from the intervention group were more likely to have had personal contact with the medical specialist, but were equally satisfied with the information compared to PCPs from the control group. Of the PCPs, 82% indicated they wish to receive a SCP in the future. PCPs who received a SCP reported that a SCP supported personal contact with the patient: 63-88% had more/better contact about diagnosis, treatment and prognosis. However, the SCP in its current format was too long and elaborate.

Conclusions
Supplying a SCP to PCPs potentially has a positive effect on PCPs' communication with the medical specialist and the patient. However, deliverance should be fully facilitated and the SCP should be concise and focused on PCPs needs, such as contact information and tailored information on patient diagnosis, treatment and possible consequences.

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Objectives
The reduction of hospital length of stay and perioperative morbidity in surgical treatment of endometrial cancer.

Methods
In April 2010, the Enhanced Recovery Programme (ERP) was introduced in Exeter. The ERP used the principles of: preoperative rehydration with glucose drinks and early postoperative feeding, maximal use of minimal access surgery, avoidance of drains and early removal of Foley catheters, planned mobilisation and discharge regimes, and avoidance of spinal/epidural anaesthesia. The effect of the change was measured on hospital length of stay, and hospital readmission rates. Other variables measured included age, use of minimal access surgery (MAS), body mass index (BMI). All consecutive endometrial cancer patients treated with hysterectomy were divided into three groups based on date of diagnosis: January 2009 - March 2010 (PreERP), April 2010 - June 2011 (PostERP1), July 2011 - September 2012 (PostERP2).

Results

<table>
<thead>
<tr>
<th>Cohort</th>
<th>PreERP</th>
<th>PostERP1</th>
<th>PostERP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>80</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>n/a</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>69</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>Laparoscopic (%)</td>
<td>12</td>
<td>29</td>
<td>60</td>
</tr>
<tr>
<td>Total bed days</td>
<td>501</td>
<td>284</td>
<td>210</td>
</tr>
<tr>
<td>Length of stay (median)</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Readmissions</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Readmission bed days</td>
<td>56</td>
<td>14</td>
<td>6</td>
</tr>
</tbody>
</table>

With a rising caseload, total bed days and median length of stay were greatly reduced. This was accompanied by reductions in number and duration of readmissions. There were no readmissions after laparoscopic surgery.

Conclusions
The ERP introduced many desirable improvements for both patient and service provider. There was no offsetting worsening in readmissions. The improvements are sustainable and can be built upon by continued focus on increasing the proportion of cases treated with MAS.
THE SWEDISH QUALITY REGISTRY FOR GYNECOLOGIC ONCOLOGY

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Objectives

Reporting to The National Swedish Cancer Registry, which started 1958, is mandatory. The coverage is over 95% and 99% are morphologically verified. However, information about treatment and follow-up is not collected. In 2004, a steering committee was formed to start a national quality registration, including all malignant gynecological tumors and covering the whole Swedish population with linkage to the cancer register. The register for ovarian, fallopian tube, peritoneal, abdominal or pelvic malignancies started in 2008, endometrial 2010, cervical/vaginal 2011, and vulvar malignancies 2012.

Methods

The registration consists of 5 web-forms; 1. Cancer registration including basic data, 2. Details on surgical treatment, 3. Details on primary non-surgical cancer treatment and tumor evaluation, 4. Details on recurrence, and 5. Follow-up data during five years. Survival is monitored via the national Cause of Death Register. Data are monitored and checked by cancer registrars at the Cancer Registry. Patients can opt-out from registration and registration is voluntary. However, hospitals are strongly encouraged by the State to participate.

Results

10 000 patients have so far been included. The coverage compared to the National Cancer Registry was 84% for ovarian/fallopian tube malignancies, 90% for endometrial, 81% for cervix/vaginal malignancies, and 61% for vulvar malignancies. Various measures are now undertaken to validate the data. Development is underway to include patient-related outcome measures.

Conclusions

The Swedish Quality Registry for Gynecologic Oncology is a population-based nation-wide web-based register including all gynecological malignancies. Its aims are both to assess the quality of medical practice and answer important research questions.
Poster Presentations: Organisation of Gynaecologic Cancer Care

ROBOTICS IN GYNAECOLOGICAL ONCOLOGY- LARGEST SINGLE CENTRE EXPERIENCE FROM THE UK.

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Objectives

Application of minimal invasive surgery in gynaecological oncology is reported since 1980’s. Uptake of laparoscopic surgery among gynaecologists has been poor with only 14% reduction in open surgery. Rate-limiting step appears to be advanced laparoscopic skills required for complex surgery. We established a robotics surgery (RS) for women with gynaecological cancers from mid 2010 and report our experience.

Methods

Prospective, observational study in a tertiary gynaecological oncology centre with 2 surgeons over the first 2 years. Patient demographics, intra and post-operative data recorded.

Results

(202) cases performed. Procedures varied from simple hysterectomy to radical hysterectomy and systematic bilateral pelvic node dissection for cervical cancer. Other specialist procedures like trachelectomy and ovarian transposition have also been undertaken with ease. BMI ranged from 17-59 (Mean 38). Median estimated blood loss overall was 50mls (5-2500). Median hospital stay was 1 day. Lymph node yield was comparable (20-56).

Conclusions

Prior to introduction of robotics review of our records revealed that atleast 64% of women especially obese patients underwent open surgery. The biggest advantage to patients is reduced blood loss, shortened hospital stay, reduced post-operative pain due to less torque on trocars and varied applications. Camera positioning by the surgeon, no camera shake, 3D image leading to greater appreciation of surgical anatomy along with better ergonomics and less fatigue beneficial to surgeons.

We are now seeking to improve our robotics program with a twofold approach. Besides advancing surgical capabilities, we are also collecting patient reported outcome measures to enhance service provided as well collaborations with engineering teams to develop better systems.
Management of Gynaecological Malignancies in the Oldest of the Old

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Objectives
Definition of geriatric patient is unavailable and cut-off age differs. Worldwide, 600 million people were noted to be > 60 years in 2000, while in 2050 this will reach 2 billion. Management of cancers in these patients is complex as the presence of co-morbidities may interact with treatment or survival.

To review our experience in management of oldest of the old, to explore feasibility and tolerability of surgery and identify factors influencing outcomes.

Methods
Retrospective study over 4 years of women age > 85 years old managed for gynaecological cancers.

Results
106 patients identified. 24 had vulvar, 3 vaginal, 8 cervical, 32 endometrial, 34 ovarian, and 5 peritoneal cancers. Mean patient age was 88.58 years (85-97). Advanced stage disease noted in 50.94 %, comorbidities in 78.3 %, and high surgical risk in 60.38 % of them. Commonest co-morbidities were aortic stenosis, atrial fibrillation, ischemic heart disease, aneurysm, hypertension, diabetes mellitus, poor eyesight, deafness, osteoarthritis, old fracture and dementia.

Conclusions
Several studies have shown that oldest of the old are managed differently to younger patients with lower odds of receiving standard care. Advancing age, is not a reliable guide to treatment decision making as recommended by International Society of Geriatric Oncology guidelines. Detailed evaluation including comprehensive geriatric assessment may help decision making during multidisciplinary discussions. Patient co-morbidities, quality of life, tumour characteristics and remaining life expectancy affects treatment recommendations.

In our opinion guideline deviation does not necessarily equal inappropriate treatment and should be tailored to a patients overall well-being.
WHAT DO OVARIAN CANCER PATIENTS EXPECT FROM THEIR DOCTORS AND THERAPY MANAGEMENT? RESULTS OF A EUROPEAN SURVEY OF NOGGO/ ENGOT-OV9

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Objectives

The primary aim of this study was to investigate information needs and preferences among patients with ovarian cancer.

Methods

A 27-item questionnaire was developed and then provided to ovarian cancer patients via internet or as a print-version in 8 European countries (Austria, Belgium, France, Germany, Italy, Poland, Rumania, Spain). The questionnaire evaluated the expectations and needs concerning their therapy management and doctor-patient communication.

Results

1743 ovarian cancer patients participated. The median age was 58 years (range 16-89). Nearly all patients (96.3%) had a primary surgery and a first-line chemotherapy (91.5%) but only more than half (56.8%) be aware of their FIGO-stage. 609 (36.8%) patients got the offer to participate on a clinical trial but more than two thirds of these patients (423) were included in clinical trials. Most of the patients were pleased with the completeness and understandability of the explanations about the therapies from their doctors. About 68 % of patients would be interested in having the opportunity to have a second opinion. The three most important aspects, which were proposed by patients to improve therapy against ovarian cancer were: no alopecia (42%), counter fatigue" (34%), and more effective therapy (29%).

Conclusions

This study underlines the need of ovarian cancer patients to discuss details concerning treatment options and clinical management with minor difference between the countries. Patients also need more information about side effects of cancer therapies and second opinion opportunities.
ESGO AFFILIATED VIRTUAL TUMOR BOARD IN ARMENIA, PRELIMINARY REPORT
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3Pathology, "Muratsan" Medical Center of State Medical University, Yerevan, Armenia
4Radiotherapy, National Institute of Oncology, Yerevan, Armenia
5Radiotherapy, Beatson Oncology Center, Glasgow, United Kingdom
6Pathology, Medical University, Graz, Austria
7University of Torino, Turin, Italy

Objectives
In October 2010 during the 1-st ESGO Basic Course in Armenia an International Multidisciplinary Cancer Conference was organized under ESGO authority. The aim of this study was to evaluate the clinical and educational efficacy of the above mentioned working group.

Methods
From ESGO: GYN Oncologist (Expert 1), Medical/Radiation Oncologist (Expert 2) and Pathologist (Expert 3). Local contributors: GYN Oncologist (Local 1), Medical Oncologist (Local 2), Pathologist (Local 3) and Radiation Oncologist (Local 4). For case submission and communication “Google Documents” Service was used. The working group was called the Virtual Tumor Board (VTB). Residents had limited access (view only mode) to the discussion. The educational value was scored by the residents.

Results
From October 2010 to April 2013 59 cases were submitted. Breast – 21 cases, ovary-12 cases, uterine corpus-14 cases and cervix-11 cases. Expert 1 and Expert 2 responded in 49 (83.1%) and 50 (84.7%) of cases, respectively, expert 3 in 29 cases (49.2%). Local 1 responded in 57 cases (96.6%), locals 2, 3 and 4 responded in 48 (82.4%) 15 (25.4%) and 9 (15.3%) cases, respectively. Discussion caused correction or changes in treatment plan in 15 (25.4%) of cases. The educational value of VTB assessed as excellent by 8 of 10 residents and as good by 2.

Conclusions
VTB is an excellent tool to obtain high standard cancer care in patients with gynecological cancer. It has also excellent educational value.
THE ROLE OF RISK OF MALIGNANCY ALGORITHM IN THE PRESURGICAL ASSESSMENT OF ADNEXAL TUMORS: A PROSPECTIVE STUDY.

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Objectives
To assess the clinical value of risk of malignancy algorithm (ROMA) in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods
Serum specimens were collected from 61 patients admitted to our Clinic because of adnexal mass. Serum specimens were collected within 72 hours before surgical operation. The definitive diagnosis of the adnexal pathology was established by the pathological examination of the excised lesions. The normal level of CA 125 and HE4 was considered less than 35 IU/ml and less than 70 pmol/L respectively. The ROMA model is calculated depending on both of HE4 and CA125 serum levels. Chi-square test was used for the statistical analysis.

Results
Seven cases were diagnosed with malignant disease (11.48%). The level of HE4 was significantly increased among patients with malignant tumors ($\chi^2(1)=44.13; p<0.001$). The level of CA125 was significantly increased among patients with malignant disease ($\chi^2(1)=14.04; p<0.001$). The results of ROMA model showed a significant statistical difference between patients with and without malignant disease($\chi^2(1)=24.14; p<0.001$). The sensitivity, specificity, positive and negative predictive values of ROMA were 100.00%, 88.89%, 53.85% and 90.16% respectively.

Conclusions
ROMA is a simple algorithm which can be used for the presurgical evaluation of adnexal tumors.
SEQUENCED COMBINATIONS OF PLATINUM DRUGS WITH BORTEZOMIB IN OVARIAN TUMOUR MODELS
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³Department of Pathology, Concord Hospital, Sydney, Australia

Objectives
Although widely used in the clinic, drug resistance is a constant problem with platinum drugs such as cisplatin and carboplatin, especially in the ovarian cancer. Cisplatin hinders its own uptake by inducing proteasomal degradation of the influx carrier copper transporter 1 (CTR1). Proteasome inhibitor bortezomib (BORT) - an anticancer drug on its own right - is found to block such degradation so that in the presence of the inhibitor cellular uptake of platinum and consequently the level of platinum-DNA binding may be increased resulting in enhanced cell death.

Methods
In this study efficacy from the sequenced combinations of cisplatin, carboplatin and oxaliplatin with BORT in the human ovarian A2780, A2780cisR, A2780ZD0473R and SKOV-3 cancer cell lines was evaluated. The levels of cellular platinum accumulation and platinum-DNA binding as well as the levels of total and oxidized glutathione were determined. Finally, changes in expression of key proteins associated with drug resistance were determined using proteomics.

Results
Presence of BORT is found to enhance cellular accumulation of platinum, the level of Platinum-DNA binding and also the oxidative stress especially in the resistant cell lines. Expression of over thirty proteins associated with drug resistance was found to be altered by the selected combinations.

Conclusions
Combinations of platinum drugs with BORT are found to increase cellular accumulation of platinum and the level of platinum-DNA binding, increase oxidative stress, and alter expressions of key proteins associated with drug resistance.
LENGTH OF HOSPITAL STAY POST-OPERATIVELY IS NOT DECREASED BY PRE-OPERATIVE ORAL CARBOHYDRATE ADMINISTRATION IN PATIENTS WITH ADVANCED OVARIAN CANCER UNDERGOING SURGERY.

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³Leeds Institute of Molecular Medicine, University of Leeds, Leeds, United Kingdom
⁴Gynaecological Oncology, St James's University Hospital, Leeds, United Kingdom
⁵Gynaecological Oncology, Royal Preston Hospital/Lancashire, Preston, United Kingdom

Objectives
Historically patients used to be fasted before surgery to ensure an empty stomach and to prevent gastric aspiration. Recent studies have indicated that oral clear fluid intake up to 2 hours before surgery remains safe while providing significant benefits by reducing anxiety levels and dryness of the mouth. If fluid intake is a safe practice, the incorporation of carbohydrate in pre-operative drinks may alleviate fasting-induced hypoglycaemia which, in turn, may have profound beneficial effects to patients who are commonly malnourished due to the disease and/or treatment. This trial was designed to study the effect of oral carbohydrate on post-operative recovery.

Methods
This project was a double blind randomised controlled trial powered to recruit 110 patients with advanced stage epithelial ovarian cancer undergoing surgery. Following ethical approval and informed consent, patients were randomly allocated into treatment (receiving carbohydrate-enriched drinks) and placebo (receiving flavoured water) groups. The drink was given as 800 mls the night before surgery and 400 mls 2 hours before the induction of anaesthesia. Primary end point of the study was post-operative length of hospital stay as a surrogate marker for post-operative recovery.

Results
Eighty patients were recruited in total. Statistical analysis has shown a significant increase in the length of hospital stay with oral carbohydrate loading when compared to zero carbohydrate flavoured water. The extent of the difference correlates with patient age.

Conclusions
Post-operative length of stay is not decreased by oral carbohydrate loading compared to flavoured water in women undergoing surgery for advanced ovarian cancer.
STUDIES ON COMBINATION OF PHYTOCHEMICALS TO OVERCOME DRUG RESISTANCE IN OVARIAN CANCER

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Background
Traditional chemotherapeutic agents act by killing cells that divide rapidly, one of the main properties of most cancer cells. And developing drug resistance is the major hurdles in cancer chemotherapy in all cancer types include ovarian cancer. One way of overcoming drug resistance is to employ combination of phytochemicals with different mechanism of action.

Aim of the study
To use combination of phytochemicals with different mode of action (Paclitaxel and Colchicine are mitotic inhibitor) with (Curcumin, Epigallocatechin gallate (EGCG) and Resveratrol are antioxidant) using different sequence of administration.

Methods
Three ovarian cancer cell lines, parent (A2780) and resistance lines (A2780CisR⁰ and A2780ZD0473R⁰) are treated with phytochemicals, individual and in binary combination using three sequences of administration. Individual treatment is done to determine the IC₅₀ values (drug concentration required for 50% cell kill) of each compound. Cell viability is quantified using the MTT reduction assay. The analysis of combination results is based on the equation derived by Chou and Talalay (1984), the actual calculations are done using CalcuSyn software.

Results
All of the selected phytochemicals are found to inhibit growth of both parent and resistant ovarian cell lines. And combination of phytochemicals showed sequence-dependent synergism.

Conclusion
Appropriate sequenced combination of phytochemical may provide a means of overcoming drug resistance.
Poster Presentations: Ovarian Cancer

AXILLARY LYMPH NODE METASTASES FROM OVARIAN CANCER: CLINICAL PATTERNS AND REVIEW OF THE LITERATURE
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Objectives
This study shows our experience on axillary metastases from ovarian cancer. We review clinical characteristics of our patients and the impact of this finding on their survival. A review of the literature is accomplished.

Methods
A total of 24 patients were included on the study. 5 patients with history of ovarian cancer and axillary metastases were identified in our database from 2002 to 2012. 19 cases were found on the literature. We reviewed clinical features, imaging studies, time to relapse and treatment of axillary disease. We compared our results with the literature’s series.

Results
56 % and 44 % of patients were staged as III and IV respectively. In 8 cases (33.3%) the axillary tumour was the initial finding. In the cases of axillary recurrence, the median time to relapse since the primary diagnosis was 28.5 months. In 41.6% of cases the diagnosis was suspected by physical examination, followed by mammogram (20.8%), ultrasonography (16.6%), PET-CT (12.5%) and CT (8.3%). The most frequent immunohistochemical pattern showed GCDFP-15 negative, Ca 125 positive, WT-1 positive, CK 20 negative and CK 7 positive. In 15 cases, the local treatment of the axillary disease is reported (7 axillary lymphadenectomies, 6 cases of node resection, 2 cases no local treatment). The median OS after the diagnosis of axillary disease was 21 months.

Conclusions
Even though axillary lymph nodes metastases in ovarian cancer are a very rare event, an accurate diagnosis is required to exclude secondary breast cancer and therefore to allow the adequate treatment.
ROLE OF DIAPHRAGMATIC SURGERY AS PART OF OVARIAN CANCER CYTOREDUCTION

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Objectives
To study the role of diaphragmatic surgery in achieving an optimal cytoreduction in advanced ovarian cancer. We analyse the surgical complications and impact on survival.

Methods
We accomplished a retrospective analysis of 50 patients with stage III/IV ovarian cancer that underwent diaphragmatic surgery during the primary debulking or relapse from 2006 to 2012. Patients were divided depending on the type of procedure: Peritoneal stripping (group 1) and resection (group 2). We reviewed the accuracy of preoperative imaging studies, complications and the impact on the cytoreductive outcome, progression free survival and overall survival.

Results
The patients included in the group 1 were 36 (72%) and the group 2, 14 (28%). FIGO stage was IIIC in 42 (84%) patients and IV in 8 (16%). Preoperatively, a PET-TC diagnosed diaphragmatic disease in the 57%. The suspicious rate was higher within the group of diaphragmatic resection (71.4% vs 42.8%). Optimal debulking (R=0) was achieved in 77.7% of patients on group 1, and in 100% on group 2. Cytoreduction with residual disease £1cm was achieved in the rest of patients of group 1 (22.2%).

Complication rates included, minor-moderate pleural effusion 24%, neumothorax 6%, respiratory distress 8%.

The PFS were 29 months (group 1) and 20 months (group 2). The OS were 70 months (group 1) and 60 months (group 2).

Conclusions
Diaphragmatic surgery improves the rates of optimal debulking in primary and recurrent ovarian cancer patients. PET-TC is helpful in the assessment of diaphragmatic disease.
PLATINUMS IN COMBINATION WITH PHYTOCHEMICALS AIMING TO OVERCOME DRUG RESISTANCE IN OVARIAN CANCER
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Objectives
Phytochemicals having chemopreventive and cytotoxic attributes can be ideal candidates for combination with targeted therapy towards overcoming drug resistance in ovarian cancer. This study aimed to investigate combined drug action from sequenced combinations of platinum drugs and selected phytochemicals.

Methods
Cytotoxicity is determined based on MTT reduction assay. Median effect analysis is done to characterize combined drug action.

Results
Results show that the combinations of platinums and selected phytochemicals produce sequence- and concentration-dependent synergism in the ovarian tumour models.

Conclusions
Combined drug actions from sequenced combinations of platinums and phytochemicals are found to vary from being highly synergistic to antagonistic.
ASSESSMENT OF LYMPHOCYTE POPULATIONS IN OVARIAN CANCER PATIENTS AND HEALTHY INDIVIDUALS AND NATURAL KILLER (NK) CELL RECEPTOR EXPRESSION

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Background
Natural Killer (NK) cells are part of the innate cellular immune defence that work hand in hand with CD8 cytotoxic T lymphocytes in being responsible for killing cells which show up as abnormal via infection by virus or mutation. Ovarian carcinoma is caused by malignant mutation in the ovarian epithelia, and numerous research had been performed on the role of T lymphocytes in this cancer.

Objectives
The project aimed to study the significance different of lymphocyte populations, particularly Natural Killer (NK) cells, involved in the peripheral blood of ovarian cancer patient

Methods
Venus blood was drawn from ovarian cancer patients before chemotherapy. Peripheral Blood Mononuclear Cells (PBMC) were isolated from 8 ovarian cancer patients and 6 age-matched healthy volunteers. Immuno-phenotyping was performed using a commercial kit to quantify the lymphocyte population and RNA isolation performed to examine the expression of KIR genes using reverse transcription polymerase chain reaction.

Results
Immunophenotyping of PBMC was successfully performed on 9 ovarian cancer patients and 6 healthy control. Near significant result was noted in the numbers of peripheral NK cells in ovarian cancer patients as compared to healthy control (p=0.0559). No other significant result were obtained for B lymphocytes, D4 and CD8 lymphocytes. Gene expression of KIR had limited success due to low number of samples

Conclusions
The initial results obtained from this study has been encouraging. The research into the NK cells as the aspect of anti-cancer immunity holds great promise. Further studies with bigger samples size will be performed to assess the significance of our results.
ECONOMIC IMPACT AMONG FAMILY CAREGIVERS OF ADVANCED OVARIAN CANCER PATIENTS

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Objectives
The life of a family changes in many ways when cancer is diagnosed. These changes regard also financial costs. To the authors' knowledge, little work has been done to estimate the costs associated with caregiving for cancer patients. We evaluated for the first time in literature the economic changes among family caregivers of advanced ovarian cancer during the first line treatment, including surgery and 6 chemotherapy cycles.

Methods
Between June 2009 to December 2012, advanced ovarian cancer patients' primary family caregivers were recruited from to the Division of Gynecologic Oncology of the University Campus Bio-Medico of Rome within 4 weeks of the patient's new diagnosis. Caregivers (N=90) reported demographic, medical information and economic cost, such as traveling to and from medical appointments, waiting with patients for appointments, missing work, attending to patients who are hospitalized

Results
Between June 2009 to December 2012, 90 advanced ovarian cancer patients' primary family caregivers were enrolled in the study. The mean age of the study cohort was 52.3 years. They reported a 3% of missing work days. The mean cost for all caregivers was 988.529 € per year. So the mean cost of each caregiver was 10.981 €/ annually.

Conclusions
This economic analysis of caregiving in advanced ovarian cancer patients reports the significant burden that cancer treatment places on both families and society. These findings underscore the importance, when appropriate, of including valid estimates of the cost of informal caregiving when evaluating the cost-effectiveness of cancer treatments.
RETROSPECTIVE STUDY OF GEMCITABINE AND CARBOPLATIN FOR JAPANESE PATIENTS WITH RECURRENT OVARIAN CANCER (KCOG-G1203S TRIAL)


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Objectives
Gemcitabine became available to the patients with recurrent ovarian cancer in Japan from 2010. The purpose of this KCOG-G1203s study is to report on the safety and efficacy of gemcitabine and carboplatin use for Japanese patients with recurrent ovarian cancer.

Methods
This is a multi-institutional study, approved by IRB of each institute. Fifty-nine patients of recurrent ovarian carcinoma received combination chemotherapy with Gemcitabine and Carboplatin from January 2010 to March 2013. The patients' medical records were retrospectively reviewed. Gemcitabine (1000 mg/m2 or 800mg/m2) was given on days 1, 8 and carboplatin AUC4 on day 1 of every 21 days.

Results
The median age was 60 years (range 29-87). The majority of patients (85%) presented with an ECOG PS of 0. The median number of previous chemotherapy regimens was 1 (range 1-6). A total of 309 cycles have been administered, with a median of 6 (range 1-15). At this stage 46 of the 59 patients are evaluable for response. Complete response, partial response, stable disease and progressive disease were observed in 9 patients (20%), 14 (30%), 17 (37%) and 6 patients (13%), respectively. The median progression-free survival time and overall survival time were 238 days (range 14-690 days) and 661 days (range 63-1062 days), respectively. The grade 3/4 toxicity of the regimen was primarily hematological, including thrombocytopenia (64%), leukopenia (58%), and neutropenia (71%).
Conclusions: Gemcitabine and carboplatin used for Japanese patients with recurrent ovarian cancer possesses a modest activity and a well-tolerated toxicity.
EVALUATION OF PLOIDY PARAMETERS IN PATIENTS WITH MALIGNANT EPITHELIAL OVARIAN TUMORS
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Objectives
Evaluate the prognostic importance of different DNA ploidy parameters in patients with malignant epithelial ovarian tumors.

Methods
Our study was carried out on 105 patients. DNA ploidy was measured in cytological materials and histological sections of malignant epithelial ovarian tumors. To identify the prognostic significance of various parameters of DNA ploidy were performed one-dimensional and multi-dimensional statistical analyzes.

Results
According to the one-dimensional statistical analysis the degree of aneuploidy (DA) is important indicator for the general survival rate of patients with malignant epithelial ovarian tumors (p <0.001).

Patients whose degree of aneuploidy measured between 30<60% has approximately 4.5 times higher risk of adverse outcome compared to patients who have adequate degree of aneuploidy DA<30%.

Patients, at which degree of aneuploidy corresponds DA>60 % (Hazard Ratio-19.38, p <0.001, C.I. 4.62-81.24) has approximately 19.38 times higher risk of the worst forecast and shorter survival rate in comparison with patients at which DA<30 %.

Multi-dimensional analysis of various ploidy indicators has shown that patients with more favorable exponents aneuploidy DA<30% and hyperploidy DH<3% has better survival rate than patients at whom degree of aneuploidy corresponds to DA>60 % and degree of hyperploidy corresponds to DH> 3 %.

Analyzing the results of the ploidy balance (PB), shows that patients with a PB<70% has about 5 times greater risk of poor outcome compared with patients in which balance adequate ploidy > 70%.

Conclusions
Evaluation of different ploidy parameters has a prognostic importance. DNA ploidy analysis allows to define malignant potential of tumours and determine prognosis.
A RARE CASE OF ISOLATED SUBCUTANEOUS IMPLANTATION OF A BORDERLINE OVARIAN TUMOR

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Objectives
Laparoscopy-related subcutaneous tumor implantations of gynecological malignancies are considered rare. We report the case of a 46-year-old woman who presented with an isolated metastasis of a borderline ovarian tumor in the abdominal wall.

Methods
The patient presented with an asymptomatic cyst with papillary excrescences in her right ovary, measuring 28 x 25 mm. CA125 was 38.7 U/ml. Patient’s concomitant diseases at time of presentation were obesity, hypothyreosis and arterial hypertension. The patient had a history of previous two laparoscopies (ectopic pregnancy 1990, sterilization 1996) and one vaginal birth.

Results
We conducted laparoscopic right adnexectomy; histopathological workup of the right ovary revealed mucinous papillary borderline tumor. Consequently, nine days later the patient underwent explorative median laparotomy with hysterectomy, left adnexectomy, omentectomy and appendectomy. No intraperitoneal implants were found. Further exploration revealed a cystic-solid structure (5 x 5 cm) in the subcutaneous fat tissue above the fascia with no contact to intraperitoneal cavity. The structure was resected; histopathological examination confirmed the diagnosis of a non-invasive implant of a papillary borderline tumor.

Conclusions
Possibly, tumor cells were displaced during previous laparoscopies (the last one fourteen years prior to presentation).
ACCURACY OF PET-CT FOR EXTRA-ABDOMINAL DISEASE AND-OR INTRA-PARENCHYMAL M ETHASTASIS (STAGE IV) IN ADVANCED OVARIAN CANCER. PILOT STUDY

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Objectives
To evaluate the accuracy of PET/CT with FDG for the diagnosis of extra-abdominal disease and/or parenchymal metastases (Stage IV) in patients with initial diagnosis of suspected ovarian cancer FIGO ≥ IIIC.

Methods
- We included 20 patients with thoracic/abdominal CT diagnosis of ovarian carcinoma ≥ FIGO IIIC stage.
- All of them with pathological study of high-grade ovarian epithelial carcinoma (excludes: low-grade serous and mucinous carcinoma)
- Whole body FDG PET-CT was performed to all patients, and it describes the location of metastases and SUV max.
- We compared the accuracy of PET-Scan vs CT Scan, to diagnose extraperitoneal disease and/or intraperitoneal metastases.

Results
PET/CT detected metastases in 9/20 patients (45%). The detection for the CT Scan was 5/20 (20%). The percentage of diagnostic PET/CT was 25% more than the CT.
The most frequent location was the extra-abdominal supra-diafragmatic lymph node (77%). Other locations were pleural metastases, Intra-hepatic and bone.

Conclusions
Whole body PET/CT with FDG has greater accuracy for the diagnosis of extra-abdominal disease or intra-parenchymal metastases (FIGO IV) of high-grade ovarian epithelial carcinoma, than CT Scan, especially for the detection of supra-diafragmatic lymph nodes.
In these cases, PET CT may help to define the most appropriate therapeutic strategy.
Poster Presentations: Ovarian Cancer

UPFRONT, INTERVAL AND SECONDARY CYTOREDUCTIVE PROCEDURES ARE OF EQUAL COMPLEXITY AND THEREFORE DEMAND THE SAME DEGREE OF SURGICAL EXPERTISE

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Objectives
Cytoreduction represents a cornerstone in ovarian cancer management. An argument to choose interval debulking (ie, after neoadjuvant chemotherapy) over upfront surgery in this setting is that the former procedure would be less extensive and therefore of decreased morbidity while dealing with reduced tumor burden. The aim of this study was to compare the extent and complexity of upfront, interval and secondary cytoreductions in patients with advanced ovarian cancer.

Methods
We reviewed the charts of women with advanced ovarian cancer treated in our center between December 2011 and April 2013. After allocation based on the type of surgery (ie, upfront, interval or secondary), we estimated both the rate of optimal debulking (ie, < 1 cm in maximum residual tumor diameter) as well as the surgical complexity utilizing the surgical complexity score (SCS) (Aletti GD, Gynecol Oncol 2007). Statistical comparisons were made using SPSS 19.0.

Results
Twenty-eight cytoreductions were attempted during the study period: 12 upfront, 12 interval and 4 secondary. Seventy-seven percent of patients in the upfront group were left optimal compared to 92% and 100% of those undergoing interval and secondary approaches. The median SCS was 9, 6 and 6 for each group respectively; this difference did not reach statistical significance (p 0.095). All upfront and secondary surgeries as well as 72% of interval debulkings required a non-standard gynecologic procedure, such us upper abdominal surgery and/or bowel resection(s).

Conclusions
Cytoreductive surgery demands a high surgical expertise extending beyond the classic gynecologic scope, regardless the timing of this procedure.
ACCURACY OF FROZEN SECTION DIAGNOSIS IN THE EVALUATION OF ADNEXAL MASS: RETROSPECTIVE EVALUATION OF 745 CASES WITH MULTIVARIATE REGRESSION ANALYSIS

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Objectives
To evaluate the accuracy of frozen section (FS) in evaluation of adnexal mass and to define clinicopathological factors associated with misdiagnosis.

Methods
The clinicopathological data of 1199 patients who underwent laparotomy for adnexal mass between 2007 and 2012 were reviewed. Results of FS and permanent pathology (PP) reports were compared with univariate and multivariate analysis.

Results
745 valid reports were evaluated. Of these; 507 (68.1%) had benign, 44 (5.9%) had borderline, 194 (26.0%) had malignant histological diagnosis at permanent section. In 717 of 745 (96.2%) patients, FS analysis agreed with PP. 28 of 745 cases (3.8%) were diagnosed incorrectly by FS. Univariate analysis showed that borderline histology (p<0.0001) and tumor size larger than 10 cm (p= 0.005) were associated with misdiagnosis of ovarian tumors by FS. Based on multivariate analysis, borderline histology (OR:14.4, p<0.0001) and tumor size larger than 10 cm (OR:2.3,
p=0.049) were the independent predictors for misdiagnosis by FS.

Table 1. Comparison of FS with PP.

<table>
<thead>
<tr>
<th>Frozen section diagnosis</th>
<th>Permanent section</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benign</td>
</tr>
<tr>
<td>Benign</td>
<td>499</td>
</tr>
<tr>
<td>Borderline</td>
<td>5</td>
</tr>
<tr>
<td>Malignant</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>507</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>98.4(499/507)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>94.5(225/238)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>97.4(499/512)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>96.6(225/233)</td>
</tr>
</tbody>
</table>

Conclusions

Frozen section evaluation of the adnexal masses provides a high accuracy. However, tumor size greater than 10 cm and borderline histology are the independent factors that adversely influence the accuracy of frozen section diagnosis. Clinicians must be aware of these pitfalls when they have to make an intraoperative surgical decision.
Poster Presentations: Ovarian Cancer

EXPECTATION OF FRENCH PATIENTS FROM INFORMATION AND THERAPY MANAGEMENT OF OVARIAN CANCER (OC): RESULTS FROM THE NOGGO-ENGOT SURVEY EXPRESSION III


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Objectives
This survey was designed to evaluate the information, needs and expectations of patients (pts) with primary or relapsed OC in different European countries. This abstract focuses on specific results from French OC pts.

Methods
257 pts filled in a 27-item questionnaire during a medical visit.

Results
Median age was 63 years (26-89). Nearly all the pts (94%) had primary surgery and adjuvant chemotherapy (95%). 50% had recurrent disease and 32% had participated in a clinical trial. At the time of the survey, 85% reported symptoms (fatigue 88%, neuropathy 55%, nausea/vomiting 40%, pain 39%). If information about chemotherapy was considered adequate for 88% of the pts, a majority of them ignored their initial disease stage (60%) and how to find more information for treatment choice (91%). Most pts (92%) preferred to get information directly from their physician. Only 7% had a contact with a self help group but 20% were interested in having such a contact. 66% express the need for more detailed information on their disease and treatments and 31% for a follow-up booklet with treatment information and detailed agenda. However, 21% of pts did not want to get negative information on their prognosis and 58% expected that treatment would cure their cancer. Having a short-time treatment with no alopecia and less fatigue was the main patients’ proposition to improve OC therapy.

Conclusions
French OC pts need for more contact with self help group and more information on their disease and its management. Direct information from their physician remains the mainstay of communication.
WHAT ARE THE REASONS FOR TUMOR RESIDUAL [TR] AFTER PROCEDURE FOR ADVANCED EPITHELIAL OVARIAN CANCER [EOC] FIGO IIIB-IV AT A SPECIALIZED CENTER?


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Objectives
Postoperative tumor residual [TR] is, aside from tumor stage, the strongest prognostic factor of EOC. Complete surgical cytoreduction (TR = 0cm) is not always feasible and depends upon surgeon’s skill, tumor and patient characteristics. We evaluate reasons for TR > 0cm at a specialized center.

Methods
Exploratory analysis of patients with advanced EOC and surgical cytoreduction obtained from a prospective registry from 2003-2012 with a median follow-up of 31 months.

Results
538 patients, median age 60 years (19-88y), FIGO IIB 7%, FIGO IIIC 60%, FIGO IV 33%. We achieved TR = 0cm in 365 patients (68%), TR = 0.1-1cm in 130 patients (24%), TR > 1cm in 43 patients (8%).

Reasons for TR > 0cm: poor performance status in 18 patients (10.4%), cardiopulmonary morbidity in 4 patients (2.3%), unfavorable tumor locations in 151 patients (87.3%) involving small bowel (mesentery/serosa): 128 patients (84.8%), portal vein, ligamentum hepato-duodenale: 17 patients (11.3%), disseminated hepatic metastases: 8 patients (5.3%), pancreas, coeliac trunc: 9 patients (6%), stomach: 7 patients (4.6%), and supradiaphragmatic tumor location: 5 patients (3.3%).

Median overall survival TR = 0cm: 52 months (95%CI: 45-58), TR > 0cm: 25 months (95%CI: 19-32); p = 0.001.

Conclusions
Over two-thirds of the patients with advanced EOC achieved a complete surgical cytoreduction with treatment at a specialized center. While we could not increase the rate of complete tumor resection above 70 +/- 4% per year, by optimizing interdisciplinary collaboration and continual quality control we kept the rate of patients with TR > 1cm below 10% for 9 of 10 years.
Objective of the study was to report feasibility and efficacy of Gemcitabine in third or higher line for recurrent ovarian cancer (OC).

Methods
From July 2005 to April 2013, 63 patients (pts) were treated with Gemcitabine as 1-hour infusion at the dose of 1000 mg/m2 on days 1 and 8 of a 21-day cycle. Toxicity profile was assessed according to NCI CTC and response was measured while met RECIST v.1.1. and CA-125 criteria described by Rustin et al. The patients' medical records were retrospectively reviewed.

Results
Patients were platinum-sensitive in 65,1% (41/63), platinum-resistant in 34,9% (22/63). 56 pts were monitored by RECIST criteria: 9/56 (16,1%) - PR, 23/56 (41,1%) - SD, 24/56 (42,9%) - PD. The biochemical response rate in 46 pts according to CA 125 levels was 30,4% (14/46) with 75% response and 19,6% (9/46) with 50%. There were not any statistically significant differences in response to gemcitabine among pts in relation to the higher number of chemotherapy line (third or more) and in relation to platinum sensitivity. In multivariate analysis primary suboptimal debulking and worse performance status (HR=2.25, 95% CI: 1.03-4.94, p=0.0424; HR=3.77, 95% CI: 1.31-10.82, p=0.0137, respectively) were independent adverse prognostic factors. We did not observe differences in toxicity after gemcitabine treatment among patients in relation to number the line of previous chemotherapy (3 vs. > 3).

Conclusions
Gemcitabine used for recurrent OC is tolerable and effective both in third and higher line and could offer a control of OC, despite previous treatment.
Poster Presentations: Ovarian Cancer

OVARIAN CANCER SYMPTOMS IN 12 MONTHS PRECEDING DIAGNOSIS: MITO-12/ENGOT OV-12 OVARIAN CANCER SYMPTOM SURVEY

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Objectives
Early diagnosis of ovarian cancer (OC) remains difficult, with no reliable screening and vague pre-diagnostic symptoms. An intergroup (MITO, MaNGO, NOGGO, BGOG, GiNECO) study was undertaken to describe patient symptoms and sentinel events along pathway to OC diagnosis. First objective was to describe the frequency and duration of symptoms within 12 months previous to OC diagnosis.

Methods
Patients with OC eligible for first-line chemotherapy were recruited to MITO7 (NCT00660842) and MITO12 (NCT01061619) studies (Nov 2008 - Apr 2013), in Italy, Germany, Belgium, France. Consenting patients completed Goff Ovarian Cancer Symptom survey, self-report instrument describing severity, frequency, duration of 23 symptoms within 8 categories (Table 1).

Results
633 patients completed surveys, median age 60 (21-87). 85% patients were stage III (420, 66%) or IV (115, 18%). At least one symptom was reported by 545 (86%) patients (Table 1). Most frequent categories were 'pain' (67%), 'abdomen' (67%) and 'eating' (57%). Most common individual symptoms were abdominal bloating (58%), pelvic pain (50%), increased abdominal girth (48%), fatigue (48%). Recruitment is ongoing through June 2013.

<table>
<thead>
<tr>
<th>Symptom category</th>
<th>N. pts (%)</th>
</tr>
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<tbody>
<tr>
<td>Pain</td>
<td>425 (67%)</td>
</tr>
<tr>
<td>Eating</td>
<td>360 (57%)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>424 (67%)</td>
</tr>
<tr>
<td>Bladder</td>
<td>213 (34%)</td>
</tr>
<tr>
<td>Bowels</td>
<td>284 (45%)</td>
</tr>
</tbody>
</table>
Conclusions
These preliminary data regarding symptoms in the 12 months prior to OC diagnosis are consistent with results of previous extra-European studies. Analyses regarding symptom severity, occurrence, duration, and geographical differences will allow further description.
Poster Presentations: Ovarian Cancer

TRABECTEDIN ALLOWS RETREATMENT WITH PLATINUM-BASED CHEMOTHERAPY IN PATIENTS WITH PLATINUM-RESISTANT/REFRACTORY (PRR) AND PARTIALLY PLATINUM-SENSITIVE (PPS) RECURRENT OVARIAN CANCER (ROC)


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Objectives
Dose-dense therapy and administration of sequential non-platinum agents in PRR ROC may play a role in reverting platinum-resistance improving the prognosis of such patients. Prolonging the platinum free-interval (PFI) is a mainstream strategy to improve survival in patients with PPS ROC. Trabectedin is a minor groove DNA-binder, which may play a role in reverting platinum resistance in patients with PRR and PPS ROC.

Methods
From 2003-2013, we retrospectively analyzed 27 patients (24 PRR and 3 PPS) treated with trabectedin 1.1-1.5 mg/m², given as a 3-h infusion every 3 weeks with antiemetic and steroid premedication. Tumor response was assessed every 12 weeks.

Results
The patients had a median age of 63 years (range: 45-81) and received a median of 5 prior chemotherapy lines (range: 1-9). A median of 4.9 trabectedin cycles (range: 1-14) was administered. The ORR was 15%, with a median duration of response of 16.5 weeks (range: 5.86-44.43), and 41% of patients achieved stable disease (SD). After progression with trabectedin, 13 patients were retreated with platinum and yield an ORR of 54% and SD in 8% of patients (clinical benefit: 61%). The median PFS after platinum rechallenge was 33 weeks (range: 17-43), and the median post-trabectedin PFI was 10 weeks (range: 3-25).

Conclusions
Sequential treatment with non-platinum/non-taxane drug trabectedin as single agent before subsequent platinum rechallenge may contribute to prolong PFI and to re-sensitize the patients with PRR and PPS ROC. Further prospective studies are necessary to determine the contribution of sequential treatments with trabectedin in these patients.
ANALYSIS OF SYMPTOMS FOR THE PREOPERATIVE PREDICTION OF MALIGNANCY OF OVARIAN MASSES IN BRAZILIAN WOMEN.

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Objectives
To evaluate whether the prevalence of specific self-reported symptoms can be used for the preoperative differentiation of ovarian malignant tumors.

Methods
For this cross sectional study, 178 women with ovarian tumor (61 with malignant tumors and 117 with benign tumors) and 150 healthy women were included. The questionnaire (Goff et al., 2007) was translated and retro-translated to Portuguese language. Women with adnexal masses were surveyed prior to surgery, before they knew their histological diagnosis. We considered a symptom positive if it occurred more than 12 times per month and for less than one year (Andersen et al., 2010). We calculated the proportion of women with each of the 22 specific symptoms in the groups of women with ovarian malignant tumors, benign tumors and healthy women. The symptoms were further subjected to the Ward’s Hierarchical Clustering Method.

Results
The proportion of women with symptoms decreased significantly from women with malignant tumors to those with benign tumors and healthy women (p<0.01). The clusters abdomen (abdominal bloating and/or increased abdominal size); pain (pelvic and/or abdominal pain) and eating (unable to eat normally and/or feeling full quickly) were the most sensitive and with best predictive positive value and were therefore chosen to be used in the symptom index (SI) calculation. The sensitivity of the SI in discriminating women with malignant from those with benign ovarian tumors was 78.3%, with a specificity of 60.3%.

Conclusions
Specific symptoms may be used to select women with ovarian malignancy among those with adnexal masses. Grant Fapesp 2012/15059-8.
ACCURACY OF FROZEN SECTION BIOPSY OF ADENEXAL MASSES

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Objectives
Evaluate the accuracy of intraoperative frozen section (FS) of adnexal masses.

Methods
151 women with an adnexal mass were included. FS biopsy was performed in 76 women. The result was compared to paraffin biopsy in different age strata. Statistical analysis: weighted Kappa statistics was used to compare FS and paraffin results.

Results
Results: 60 women were aged ≥ 40 years and 16 <40 years. Of 23 cases considered malignant in FSs, 21 were confirmed in paraffin, one was non-neoplastic and one was benign. Four tumors rendered as borderline in FS, all were confirmed in paraffin. Of the 37 considered benign in FS, 36 were confirmed as benign in paraffin and one was rendered as non-neoplastic. Of the 12 tumors initially evaluated as non-neoplastic, 8 were confirmed and 4 were benign. In young women, of 5 cases considered malignant in FS, 4 were confirmed and one was benign. In one case considered benign with FS, paraffin revealed malignancy. In patients ≥40 years, 1 case rendered as benign in FS was later considered malignant in paraffin. In women ≥40 years, epithelial cases prevailed in paraffin (72/110 cases), whereas in women <40 years, 54% were germ cell tumors (22/41 cases).

Conclusions
Conclusions: The overall accuracy of FS was 90.79% (93.75% in women <40 years and 90% in women ≥40 years). Since imaging tests cannot be used alone to guide surgical procedure, this study corroborates the concept that FS has sufficient accuracy to determine intraoperative conduct in relation to malignancy, even in young women.
OVARIAN GRANULOSA CELLS TUMORS. RETROSPECTIVE ANALYSIS OF 34 CASES IN ONE CENTRE

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Objectives
Granulosa cells tumors of the ovary (TCG) are a type of infrequent neoplasias which represent less than 5% of ovarian tumors. The aim was to analyze the diagnosed TCG cases, their treatment, predictive factors and their evolution.

Methods
A retrospective study was done in 34 patients with a TCG diagnosis in one institution between January 1990-January 2013. The tumor staging, residual disease, age, size, surgery type and histology have been described as predictive factors.

Results
The average age was 48 years old (range: 14-77). The mean follow-up was 82.3 months (2-231). 82.3% were diagnosed in early stage (I-II) and 14.7% in late-stage (III). Surgical treatment had been made in all the cases with fertility-sparing staging in 10 patients. 20.6% had needed a adyuvant chemotherapy. According to histology 28/34 was TCG adult-type and 6/34 young-type. 5 patients reported a recidive (14.7%) with a mean disease-free interval of 45.4 months (10-122). The mean overall survival was 82 months (2-231). There were 3 death (8.8%). Applying a univariate analysis we found three significant factors for overall survival: stage (p=0.004), recurrence (p=0.004) and adyuvant chemotherapy (p=0.007). However, in a multivariate analysis, could not find significant difference.

Conclusions
TCG are unusual tumors with a long natural development. This analysis shows that stage, presence of recurrence and adyuvant chemotherapy are significant prognostic factors for overall survival in our serial.
INTRATUMORAL LYMPHOVASCULAR DENSITY IN MUCINOUS OVARIAN CARCINOMAS: LOWER VALUES IN METASTATIC TUMORS

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Objectives
Ovarian mucinous metastases commonly present as the first sign of the disease. They are capable of simulating primary tumors, leading even experienced pathologists to diagnose incorrectly a secondary deposit as a primary neoplasm. Our aim was to investigate the role of the intratumoral lymphatic vascular density (LVD) in the differential diagnosis of primary or secondary mucinous ovarian tumors.

Methods
A total of 124 cases of mucinous tumors in ovary, 63 of them known as primary and 61 metastatic, presenting borderline and malignant histology were selected and reviewed. The two groups were compared according age of patients, gross and microscopic features, and immunohistochemistry profile. The intratumoral LVD was quantified by counting the number of vessels stained by the D2-40 antibody.

Results
In the univariate analysis, metastatic tumors occurred in older patients and showed higher proportion of tumors below 10.0 cm, bilaterality, extensive tumoral necrosis, extraovarian extension, and immunoreexpression of CK20, CDX2, CA19.9 and MUC2. They presented lower expression of CK7, CA125 and MUC5AC. DVL was higher among primary tumors (58% vs. 37.7%). After multivariate analysis, the best predictors of a secondary tumor were size 10.0 cm or less, bilaterality and CK7 negativity. Negative MUC2 was an important factor favor primary tumor. This model allows classifying correctly 90.0% of all cases, including 92.2% of primary tumors and 86.2% of metastases.

Conclusions
Although we observed higher intratumoral LVD in primary tumors when compared with the secondary lesions, it was not strong enough to help in the distinction between these tumors.
Poster Presentations: Ovarian Cancer

INTRAVENOUS AND ORAL TREOSULFAN IN THE ROUTINE TREATMENT OF OVARIAN CANCER: RESULTS OF A GERMAN NON-INTERVENTIONAL STUDY


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Objectives
Data about routine systemic treatment of patients with ovarian cancer are still limited. The alkylating agent treosulfan is approved as oral (p.o.) and intravenous (i.v.) form for ovarian carcinoma. This NIS analyzed the clinical practice of the use of treosulfan in Germany evaluating mode of application, toxicity, response and survival.

Methods
Ovarian cancer patients who received treosulfan either i.v. (5000 - 7000 mg/m² d1, q21 to 28d) or p.o. (400 - 800 mg/m² d1-14 or 21, q28d) for ≥ 1 cycle were included into the study.

Results
248 patients with median age 70 years (range 36-92) were recruited into the study (47% ≥ 70 and 45% <70 years), receiving at least one therapy cycle. Most patients presented serous histology (131, 52.8%) with advanced stage disease FIGO III (122, 49%) or IV (55, 22%). Median ECOG was 1 (n=0-2), cardiac co-morbidity was common (31%) and treosulfan was administered commonly in the second (26%), third (21%) or fourth line (17%). 155 patients received i.v. and 93 p.o. treatment, whereas dose modifications resulted mostly due to hematological toxicity (46%). Main reason for therapy discontinuation was progressive disease (38.5%). Response was observed in 25.8%, disease stabilization in 28.6 % and progress in 45.6%. Median progression-free survival was 201 days. A subgroup analysis of patients < and ≥ 70y will be presented at the meeting.

Conclusions
Treosulfan presented in predominantly elderly and heavily pre-treated patients with ovarian cancer a clinical relevant efficacy and well-manageable mostly haematological toxicity, which resulted in a positive therapeutic index.
Poster Presentations: Ovarian Cancer

SURVIVAL AND REPRODUCTIVE OUTCOMES AFTER FERTILITY-SPARING MANAGEMENT FOR MALIGNANT OVARIAN GERM CELL TUMOR

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Objectives
To analyze survival and reproductive outcomes including menstrual function of patients who were treated with fertility-sparing surgery followed by adjuvant chemotherapy for malignant ovarian germ cell tumors (MOGCTs).

Methods
We performed a retrospective review of patients who were treated for MOGCTs between 1990 and 2011 at Asan Medical Center (AMC, Seoul, Korea). Patients who underwent fertility-sparing surgery were included. Demographic and clinicopathologic data were gathered from patients' medical records and a telephone questionnaire was performed to gather data regarding reproductive and menstrual function.

Results
Fertility-sparing surgery was performed in 132 of 158 patients with MOGCTs. The mean age at the time of diagnosis was 23 years (range, 6-45 years). Histologic subtypes were as follows: immature teratoma (32.5%), dysgerminoma (31%), yolk sac tumor (12.8%), choriocarcinoma (2%), and mixed germ cell tumor (20.4%). Ninety-nine patients (75%) received adjuvant chemotherapy with 96 patients (97%) receiving bleomycin, etoposide and platinum (cisplatin or carboplatin). Seven patients had recurrence and two of them died of disease after median follow-up time of 64 months. The 5-year overall survival was 95%. Sixty-eight were contacted and 52 of them received adjuvant chemotherapy. Fifty-four patients (79.4%) had normal menstrual cycles, seven (10%) had irregular menstrual cycles, four (5.9%) were premenarchal, and three (4.7%) were menopaused. Twelve (55%) of 22 patients who tried pregnancy had successful spontaneous pregnancies, resulting 16 live births.

Conclusions
Fertility-sparing surgery followed by adjuvant chemotherapy was safe and effective, and reproductive outcomes including menstrual function was very promising.
Poster Presentations: Ovarian Cancer

HYPERTHERMIC INTRA PERITONEAL CHEMOTHERAPY FOR THE TREATMENT OF THE FIRST RELAPSE OF EPITHELIAL OVARIAN CANCER: A MULTI INSTITUTIONAL SERIES OF 314 PATIENTS

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Background
Patients treated for an Advanced epithelial ovarian cancer (EOC) will experience frequently a peritoneal relapse within a period of 2 years. Hyperthermic Intra Peritoneal Chemotherapy (HIPEC) is an heavy option for the treatment of this peritoneal failure of conventionnal strategies.

Methods
A retrospective multi institutional cohort of patients treated for an EOC with HIPEC was performed from 13 French centers. We focused on patients treated for the first relapse treated with secondary cytoreductive surgery SCS and HIPEC. The extent of carcinomatosis was assessed with the Peritoneal Cancer Index (PCI) and the resection with the CC-score (CC-S). Baseline risk factors were assessed using univariate and multivariate Cox proportional hazards model.

Results
314 patients were included, among which 166 (53%) were chemoresistant (relapse <6 months after the end of initial treatment) and 148 (47%) chemosensitive. All patients received a previous secondline systemic chemotherapy before SCS and HIPEC.

The median PCI was 7. A complete SCS (CC-0) was obtained in 248 patients (79 %). Mortality rate was 1% and severe morbidity rate, 31%.

The median overall survival was 47 months with no difference between chemosensitive or chemoresistant group. Prognostic factors for OS were the PCI and the CCS.

Conclusions
Heavy therapy combining optimal cytoreductive surgery and HIPEC is feasible and may achieve long-term survival in highly selected patients with a first recurrence of ovarian carcinoma. We did not found any survival difference between the chemosensitive and the chemoresistant populations.
IMMUNOLOGICAL RESPONSE AFTER WT1 MRNA-LOADED DENDRITIC CELL IMMUNOTHERAPY IN OVARIAN CARCINOMA AND CARCINOSARCOMA

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Objectives
Ovarian cancer remains an important cause of death, making the search for new therapies mandatory. Dendritic cell (DC) based immunotherapy is relatively new in ovarian cancer.

Methods
Two women with respectively progressive ovarian carcinosarcoma (OCS) and serous epithelial ovarian cancer (EOC), received 4 weekly vaccines of WT1 mRNA-loaded DCs. During their disease course, both had relapsed at least twice. Immunotherapy outcome focused mainly on immunological response.

Results
The technique was feasible with no toxicity signs. In an ex vivo stimulation assay, both patients showed an increase in CD137+ T cells and IL-10 after three vaccinations. Moreover, the patient with OCS showed an increase in IL-2 in the supernatant, the EOC patient showed increase in IFN-γ, TNF-α and NK cells. There was no increase in WT1 specific T cells. Unfortunately, the patients showed progression after four vaccines. They continued with conventional therapies. The OCS and EOC patient had a remarkably long survival of respectively 19 and 12 months after immunotherapy stop, leading to an overall survival of respectively 70 and 64 months.

Conclusions
We report the first two cases of ovarian cancer treated with WT1 mRNA-loaded DC immunotherapy. The technique was safe and led to an immunological response.
Poster Presentations: Ovarian Cancer

METRONOMIC ORAL CYCLOPHOSPHAMIDE IN THE SALVAGE TREATMENT OF HEAVILY TREATED OVARIAN CANCER PATIENTS: A RETROSPECTIVE, MULTICENTER STUDY
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Objectives
The aim of this multicenter, retrospective study was to evaluate the efficacy of metronomic oral Cyclophosphamide (Endoxan®, Baxter, Italy) (CTX) in very heavily treated relapsed ovarian cancer (ROC) patients.

Methods
Response to treatment was classified according to RECIST criteria. Progression-free (PFS), and overall survival (OS) were also assessed.

Results
47 patients were analyzed: 29 (61.7%) were platinum sensitive, and 18 (38.3%) platinum refractory/resistant. Median age was 72 years (range: 40-80); median number of previous regimens was 4 (range: 1-9). In the whole population, overall response rate (ORR) was 23.4%; stable disease (SD) was observed in 11 patients (23.4%), for a rate of clinical benefit of 46.8%. In platinum refractory/resistant disease, ORR was 12.9%. Overall, median PFS and OS were 5, and 11 months, respectively. The median number of cycles administered was 5 (range: 2-35). There was 1 case experiencing Grade 3 asthenia and Grade 2 nausea/vomiting; only 1 patient was shown not to tolerate oral administration of the drug due to gastritis, and was triaged to intravenous CTX route. No case of hematological toxicity was documented.

Conclusions
Metronomic oral CTX, retains its efficacy in terms of ORR and long lasting clinical benefit in heavily treated ROC patients, with negligible toxicity.
Poster Presentations: Ovarian Cancer

HUMAN OMENTAL-DERIVED ADIPOSE STEM CELLS: MODULATOR OF OVARIAN CANCER PROLIFERATION, MIGRATION AND CHEMORESISTANCE
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Objectives
Adipose tissue contains a population of multipotent mesenchymal stromal cells (ASC) which exhibit tumor tropism, similar to bone marrow derived mesenchymal stem cells (MSC). Excess visceral adipose tissue increases the risk of ovarian cancer and the omentum is a prominent site for ovarian cancer metastasis. We hypothesize that the omentum serves as a source of ASC which promote ovarian cancer progression.

Methods
ASC were isolated from the omentum (O-ASC) of three patients with ovarian cancer. Gene expression array profiling was performed using Nimblegen arrays. The impact of stromal cells on proliferation and chemoprotection and radioprotection of ovarian cancer cells was tested with co-culture assays. Transwell migration assays were performed with conditioned media from O-ASC and control cell lines. O-ASC engraftment was tracked by injecting GFP labeled O-ASC into nude mice bearing SKOV3 xenografts.

Results
Human O-ASC were detected engrafted within the stroma of human ovarian cancer xenografts. O-ASC significantly promoted in-vitro proliferation and migration of ovarian cancer cell lines: OVCA 429, OVCA 433, A2780, SKOV3. Co-culture of ovarian cancer cells with O-ASC increased resistance to chemotherapeutic drugs and radiation. Microarray data showed that O-ASC4 and O-ASC5 are similar in gene expression profiles in contrast to O-ASC5 grouped with BM-MSC and sq-ASC in hierarchical clustering.

Conclusions
Adipose stem cells derived from human omentum promote proliferation, migration, chemo and radio-resistance of ovarian cancers. Clinical isolates demonstrate heterogenous effects in-vitro. Future studies will determine if tumor promoting effects of O-ASC can be predicted on the basis of clinical or disease related characteristics.

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A PHASE 1 STUDY OF ORAL OR INTRAVENOUS RUCAPARIB IN COMBINATION WITH PLATINUM-CONTAINING CHEMOTHERAPEUTIC REGIMENS: ANALYSIS OF PATIENTS WITH OVARIAN OR PERITONEAL TUMORS

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Objectives
Poly (ADP-ribose) polymerase (PARP) inhibition may increase efficacy of DNA-damaging agents. Rucaparib is a potent and selective PARP 1/2 inhibitor being developed for treatment of platinum-sensitive ovarian cancer (OC). This study evaluated the tolerability of oral or intravenous (iv) rucaparib, combined with carboplatin, carboplatin/paclitaxel or cisplatin/pemetrexed, in a 3+3 ascending dose design. Results in the ovarian/primary peritoneal cancer subgroup are presented here.

Methods
Patients aged ≥18 with advanced solid tumors, ECOG 0 or 1, were included. Measurable disease was not required. Chemotherapy was given D1 and rucaparib on D1-3 (iv) or D1-14 (oral) every 21 days.

Results
So far in dose finding cohorts, 14 pts (median age 62 yrs [range 38 – 73]; 6 ECOG PS=0) with ovarian/primary peritoneal cancer have been enrolled, 7 on the oral rucaparib/carboplatin arm, 4 on the iv rucaparib/carboplatin/paclitaxel arm and 3 on the iv rucaparib/cisplatin/pemetrexed arm. Two patients experienced grade 3/4 dose-limiting toxicity (neutropenia and thrombocytopenia) at AUC5 carboplatin/360 mg oral rucaparib. Evaluation of AUC5 carboplatin/240 mg oral rucaparib is being completed. Adverse events related to study drugs in ≥5 pts, all grades, include nausea (n=10), fatigue (n=6), neutropenia (n=6), constipation (n=5), diarrhea (n=5). So far, two pts (OC, BRCAwt, carboplatin/oral rucaparib; OC BRCA1mut, cisplatin/pemetrexed/iv rucaparib) had partial responses. Seven additional pts had stable disease >12 wks. Overall disease control rate (CR+PR+SD>12 wks) in evaluable patients across all dose levels and regimens was 75%.
Conclusions
Rucaparib combined with platinum-based regimens exhibits clinical activity. Further studies in platinum-sensitive and homologous recombination repair deficient populations are warranted.
Poster Presentations: Ovarian Cancer

LAPAROSCOPIC SURGICAL STAGING OF OVARIAN TUMORS
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Objectives
To evaluate the feasibility of laparoscopy for the management of early-stage ovarian tumors.

Background: The classical surgical treatment in patients with ovarian cancer is laparotomy. However, with the expansion of endoscopic techniques, in early ovarian tumors, an alternative could be a laparoscopic approach. There are a lot of advantages such as a less traumatic technique, reduced morbidity, a shorter period of recovery and hospitalization.

Methods
The study included 33 patients, who had been diagnosed with ovarian tumors and underwent laparoscopic surgery. In some cases, it was their first surgery (36.4%), in others, restaging (63.6%). Medical records from January 2009 to December 2012 were reviewed. Descriptive and comparative analysis with T-Student, chi-squared test, and Kaplan-Meier were used.

Results
81.8% of patients were at stage I; 3% stage II and 15.2% stage III. According to histology: 42.4% invasive epithelial tumors; 51.5% borderline and 6% nonepithelial tumors. The patients’ median age was 44.5 years (25-71); 75.8% were menopausal; the median BMI was 25.56 (19-38), and 57.6% had undergone previous laparotomy. 5 patients underwent fertility-sparing versus 28 radical operation. As mean surgical outcomes: operative time 230,91 minutes; 180,65 ml blood loss and 9,1% postoperative complications. One case was converted to laparotomy. The mean follow-up period was 21,45 (3-45). Overall survival at 1 year was 92%.

Conclusions
Laparoscopic staging in ovarian tumors is feasible in selected patients in our experience, although it should be performed by experienced departments of gynecological oncology.
Poster Presentations: Ovarian Cancer

PREDICTION OF COMPLETE CYTOREDUCTION IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER: FDG-PET/CT AND STAGING-LAPAROSCOPY VS. AGO-SCORE.

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Objectives

to investigate the best diagnostic and staging strategy for recurrent ovarian cancer.

Methods

The negative predictive value, specificity, positive predictive value, sensitivity, and accuracy rates of the fluorine-18-fluorodeoxyglucose positive emission tomography computed tomography (FDG-PET/CT), staging laparoscopy, AGO-score evaluation in identifying surgically treatable/untreatable patients are assessed in a consecutive series of 155 recurrent ovarian cancer cases. Moreover, the diagnostic performance of each staging procedure in the evaluation of the number of nodules is analyzed.

Results

The negative predictive value of the laparoscopy staging was 98.0%, specificity 84.0%, positive predictive value 88.0%, sensitivity 98.0%, and accuracy rate 92.0%. Negative predictive value, specificity, positive predictive value, sensitivity, and accuracy rate of AGO-score evaluation were 84.0, 60.0, 66.0, 94.0 and 69.0%, respectively. Combined radiological and laparoscopic evaluation showed a negative predictive value of 91.0%, a specificity of 88.0%, a positive predictive value of 91.0%, a sensitivity of 94.0%, and an accuracy rate of 92.0%.

Conclusions

The combination of FDG-PET/CT and staging laparoscopy has a significant effect on the multimodal approach to the population of patients with recurrent ovarian cancer, while AGO-score evaluation alone, does not have a role for identifying surgically treatable/untreatable patients. FDG-PET/CT and staging laparoscopy should be considered complementary, because of the potential of each one to identify a different setting of the disease.
Poster Presentations: Ovarian Cancer

GLUTAMINE AND CYSTEINE CONTRIBUTE FOR OVARIAN CLEAR CELL CARCINOMA SURVIVAL (OCCC), THROUGH MTOR ACTIVATION AND GLUTATHIONE SYNTHESIS

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Objectives
Clear cell carcinoma (OCCC) is a rare type of ovarian cancer, is highly chemoresistant and has a very poor prognosis. Unique histology due to lipids and glycogen accumulation and mTOR activation are OCCC features. Metabolism is a cancer hallmark and the ability of OCCC to accumulate glycogen can be a clue that glucose is not the main carbon/energy source. Amino acid metabolism is often altered in cancer. Glutamine can be used as a non-glucose carbon source. Cysteine is the main sulfur source in mammals. We aimed to evaluate the role of glutamine and cysteine in OCCC.

Methods
We used an OCCC cell line - ES2 - cultured with glucose or glutamine both alone or in combination with cysteine. Glucose and glutamine metabolism was evaluated by NMR. Cell cycle was evaluated by flow cytometry, using propidium iodide labelling. The expression of mTOR pathway elements and cysteine degradation genes (GOT1, CTH, MPST) was evaluated by RQ-PCR.

Results
ES2 cells perform glutaminolysis, synthesising glutamate and alanine. Cell cycle activity is equivalent in cells grown in glucose or glutamine. Glutamine induces leucine uptake and RRAGA/B/C/D and mTOR complex expression. Cysteine increases cell cycle rate in the presence of glucose and glutamine. However, with glutamine and cysteine cell cycle rate is so high being S phase undetectable. Cysteine induces CTH and MPST overexpression.

Conclusions
Glutamine is a carbon/energy source in OCCC. Cell cycle can be sustained by mTOR activated by glutamine/leucine exchange, and increased by glutathione synthesis, using glutamate from glutaminolysis and cysteine.
Objectives
Patients with early stage epithelial ovarian cancer should be optimally staged, or alternatively receive adjuvant chemotherapy. However, in grade III tumors there is lack of consensus about adjuvant chemotherapy. The purpose of the study was to investigate the clinical practice of the application of adjuvant treatment in patients with early stage epithelial ovarian cancer in Comprehensive Cancer Center South (CCCS), a region in The Netherlands.

Methods
A retrospective analysis was performed on all patients (n=135) with FIGO stage I-IIa epithelial ovarian cancer, diagnosed between January 2006 and December 2010 at CCCS. Patient charts were reviewed for data of both patient and tumor characteristics and applied treatment. Primary outcome was defined as the percentage of patients who received adjuvant chemotherapy. Secondary outcomes were comprehensiveness of the staging procedure, recurrence rate and disease specific and overall survival.

Results
In CCCS, 40% (n=54) of the patients with early stage epithelial ovarian cancer was treated with adjuvant chemotherapy. These patients differed significantly compared to patients without adjuvant chemotherapy (n=81) with respect to: non-optimal staging procedure, and grade II-III tumors. Optimal staging was accomplished in 50% of the patients. Predictors for non-optimal staging were: advanced age (OR 1.05, 95%-CI 1.02-1.09), comorbidity (OR 16.55, 95%-CI 1.87-147) and treatment outside a gynecological oncology center (OR 3.60, 95%-CI 1.05-12.37).

Conclusions
In early stage ovarian cancer, adjuvant chemotherapy was applied in 40% of the patients, mostly due to a non-optimal staging procedure. Involvement of gynecological oncology centers may improve staging procedures, and hence reduce adjuvant chemotherapy in early stage ovarian cancer.
Poster Presentations: Ovarian Cancer

HE4 GENE EXPRESSION IN OVARY, FALLOPIAN TUBE AND OVARIAN CANCER

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Objectives
HE4 protein is the marker of epithelial ovarian cancer (EOC). It is also known as a protein of Müllerian origin. Recently, it is supposed that EOC does not derive from ovarian surface epithelium, but from tissues of Müllerian origin, particularly from the fallopian tube. This study was designed to compare the level of HE4 gene (WFDC2) expression in normal ovary, fallopian tube and EOC.

Methods
EOC specimens were obtained during surgical procedures from 30 patients (FIGO stage I, II and III). To compare it with normal gynecological tissues, we obtained 10 samples of normal ovaries and 10 samples of fallopian tubes. Total RNA was isolated from tissues and reversely transcribed into cDNA. Relative WFDC2 expression level was measured by real-time PCR and was analyzed statistically (Mann-Whitney test, Kruskal-Wallis test)

Results
All investigated specimens presented WFDC2 transcripts. EOC samples distinguished themselves by much higher relative WFDC2 expression in comparison to normal ovaries (p=0.003). Transcriptional activity of WFDC2 in EOC specimens and in normal fallopian tubes was comparable (p>0.05). Lower expression was observed in FIGO stage I and II, and in grade 1 cases of EOCs.

Conclusions
We showed that high expression of WFDC2 is observed in both EOC and the fallopian tube, but in normal ovaries we observed low expression. Our results confirmed resemblance of EOC and fallopian tube tissues and showed the potential role of fallopian tube in ovarian cancer pathogenesis.
PROGNOSTIC SIGNIFICANCE OF PERITONEAL CANCER INDEX (PCI) IN ADVANCED OVARIAN CANCER AFTER COMPLETE CYTOREDUCTIVE SURGERY

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Objectives
PCI is quantitative prognostic indicator for palliative and curative management of peritoneal carcinomatosis in gastrointestinal malignancy. In the current retrospective study, we aim to define the significance of PCI in primary macroscopically complete resected epithelial ovarian cancer (EOC) patients.

Methods
Between January 2007 to July 2012, 495 primary EOC patients received surgical treatment within our institution. From this collective of patients, we excluded with history of neo-adjuvant chemotherapy, completion cytoreductive surgery and macroscopically residual tumor mass after surgery, due to limitation in accurate describing the PCI. In the end 89 women, mean age 59.01 (32-86), were included in our analysis. Correlation between PCI score and clinical factors were analyzed using Kendall’s tau b. Univariable and multivariable survival analysis were performed with Kaplan-Meier method and Cox Regression models.

Results
Increasing value of PCI scores was associated with advanced FIGO stage (p=0.007), present of ascites (p<0.001) and lymph node involvement (p=0.029). The best cut-off value of OAS and PFS were 16 (p=0.004) and 11 (p=0.001). Estimated 2-years OAS rate for the patients with PCI ≤16 were 88.0 months and patients with PCI >16 were 52.5 months. High risk of PCI score >16 for OAS and >11 for PFS remained significant also after adjustment for age at diagnosis, present of ascites, histology and FIGO stage (HR 3.42; 95%CI 1.08-10.81 and HR 3.76; 95%CI 1.76-8.04)

Conclusions
PCI Score is potential prognostic indicator for PFS rate in ovarian cancer patients. However, OAS rate during complete resection can be only slightly predicted using PCI score.
Poster Presentations: Ovarian Cancer

GENE EXPRESSION PROFILE AS A PROGNOSTIC MARKER IN EPITHELIAL OVARIAN CANCER

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Objectives
In clinical practice epithelial ovarian tumors with the same istotype and advanced FIGO stage, treated with the same standardized protocols, have different evolution and overall survival (OS). Nowadays, classic prognostic factors are often unable to define a correct prognosis.

Methods
We retrospectively evaluated 37 serous epithelial ovarian cancer patients (FIGO stage III and IV) treated with surgery and chemotherapy based on Paclitaxel and Carboplatin, from January 1998 to December 2008. Patients were stratified into 2 groups, based on OS: 10 long-term (>84 months) and 27 short-term (<36 months) survival. Gene expression profiles were obtained from frozen tissues and analyzed to underline differences between the two groups.

Results
A total of 628 genes were discovered to be differently expressed in long vs. short patients (up or down regulated). According to literature, we studied the role these genes assume in different pathways (ECM-interaction pathways, complement and coagulation cascade, focal adhesion and others) and their connection with the tumor onset, growth and outcome.

Conclusions
In long-term survival patients all genes appear down-regulated, suggesting a favorable profile of these tumors. In conclusion, it is possible to define differences in gene expression which are able to justify and explain so different outcomes in apparently similar diseases.
Role of Pelviperitonection in Primary and Interval Surgery in Patients with Primary Advanced Ovarian Cancer

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Objectives
To assess the role of pelviperitonection in Primary Ovarian Cancer surgery and compare its morbidity, intra and post-operative complications and survival as primary or interval surgery.

Methods
Patients with Advanced Ovarian Cancer and peritoneal carcinomatosis who underwent pelviperitonection at primary or interval surgery from January 2005 to December 2011 at University Hospital Vall d’Hebron.

Results
From 59 patients included, 49 (83.05%) underwent primary debulking. In 40.6% tumor reduction was complete and in 35.6% residual tumor was <1 cm. 47 patients (79.6%) had an intraoperative complication (blood transfusion, tearing great vessels, urinary tract injury or hemorrhagic shock). Postoperative complications were seen in 25 patients (42.37%). There were no statistically significant differences between the degree of cytoreduction achieved or intra- and post-operative complications in cases of primary versus interval debulking surgery (p = 0.319, p = 0.712 and p = 0.673 respectively).

The median overall survival was 47.7 months (95% CI: 22.2-73.1). No statistically significant differences in survival according to the type of surgery and adjusting for tumor residual were seen.

Conclusions
Tumor residual after surgery is the main prognostic factor in patients with ovarian cancer. Pelviperitonection is a safe surgical procedure necessary to achieve complete tumor reduction in cases of advanced ovarian cancer with peritoneal carcinomatosis at primary and at interval surgery.
RESULTS OF A PHASE I TRIAL OF HYPERThERMIC INTRAPERITONEAL CISPLATIN AFTER NEOADJUVANT CHEMOTHERAPY AND CYTOREDUCTIVE SURGERY AND FOLLOWED BY BEVACIZUMAB IN INITIALLY UNRESECTABLE OVARIAN CANCER

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Objectives
The aim of this study was to identify the recommended dose of cisplatin for hyperthermic intraperitoneal chemotherapy (HIPEC) at complete cytoreductive surgery (CCRS) after neoadjuvant carboplatin and paclitaxel (CP).

Methods
Patients were treated with 6 cycles of CP followed by CCRS and HIPEC using cisplatin heated for one hour at 42°C±1°C. Four dose levels of cisplatin were tested: 50, 60, 70 and 80 mg/m². Dose limiting toxicities (DLTs) were defined as a grade > IIIb surgical adverse event according to the Dindo classification, during the 1st post-operative month. After surgery, maintenance bevacizumab (15mg/kg) was offered for 22 cycles, every 3 weeks.

Results
From 08/11 to 10/12, 30 patients were recruited in 7 comprehensive cancer centers. Median age was 58 (range 22-66) No DLT occurred at the first 3 dose levels (N=4, 4 and 5 pts respectively). At dose level 4 (80mg/m², N=17), four DLTs occurred: 2 renal failures, 1 peritonitis and 1 hemorrhage. Eight weeks after surgery, creatinine clearance was reduced to < 30 ml/min in 3 (10%) patients (all in the 80mg/m² dose level), and between 30 and 60 ml/min in 6 (20%) patients. Twenty patients received at least 1 course of maintenance bevacizumab and 10 did not (4 due to previous DLT, 2 due to progression and 4 for miscellaneous reasons).

Conclusions
We recommend a dose of 70 mg/m² considering prolonged impairment of the renal function observed at the level 4. Renal toxicity appears as the limiting morbidity of cisplatin-based HIPEC.
EVALUATING THE ACCURACY OF FROZEN SECTION IN BORDERLINE OVARIAN TUMORS.
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Objectives
The objective of this study was to evaluate accuracy of frozen section in borderline ovarian tumors and to determine the tumor characteristics that lead to higher likelihood of Inaccurate Intraoperative Diagnosis (IAIOD).

Methods
This was a retrospective chart review of 622 consecutive cases that were diagnosed with pelvic mass and underwent surgery between 2006-2011. Of these, 52 were diagnosed as borderline ovarian tumors by frozen section. Experienced pathologists performed these frozen sections. Terms such as “at least borderline” were also evaluated to help stratify patients. Frozen section and final permanent histology reports were compared. Patient and tumor characteristics that may cause IAIOD such as age of patient, histological subtype, size of tumor, bilaterality, CA-125 levels were studied. Staging was performed when borderline or malignant ovarian tumors were identified by frozen section.

Results
Agreement of the frozen section results with final pathology was observed in 37 out of 52 patients with a diagnostic accuracy of 71.15 %. Under diagnosis occurred in 12 out of 52 patients and over diagnosis occurred in 3 out of 52 patients. None of the variables (age of patient, size of tumor, bilaterality, CA-125) were significant (p>0.05) in causing IAIOD.

Conclusions
In our study, the rate of IAIOD was high despite experienced pathologists and using “at-least borderline” terminology. Traditionally described features leading to inaccuracy with frozen sections, such as large tumors with mucinous histology did not increase the risk of IAIOD. Given this information, full staging of all borderline ovarian tumors identified at time of frozen section should remain the standard of practice.
Poster Presentations: Ovarian Cancer

CAN PURE MUCINOUS BORDERLINE OVARIAN TUMOR RECUR ACTUALLY?: CLINICAL ANALYSIS OF 373 CASES OF MUCINOUS BORDERLINE OVARIAN TUMOR IN SINGLE INSTITUTE IN KOREA

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Objectives
Classification of mucinous borderline ovarian tumor(MBOT) is very complicated, the clinical course about recurrence and metastasis of which is not completely concluded. The authors give a new opinion about necessity of closed follow-up for recurrence detection of pure MBOT among a lot of controversy.

Methods
Medical records and pathologic slides were reviewed retrospectively about the clinical course of 373 cases of MBOT in Asan Medical Center in Korea from 1991 to 2012.

Results
Total 11 cases recurred and were reviewed again by pathologist. 3 cases had initially intraepithelial carcinoma(IEC) component on review. 6 of the others 8 cases recurred as pure MBOT. Pathologic review could not be performed in 2 cases, which eventually recurred as invasive carcinoma(IC). Inferring from their poor prognosis, they might be originally IEC or IC. The recurrence rate of pathologically reviewed pure MBOT was 1.1%(4/373). A thing worthy of note is that 3 cases recurred at the contralateral ovary, 2 cases were endocervical type and 1 case was initially mixed epithelial type arising from endometriosis. That might mean not recurrence but newly developed tumor associated with endometriosis. Moreover it could be progression of residual tumor because most patients were young women and surgeon would debulk less radically.

Conclusions
The recurrence rate of pure MBOT might be much lower than rate reported so far. The authors suggest carefully that if surgeon debulk completely in non-mixed, non-endocervical type of pure MBOT with stage Ia and Ib, the physician might reduce or omit unnecessary repetitive checking-up of tumor marker and imaging study for the long term.
Poster Presentations: Ovarian Cancer

PANOBINOSTAT / CARBOPLATIN DELAY POSTSURGICAL RELAPSE OF OVARIAN CARCINOMA IN AN ORTHOTOPIC MOUSE MODEL

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Objectives
Despite improvement in treatment of ovarian cancer the overall survival rate is still below 45%. Clinical failures of drugs against novel targets, which demonstrate efficacy in preclinical models, suggest the limited predictive value of current preclinical models. Recently we have established a surgical, orthotopic mouse model for ovarian cancer treatment that represents a more clinical relevant system for identifying agents that can modify treatment outcome in humans. Inhibitors of histone deacetylase (HDACi) activity are emerging as a potentially important new class of anticancer agents and this study is aimed to assess the antitumor effect of the novel HDACi panobinostat in the established in vivo model.

Methods
Luciferase transfected ovarian cancer cells, SKOV-3, were injected orthotopically into the ovaries of NOD/SCID mice. Disease development and effect of clinical standard treatment including hysterectomy, bilateral salpingoophorectomy and adjuvant regime with carboplatin together with panobinostat was evaluated by bioluminescence imaging (BLI) and survival.

Results
Orthotopic tumor growth following implanting of bioluminescent SKOV-3 cells in the bursa of mouse ovaries resulted in disease analogous to de novo human ovarian cancer. Surgery followed by combination treatment with carboplatin and panobinostat resulted in plateau of bioluminescence suggesting disease stabilization and significant longer survival ($p < 0.05$) compared to surgical control group. Treated mice tolerated the combination of surgery and panobinostat/carboplatin without significant loss of weight.

Conclusions
Surgical treatment with follow up carboplatin and panobinostat resulted in significant longer survival compared to surgical control and this was visualized by mean of BLI.
Poster Presentations: Ovarian Cancer

PROGNOSTIC FACTORS OF GERM CELL AND SEX CORD- STROMAL OVARIAN TUMORS IN PEDIATRIC AGE

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Objectives
To study the clinico-pathologic features and prognosis of our managed cases of germ cell and sex cord- stromal ovarian tumors in pediatric age for 5 years.

Methods
This retrospective study included all managed cases of malignant germ-cell and sex cord-stromal tumors in the pediatric age (less than 18 years). The medical records of the admitted cases from first of January, 2008 to 31 December, 2012 were reviewed and the following information was collected: patient age, clinical presentation, surgical stage, tumor histology, therapy, clinical course, and outcome. Serum alpha-fetoprotein on admission was studied.

Results
The study included 42 pediatric cases of germ-cell and granulosa cell tumors of the ovary. Mean age of the cases was 11.26 years (range: 7-15 years). Abdominal pain was the commonest presentation. Twenty-two cases (52.4%) were diagnosed as stage I disease. Twenty-eight cases (66.7%) were exposed to fertility sparing surgery. Age of the patient and site of tumor were significantly correlated to the survival (p value: 0.04 & 0.09 respectively). The correlations of stage of the disease, use of pre-operative chemotherapy, and type of surgical interference were highly significant (P value: 0.007, 0.001, and 0.001 respectively). Tumor size and histologic types were not significantly correlated to survival (P: 0.19 & 0.67 respectively).

Conclusions
The cumulative survival rate was 76.2 %. The correlations of stage of the disease, use of pre-operative chemotherapy, and type of surgical interference were highly significant. Tumor size and histologic types were not significantly correlated to survival. Initial level of alpha-fetoprotein was not significantly correlated to survival or recurrence.
TUMOUR ACTIVE PHYTOCHEMICALS IN COMBINATION WITH TARGETED THERAPY TO OVERCOME DRUG RESISTANCE IN OVARIAN CANCER

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Objectives
To apply combinations of platinum drugs and phytochemicals towards overcoming drug resistance in ovarian cancer

Methods
Cell culture to determine activity of drugs alone and in combination based on MTT reduction assay, proteomics to determine changes in expression of key proteins associated with drug resistance using 2D gel electrophoresis and mass spectrometry, determination of changes in glutathione level as a measure of cellular oxidative stress

Results
Platinum drugs and phytochemicals including reserveratrol, EGCG, curcumin, genistein and thymoquinone are found to produce sequence and concentration dependent synergism in ovarian tumour models. Generally administration with 2 to 4 h time gap are found to be more synergistic than the bolus. Over thirty proteins including molecular chaperones, stress related proteins, proteins involved in detoxification and drug resistance, and mRNA processing proteins have been identified and are believed to be associated with platinum resistance. Whereas platinums down regulate GSH level, a number of phytochemicals do the converse.

Conclusions
If confirmed in vivo, appropriate sequenced combinations of phytochemicals and targeted therapy can provide a means of overcoming drug resistance in ovarian cancer.
PERSONALIZED CANCER THERAPY FOR OVARIAN CANCER PATIENTS.
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Objectives
Our objective was to isolate potential ovarian metastatic cells from patients and correlate their in vitro response to the chemotherapy observed in the patient.

Methods
Primary cultures of ovarian cancer cells (peritoneal fluid) were obtained with signed informed consent from a network of Chilean hospitals. Chemotherapy response was assessed by MTS and data correlated with CA125 levels, imaging and medical criteria.

Results
Analysis of 59 assays for ovarian cancer patients with clinical follow-up demonstrated a median of progression free survival (PFS) of 16 months for patients predicted to respond to treatment showed by our assay, but only an average of 2 months of PFS in patients that the assay predicted no response.

Conclusions
When using exclusively cancer cells extracted from ascites we demonstrate a clear distinction in time to relapse between patients predicted or not predicted to respond to treatment in our assay. Our results demonstrate the requirement of the medical community to consider reevaluating this procedure and to take this research to the stage of randomized clinical trials.
Poster Presentations: Ovarian Cancer

CIRCULATING SVCAM-1 CONCENTRATION IN ADVANCED OVARIAN CANCER PATIENTS: CORRELATION WITH ASCITES

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Objectives
Vascular cell adhesion molecule-1 (VCAM-1) is associated with ovarian cancer progression, however the origin of its soluble form (sVCAM-1) in serum is not known. Purpose of this study was to elucidate if the concentration of sVCAM-1 in serum correlate with concentration in ascites, that represents local tumor environment, clinicopathological characteristics, inflammation markers and patients outcome

Methods
36 patients with FIGO stage III and IV ovarian cancer were included. Serum for sVCAM-1 analysis was obtained prior to surgery. Ascites samples were collected on the beginning of operation. Clinical data (tumor size, FIGO stage, grade, CRP and WBC levels) were collected from patient’s medical records. sVCAM-1 was analyzed with flow cytometric bead-based assay. Median (range) follow-up was 12 (4-24) months. Pearson’s and Spearman’s correlation coefficients were used to calculate the strength of paired data relationship. Mann-Whitney test was used to compare continuous parametric and non-parametric variables.

Results
Mean sVCAM-1 concentrations were 1639.39 ± 537.26 ng/ml and 817.95 ± 287.72 ng/ml in serum and ascites respectively. Strong correlation was demonstrated between the two compartments (p<0.001). Serum sVCAM-1 weakly correlated with tumour size (p=0.038), there was no correlation with inflammatory biomarkers, FIGO stage and grade (p>0.05). 4 out of 5 patients died before chemotherapy was started, all with significant higher sVCAM-1 (p=0.02).

Conclusions
Serum sVCAM-1 in advanced ovarian cancer patients correlate with sVCAM-1 in ascites thus expressing the biologic potentials in tumor local environment and not with systemic inflammatory response. Higher levels of sVCAM-1 might be prognostic factor for poor outcome, but the cut-off point needs to be validated.
Poster Presentations: Ovarian Cancer

EXTENSIVE UPPER ABDOMINAL SURGERY FOR BULKY STAGE IIIC AND IV OVARIAN CANCER: IS IT JUST A “BELIEF”?  
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Objectives
The aim of the study is to evaluate the survival benefit of extensive upper abdominal surgery (EUAS) for stage IIIC and IV ovarian cancer with bulky upper abdominal disease (UAD).

Methods
A single institute, observational study was conducted between 2009 and 2011 based on different surgical teams. Team A is the “believers” of EUAS, Team B not believing EUAS. The EUAS was performed in 58% (29/50), 7.4% (9/122) of the patients by team A, B, respectively. All patients underwent primary cytoreductive surgery with the goal of optimal outcome, neither interval cytoreduction nor palliative surgery being included. The optimal cytoreduction (≤1cm) achieved in the pelvis, middle abdomen, and upper abdomen were 87.8%, 89.5%, and 62.2%, respectively. The residual disease was reviewed in the pelvis, middle abdomen, and upper abdomen, respectively. Progression-free survival (PFS) was evaluated using Kaplan-Meier method, a difference comparison using Cox regression model.

Results
The median follow-up was 29.6 months. The median PFS were 17.8 mos. and 12.4 mos. in EUAS group and non-EUAS group (P=0.075, HR=0.701, 95%CI 0.474-1.038), with a 2-yr survival was 87% and 67%, respectively. Residual disease in the pelvis, residual disease in the upper abdomen, and FIGO stage were the predictors of PFS by Cox regression analysis.

Conclusions
Extensive upper abdominal surgery lengthens the progression-free survival of ovarian cancer patients with bulky upper abdominal disease. But a well-designed randomized trial is needed to confirm the results.
ACCURACY OF FROZEN SECTION DIAGNOSIS OF BORDERLINE OVARIAN TUMORS
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Objectives
The objective of this study was to determine between the clinicopathological parameters and the incidence of invasive cancer in ovarian masses diagnosed as borderline tumor at the time of frozen section.

Methods
We performed a retrospective review of all patients diagnosed with ovarian borderline tumor on frozen section at our institution between 2003 and 2012. Clinical and pathologic data were extracted and frozen section and permanent histology analyses were compared. Multivariate regression analysis was used to assess the influence of clinicopathological parameters.

Results
A total of 179 patients were identified, of which 155 (86.6%) had borderline on frozen biopsy that was confirmed on final pathology. In 18 (10.1%) patients, borderline tumor was diagnosed on frozen biopsy but was reclassified as invasive cancer on final pathology. Six patients (3.3%) had borderline tumor on frozen biopsy but benign pathology on final diagnosis. Based on histologic evaluation, 112 tumors (62.6%) were mucinous, 58 (32.4%) were serous, and 9 (5.0%) tumors were mixed, endometrioid, or clear cell. Based on multivariate analysis, mucinous histology (odds ratio [OR], 1.49; P < 0.01) and laparoscopic approach (OR, 2.12; P < 0.01) were significant predictors for underdiagnosis by frozen biopsy.

Conclusions
Frozen section analysis of BOTs has low accuracy, sensitivity, and positive predictive value, and underdiagnosis and overdiagnosis are frequent. Therefore, surgical decision-making for BOTs based on frozen section diagnosis should be done carefully, especially in tumors with mucinous histology or laparoscopic approach.
A RETROSPECTIVE ANALYSIS OF TRABECTEDIN (T) USE IN OVARIAN CANCER PATIENTS: A MULTICENTRIC ITALIAN EXPERIENCE.

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Objectives
Since 2011, T is reimbursed in Italy for ovarian partially-sensitive cancer patients in association with liposomal-doxorubicin. Nevertheless, some women receive T alone or in advanced lines of therapy. Thus, we evaluate the impact of T treatment in the daily practice.

Methods
We reviewed data of T use in ovarian cancer patients of 5 Italian hospitals.

Results
Since October 2010, 55 women received T, with a median age of 53 years (range,39-79), mainly as 4th line of treatment. 274 cycles were infused, with a median number of 5 (range,1-15). 29 pts progressed, 21 are still on therapy, and 5 have not yet progressed. In this series, median progression-free survival (mPFS) was 5.3m (range,2.4-26.4). When T was administered as a 2nd or 3rd line of therapy, mPFS was 9.2m (range,2.6-26.4), without differences according to the administration’s line, and to the combination or not with pegilated-doxorubicin. mPFS was, instead, 5.4m (range,2.4-17.9), when T was used in more advanced lines. Grade 3 and 4 toxicities were rare, with neutropenia, liver enzyme elevation, and asthenia in 11%,4% , and 4% of patients, respectively, without relation to the line of treatment. Actually, thrombocytopenia and anemia were twice as frequent in advanced lines as in early ones. No severe cardiotoxicity was detected.

Conclusions
Our data are consistent with previous trials. In daily practice, activity was maintained until the 3rd line of therapy. Moreover, it is of note that toxicity does not significantly increase with advanced lines, while activity it is only slightly lower than in early ones.
Poster Presentations: Ovarian Cancer

BLOOD PLASMA FOURIER TRANSFORM INFRARED AND RAMAN SPECTROSCOPY FOR NON-INVASIVE DETECTION OF OVARIAN CANCER


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Objectives

Robust diagnosis of ovarian cancer with blood based analysis remains a challenge. The aim of this study is to determine whether two novel metabolomic approaches (ATR FTIR & Raman spectroscopy) can discriminate between ovarian cancer and controls using peripheral blood samples.

Methods

Blood samples were obtained from ovarian cancer (n=30) and control subjects (n=30) following which plasma and serum were isolated using standardized procedures. To obtain Infrared spectra, serum and plasma samples were mounted on low-e glass slides and were interrogated with ATR-FTIR spectroscopy. Raman spectra were obtained after mounting blood plasma (n=8) on aluminium stubs, drying and analyzing with InVia Renishaw Raman spectrometer. The spectra were processed using MATLAB R2010a. For the analysis of Raman spectra (n=400), we applied principle component analysis followed by linear discriminant analysis. For ATR spectra (n=2,400) linear discrimination analysis was used. The support vector machine classifier was employed to obtain classification accuracy rate (average between sensitivity and specificity).

Results

Statistically significant difference was observed between spectra of ovarian cancer versus control for ATR-FTIR (Fig 1) and Raman spectroscopy (p<0.001). Support vector machine classifier showed classification accuracy of 74 % for Raman spectra and 93.3 % for ATR-FTIR spectra of blood plasma. The spectral biomarkers responsible for segregation were vibrations of proteins, lipids and DNA.
Conclusions

ATR-FTIR spectroscopy of blood plasma provides highly accurate diagnosis of ovarian cancer. The accuracy of Raman spectroscopy can be enhanced by using surface enhanced Raman spectroscopy with silver/gold colloids.
Poster Presentations: Ovarian Cancer

ULTRASOUND AND STAGING OF OVARIAN CARCINOMAS

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Objectives
Ultrasound is regularly used for evaluation of adnexal masses. The aim of this study was to determine if ultrasound parameters are linked with the FIGO stage of ovarian carcinomas.

Methods
Study involved all women operated due to ovarian carcinomas throughout a period of 36 months in the Clinic for Ob/Gyn, Clinical Center of Serbia. Upon admission we assessed if the tumor was multilocular, bilateral; had solid parts, septa, mixed consistency and papillae. Tumor diameter (<5cm, 5-10cm, >10cm) and Doppler RI and PI were also evaluated, and the presence of ascites was noted. Obtained data were compared with histopathological findings of tumors and FIGO staging, and statistically analyzed.

Results
There were 126 ovarian carcinomas registered, the most in FIGO stage IIIC (χ²=148.990; p=0.000) There were significant differences between FIGO stages only for solid parts (F=2,906; p=0.003) and ascites (F=2.027; p=0.037). St Ib had the least and IIIC the most solid parts, Ib was almost never accompanied by ascites and IV almost always. On the other hand, presence of solid parts (p=0.187; p=0.002), ascites (p=0.228; p=0.000), bilaterality of the tumors (p=0.164; p=0.008) and Doppler RI (p= - 10.173; p=0.005) were significantly correlated with FIGO stages of investigated malignant tumors. Tumors of higher stages had more solid parts, ascites and were usually bilateral, but had lower values of RI.

Conclusions
Ultrasound parameters are found to be good predictors of malignant tumors stage, and therefore, detailed ultrasonographic scan should always be performed in all patients with adnexal masses.
DIAGNOSTICS OF MALIGN OVARIAN TUMORS BY ULTRASOUND AND CA 125 – OUR EXPERIENCE

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Objectives
The aim of the study is to evaluate retrospectively a sensitivity and specificity of CA 125 and “simple rules” ultrasound (US) criteria in the hands of an experienced sonographer in diagnostics of malign ovarian tumors.

Methods
Patients with suspicious adnexal masses (2010 – 2012), was conducted US and CA 125 was taken. According to final histology we evaluated the sensitivity and specificity of pre-operative staging. We have used the 2-step model (IOTA) for diagnostics an OC and borderline tumor (BTO) by US. The reference level for positivity of CA 125 is determined to ≥ 35 kU/L.

Results
In 2010 - 2012 we evaluated 347 tumors (125 malign – 101 invasive OC and 24 BTO, 222 benign). Malign ovarian tumor was detected by US in 118 (sensitivity 94 %, specificity 93 %) and by CA 125 in 93 cases (sensitivity 68 %, specificity 69 %). Invasive OC was diagnosed by US in 99 (sensitivity 98 %, specificity 93 %), BTO in 19 cases (sensitivity 79 %, specificity 93 %). Invasive OC was diagnosed by CA 125 in 80 (sensitivity 74 %, specificity 69 %), BTO in 13 cases (sensitivity 46 %, specificity 69 %).

Conclusions
Pre-operative US divides accurately adnexal masses in benign and malign. The sensitivity and specificity of CA 125 for detection of malign ovarian tumor is lower than US, most for early stages of OC and BTO.
MALIGNANT MELANOMA IN PREGNANCY – FASTEST GROWING PROBLEM
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Objectives
Malignant melanoma is the fastest growing malignancy in pregnant women population. Incidence in literature is from 2.8-10/10000 pregnancies.

Aim was to see the rate of it in our Maternity ward, during the period of 14 years, and outcome of it, toward mother and neonate.

Methods
Maternity ward of Clinic Narodni front, Belgrade, had 35 (13 first time diagnosed, 22 imported) cases of melanoma in last 14 years (96781 deliveries)( 3.61/10000). Ones diagnosed during pregnancy-none had any malignancy before. Average gestation of diagnosis-23 +3 weeks.

Results
5 delivered vaginally, 8 by CS. Chemotherapy treatment 4, chemotherapy + surgically 3, and surgically in 6 cases. Surgical treatments -performed in our Clinic. Chemotherapy of all in Institute Of Oncology, CCS supervised by an obstetrician. Average term of delivery- 33 weeks, 5 days; Apgar score 7.23/7.9; average body mass 2415 grams; duration of hospitalization 8.7 days. 1 newborn had cutaneous markings-malignant-transferred during cordocentesis operated one day after delivery. 4 women died in 5 year period, 2 in 10 years. 7 are still in screening protocol. 3 had another child after. Surgical treatment had 8 - depending of localization and level of malignancy. 1 patient treated urgently after delivery - metastases inside of the eyeball-removed.

Conclusions
Malignancy level was high at the diagnosis. Therapy-radical and prompt-problem - saving the mother, fertility and after pregnancy. Incidence growth-341% in 14 years-the most vigorous problem for obstetricians, surgeons and pediatricians in time to come, concerning malignant diseases. ALWAYS TO THINK ABOUT.
FERTILITY SPARING SURGERY IN EARLY STAGE EPITHELIAL OVARIAN CANCER: A PROSPECTIVE STUDY IN A TERTIARY CENTER.

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Objectives
Fertility sparing surgery (FSS) is a strategy often considered in young patients with early epithelial ovarian cancer (eEOC). In this prospective study we investigated the role of FSS in eEOC who underwent comprehensive surgery.

Methods
We prospectively recruited 124 patients diagnosed with apparent eEOC (FIGO stage I and II) between January 2003 and January 2011. Twenty-four underwent FSS. Eighteen out of 24 women were one to one well matched and balanced for stage, histotype and grading with a group of patients underwent to radical comprehensive staging (RCS). Demographics, surgical procedures, morbidities, pathologic findings, recurrence rate, pregnancy rate and correlations with DFS were assessed.

Results
A total of 36 (18 FSS, 18 RCS) patients had a complete surgical staging including lymphadenectomy and were therefore analyzed. Seven patients experienced a recurrence: 4 (22%) in the FSS group and 3 (16%) in the control group (p=NS). Sites of recurrence were: residual ovary (2 cases), abdominal wall and peritoneal carcinosis in FSS group; pelvic (2 cases) and abdominal wall in control group. Recurrences in FSS group appeared earlier (mean 10.3 months) than in RCS group (mean 53.3 months) p<0.001.

DFS were comparable between the two groups (p:0.44). No deaths were reported. All the patients in FSS group recovered a regular period. Thirteen out 18 (72.2%) attempted to have a pregnancy. Five (38%) achieved a spontaneous pregnancy with full term delivery.

Conclusions
FSS in eEOC underwent comprehensive surgical staging is feasible in an oncofertility view. Our follow-up data are encouraging, clearer data are warranted by prospective controlled studies.
PROGNOSTIC VALUE OF SCCA TUMOR MARKER IN PATIENTS WITH CERVICAL CANCER
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Objectives
Squamous cell carcinoma antigen (SCCA) level in blood serum is proved to be valuable for diagnosis and monitoring of patients with cervix carcinoma. Since cervix carcinoma as a rule originates from squamous epithelium, SCCA estimation in blood serum is significant for the study of the disease development.

The aim of the study was to follow SCCA level in patients with cervix carcinoma with primary and metastatic disease for determination of recurrence probability value.

Methods
Changes in SCCA level in blood serum and clinical data were analyzed within 224 patients with cervix carcinoma I-IV stage. 171 patients were diagnosed with primary cancer; recurrence was confirmed in 53 patients. SCCA concentration in blood serum was determined by chemiluminescent immunoassay at micro particles (HIAM). Statistic analysis was made at Statistica 6.0.

Results
It was confirmed that SCCA level in patients with primary cervix cancer with metastases in regional lymph nodes was higher as compared with the SCCA level in patients without metastases (5.6 ±1.4 ng/mL vs 2.3 ± 0.1 ng/mL), p < 0.05. SCCA level in blood serum was increased in 86.4 % of patients with the recurrence. It amounted to 19.4 ± 3.7 ng/mL (from 0.5 to 70.0 ng/mL).

SCCA value in blood serum was increased in 60.4 % of patients with cervix carcinoma IB-III stage. Test-sensitivity increases from 7.8 % (I stage) to 77.8 % (III stage).

Conclusions
SCCA level in blood serum can be considered as a sensitive method in prognostic study and determination of disease stage in of patients with cervix carcinoma.
COMPLEX ADNEXAL MASSES DIAGNOSED AND TREATED DURING PREGNANCY: REVIEW OF A CASE SERIES
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Objectives
To expose a case series of complex adnexal masses diagnosed and treated during pregnancy.

Methods
We conducted a retrospective study of 11 patients collected between 2009 and 2013 at a tertiary hospital. Treatment (conservative or surgical), follow-up and timing of delivery was decided between a multidisciplinary team. Surgical management was chosen when ultrasound and/or MRI appearance, tumor markers or symptoms were suspicious of malignancy.
- Approach: Laparoscopy or laparotomy depending on gestational age and mass size.
- Procedure: Peritoneal washing, cystectomy/oophorectomy or salpingo-oophorectomy and inspection of peritoneum, contralateral adnexa and abdominal cavity (biopsy if necessary).
- Follow up: clinical and ultrasound control every 4 weeks.

Results
Mean age was 28 years. 64\% were diagnosed during the first trimester. Surgery took place often (6 cases) during the second trimester. Midline laparotomy and salpingo-oophorectomy were mostly performed. There were no postoperative complications.
Pathology results: 6 malignant (4 borderline, 1 dysgerminoma 1 cistoadenocarcinoma)
Staging: 5 were IA and 1 IB FIGO stage.
Delivery was eutocic at term in 9 cases. There were 2 scheduled C-sections.
Follow-up: ultrasound and tumor markers quarterly during the first year, semiannual the second and annually thereafter.
Only one patient with a borderline tumor suffered a recurrence

Conclusions
The use of ultrasound has increased the detection of asymptomatic complex adnexal masses. This allows to perform surgery during the second trimester which has showed low risk of complications.
Conservative management can be a safe and less aggressive option in case of borderline and early stage tumors.
Poster Presentations: Fertility / Pregnancy

ANTI-MULLERIAN HORMONE AS A MARKER OF OVARIAN RESERVE IN PATIENTS WITH GERM CELL OVARIAN TUMORS WHO HAVE UNDERGONE FERTILITY-SPARING TREATMENT

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Objectives
Malignant ovarian germ cell tumors (MOGCTs) affect young women and are treated by surgery plus chemotherapy. There is a fairly literature on reproductive function after chemotherapy for MOGCTs, albeit exclusively retrospective. The loss of follicles by surgery and chemotherapy results in decreased ovarian reserve, which consecutively affects reproductive capacity. The aim of the study was to evaluate the role of Anti-mullerian hormone (AMH) as a marker of ovarian reserve in MOGCTs patients after treatment.

Methods
We report our experience in preservation of fertility for 4 patients referred to San Raffaele Hospital Oncofertility Unit.

Results
Average patients age was 17 (14-21). Two patients were affected by mixed germ cell tumors (stage IIIC and IIB) and two by disgerminomas (stage IC and IV). All patients had received fertility sparing surgery plus BEP chemotherapy. The two patients affected by mixed tumors received a salpingooophorectomy plus contralateral cystectomy. After 12 months from the end of treatment AMH levels have been evaluated. The results were: AMH= 0.1 ng/ml (age=16 years), AMH=0.7 ng/ml (age=18 years), AMH= 2.3 ng/ml (age=21 years), AMH= 2.7 ng/ml (age=23 years). We reported lower AMH levels in these patients than in healthy general population: AMH levels were under the 25th age-specific percentiles of AMH nomogram. We offered to the two younger patients a oocyte cryopreservation. We obtained two and six oocytes, respectively.

Conclusions
Although patients receiving chemotherapy may retain fertility, their window of fertility may be shortened. AMH, as a marker of ovarian function, can improve identification of patients to address to fertility preservation strategies.
QUALITY OF LIFE IN GYNAECOLOGICAL CANCER SURVIVORS
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Objectives
Evaluation of the quality of life of women, who were treated for genital cancer and later supervised in the Department of Gynecology & Obstetrics of Hospital of Lithuanian University of Health Sciences, using the FACT-G and Rosenberg’s Self-Esteem Scale.

Methods
The study involved 100 women, who filled in the FACT-G and the Rosenberg Self-Esteem questionnaire.

Results
Quality of life analysis was based on the 93 eligible questionnaires. A worse quality of life was rated by 57 (61.3%); 28 (49.1%) of them have a low self-esteem and 29 (50.9%) reported normal self-esteem. A better quality of life was indicated by 36 women (38.7%); 12 - had a low self-esteem(33.3%), 24 – reported having a normal self-esteem (66.7%) (p = 0.1, Pearson’s correlation coefficient r = 0.15). The quality of life was the worst among the women suffering from the stage II disease, but the difference was not statistically significant. Patients, who had the laparoscopic surgery rather than the laparotomy (22.6 ± 4.8 and 18.9 ± 5.3 points, p = 0.004), and patients who underwent a more radical surgical procedure (removal of lymph nodes), reported a significantly better well-being and a better quality of life.

Conclusions
Functional and physical conditions of the patient alone are not sufficient for an accurate evaluation of the patient’s well-being and such subjective assessment criteria as emotions and acceptance one’s illness are crucial for evaluating the quality of life.
DEPRESSION AND ANXIETY AS A PART OF QUALITY OF LIFE IN WOMEN WITH GYNECOLOGICAL AND BREAST CANCER

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Objectives
Depression and anxiety are a characteristic of patients with cancer and are connected with the quality of life. The aim of the study was to estimate depression and anxiety in cases of gynecological and breast cancer.

Methods
Depression and anxiety were conducted in 140 patients (120 with gynecological and 20 with breast cancer) and 120 controls. Determination the level of depression (Self Rating Depression Scale-SDS) and test anxiety (Self Rating Anxiety Scale-SAS) we used.

Results
Patients with gynecological have mild, moderate and severe anxiety (97, 16 and 7, respectively), and patients with breast cancer there were 10, 8 and 2 respectively. Mild, moderate and severe depression (87, 23 and 10 respectively) in gynecological cancer, in 10, 9 and 1 respectively in breast cancer were found. In gynecological cancer mild anxiety in 80% and moderate and severe anxiety in 20% of the cases were detected in contrast in breast cancer mild anxiety only in 50% and moderate and severe anxiety in 50% of the cases were detected. In gynecological cancer moderate and severe depression was in 28% of the cases in contrast in breast cancer moderate and severe depression in 50% of the cases was found. The patients with gynecological and breast cancer have increased levels of anxiety and depression. In the control group were not identified such changes.

Conclusions
Patients with breast and gynecological cancer have elevated level of anxiety and depression and quality of live is reduced in both groups, but is worst in breast cancer.
IMPACT OF SELF-REPORTED URINARY INCONTINENCE ON DAILY LIFE AND SEXUALITY AMONG GYNECOLOGICAL CANCER SURVIVORS FOLLOWING PELVIC RADIOThERAPY

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Objectives

Patient-reported urinary incontinence and consequences on daily life functioning among gynecological cancer survivors after pelvic radiotherapy is rare in the literature.

Methods

In 2006, 789 patients, who received pelvic radiotherapy as part of treatment for gynecological cancer during 1991-2003, at two university hospitals in Sweden, were included in a population-based study. 478 frequency-matched control women were recruited from the Swedish Population Registry. They received a validated postal questionnaire including 351 questions, covering symptoms from pelvic organs, quality-of-life, demographics and daily-life-functioning.

Results

Six hundred and sixteen (78%) gynecological cancer survivors and 344 (72%) control women participated. Mean follow-up after radiotherapy was 6.2 years. Cancer survivors reported a significantly higher occurrence of urinary incontinence with urge (35%) and without urge (15%) compared to control women (19% and 7% respectively). After adjustment for known risk factors Odds Ratio (OR) for urinary incontinence was 1.80 (95% CI 1.27-2.55). For survivors treated with radiotherapy alone, OR was 2.25 (95% CI 1.20-4.22). Twenty-three percent of survivors with urge incontinence, treated with radiotherapy only, needed to void more often than every hour, even during night. When feeling the need to void, two thirds of affected survivors had less than 5 minutes to reach a toilet. Furthermore, 26% of affected survivors reported that urinary incontinence kept them from partaking in social as well as sexual activities.

Conclusions

Gynecological cancer survivors, treated with pelvic radiotherapy, have an increased risk of urinary incontinence with and without urge, compared to controls. Urinary incontinence affects daily-life-functioning and sexual activity.
IMPACT OF CLOSE RESECTION MARGINS ON OUTCOMES OF PATIENTS WHO UNDERWENT EXENTERATION FOR RECURRENT PELVIC MALIGNANCIES; A RETROSPECTIVE ANALYSIS AND LITERATURE REVIEW

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Objectives
Pelvic exenteration is an uncommonly performed procedure involving removal of the vagina, cervix, uterus, fallopian tubes, ovaries, urethra, bladder, ureters, rectum and anus. It is done to treat the recurrence of gynaecological, colorectal and urological cancers confined to the pelvis. Overall 5 year survival is 20-50%, however, it remains a curative option for the recurrence of these cancers.

To describe the indication, long and short term outcomes of exenterations performed at the Gynaecological Oncology Centre at Wolverhampton and to identify if resection margins correlate to better outcomes.

Methods
A retrospective study using patient notes and the Somerset Cancer Register recording demographics, surgical indications, complications, duration of hospital stay, estimated blood loss, histology and overall survival rates. Paper databases were searched to identify cancer patients who had exenterations in the last 15 years.

Results
23 women were identified, four of which no longer had paper or electronic notes available. 19 sets of notes were used. Indications for surgery were endometrial or cervical cancers, with vaginal, urological and colorectal cancers making up a smaller percentage. Resection margins ranged from under 1millimetre to 10millimetres. The longest hospital stay was 7 months. 11 of the 19 women are still alive today. The 3 women with margins 1-2mm all died within 2 years of surgery. The woman with a margin of 10mm is alive 15 years after surgery.

Conclusions
This is an uncommonly performed procedure so recommendations are difficult to make. With this small cohort, bigger resection margins are associated with increased survival times.
A NEW METHOD ASSESSING VAGINAL MORPHOLOGICAL CHANGES IN CERVICAL CANCER SURVIVORS

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Objectives
Women treated for cervical cancer have persistent changes in their sexual function, resulting in considerable distress. Little is known about the morphology of the vaginal wall after treatment and its role on sexual health, while late effects of radiotherapy are well known in the bladder and intestines. We have developed a method to examine the morphology of the vaginal wall in vaginal biopsies in cervical cancer survivors.

Methods
We included 10 patients treated for cervical cancer and 10 healthy controls. The patients were treated with surgery, radiotherapy or combined treatment. Clinical examination was performed for grading of vaginal atrophy, telangiectasia and pelvic fibrosis. Vaginal biopsies were taken and analysed using immunohistochemistry and morphometry.

Results
The cervical cancer survivors had marked morphological vaginal changes compared to the controls, shown in figure 1. Clinical examination showed different degrees of atrophy, telangiectasia and pelvic fibrosis. Our methods for examination, sampling and analysis were feasible and functional.

Conclusions
After treatment of cervical cancer there are morphological changes in the vaginal wall, which may have a central role in the development of sexual dysfunction. We have developed a functional method for estimating the clinical and histological changes. The clinical implications and replication of the findings in a larger population are now studied, focusing on the radiotherapy effects. This will give tools for further preventive actions and targeted interventions.
THE IMPACT OF OVARIAN CANCER TREATMENT ON WOMEN'S SEXUAL WELLBEING

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Objectives
We have previously reported that women treated for ovarian cancer experience persistent psychological and physical problems. Sexual functioning was highlighted as a particularly significant factor and we sought to investigate this further.

Methods
A validated tool, the Fallowfield Sexual Activity Questionnaire, was used to obtain information from women more than six months following a diagnosis of ovarian cancer.

Results
We obtained responses from 102 women, with a mean age of 51.3 (range 18-77). Across all responders, 63% of women reported their diagnosis of ovarian cancer had changed their sex life in a negative way. Of women not sexually active (54%), the most common reasons given for this were a lack of interest in sex (27%), physical problems that prevented sex (20%) and no partner (19%). For women who were sexually active, 43% had little or no desire for sex. Fatigue was a very significant preventative factor for 30% of women. Physical factors also contributed to sexual problems; 77% reported pain or discomfort during sex and 87% had experienced vaginal dryness. Women reported that their diagnosis had a negative impact on the amount of sexual activity they were engaging in, with 36% not satisfied with the frequency.

Conclusions
The majority of women diagnosed with ovarian cancer experience a negative impact on their sex lives. Many of the associated problems are potentially reversible and clinicians should be open to raising these issues with their patients. Dedicated support for sexual wellbeing should be considered in future survivorship initiatives.
Poster Presentations: Quality of Life after Treatment of Gynaecologic Cancer

RECONSTRUCTIVE AND COSMETIC SURGERY IN ONCOGYNECOLOGY

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Objectives

Our aim was to present our results in cosmetic and reconstructive surgery in the field of oncogynecology, especially after radical surgical treatment of vulvar cancer, to offer options to improve the patients' quality of life. Radical surgery connected with vulvar cancer causes significant physical and psychological problems after treatment.

Methods

Reconstructive surgery was primarily used when treating such malignant tumors as vulvar cancer. The goal was to achieve smaller post operative surgical defects, and shorter hospital stays. Our surgical technique was used after am-block vulvectomy. The surgical technique used most was done with myocutaneous flaps from musculus tensor fasciae latae and musculus gluteus maximus. Fifty cases over 10 years were treated with this technique.

Results

With all techniques, preservation of the blood supply of the skin and the subcutaneous tissue was achieved. Only cutaneous flaps with subcutaneous tissue were used which were considered most suitable in such cases. The plastic surgery using skin and subcutaneous tissue gave the best results in our study. With this technique, the healing process is 2-3 weeks compared to that of radical vulvectomy without using reconstructive surgery- where the healing process is up to 3 months.

Discussion: The oncogynecological radical surgery especially connected with vulvar cancer is a big challenge to treat. We shared our experience in this field.

Conclusions

With our research work we tried to achieve better quality of life of our patients giving them a nice cosmetic and aesthetic effect after difficult and radical surgical procedures, especially connected with vulvar cancer.
THE IMPORTANCE OF NERVUS GENITOFEMORALIS VARIATIONS OBSERVED DURING PELVIC LYMPH NODE DISSECTIONS AND THE AFTERMATH FOR THE QUALITY OF LIFE OF FEMALE PATIENTS

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Objectives
To visually categorise and present the main variations of Nervus Genitofemoralis (NGF) through careful in vivo visualisations during lymph node dissections. This will reduce the risk of NGF inadvertent lesions, thus preserving the quality of life postoperatively.

Methods
Open abdominal surgery of 346 patients aged 26-81 with different oncogynaecological diseases. Within their treatment (February 2010-2013), pelvic +/- para aortic lymph node dissections were performed. Of these patients, 33 (aged 39-81) were randomly selected for thorough presentation of the NGF branches, laterally from the common and external iliac arteries to the deep iliac circumflex vein. A day before and a month after the operation, the patients were asked to complete a questionnaire to detect their skin sensitivity in the NGF innervated areas. For comparison, other 70 patients were asked to complete the same questionnaire, without being subject to a detailed NGF presentation.

Results
In vivo three main NGF variations: branching at the external iliac artery level to a femoral and genital branch (21 patients, 63.63%), two different branches: femoral and genital, at the common iliac artery level to the deep iliac circumflex vein (24.24%), a single NGF without branching to the deep iliac circumflex vein (12.12%).

80% of the 70 surveyed reported satisfactory sensitivity on the mons, labia, thigh internal surface vs. 88% of those 33 selected for detailed NGF presentation.

Conclusions
NGF is not a constant anatomical structure. Its variations' knowledge during surgeries could improve postoperative quality of life.
Poster Presentations: Quality of Life after Treatment of Gynaecologic Cancer

SEXUAL DYSFUNCTION IN SURVIVORS FROM CERVICAL CANCER

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Objectives

To evaluate the prevalence of sexual dysfunction among survivors who had suffered from cervical cancer, and to find out risk factors associated with the sexual dysfunction.

Methods

From July 2011 to June 2012, we performed a cross-sectional study of cervical cancer survivors (≥20 years old) who had no evidence of residual or recurrent disease. Comprehensive history taking, anthropometric measurement, laboratory testing, and questionnaire administration were performed for each of the total 106 patients. The modified version of Female Sexual Function Index (FSFI-LL) was used to assess the key dimension of female sexual functions.

Results

The median age of enrolled subjects was 54 (32-69) years, and the rate of female sexual dysfunction measured by FSFI-LL was 73.9% (68/92). Sexless women who had no sexual activity over half-year were counted as high as 24.5% (26/106), although more than half (53.8%; 57/106) of enrolled women were sexually active. The most compromised domains of female sexual functions were ‘desire (50%; 46/92)’ and ‘arousal (48%; 45/92), followed by ‘orgasm (27.2%)’, ‘satisfaction (25%)’, ‘pain (17.4%)’, and ‘lubrication (16.3%)’. Menopause (95.6 vs. 79.2%), partner’s sexual dysfunction (27.9 vs. 0.0%), and depression (22.8 vs. 0.0%; measured by Beck’s depression inventory) were significantly more frequent in affected women (n=68) compared with non-affected survivors (n=24) (p<0.05). However, age, radical hysterectomy, pelvic irradiation and/or chemotherapy did not affect the female sexual functions.

Conclusions

Female sexual dysfunction was very prevalent, and a significant portion of cervical cancer survivors seemed to avoid sexual activity. More concerns including emotional and hormonal support should be given to these cancer survivors.
ILEUS AFTER RADIATION THERAPY FOR CERVICAL AND ENDOMETRIAL CANCER

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Objectives
To determine the incidence, treatment options and mortality rate of bowel obstruction following radiation therapy.

Methods
Between 2005 - 2011, a total 762 patients with a pathological diagnosis of cervical (N=464) and endometrial (N=298) cancer received primary or adjuvant radiation therapy at the Hospital of Lithuanian University of Health Sciences Kauno klinikos. A retrospective analysis was performed to determine the incidence, treatment options and mortality rate of bowel obstruction following radiation therapy.

Results
The incidence of an ileus following radiation therapy for cervical and endometrial cancer was found to be 4.7% (N=22) and 6.4% (N=19) respectively (total incidence 5.3%). The median time from the last radiation traction to an ileus was 12 months. 73% (N=30) of the patients underwent surgery and 27% (N=11) were treated conservative, and mortality rate was 23.3% (N=7) and 9% (N=1) respectively (p=0.308).

Conclusions
Ileus after radiation therapy for cervical and endometrial cancer is an serious complication which mostly need for surgery and have high risk for postoperative mortality.
Poster Presentations: Quality of Life after Treatment of Gynaecologic Cancer

PREVENTION OF VAGINAL STENOSIS AND QUALITY OF LIFE IN WOMEN SUBMITTED TO PELVIC RADIOTHERAPY AND BRACHYTHERAPY – PRELIMINARY RESULTS.

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Objectives
Pelvic Radiotherapy and Brachytherapy play a fundamental role in the treatment of Gynecologic malignancies. These treatments are not exempt of toxicities. Vaginal stenosis develops in up to 88% of patients, compromising their sexual activity, quality of life and clinical surveillance. Therefore the need to prevent this condition is evident.

Objectives: Present the preliminary data of vaginal stenosis prevention methods, and quality of life of these patients.

Methods
Retrospective analysis of 89 patients with Gynecologic tumors, submitted to Radiotherapy (IMRT/3DCRT) and/or Brachytherapy (3D, HDR, guided by CT), between 2011-2012, proposed to prevent vaginal stenosis. Prevention started 2 weeks after the end of Radiotherapy, using one or more of the following techniques: vaginal dilator, modified Nunns' technique or sexual intercourse, according to patient’s preference.

Results
43% had Cervical tumors. With an average age of 59 (26-80), 88% underwent pelvic Radiotherapy, and 97% Brachytherapy. Compliance to the selected method was 86%, and the most used were: dilator (21%), modified Nunns’ technique (19%), and modified Nunn’s technique combined with sexual intercourse (19%). 27% of patients performed prevention 3 times/week. Dyspareunia occurred in 33%. One-year overall survival was 96%, and disease free-survival 78%. None of the patients had significant vaginal stenosis.

Conclusions
Given the short follow-up, it is not yet possible to evaluate the efficacy in preventing vaginal stenosis. An excellent compliance was obtained. With the continuing practice of these methods, it is our aim to analyse these methods’ efficacy in the prevention of vaginal stenosis, and their contribution to the patients’ quality of life.
Poster Presentations: Quality of Life after Treatment of Gynaecologic Cancer

CARDIOVASCULAR ADVERSE EVENTS WITH ADJUVANT ENDOCRINE THERAPY FOR EARLY BREAST CANCER. TAMOXIFEN VS AROMATASE INHIBITORS: SYSTEMATIC REVIEW – EVIDENCE FROM RCTS

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Objectives
The risks/benefits of endocrine therapy [tamoxifen/aromatase inhibitors (AI)] for women with breast cancer must be carefully weighed to consider long term outcomes. The objective of this study was to review the risk of cardiovascular disease with endocrine monotherapies for breast cancer in post menopausal women.

Methods
We included randomized controlled clinical trials (RCTs) of women diagnosed with early invasive operable breast cancer. We then searched for RCTs that compared monotherapy of either tamoxifen or AI using MEDLINE and EMBASE databases. As RCTs report their results at different time points, we compared adverse reporting at three defined time periods (less than 3, 3 to 5, and more than 5 years).

Results
Two RCTs, Arimidex Tamoxifen Alone or in Combination (ATAC) and Breast International Group trial (BIG) were identified. These two parent trials resulted in ten subsequent published trial reports. Over 14,000 patients were included in this review. The reported risks of stroke, ischemic heart disease and other cardiovascular events with tamoxifen compared to AI was different between RCTs (See table).

<table>
<thead>
<tr>
<th>Duration of follow-up / Cardiovascular risks</th>
<th>Tamoxifen vs AI - OR[95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ATAC</td>
</tr>
<tr>
<td>First 3 years</td>
<td>2.12[1.38, 3]</td>
</tr>
<tr>
<td></td>
<td>.26</td>
</tr>
<tr>
<td>Between 3-5 years</td>
<td>2.08[1.38, 3]</td>
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<tr>
<td></td>
<td>.15</td>
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<tr>
<td>Over 5 years</td>
<td>1.43</td>
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<tr>
<td></td>
<td>[1.03, 1.99]</td>
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</table>

Conclusions
These discrepancies may be due to differences in adverse outcome capturing, reporting and study populations. Population level data looking at adverse outcomes in breast cancer patients is warranted. This would facilitate informed therapy selection between treatment options.
PATHOGENESIS OF HAND-FOOT SYNDROME INDUCED BY PEG-MODIFIED LIPOSOMAL DOXORUBICIN

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Objectives
PEG-modified liposomal doxorubicin (PEGL-DOX) is an excellent treatment for recurrent ovarian cancer, but frequently results in Hand-Foot Syndrome (HFS). But pathogenesis of HFS have been uninterpreted still now. We report the details of experiments for the purpose of revealing pathogenesis of HFS.

Methods
We prepared HFS rat model and carried out in vivo experiments about skin tissue analysis in rat paws, analysis of expressing cytokines for the purpose of revealing pathogenesis of HFS, and in vitro experiments using HaCaT(derived from human keratinocytes)&Normal Human Dermal Fibroblasts (NHDF) cells to measure DOX toxicity. To test the toxicity in the presence of copper ions, copper chloride were added to DOX media, and the survival rate and the inflammatory cytokines were measured. Finally, to test the degree of inhibition of reactive oxygen species(ROS) by superoxide dismutase(SOD), SOD was added to the medium, and the survival rate was again measured.

Results
Injections of PEGL-DOX yielded an HFS-like disease state. Antibody array showed increased expression of chemokines and cytokines in vivo. DOX and Cu(II) ions increased production of chemokines and cytokines and lowered cell survival rates in vitro, which were rescued by SOD.

Conclusions
We propose that HFS develops due to the combination three primary factors: (1) the inherently strong cytotoxicity of DOX, (2) the ability of PEGL-DOX to remain in circulation for extended periods of time as a PEG-modified liposome, and (3) the abundance of metal ions in the skin tissue. In the future, we plan to develop preventative as well as therapeutic treatments by trapping the ROS.
Poster Presentations: Vaginal and Vulvar Cancer

FDG PET-CT IN PRE-OPERATIVE ASSESSMENT OF VULVAL CARCINOMA. A SINGLE INSTITUTION’S EXPERIENCE OVER FOUR YEARS

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Objectives
Radical vulvectomy and groin node dissection are the mainstay of surgical management and cure of vulval cancer. Groin lymphadenectomy has a significant morbidity and sentinel lymph node (SLN) sampling is emerging as a valid alternative in selected cases. Better radiological prediction of nodal status could be useful in selecting patients for SLN.

Methods
A review of 78 patients with primary vulval cancer over a four year period (2009-12).

Results
Twenty-two patients had PET-CT and surgery. No patient had evidence of disease outside the vulva and groins. Six with FDG-avid lymph nodes had histological confirmation of metastases (5>one node involved). A further six patients with negative PET CT had nodal metastases (4 single, 2 multiple nodes involved). Test sensitivity was calculated at 50%, specificity and positive predictive value both 100% and the negative predictive value at 62.5%. The FDG-avidity of the primary vulval tumour was higher (mean SUV 13.7) in true positive than in false negative cases (mean SUV 3.5) p<0.001.

Conclusions
The sensitivity of PET-CT may be limited by poor FDG avidity in the primary tumours and the negative predictive value limits its potential to spare women the morbidity of groin node dissection. By comparison, the excellent positive predictive value, could select out patients with stage III disease if we had an alternative to the current standard of full lymphadenectomy prior to radiotherapy. Within the limitations of current standard practice the finding of FGD avid groin nodes can only be used to spare the additional cost of sentinel lymph node sampling.
Poster Presentations: Vaginal and Vulvar Cancer

AN EARLY INSTITUTIONAL EXPERIENCE USING INTENSITY-MODULATED (IMRT) RADIATION THERAPY FOR VULVAR CANCER

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Objectives
Despite a lack of data, IMRT is used for vulvar cancer (VC) at many centers. Theoretically, IMRT provides better normal tissue sparing than conventional radiotherapy and can be used to deliver a concomitant radiotherapy boost, decreasing treatment duration. Here we present our experience treating VC with IMRT.

Methods
From 2005 to 2012, 27 patients were treated with IMRT. 67% had FIGO 2009 stage III-IV disease. Treatment rationale varied: 17 patients (63%) were treated at initial presentation, 9 as primary therapy and 8 adjuvantly. 10 patients (37%) were treated for locoregional recurrence. Median dose was 59.4 Gy. 20 patients (74%) received concurrent chemotherapy.

Results
Median follow-up was 28 months. 5 patients (18%) required a treatment break for acute toxicity. Early toxicities included skin effects gr 1-2 (n=18, 67%) and gr 3 (n=8, 30%), and diarrhea gr 1-2 (n=14, 52%). Late toxicities included vaginal stenosis gr 1-2 (n=3, 11%) and gr 3 (n=2, 7%), lymphedema gr 1-2 (n=5, 18%), and radiation necrosis (n=4, 15%). Of 22 patients who got vulvar treatment, vulvar control was 41% at 24 months. When excluding patients treated for recurrent disease, vulvar control was 65%. Of 25 patients who got nodal irradiation, nodal control at 24 months was 78%. 2-year overall survival was 58%.

Conclusions
In this heterogenous population, IMRT resulted in locoregional control rates on par with historical data, and most patients avoided serious toxicity. The low incidence of VC may preclude prospective studies of IMRT; however, our experience provides some rationale for IMRT going forward.
Poster Presentations: Vaginal and Vulvar Cancer

PERSPECTIVES OF PDT OF VULVA DISEASES
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Objectives
One of modern perspective techniques for background and precancer vulva diseases treatment is photodynamic therapy (PDT).

Methods
44 female patients (25-83 years ago) were treated: 15 with vulva lichen sclerosis, 20 with vulvar squamous cell hyperplasia, 9 with high grade vulval intraepithelial neoplasia (VIN II-III). PDT was performed using chlorine-derivative photosensitizer in dose of 1 mg/kg, which was injected intravenously with 200 ml of saline solution during 30 minutes. Laser irradiation was performed under general anesthesia or spinal anesthesia in 2.5-3 hours after injection. In follow-up clinical monitoring, vulvoscopy, cytological and morphologic (biopsy) data were used. 2-year long-term results were analyzed.

Results
Epithelization of the specified areas started in 7-10 days after treatment and finished in 3-4 weeks. Treatment effectiveness was evaluated by clinical results and morphological data. Complete response has been achieved in 13 of 15 female patients with lichen sclerosis, in 17 of 20 cases of vulvar squamous cell hyperplasia and in 7 of 9 female patients with VIN. Partial effect was observed in 2, 3 and 2 cases respectively. In cases of partial effect additional PDT procedures were conducted so that the complete effect was achieved. No cases of complications and side-effects were observed.

Conclusions
PDT being radical but careful is a method of choice for treatment of vulva diseases. Application of PDT for different pathologies requires different regimes of the light irradiation which will allow to obtain optimal functional results, it is the subject of further investigation.
IMPACT OF TRIPLE INCISION VULVECTOMY ON QUALITY OF LIFE AND PELVIC FLOOR OUTCOMES IN WOMEN WITH VULVAL CANCER
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Objectives
Although vulval cancer often necessitates invasive surgical treatment, little is known about the long-term outcomes of surgery. We assessed the impact of surgical treatment for vulval cancer upon a woman's quality of life and bowel, vaginal, urinary and sexual functioning during the first year post therapy.

Methods
Prospective, longitudinal mixed-methods study. At baseline (pre-treatment) and then at routine follow-up every 3 months during the first year post-treatment 23 women completed the EORTC QLQ C30, SF-36 and an electronic pelvic floor assessment questionnaire (ePAQ-PF). Semi-structured qualitative interviews were carried out with 11 of the women.

Results
Mean age was 59.9 years (SD=15.3; range=23.8-86.6yrs). Mean BMI was 30.0 (SD=4.5; range=24.4-38.2). Seventeen of the women had early stage cancer (Stage 1 to 2B) and six women had advanced stage of disease (Stage 3). The questionnaires revealed that general health, role, social and physical functioning, fatigue and pain were significantly worse at follow-up (p = < 0.05). Compared to baseline, women with early stage vulval cancer experienced significantly worse physical functioning and fatigue following treatment. Increase in age and BMI were significantly linked to worse outcomes. Qualitative analysis revealed multiple side effects of treatment including lymphoedema, pain, lethargy, wound infection, and urinary/faecal incontinence which women perceived as severe and enduring.

Conclusions
For women with vulval cancer the impact of surgery appeared to most negatively affect physical functioning and increase fatigue and pain post treatment. Better management of treatment side effects may lead to improvements in quality of life during the first year of treatment.
NON-HPV ASSOCIATED VULVAR DISEASE: CHARACTERIZING AN AGGRESSIVE ENTITY AS A STEP TOWARD IMPROVED MANAGEMENT

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Objectives
Vulvar squamous cell carcinoma (VSCC) may develop through HPV-associated or non-HPV-associated mechanisms. Differentiated VIN (DVIN) is the purported precursor lesion in the latter, with clinical and pathologic differences compared to 'usual type' VIN. We reviewed the pathologic features and clinical outcomes of this less well-understood entity, in order to assess the adequacy of our current management and diagnostic capability.

Methods
10 cases of DVIN without invasive carcinoma and 20 cases of DVIN with adjacent VSCC were identified. Patient characteristics, treatments, recurrence, pathology, immunohistochemistry, and HPV PCR were determined.

Results
DVIN patients were older (75.1 years) non-smokers with normal Pap smear history. The most common pre-surgical diagnosis in both DVIN and DVIN+VSCC group was 'well-differentiated invasive VSCC'. Median lesion size was 4.2 cm with median depth of invasion for cases associated with VSCC measuring 4 mm. 42% of nodal dissections yielded positive nodes. Radical vulvectomy (54%) and wide local excision (46%) resulted in positive margins in 10%. Time to recurrent DVIN or VSCC was short (median 18 months) with 10 deaths in the DVIN+VSCC group over median 3.5 years follow-up. p53 over-expression or complete loss of expression was observed in 71% of cases, p16 expression in only 2 cases (one DVIN or 16.6% tested, one DVIN/SCC or 5.6% tested) but HPV PCR revealed HPV16/18 in an additional 4 cases of DVIN/SCC for overall concordance rate HPVPCR/p16IHC of 75%.

Conclusions
Isolated DVIN is rare, more commonly adjoining VSCC, and rapid recurrence common. Accurately diagnosing non-HPV associated DVIN+VSCC is challenging but there are major prognostic implications that may prompt repeat surgery, adjuvant therapy, or more frequent surveillance.
Electrochemotherapy (ECT) is an attractive treatment for solid cutaneous tumours with a good response rate (55-92%). No studies have evaluated ECT performed in vulvar cancer. The aim of our study was to evaluate the safety, local tumour efficacy and relief of symptoms of ECT treatment in patients affected by recurrence of squamocellular vulvar cancer (V-SCC) unsuitable for standard treatments.

Methods
We enrolled nine patients with histological diagnosis of recurrence of V-SCC. Intravenous Bleomycin was injected under general sedation after an accurate mapping of all lesions and ECT was performed. Patients were reviewed after one, three and six months. Response to therapy was evaluated using RECIST criteria and quality of life was evaluated via questionnaires.

Results
The median age was 84 years (range 80-90 years). The main location of recurrences was the vulva (87.5%). Multiple lesions were present in 25% of cases. No peri-operative complications were observed. Response to therapy was complete in 62.5% of patients, partial in 12.5%, no change was observed in 12.5% and progression of disease in 12.5% of patients respectively. Evaluation of symptoms showed a significant reduction of pain (p<0.03), bleeding (p<0.04), odour (p<0.04) and urinary discomfort (p<0.04). We observed two relapses at four and seven months after treatment. After nine months fifty percent of patients were alive.

Conclusions
Our preliminary study showed that ECT is a suitable procedure in elderly patients with loco-regional vulvar cancer relapses. ECT can be used as palliative therapy and the treatment relieves symptoms and improves quality of life.
EFFECTIVENESS OF CO2 LASER VAPORIZATION IN THE TREATMENT OF VAGINAL INTRAEPITHELIAL NEOPLASIA

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Objectives
To review a large cohort of patients with vaginal intraepithelial neoplasia (VAIN) and to evaluate the outcomes of treatment with CO2-laser vaporization.

Methods
291 patients were diagnosed with VAIN at Sant’Anna Hospital of Turin, from 1995 to 2011. A retrospective chart review was performed. Primary outcomes were VAIN recurrence and progression to invasive vaginal carcinoma.

Results
Among 291 patients 285 (98%) were treated with CO2-laser vaporization; among them 110 were VAIN 1 (38.6%), 136 VAIN 2 (47.7%) and 39 VAIN 3 (13.7%). The median age was 38 years (range 14-76); 18 (6.3%) patients underwent a hysterectomy before the diagnosis of VAIN. VAIN-CIN and VAIN-VIN were associated in 231 (81%) and 9 (3%) women, respectively. Median follow up was 60 months (range 8-204). 71 out of 285 (25%) patients had a VAIN first recurrence. In particular 22% of VAIN1, 27% of VAIN2 and 26% of VAIN3 relapsed. Median time to first recurrence was 7 months for VAIN1, 6 for VAIN2, and 4.3 for VAIN3. 61 out of 71 women were submitted to a second CO2-laser application. 23 patients developed further VAIN recurrences and 11 of them were submitted again to CO2-laser vaporization. 260 (91%) laser treated patients are free from VAIN at follow-up, 14 (5%) have a persistence of VAIN; any patients progressed to invasive vaginal carcinoma.

Conclusions
CO2-laser vaporization is an effective treatment of VAIN, but careful, long term follow up is needed for these women because VAIN often recurs; most of recurrences can be successfully laser retreated.
THE IMPACT OF THE SELF-MANAGEMENT INTERVENTION ‘WOMAN-PRO II PROGRAM’ ON SYMPTOM PREVALENCE OF PATIENTS WITH VULVAR NEOPLASIA: A MIXED-METHODS STUDY-PROTOCOL

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Objectives
In vulvar neoplasia (VN), surgical interventions cause multiple symptoms, distress, complications, and influence the quality of life of affected women and health care costs negatively. Symptoms and symptom distress can be reduced by providing adequate treatment. This study aims to test the impact of standardized care and the WOMAN-PRO II program on symptom prevalence in women with VN after surgical treatment.

Methods
In this sequential explanatory mixed-methods project, a randomized phase II study will be followed by a qualitative sub-study. Ninety patients with VN and treated surgically will be recruited in six hospitals in Switzerland, Austria and Australia. Patients will be randomly assigned to standardized care or the self-management intervention WOMAN-PRO II program, which includes counselling sessions of specially trained gynaecology-oncology nurse specialists. Counselling and quantitative data collection of both interventions will take place at six predefined points of time between diagnosis and week 24 following surgery.

Results
The primary outcome is symptom prevalence. Secondary outcomes will be collected for explorative reasons (i.e. distress, quality of life, and costs). Mixed linear regression analysis will be used for quantitative data analysis. Twenty interviews with women who received the WOMAN-PRO II program and a focus-group interview with the gynaecology-oncology nurse specialists will be conducted. Qualitative data will be analysed by using thematic analysis and critical hermeneutic reflection.

Conclusions
This study will evaluate the impact of the WOMAN-PRO II program on symptom prevalence, patient-reported outcomes and clinical parameters, and inform the design of a possible phase III study on the clinical efficacy of the program.
SUBTYPES OF CYTOTOXIC LYMPHOCYTES AND NATURAL KILLERS INFILTRATING CANCER NESTS CORRELATE WITH PROGNOSIS IN PATIENTS WITH VULVAR SQUAMOUS CELL CARCINOMA.

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Objectives
We have already revealed that adaptive immune effectors (CD8+ and CD4+ lymphocytes) do not influence the prognosis in vulvar squamous cell carcinoma (vSCC). Therefore, we tried to clarify the prognostic role of innate immunity and granzyme B dependent cytotoxicity as defined by intratumoral infiltrates of T lymphocytes and natural killer cells (CD56+ and expressing granzyme B + [GrB+]).

Methods
We analyzed 76 primary vSCCs and 35 lymph node metastases obtained from 76 patients with full clinical history. Distribution and density of GrB+ and CD56+ cells within cancer tissue were evaluated by immunohistochemistry and correlated with clinicopathological features, commonly recognized prognostic factors as well as the overall survival (OS).

Results
We analyzed infiltration of immune cells within cancer nests (intraepithelial infiltration). Intensity of intraepithelial (IE) GrB+ cells within primary tumor was inversely correlated with age ($r = -0.333$, $p = 0.004$) and positively correlated with tumor grade ($r = 0.304$, $p = 0.009$), while intensity of IE CD56+ cells at primary site was correlated with depth of invasion ($r = 0.339$, $p = 0.003$) and risk of recurrence ($r = 0.295$, $p = 0.011$).

The median OS was 41.16 months (range 1.7-98.43). High IE GrB+ infiltrates predicted longer OS among patients without metastases ($p = 0.028$). High IE CD56+ infiltrates were correlated with longer OS in patients with metastatic dissemination ($p = 0.0019$).

Conclusions
IE GrB+ infiltrates indicating combined cytotoxicity of adaptive and innate immune effectors predict longer OS among vSCC patients with local disease. The mechanism of the suggested protective role of IE CD56+ infiltrates at primary site in metastatic cases requires further investigation.
Poster Presentations: Vaginal and Vulvar Cancer

CDKN2A (P16) AND HRAS ARE FREQUENTLY MUTATED IN VULVAR SQUAMOUS CELL CARCINOMA
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Objectives
Vulvar cancer develops through two different etiologic pathways. The first is associated with HPV-infection and the second with lichen sclerosis and mutations of the TP53-gene. Studies on other somatic mutations in vulvar cancer are limited. Here we investigated the prevalence of genetic mutations in 100 vulvar squamous cell carcinomas (VSCC).

Methods
One-hundred paraffin embedded tissue samples of VSCCs were tested for HPV-infection, sequenced for TP53 exon 5-8 and screened for mutations on 12 different genes (BRAF, CDKN2A(p16), CTNNB1, FBXW7, FGFR2, FGFR3, FOXL2, HRAS, KRAS, NRAS, PIK3CA, and PTEN), using a MALDI-TOF (Matrix Assisted Laser Desorption – Time of Flight) based oncologic mutation panel.

Results
Mutations were detected on 6 different genes. Of one-hundred VSCCs, 58 tumours contained at least one mutation. Forty-three tumours harboured mutations on TP53, 12 on HRAS, 11 on CDKN2A, and 6 on PIK3CA. CTNNB1 and KRAS were mutated in 1 patient each. Eighteen patients were hr-HPV positive, with only one having a somatic mutation (TP53). Five-year disease specific survival was worse for mutated patients (63% vs 87%, p=0.003), which is greatly affected by the poor survival in HRAS-mutated patients (37% vs 78% p=0.001). After multivariate analysis, the risk of disease specific death was higher in patients with any somatic mutation (HR 3.3, 95%CI 1.1-10.2).

Conclusions
Somatic mutations were detected in 58% of VSCCs. HPV-infection and TP53-mutations play a key role in the development of VSCC, but CDKN2A(p16), HRAS and PIK3CA mutations are also frequently seen in HPV-negative patients. Patients with somatic mutations, and especially HRAS-mutations, have a significantly worse prognosis than non-mutated patients.
STRUCTURAL EQUATION MODELING - TOOL IN ASSESSING EXPECTATIONS OF PATIENTS TREATED FOR OVARIAN CANCER IN A ROMANIAN TERTIARY CANCER CENTER.

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⁵Gynecologic Oncology, Charite, Berlin, Germany

Objectives
The primary goals of this study were to argue with more powerful statistical and analysis instruments concrete associations, dependencies and correlations between expectations with regard to the physician–patient communication and treatment management. The working hypothesis, based on literature data and empirical observations from a tertiary cancer center in Romania is that there is an association between three factors (physician’s evaluation by the patient, the result of therapy (from the perspective of patient) and the need for changes in treatment (from the perspective of patient)), which loops the doctor – patient relationship and treatment approach.

Methods
We used the responses to the questionnaire entitled: Expression OVAR III, an European-wide survey on the internet or on hard-copies among patients diagnosed with ovarian cancer and for data analysis: Mplus and LISREL v.3.0 (Student) v.8.8.

Results
108 patients treated for ovarian carcinoma answered the questionnaire. 73.8% of patients scored 9 or 10 (out of 10) when assessing the therapy’s success. The most efficient and patients’ needs-oriented source of information is considered to be the treating doctor (87%). The empirical observations that came out of the descriptive statistics were once more confirmed using the confirmatory factor analysis (CFA). Our hypothetical models were tested using structural equation modeling (SME).

Conclusions
This study underlines the key role of the physician as the main point of contact for patients with ovarian cancer. The physician’s role is essential not only as a source of information about the disease and various treatment options but also in coping with the disease.
MANAGEMENT OF TOTALLY IMPLANTABLE VENOUS ACCESS PORT DRUG EXTRAVASATION: RETROSPECTIVE EXPERIENCE OF A CANCER CENTER.

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Objectives
Widely used in oncology, totally implantable venous access ports (TIVAPs) are essential in delivering chemotherapies. Nevertheless, TIVAPs are subject to complications that not only can be severe, but can also delay treatment. Data concerning drug extravasation (DE) in this context is scarce. We aimed to determine DE management in our center.

Methods
Thirty patient files having presented one or multiple DE were retrospectively reviewed.

Results
33 events (age 47.6 [1–79]; BMI 24.9 +/- 6.2; 21 women) were identified from February 2007 till February 2013. Delay between TIVAP insertion and its first use was 12.3 +/- 9.6 days, and was 372 +/- 748.6 days between insertion and DE. The majority of implicated agents were vesicants (51.5%). 45.5% were irritant type agents and 3% non-vesicant. We reported one intra-pleural DE. Needle malposition was identified in 24.4% of cases. Surgical exploration was undertaken in 97% of cases, in the first 24 hours (90.6%). Surgical lavage and extraction of TIVAPs was realized in 87.5% and 53.1% of times respectively. 5 patients (age 55.2 [44–69]; BMI 30.3 +/- 5.1) were subject to surgical re-intervention for unsatisfying local outcome (mean delay 33 days [8-58]). Vesicant agents (3 cases) or oxaliplatin (2 cases) were implicated. Skin graft was necessary in one of those cases. Local outcome was always satisfying.

Conclusions
Symptom aggravation is a possibility after acute DE, hence regular and repeated clinical surveillance. Oxaliplatin acted like a vesicant agent. Personnel's training is essential for prevention and successful management of DE.
Poster Presentations: Miscellaneous

OUTCOME OF THE SURGICAL MANAGEMENT OF BOWEL OBSTRUCTION IN WOMEN PREVIOUSLY TREATED WITH ABDOMINAL/PELVIC RADIOTHERAPY FOR GYNAECOLOGICAL MALIGNANCY

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Objectives
Bowel obstruction (BO) in previously irradiated gynaecological cancer patients may be due to radiation effects on the bowel or recurrent disease or both. We report our experience in the surgical management of 52 consecutive patients.

Methods
Data were collected for all women who had surgery for BO post radiotherapy from November 1987 to April 2013. We exclude from this series women who had surgery for intestinal fistula(e).

Results
55 laparotomies for 52 women. Median age at surgery 51 years (30–80). Median time from completing radiotherapy to surgery 12 months (range 3 days – 290 months). 26 (47%) did not have relapsed disease.

<table>
<thead>
<tr>
<th>Surgical findings and procedures</th>
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<tbody>
<tr>
<td>Bowel perforation</td>
<td>0</td>
</tr>
<tr>
<td>Ischemic bowel</td>
<td>2</td>
</tr>
<tr>
<td>Recurrent disease</td>
<td>29</td>
</tr>
<tr>
<td>Bowel resection</td>
<td>22</td>
</tr>
<tr>
<td>Bypass procedure</td>
<td>23*</td>
</tr>
<tr>
<td>Mucous fistula</td>
<td>10</td>
</tr>
<tr>
<td>Colostomy</td>
<td>12**</td>
</tr>
<tr>
<td>Ileostomy</td>
<td>9</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>12</td>
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<tr>
<td>Jejunostomy</td>
<td>9</td>
</tr>
</tbody>
</table>

* 4 also had bowel resection
** Additionally 4 had previous colostomy

Median post-operative stay was 22 days (range 2 – 195). Successful palliation (adequate oral intake at least 60 days postoperatively) was achieved in 35 of the 44 (80%) women for whom data were available. There were 11 Clavien Grade III – IV post-operative complications within 30 days, including 1 death on day 2. After median FU of 7.5 months (range 1–208), 14 of the 52 women are alive, 12 free of disease.

Conclusions
Prior radiotherapy poses specific surgical challenges in bowel obstruction, which was relieved in 80% with acceptable mortality and morbidity rates. Almost 50% did not have relapsed disease as cause of obstruction.
FEASIBILITY OF ROBOTIC EXTRAPERITONEAL PARAAORTIC LYMPHADENECTOMY FOR GYNECOLOGIC CANCER.

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Objectives

Robotic surgery has been developed in gynaecological oncology for several years now. Difficult surgical procedures associated with long learning curve may appear to be a good indication of this technique. The aims of our study were to describe the technique, the feasibility and the results of robotic extraperitoneal paraaortic lymphadenectomy.

Methods

Prospective evaluation of consecutive patients undergoing robotic extraperitoneal paraaortic lymphadenectomy using the Da Vinci system. Extrapertoneal paraaortic lymphadenectomy was performed using a similar surgical technique as previously described by laparoscopy. The procedure was carried out using four port sites: one for the camera, one each for the no. 1 and no. 3 arms of the Da Vinci robot system, and one for the assistant.

Results

Fifteen patients were included in the study (10 cervical and 5 endometrial cancers). The robot-assisted procedure was completed in all patients except two (pneumoperitoneum leakage, and bad trocar position). Five patients with endometrial cancer had a transperitoneal bilateral pelvic lymphadenectomy and hysterectomy, and 1 patient with advanced cervical cancer had anterior pelvectomy. The median age of patients was 56 [42-65] and BMI 24.3 [21.3-26.1]. The median operating time was 240 min [165-300]. The median number of paraaortic lymph nodes removed was 19 [8-25], the decrease in haemoglobin was 1.2 g/dL [0.95 -2.4] and the hospital stay was 5 days [3.5-6.5]. There was one intraoperative (bilateral pneumothorax) and three postoperative complications (desaturation, blood transfusion, sepsis on digestive fistula).

Conclusions

Robotic-assisted extraperitoneal paraaortic lymphadenectomy carried out using the Da Vinci system appears feasible and safe.
INTRAOPERATIVE CELL SALVAGE IN WOMEN WITH SUSPECTED OR KNOWN GYNAECOLOGICAL MALIGNANCY: RESULTS OF FEASIBILITY STUDY

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Objectives

Intraoperative cell salvage (IOCS) involves the return of autologous erythrocytes to the bleeding patient. Despite potential to minimise the known morbidity of allogeneic transfusion, the use of IOCS in gynaecological oncology remains limited. We aimed to assess the feasibility of IOCS in patients undergoing laparotomy for known or suspected gynaecological malignancy at the Royal Cornwall Hospital, Truro.

Methods

We retrospectively evaluated cases of laparotomy for suspected gynaecological malignancy. Criterion for IOCS was anticipated haemorrhage exceeding one litre. Endpoints included haemoglobin difference, postoperative iron use, hospital stay and postoperative complication rate. Age, ASA grade, estimated blood loss (EBL), and operative duration were also recorded. Baseline morbidity was compared using a validated measure (surgical APGAR). Data are reported as median and range throughout.

Results

63 patients underwent laparotomy (suspected cancer of ovary, endometrium, vagina, and cervix). 17 received IOCS and 6 postoperative allogeneic transfusion. 20 oncological patients remained untransfused and 20 had benign histology. Age, ASA status, and surgical APGAR were similar in oncological patients. IOCS patients had equivalent EBL to allogeneic recipients (p=>0.05). Operative time was similar amongst transfused groups (IOCS 210 minutes (90-390) vs. donor 278 minutes (240-360); p=>0.05). EBL was positively correlated with operative duration in IOCS patients (Spearman’s R 0.48; p=<0.05). Postoperative haemoglobin concentrations were equivalent in transfused groups (IOCS -1.6 (-3.7 to +2.1) vs. donor -1.7 (-2.4 to +2.3); p=>0.05). There was no difference in early postoperative complication rate or iron use (p=0.76 and p=0.56 respectively). IOCS recipients were discharged earlier than allogeneic patients (p=0.02).

Conclusions

IOCS appears a feasible and effective alternative to allogeneic donor transfusion in patients with gynaecological cancer.
Poster Presentations: Miscellaneous

LEIOMYOSARCOMA OF THE RIGHT ILIAC VEIN PRESENTING AS A PELVIC MASS: A CASE REPORT
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Objectives
Leiomyosarcoma of the iliac vein is a very uncommon tumor, sometimes presenting as a pelvic mass. Prognosis is usually poor and the best treatment is unknown. Radical excision appears to offer the best chance of cure, while the possible benefits of adjuvant therapy have not been proven.

Methods
A 74-year-old woman had right leg edema. Venous color doppler was normal. Abdominal ultrasound and magnetic resonance scanning demonstrated a mass of 70 mm in the right pelvis with a well-defined profile, not homogeneous after contrast enanchement. The lesion was in close contact with the iliac vessels and the right iliac vein profile was incorporated in the mass. Computed tomography of upper abdomen didn't show metastatic lesions. Serum markers were in the normal range.

Results
The patient underwent an exploratory laparatomy by a team of gynaecologic oncologists for the suspicion of ovarian cancer, but a retroperitoneal tumor of the wall of right common iliac vein and external iliac vein was found. With the help of a vascular surgeon the tumor was resected en bloc and polytetrafluoroethylene grafts were used to reconstruct the vessels. Postoperative course was uneventful. At histological examination a leiomyosarcoma of the iliac vein was found. The patient received adjuvant chemotherapy. No signs of recurrence or postoperative complications were detected 14 months after surgical resection.

Conclusions
Leiomyosarcoma of iliac vein is a rare option to consider in the management of a pelvic mass. Radical surgical excision with polytetrafluoroethylene grafts reconstruction followed by adjuvant chemotherapy was feasible and effective.
THE DANISH GYNECOLOGIC CANCER DATABASE (DGCD). A NATIONWIEDE CLINICAL DATABASE IN GYNECOLOGICAL CANCER.

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Objectives
To present implementation, use and success of the clinical nationwide Danish Gynecological Cancer Database (DGCD) for quality control and research.

Methods
January 2005 DGCD was launched in Denmark. Hospitals connect through Virtuel Private Network (VPN). DGCD may function as an electronic patient file with datafiles for history, findings at admission, staging, operation, nursing, complications, pathology, oncology, follow up and survival.

It is compulsory to register gynecologic cancer patients. Missing patients are recorded by linkage to the Pathology register and the administrative National Patient Register. Lists with missing patients are quarterly mailed to departments.

A SAS outdata system is part of DGCD and gives possibility to withdraw time close data and reports for own statistics. The DGCD secretariat can withdraw national data and statistics. The civil registration number (CPR) gives possibility to connect to other registers including the Danish Cancer Biobank.

Results
Extensive year reports are published. In the 2011 year report 12,959 patients were presented with an average coverage on 96.8% and data completeness on 93.1%. Distributions in age, ASA, BMI, other diseases and stages were as expected when stratified for cervical-, ovarian- and endometrial cancer. Ovarian cancer was reported for 3067, peritoneal 313, tubal 197 and borderline tumors 1114 patients. Total 2467 had cervical, 4718 endometrial cancer and 463 hyperplasia with atypia.

Several quality, research and PhD studies are based in DGCD.

Conclusions
DGCD is a national success and gives tremendous possibilities for quality control and research.
OBJECTIVES
Through Danish CancerBiobank (DCB) to ensure collection of blood and tissues optimal for translational research from all patients diagnosed with primary cancer.

METHODS
The infrastructure was established through the Departments of Pathology and Departments of Clinical Biochemistry at the six University hospitals in Denmark. All departments agreed on national technical recommendations. A national on-line database was established to registry information such as pre-analytical factors, laboratory procedures and verification of the diagnosis of the collected tissues. The database is linked to the national pathology register (http://www.patobank.dk/) and the data can be combined with Danish clinical databases and other registers relevant for research.

RESULTS
DGC was implemented in January 2010. In 2012 biological materials from 9,609 patients have been collected, a total of 11,121 blood samples and 6,814 tissue samples equivalent to a 30% coverage of all patients with primary cancer. From 3,056 tissue samples a corresponding blood sample was collected. A twofold increase of material collected is observed from 2010 to 2012. Today DCB is responsible for collecting biological materials for 35 research projects.

CONCLUSIONS
The DCB is unique nationally and internationally, due to: 1) National recommendations for handling of biological materials 2) Centralized nationwide data registration 3) Information of both blood and tissue for the single patient 4) Connection to the final diagnosis through Patobanken and 5) Connection to the nationwide clinical databases and other national registries. The success for DCB will be translational research results of clinical importance for cancer patients.
STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR GYNAECOLOGICAL MALIGNANCY: INITIAL EXPERIENCE AND RESULTS

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²Department of Physics, The Royal Marsden NHS Foundation Trust, London, United Kingdom

Objectives

The Cyberknife radiosurgery system delivers highly conformal radiation and may be useful for treating disease related to gynaecological malignancy, particularly in sites of previous irradiation or isolated relapse which pose a challenging clinical problem.

This study reviews the indications, toxicity and early efficacy data of patient’s receiving Cyberknife SBRT for gynaecological malignancy at our institution.

Methods

Cases receiving Cyberknife SBRT to gynaecological targets were retrospectively identified. Details on primary site, SBRT target and previous irradiation were obtained from patient electronic records. Radiotherapy toxicity was graded using CTCAE v4.0. Follow up consisted of clinical examination, tumour marker evaluation and radiological assessment. In-field local control and time to progression were calculated from the day of completing SBRT until the date of radiological evidence of progression using standard RECIST criteria.

Results

14 patients were treated from 08/2011-04/2013. Median age was 61 years (range 26-76). Primary sites included cervix, endometrium, vagina and ovary. Sites for SBRT were cervix (2), lymph nodes (5), vagina (2), spine (1) and pelvic side wall (4). 7 patients were reirradiated (median previous dose 50.4Gy), 3 received SBRT as a boost after conformal RT.

Median follow up was 9 months (range 1-20). Acute toxicity was minimal: 71% G0, 14% G1, 14% G2 (pain during SBRT). No late toxicity has been experienced. Local control is 93%, a single patient experienced in-field relapse at 17 months. 21% (3/14) have relapsed at distant sites, time to relapse 3-17 months.

Conclusions

A variety of gynaecological targets are suitable for SBRT which has limited toxicity and promising early results.
Objectives
Innovations often increase the cost of medical strategies without radically improving the outcome. Robotic techniques are known to be expensive, but may lead to decrease hospitalization costs, and improve patient’s related outcomes. In this context, the ultimate benefit for society remains to be established.

Methods
The objective of this study was to compare the costs, pain and satisfaction in patients treated with conventional laparoscopy (n=226) vs robotic-assisted laparoscopy (n=80). This study was multicentric. Costs were calculated using the micro-costing method. We analyzed robot-specific direct costs, operating room costs and hospitalization costs.

Results
Given an average of 165 cases performed a year with the robot, robot-specific costs represent 2,213€ per intervention, and robot-specific surgical supplies represent 957€ per intervention. The surgical supplies specific to conventional laparoscopy amount to 1,432€, which is significantly higher than robotic supplies (p<0.001). Hospitalization costs was decreased for the robotic strategy (2,380€ vs 2,841€, p<0.001) due to a reduced time spent in the intensive care unit (0.38 days vs 0.85 days). Operative room costs were higher for the robotic strategy (1,490€ vs 1,311€, p=0.0004) because of an increased length of procedure (4.98h vs 4.38h).

Conclusions
The most important driver of additional cost is the fixed cost of the robot. This cost was not overcome by reduced room costs. Efficiency of the robot would be higher if the number of cases per year was increase or if the purchase price of the robot was reduced. A shorter learning curve may also allow for a decrease of operative room costs.
ROLE OF INTRAOPERATIVE RADIATION THERAPY (IORT) IN THE MANAGEMENT OF PATIENTS WITH RECURRENT GYNAECOLOGICAL CANCER

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²Department of Radiation Oncology, University Clinic of Freiburg, Freiburg, Germany

Objective
The aim of this retrospective analysis was to evaluate the contribution of IORT to the management of patients with recurrent gynaecological cancer.

Methods
Between 2005 and 2012, 31 women with localised recurrence of a gynaecological cancer were eligible for tumor resection in combination with IORT. The median age was 62 years.

Results
Surgery consisted of local tumor excision, extensive tumor resection, exenteration, lymphnode dissection or radical vulvectomy. 19 patients were treated with IORT with a median dose of 15 Gy (range 8-18 Gy). The most common target of the IORT was the pelvic sidewall. In 12 patients we did not apply the planned IORT due to complete tumor resection, an extensive non resectable tumor burden or the risk of complications. After tumor resection 9 patients received external beam radiotherapy, 5 patients received chemotherapy and two patients anti-hormonal treatment. For 12 patients no further therapy was necessary after surgery. Follow-up was 14 months (range 1-65), progression free survival 5 months (3-14). IORT was tolerated without severe side-effects.

Conclusions
In carefully selected patients IORT and cytoreductive surgery contributed to local control and disease palliation. The combined approach appeared to be especially suitable for women who received prior conventional radiotherapy and were therefore not eligible for further external beam treatment. Because of the small cohort and subsequent third and fourth line therapies efficacy data for IORT cannot be provided. In some cases, however, IORT may have prolonged the progression free interval and may therefore have delayed the necessity for further treatment.
Poster Presentations: Miscellaneous

IS ROBOT-ASSISTED SURGERY A SAFE ALTERNATIVE FOR MORBID OBESE PATIENTS IN A GYNAECOLOGIC POPULATION?
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Objectives
Minimal invasive surgery offers many advantages over open surgery for gynaecologic patients and has become standard procedure for several indications. The last decade there is also an increase in the use of robot-assisted laparoscopy. Robotic-surgery still has high costs compared to conventional laparoscopy, but may be beneficial to morbid obese patients. The prevalence of obesity is increasing and obesity is a well-known risk factor for per-operative and post-operative complications. Furthermore, the rate of conversion from laparoscopy to laparotomy is increased in an obese population. We investigated whether robot-assisted surgery is a safe alternatives for obese gynaecologic patients.

Methods
All patients undergoing robot-assisted gynaecological surgery between 2007 en 2011 in our hospital were eligible. Procedures were performed with the daVinci® Surgical System. Conversion rate, blood loss, length of surgery, adverse events and admission time were collected and analysed.

Results
Of 89 women undergoing robot-assisted surgery, 35 patients had a BMI of ≤ 25.0 and 29 patients had a BMI > 30 kg/m². In the (morbid) obese group no conversions occurred. Total blood loss and length of surgery were not significantly different between groups. Also, incidence of adverse events and admission time (4.6 vs 3.6 days p=0.244) were comparable.

Conclusions
In our (morbid) obese patients, robot-assisted surgery was shown to be a safe procedure. Because conversion to open surgery did not occur, this was not further increasing costs like in conventional laparoscopy. RCT's including cost benefit analyses need to confirm optimal minimal invasive approach and patient selection.
MANAGEMENT OF INTRAVENOUS LEIOMYOMATOSIS WITH INTRACARDIAC EXTENSION: CLINICAL ANALYSIS OF 11 CASES

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Objectives
To report the results of surgical management of intravenous leiomyomatosis with intracardiac extension at Peking Union Medial College Hospital.

Methods
We reviewed a cohort of 11 patients with intravenous leiomyomatosis extending to the right heart chambers, focusing on the clinical characteristics, the results of surgical management, and prognosis.

Results
The mean age of the patients was 41.2± 6.0 years. The clinical manifestations of intravenous leiomyomatosis are various and nonspecific, including pelvic mass, exertional dyspnea, palpitation, swelling in the lower extremity, abdominal distension, syncope and skelalgia. All the patients had history of uterine leiomyoma and 10 patients (90.9%) had undergone uterine leiomyoma operation. Preoperative image findings showed that all the tumors originated from gonadal or iliac veins and extended into right cardiac chambers through inferior vena cava (64% in right atrium alone, 36% in both right ventricle and atrium). After careful preoperative evaluation, one-stage surgical removal of intracardiac, intracaval and pelvic tumors were successful performed in 3 patients and two-stage operation in 8 patients. All operations were performed without severe surgical-related complications or death. Eight (72%) patients received hormone therapy postoperatively. Follow-up was 100% complete at a mean of 37.8 months. Pelvic tumor recurrence occurred in one patient (9%) but the patient survived and no reoperation was required.

Conclusions
Intravenous leiomyomatosis with intracardiac extension should be considered in a female who presenting with an extensive mass from inferior vena cava into the right-sided cardiac chambers. Full-scale preoperative evaluation, complete tumor resection, and multidisciplinary cooperation are crucial for successful treatment.
MITOCHONDRIAL DNA GENOTYPING: A NEW TOOL FOR SYNCRONY CANCER DETECTION

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Objectives
Simultaneous independent primary tumors of the female genital tract occur in 1–2% of gynecological cancer patients, 50–70% of which are synchronous tumors of the endometrium and ovary. Guidelines for determining the nature of simultaneously detected tumors, based on surgical and histopathological findings, are often ambiguous and may require further molecular analyses. Such approach is necessary to indicate correct prognosis and hence treatment. We demonstrated on a previous case report the role of mitochondrial DNA (mtDNA) sequencing in a woman with a suspected synchrony. Based on this data, we want to demonstrate how the use of mtDNA screening for diagnosis of synchrony in simultaneously diagnosed endometrial and ovarian carcinoma can be informative when the usual guideline approaches were unsuccessful.

Methods
We performed histopathological, canonical molecular analysis (microsatellite instability and β-catenin immunohistochemical staining) and mtDNA sequencing in 11 samples of women with suspected synchronous endometrial and ovarian cancer.

Results
Microsatellite instability and β-catenin immunohistochemical staining were informative in 2/11 (18%) and in 0/11 (0%) analyzed cases, respectively. On the opposite, mitochondrial analysis was informative for metastatic/synchronous disease in 5/11 (45%) cases. In particular, in these 5 women the histopathologic diagnosis indicated 3 synchronous tumors and 2 metastatic disease, while the mtDNA analysis everted the diagnosis in 3 cases from synchronous to metastatic cancer.

Conclusions
Mitochondrial DNA sequencing may provide a cheap and useful contribution to indisputably recognize the synchronous nature of simultaneously detected endometrial and ovarian carcinomas. This molecular tool could drastically change the final staging and clinical management for these patients.
FREQUENCY, CLINICAL PATTERN AND OUTCOME OF PERIOPERATIVE VENOUS THROMBOEMBOLISM WITH GYNECOLOGIC DISEASES

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Objectives
A venous thromboembolism (VTE) is prevalent in patients with gynecologic malignant diseases. The aim of this study was to identify risk factors for perioperative VTE in gynecologic disease patients.

Methods
We analyzed 1,756 patients who underwent laparotomy at Kumamoto University Hospital between January 2007 and December 2011. All clinical and pathology records were reviewed. We have comprehensively investigated incidence, clinical pattern and outcome and also detected risk factors for VTE in association with gynecologic disease.

Results
Of the cases we examined, VTE was identified in 23 (1.3%). Pulmonary embolism (PE) was also seen in 18 (1.0%). Among the patients of VTE, twenty patients (87.0%) had gynecologic malignancies and three patients (13.0%) had benign diseases. The incidence of VTE was higher in patients with ovarian cancer than in those with other gynecologic diseases. In ovarian cancer patients, multivariate analysis revealed that an age≥55 years, BMI≥25kg/m², D-dimer≥1.5µg/ml and clear cell adenocarcinoma were independent risk factors for VTE. The patient numbers of pre- and post-gynecologic surgery were 12 (54.5%) and 10 (45.5%), respectively.

Conclusions
In this study, we suggested that VTE is frequently encountered in the preoperative period of gynecologic disease. Preoperative VTE-screening should be performed to prevent life-threatening complication in the gynecologic field, especially when patients have risk factors such as older age, higher BMI, D-dimer≥1.5µg/ml, and clear cell adenocarcinoma.
Poster Presentations: Miscellaneous

TRABECTEDINE TREATMENT IN ADVANCED GYNECOLOGICAL CANcer – EXPERIENCE AND RESULTS
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Objectives
Trabectedine is used for the treatment of relapsed advanced gynecological cancer. In this study we analysed the response rate and incidence of side effects of Trabectedine used in palliative treatment setting in non-selected patients.

Methods
Retrospective descriptive analysis using data of 26 non-selected patients undergoing palliative Trabectedine treatment of advanced gynecological cancer in two gynecological oncology units 01/2010 -03/2013. Trabectedine therapy was given at least as a 2nd-line therapy (mono-/combination therapy).

Results
113 therapeutic cycles were evaluated; mean follow-up time 481 days +/-218 (16 months +/-7,2). Administration of all planned 6 cycles (complete response 47,8%): 11/23 of the total(T); ovarian cancer patients(OC): 6/16 (37,5%). Without progression to date: 3/23 pat. (11,5%, mean follow-up time 282 days=9,4 months).

Tumor progression during treatment(partial response > 3 cycles n=4): T: 12/23 patients(52%), OC 10/16 pat.(62,5%). Overall response (complete and partial) 65,2%(15/23)
Reinduction therapy: Platinum therapy administration after progression during treatment 6/11(54,5%). Reinduction therapy after complete response 7/12(63,6%)
Median time to progression (TTP): T: 185 (+/-120) days (=6mo +/-4), OC: 230 (+/- 146) days (=7,6mo +/-5). 2nd line therapy: 229 (+/-154) days, 4th line therapy: 146 (+/- 75) days.
Side effects: severe neutropenia (G3/G4): 5/26 pat.(19,2%), thrombocytopenia (G3/G4) 3/26 pat.(11,5%), sepsis (n=1), sepsis of port-a-cath (n=1), duodenal fistula (n=1)
Discontinuation of therapy after one cycle 3/26 patients(11,5%). Dose reduction in 7/23 patients(30,4%).

Conclusions
Irrespective of the previous treatment Trabectedine shows good response rates and acceptable toxicity in patients with advanced gynecological cancer. Reinduction of therapy was possible in most patients.
THE RISK FACTORS FOR DEVELOPING ANAL HPV INFECTION IN WOMEN WITH CIN 2+
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Objectives
About 90% of anal cancers are associated with the human papillomavirus (HPV) infection. The aim of our study was to describe the risk factors for development anal HPV infection in HIV-negative women treated for high-grade cervical intraepithelial neoplasia (CIN 2+).

Methods
Altogether 272 women were enrolled. The study group included 172 women who underwent conization for CIN 2+. The control group consisted of 100 women with non-neoplastic gynecologic diseases. All participants completed a questionnaire detailing medical history and sexual risk factors and were subjected to the anal and cervical HPV genotyping using Cobas HPV test.

Results
Concurrent cervical and anal HPV infections were detected in 42.4 % women of the study group, and in 8.0 % women of the control group. This subgroup (n=73) reported significantly more occasional contact with anus according to reference group with no contact (OR 2.62; p=0.008) and common contact with anus (OR 1.96; 95 % CI: 1.02-3.73, p=0.049). Any frequency of anal contact (occasional and common) was significant (OR 2.43; p=0.010) in contrast to practising of anal intercourse (OR 1.54; p=0.176). Other evaluated risk factors (smoking, autoimmune disease and/or condylomata acuminata, early sexual debut, high number of sexual partners, unprotected vaginal coitus, practising of anal coitus) did not reach level of significance.

Conclusions
Anal high-risk HPV infection is significantly more frequent in women with CIN 2+. Any type of contact with anus with any frequency is showed as an important risk factor for concurrent cervical and anal infection among patients with CIN 2+. 
THE QUALITY OF ONLINE CONSUMER INFORMATION ON GYNAECOLOGICAL CANCERS

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Objectives
With the growing access to the WWW, Internet has become an important source of consumer health information. However, in the absence of a uniform system of quality control, the information provided may not always be reliable. The aim of this study was to assess the quality of information about symptoms, signs, and treatment for gynaecological cancers using validated instruments.

Methods
Using the Alexa Rank, 35 most frequently visited sites referring to 7 types of gynaecological malignancies were chosen for quality assessment. They were categorised according to affiliation, specialisation, content type and checked for the presence of the Health on the Net (HON) seal. The quality of information was evaluated using 3 instruments: the Flesch Reading Ease Score, the JAMA benchmarks and the DISCERN instrument.

Results
Only 25.7% of the websites achieved all JAMA benchmarks and 28.6% displayed the HON seal. The mean readability scores were 44.66 and 41.18 for symptoms and signs, and treatment information respectively. No significant difference has been found in terms of readability among the sites that did or did not display the HON seal. The websites with better readability did not achieve significantly more JAMA benchmarks than those with worse readability. However, the good quality sites had a significantly better readability compared to the poor quality sites (p=0.048).

Conclusions
The findings show that online health information concerning gynaecological cancers is generally difficult to read and understand. Good quality information concerning treatment was easier to read compared to the poor quality information, however, no other association between quality assessment and readability has been found.
ANGIOSARCOMAS OF GYNECOLOGIC ORIGIN: A CLINICOPATHOLOGIC REVIEW AND QUANTITATIVE ANALYSIS OF SURVIVAL
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Objectives
There is lack of consensus on risk factors for poor outcome and optimal treatment for angiosarcomas of the female genital tract (FGT). We performed a clinicopathologic review and survival analysis.

Methods
Published English literature was reviewed for angiosarcomas of the vulva, vagina, uterus, and ovary. Survival was evaluated by Kaplan-Meier analysis and the effect of clinical and demographic variables on survival by Cox regression analysis.

Results
51 patients were identified, with a median age of 47 (range 17-87) years. Two of the patients had an angiosarcoma of the vulva, two of the vagina, 18 of the uterus and 29 of the ovary. Five-year overall survival was 27% (SE 8%). Pooled hazard ratios of age at diagnosis and tumor size≥5 cm were 1.04 (95%-CI 1.00-1.08) and 8.86 (95%-CI 0.93-84.07), respectively. The majority of patients presented with locoregional disease, having surgery as their primary intervention. Overall, adjuvant therapy significantly improved survival (HR=0.17; 95%-CI: 0.05-0.59, adjusted for age and tumor size). Adjuvant treatment consisted of radiotherapy for angiosarcomas of the vulva, vagina and uterus and chemotherapy for ovarian angiosarcomas. Subgroup analysis by FGT site was hampered by the small number of cases.

Conclusions
This review supports the use of surgical and adjuvant radiotherapy for angiosarcomas of the vulva, vagina and uterus. Cytoreductive surgery and adjuvant chemotherapy remain the primary treatments for angiosarcomas of the ovary.
RETROSPECTIVE ANALYSIS OF 59 CASES OF PELVIC-PERITONEAL TUBERCULOSIS IN A GYNAECOLOGIC ONCOLOGY CLINIC

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Objectives
Despite increasing awareness and the availability of better imaging and other diagnostic methods, pelvic-peritoneal tuberculosis remains a difficult diagnosis to establish due to its non-specific nature. Here, we report a retrospective study of clinical and laboratory features of 59 patients who received the diagnosis of pelvic-peritoneal tuberculosis in a gynaecologic oncology clinic in Turkey.

Methods
The medical records of relevant patients, managed between January 1995 to December 2012 at our institution, were reviewed.

Results
The mean age of the patients was 46.2 (range 24–75). The mean CA-125 level was 212.2 IU/ml (range 5–677). Among the 59 patients, 47 patients (79.6%) had detectable pelvic mass in preoperative period, 53 patients (89.8%) had elevated levels of CA-125 and, 38 patients (64.4%) had ascites. Preoperative chest radiograms revealed findings indicating tuberculosis only in one patient, and non-specific abnormalities in five. We performed surgical intervention in 53 of 59 patients with the suspicion of ovarian cancer. Three of the patients received the diagnosis of tuberculosis by laparoscopic peritoneal biopsy, and the remaining by laparotomy. In all patients the diagnosis of pelvic-peritoneal tuberculosis was confirmed by paraffin-embedded evaluation. In seven patients, concurrent gynecologic malignancies were detected.

Conclusions
Oncologist and surgeons should remain cognizant of the possibility of tuberculous infection in a woman with pelvic mass, ascites or elevated levels of CA-125, particularly in developing countries.
VALUE OF CLAVIEN-DINDO CLASSIFICATION OF COMPLICATIONS IN GYNAECOLOGICAL ONCOLOGY

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Objectives
The published overall incidence of serious postoperative complications ranges from 3% to 16%. We regularly review the postoperative complications in our quarterly morbidity and mortality meetings and recently introduced the Clavien Dindo classification for all surgical disciplines.

Methods
Postoperative complications were prospectively documented for all surgical cases and recorded in our Surgical Database. The Clavien-Dindo Classification was used for grading complications. We reviewed all patients who underwent a surgical procedure for a gynaecological cancer in our institution between January 2011 and January 2013.

Results
Total number of procedures performed was 820, 618 major and 202 minor procedures. 2.8% (n=23) of all cases concerned emergency procedures. 170 (27.5%) patients had complications classified as Clavien I-II, which include any deviation from the normal postoperative course, requiring medication, blood transfusion, total parenteral nutrition. Thirty patients (4.8%) had a Clavien III complication, which includes all complications requiring surgical, endoscopic or radiological intervention. Three patients (0.5%) were classified as Clavien IV, which include single and multi-organ failure. There were three (0.5%) deaths (Clavien V), each of which occurred within 30 days after an emergency procedure. The incidence of major complications (Clavien III-V) is 5.8%.

Conclusions
The incidence of serious postoperative complications in our patient population is 5.8%. This includes the overall rare risk of death of 0.5%, and all deaths were recorded following emergency procedures. These numbers are comparable to rates published in the literature. This classification facilitates comparative analysis of postoperative complications from different time periods in the same unit and from different units.
NEITHER ROMA NOR HE4 CAN IMPROVE THE DIAGNOSTIC VALUE OF CA125 IN PREDICTING PRESENCE OF INVASIVE IMPLANTS WITHIN BORDERLINE OVARIAN TUMORS (BOT)

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Objectives
Presence of invasive implants (InvImp), quality of surgical staging and residual tumor mass were shown to be major prognostic factors for BOT. Currently, there are no biomarkers that can predict the various types of BOT. Aim of our study was to assess the value of individual CA125 and HE4 values, or in combination within ROMA score for detecting BOT, and for predicting the presence of InvImp.

Methods
We enrolled 167 patients, (104-benign diseases, 48-BOT and 15-BOT with InvImp). Blood was collected prior surgery. HE4 and CA125 were determined using ELISA technique. The performance of HE4 and CA125 were analysed using the receiver operator characteristic (ROC) and logistic regression.

Results
HE4 and CA125 in BOT with InvImp (median=73.85 pmol/L and 49.5IU/ml) were significantly increased compared to benign diseases (median=48 pmol/L and 18.5IU/ml; p=0.009 and 0.001, respectively) and slightly increased compared to BOT without InvImp (median=61.45 pmol/L and 26.5IU/ml; p=0.822 and 0.201, respectively). HE4 and CA125 cut off values of 65 pmol/L and 60 IU/ml, respectively were independent predictive factors for the presence of InvImp (p=0.018, OR=5.32, 95%CI=2.31-36.36 and p=0.031, OR=4.83, 95%CI=1.16-20.13, respectively). ROMA (p=0.002, RR=9.17, 95%CI=2.31-36.36) performed better than HE4 or CA125 alone. The OR of a high ROMA score were 0.082 (95%CI: 0.02-0.34; p=0.001) for benign diseases and 0.27 (95%CI: 0.05-1.42; p=0.123) for BOT without InvImp compared to BOT with InvImp.

Conclusions
CA125, HE4 and ROMA score cannot predict sufficiently InvImp in BOT. Further multicenter prospective studies are needed for the development of reliable biomarkers for BOT.
Poster Presentations: Ovarian Cancer

IL-6 BLOCKING OVERCOMES PLATINUM DRUG RESISTANCE IN OVARIAN CANCER AND UTERINE SEROUS CANCER

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Objectives
To study the role of IL-6 in inducing platinum-resistance in ovarian and endometrial cancer and to determine the effect of IL-6 blockers on chemo-efficacy.

Methods
Human ovarian (SKOV-3, OVCAR-3, ES-2) and uterine serous (USPC-2) cancer cell lines, were treated with cisplatin and Anti IL-6 antibody (Siltuximab) or si-RNA. IL-6 signaling and chemosensetivity were determined using different methods.

Results
Platinum-resistant cells increased IL-6 secretion levels upon treatment with Cisplatin (3.2-31.29 folds, P values 0.02-0.0006). Furthermore, Siltuximab increased sensitivity to Cisplatin in platinum-resistant cells, USPC-2; RR-3.125, (p=0.0005) SKOV-3 RR-1.6-1.77 (p<0.039). Knockdown of IL-6 levels by si-RNA increased cancer cell sensitivity to Cisplatin; USPC-2 showed up to 20% increase in Cisplatin cytotoxicity (p<0.042), while OVCAR-3 and ES-2 showed a 10% increase (p<0.042). Siltuximab significantly inhibited cancer cells movement in a wound healing model by up to 44.6% (USPC-2, p<0.001).

Conclusions
We showed that in ovarian and endometrial cancer cell lines, Cisplatin induces IL-6 secretion and IL-6 inhibition can sensitize cancer cells to Cisplatin and inhibit cancer cells movement. We are currently investigating the potential combination therapy of Siltuximab and Cisplatin in vivo. Developing targeted treatment modality that will increase chemo-sensitivity based on IL-6 could prolong survival of ovarian patients.
PROGNOSTIC MODEL FOR SURVIVAL OF EPITHELIAL OVARIAN CANCER PATIENTS TREATED WITH PRIMARY OR INTERVAL DEBULKING SURGERY

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Objectives
At present, predicting survival of patients with epithelial ovarian cancer (EOC) is based on population prognosis using a single prognostic factor. Combination of all known prognostic factors would facilitate prediction on the level of the individual patient. The aim of this study was to develop a prognostic model to predict five year disease specific survival in epithelial ovarian cancer patients.

Methods
We performed a retrospective cohort study of all EOC patients treated with primary debulking and adjuvant chemotherapy or neo-adjuvant chemotherapy and interval debulking surgery in three gynaecological-oncologic centres between 1998 en 2010. Primary outcome of our study was disease specific survival. We considered 12 potential predictors for the Cox proportional hazard model. The Lasso method was used for selection of predictors and to correct for overfitting. Performance was evaluated by discrimination and by calibration.

Results
In total, 840 patients were eligible for the study of whom 489 (58%) patients died from EOC within 5 years. FIGO stage, residual tumour, type of surgery, histology, performance scale, age, amount of ascites and a family history suggestive of breast or ovarian cancer were predictive of 5-year survival. The final model showed good discrimination (c-statistic 0.71; 95% CI 0.69-0.74) with an accurate calibration.
Figure 1 shows the developed nomogram.

Figure 1 Nomogram to predict 1-year, 3-year and 5-year survival for patients with epithelial ovarian cancer. Coefficients are based on the lasso method.

Conclusions
Our prediction model provides an individual five-year survival prognosis for patients with all stage epithelial ovarian cancer. This could be used for counselling of patients or to select patients for trials.
INTRODUCTION OF STAGING LAPAROSCOPY IN THE MANAGEMENT OF ADVANCED EPITHELIAL OVARIAN, TUBAL AND PERITONEAL CANCER: IMPACT ON PROGNOSIS IN A SINGLE INSTITUTION EXPERIENCE

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Objectives
To evaluate the prognostic impact of routinely use of staging laparoscopy (S-LPS) in patients with primary advanced epithelial ovarian cancer (AEOC)

Methods
All women were submitted to S-LPS before receiving primary debulking surgery (PDS) or neoadjuvant treatment (NACT). The surgical and survival outcome were evaluated by univariate and multivariate analysis.

Results
Among 300 consecutive patients submitted to S-LPS no complications related to the surgical procedure were registered. The laparoscopic evaluation showed that almost half of the patients (46.3%) had an high tumor load. One-hundred forty-eight (49.3%) women were considered suitable for PDS and the remaining 152 (50.7%) were submitted to NACT. The percentages of complete (residual tumor, RT=0) and optimal (RT< 1 cm) cytoreduction of PDS and interval debulking surgery (IDS) were 62.1% and 57.5%, 22.5% and 27.7%, respectively, p=0.07). The post-operative complications of NACT/IDS group were lower than PDS group (p=0.01). The median progression free survival in women with RT=0 at PDS was 25 months (95% CI, 15.1 - 34.8), which was statistically significant longer than in all other patients, irrespective of the type of treatment they received (p=0.0001). At multivariate analysis, residual disease (p =0.011) and performance status (p = 0.016) maintained an independent association with the PFS.

Conclusions
Including S-LPS in a tertiary referral center for the management AEOC does not appear to have a negative impact in terms of survival and it may be helpful to individualize the treatment avoiding unnecessary laparotomies and surgical complications.
Poster Presentations: Ovarian Cancer

AUTOTAXIN INHIBITORS AS A POTENTIAL TREATMENT FOR OVARIAN CANCER

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Objectives

Autotaxin is an extracellular phospholipase D that is a major contributor to the synthesis of the bioactive lipid lysophosphatidic acid (LPA) via the hydrolysis of lysophosphatidyl choline (LPC). LPA is a lipid mediator which has been implicated in many physiological and pathological processes, including cell migration and invasion, proliferation and survival. The most potent autotaxin inhibitor described to date is the LPA analogue S32826. However when studied using in vivo models it was found to lack sufficient stability. Polymers are becoming an increasingly useful tool in the delivery of drugs and have the potential to improve the pharmacokinetic properties of small molecules. We wished to evaluate whether dendrimer conjugates of autotaxin inhibitors would retain activity against ovarian cancer cells.

Methods

We synthesized an analogue of the previously described autotaxin inhibitor S32826 and coupled it to a dendrimer. The conjugate was evaluated in assays to measure apoptosis and inhibition of cell migration.

Results

The drug-dendrimer conjugate was found to inhibit autotaxin activity in the FS3 and bis-pNPP assays. Evaluation of the conjugate in a cell migration assay showed the inhibitor was able to decrease cell migration in an ovarian cancer cell line modified to overexpress autotaxin. Furthermore the conjugate potentiated apoptosis induced by carboplatin when assessed for caspase 3/7 activity.

Conclusions

We conclude that dendrimer conjugates offer a potential route to improve the delivery of autotaxin inhibitors.
AGE-SPECIFIC PROGNOSTIC FACTORS FOR SURVIVAL IN YOUNG PATIENTS WITH ADVANCED OVARIAN CANCER: AN ANALYSIS OF THE FOUR PROSPECTIVE PHASE III TRIALS FROM THE AGO-STUDY GROUP

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Objectives
We examined the prognostic factors for progression-free (PFS) and overall survival (OS) survival in patients with advanced ovarian cancer treated with platinum/taxane-based chemotherapy and the effect of young age.

Methods
The AGO, GINECO, NSGO intergroup studies Ovar 3, 5, 7 and 9 databases were merged to identify 294 patients < 40 years and 4761 patients > 40 years. We conducted survival analyses, linear regressions, and cox proportional hazard regression models.

Results
For patients < 40 years, the crude median PFS was 28.9 months and the median OS was 75.3 months. For patients > 40 years, the crude median PFS was 18.1 months and the median OS was 45.7 months (all differences: p < 0.001). In the multivariate analysis, young age had a statistically significant better OS (HR: 0.74, 95% CI: 0.60, 0.92; p=0.007), although in young patients, mucinous tumors were more frequent (13 % vs 4 %) and more aggressive compared with serous tumors (HR: 3.66, 95% CI: 1.82, 7.37). The effect of dose reduction had more impact in patients < 40 years (HR 1.32, 95% CI: 0.69, 2.52) than in patients > 40 years (HR1.04, 95% CI: 0.92, 1.17).

Independent survival risk factors were similar in both age groups: FIGO stage, grading, residual tumor and number of chemotherapy cycles. Increasing number of cycles > 6 did not contribute to prognostic performance.

Conclusions
Prognostic factors in young patients with ovarian cancer were similar to patients older than 40 years. However, younger age was an independent prognostic factor for overall survival.
Poster Presentations: Ovarian Cancer

SENTINEL NODE IN OVARIAN CANCER: A FEASIBILITY STUDY.
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Objectives
Sentinel lymph node surgery is to determine whether cancer has spread to the first lymph node or sentinel node (SN). The aim of this study is to determine whether a SN procedure in ovarian cancer is feasible when the tracers are injected into the ovarian ligaments instead of in the ovarian capsule, this to avoid possible spillage of tumour cells.

Methods
Patients with a high likelihood of having an ovarian malignancy in whom a median laparotomy with frozen section is planned, and patients with endometrial cancer with a staging laparotomy are included. Before staging, blue dye and radioactive colloid are injected into the ovarian ligament and the infundibulopelvic ligament.

Results
Ten patients were included: three with endometrial cancer, seven with an ovarian tumour (6 benign, 1 malignant). In nine patients we were able to identify the SN. The patient without SN identification had pathological enlarged lymph nodes. Locations of the SN were ipsilateral para-aortal (n=6), ipsilateral pelvis and para-aortal (n=2), and bilateral pelvis and ipsilateral para-aortal (n=1). In three patients the SN’s were removed (2 endometrial cancer, 1 ovarian cancer). One patient with endometrial cancer had metastases in the lymph nodes, including the SN.

Conclusions
These preliminary data on SN recognition in ovarian cancer by injection of tracer into the ovarian ligaments are very promising. A SN procedure could prevent unnecessary lymph node dissection with associated morbidity. When the results are confirmed, we are planning a multicenter study to test the accuracy of this technique.
AN EVALUATION OF CLINICAL FEATURES THAT CHARACTERIZE LONG-TERM, DISEASE-FREE SURVIVAL IN ADVANCED STAGE SEROUS OVARIAN CANCER; KOREAN SINGLE INSTITUTE RETROSPECTIVE STUDY

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Objectives

The objective of this study was to define clinical characteristic patterns associated with favorable survival.

Methods

Clinical characteristics from 50 stage III/IV serous ovarian cancer patients who were diagnosed and treated ovarian cancer in Asan Medical Center from 2001 were analysed. This include 30 long-term, disease-free survivor(LTDFS) who lived disease freely>5 years and 20 patients with poor outcome(PO) who died in 6 month from ovarian cancer diagnosis.

Results

<table>
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<th>LTDFS (&gt;60 months)</th>
<th>PO (&lt;6 months)</th>
<th>p-value</th>
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<td>Age (yrs)</td>
<td>55.20±8.28</td>
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<td>Weight Change (Kg)</td>
<td>0.43±4.04</td>
<td>-3.01±4.17</td>
<td>.005</td>
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<td>Preop CA-125 (IU/mL)</td>
<td>2378.12±5673.56</td>
<td>2655.16±3291.02</td>
<td>.845</td>
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<td>CA-125 level after 1st course of chemotherapy</td>
<td>67.18±88.02</td>
<td>487.94±691.98</td>
<td>.002</td>
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<td>CA-125 ratio</td>
<td>0.168±0.325</td>
<td>0.333±0.357</td>
<td>.098</td>
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<tr>
<td>No. of metastatic lymphnodes</td>
<td>5.10±11.80</td>
<td>10.83±11.17</td>
<td>.103</td>
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<td>No. of dissected lymphnodes</td>
<td>41.50±16.72</td>
<td>39.89±17.97</td>
<td>.755</td>
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<tr>
<td>No. of supportive family members</td>
<td>5.40±2.61</td>
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<table>
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<tr>
<th></th>
<th>LTDFS (&gt;60 months)</th>
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<td>Underlying Disease</td>
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</table>

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Conclusions
Differences in survival of advanced ovarian cancers are reflected by distinct patterns of clinical characteristics. Decreased CA-125 level after 1st course of chemotherapy is clinically significant favorable factor for longer survival. Other socioeconomic distinction should be further evaluated.
DISTRIBUTION OF HISTOPATHOLOGY IN STAGE 1A EPITHELIAL OVARIAN CANCER

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Objectives
To identify the distribution of the histopathology types in stage 1A EOC cases in two cancer centers in the UK and compare the results with the available published data.

Methods
We identified retrospectively stage 1A EOC patients who underwent primary surgical treatment and searched the available literature regarding the histopathology distribution of stage 1A EOC.

Results
From 01/01/2003 to 31/07/2009, 94 patients with stage 1A EOC were treated at St Bartholomew’s and University College Hospitals. 47 cases were borderline tumours and 47 were stage 1A. 50% of stage 1A cases in both centers were mucinous tumours, followed by serous, clear cell and mixed types.

Conclusions
In our study the majority of stage 1A EOC were mucinous and serous, a significant difference with international studies, where serous and clear cell are the most frequent histopathological types. This may partly be due to different thresholds in diagnosing mucinous carcinoma but the fact that the two Centers showed a similar proportion of mucinous carcinomas suggests this is a true incidence in our Centers.

Our findings support the hypothesis that there are important biological differences in the behavior of the major tumor types between early and advanced cases of EOC, with important clinical implications.

Awareness of the histopathological type distribution of stage 1A EOC cases may guide ovarian cancer screening research. It could also aid management guidelines, including pre-operative patient counselling and planning for intra-operative frozen section diagnosis, since currently there is no international consensus regarding the treatment of stage 1A EOC.
THE ROLE OF SECONDARY CYTOREDUCTIVE SURGERY (SCR) IN RELAPSED EPITHELIAL OVARIAN CANCER (EOC)

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³Radiology, The Royal Marsden NHS Foundation Trust, London, United Kingdom

Objectives
To evaluate the role of surgery for relapsed epithelial ovarian cancer (EOC) so as to define criteria for complete secondary cytoreductive surgery (SCR).

Methods
86 women with relapsed EOC underwent secondary cytoreductive surgery between 1996-2010.

Results
Median age at time of surgery for relapsed EOC was 58 years (range, 29-77 years). All patients had received at least one line of platinum-based chemotherapy. Median time from diagnosis of primary disease to surgery for relapsed disease was 38 months (range, 7-219 months). 71% underwent complete cytoreductive surgery with a median survival significantly longer than those who had macroscopic disease (56.3 v 33.1 months, p <0.001). Similarly, median survival was also longer in patients who underwent cytoreductive surgery at first relapse compared to surgery at subsequent relapse (64.4 v 33.6 months, p < 0.001). The operative morbidity and mortality rates were 21% and 1.2%, respectively. Optimal debulking (< 1cm residual disease) at primary surgery and single site of recurrence were identified as predictors for complete SCR, p=0.015 and p < 0.001. Complete secondary cytoreductive surgery was predictive for survival (p=0.001). The median overall survival (OS) was 49.3 months (range, 39-59.7 months).

Conclusions
Complete SCR was more likely to be achieved if optimal cytoreduction was achieved at primary surgery.
Poster Presentations: Ovarian Cancer

FIBROBLAST GROWTH FACTOR RECEPTOR 4 (FGFR4) IMMUNOHISTOCHEMISTRY IS NOT ASSOCIATED WITH OUTCOME BUT WITH POSTOPERATIVE RESIDUAL DISEASE IN HIGH-GRADE SEROUS OVARIAN CARCINOMA (HGSC).

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Objectives
Overexpression FGFR4 and its ligand, FGF-1, have been associated with poor overall survival in HGSC. In addition, a polymorphism within the FGFR4 gene is associated with platin sensitivity and improved overall survival (multivariable hazard ratio 0.49, p=0.006). This study was designed to validate the prognostic impact of FGFR4 in HGSC.

Methods
This study includes 611 patients with HGSC of 3 population-based cohorts from British Columbia. FGFR4 immunohistochemistry was performed using two different anti-FGFR4 antibodies (Sigma, HPA027273 & SantaCruz sc-124) on tissue microarrays. Staining intensity was graded absent, weak, intermediate or strong. Uni- and multivariate proportional hazard models were used to correlate important prognostic factors with overall survival.

Results
601/611 HGSC were evaluable for FGFR4. Median follow-up was 3.55 years with 398 (66.2%) deaths. The sc-124 anti-FGFR4 antibody didn’t show any prognostic impact, neither in patients with or without postoperative residual disease. In contrast, we observed a weak correlation between the HPA027273 antibody and OS. Statistical significance was almost lost when correcting for postoperative residual tumor in the multivariate analysis (p=0.04). Residual tumor and FIGO stage showed the strongest association with OS (p<0.0001 and p=0.0003). Correlation between the staining intensities of the antibodies was poor (r²=0.21). The HPA027273 antibody was associated with postoperative residual disease (p<0.0001).

Conclusions
We were unable to confirm the independent prognostic impact of FGFR4 expression in a larger cohort of HGSC. The strong correlation between high FGFR4 expression and postoperative residual disease suggests FGFR4 to play a role in tumor progression.
PHASE 1 STUDY OF CONTINUOUS ORAL RUCAPARIB: ANALYSIS OF PATIENT SUBGROUP WITH OVARIAN/PERITONEAL CANCER


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7Center for Early Drug Development, Dana Farber Cancer Institute, Boston, USA

Objectives
Rucaparib, an oral small molecule inhibitor of poly (ADP-ribose) polymerase (PARP) 1 and -2, is being developed for treatment of platinum-sensitive ovarian cancer. Primary objectives of this study were to define the maximum tolerated dose (MTD), recommended Phase 2 dose (RP2D), and PK of continuous oral rucaparib. This analysis describes the patient subgroup with ovarian or primary peritoneal cancer.

Methods
Patients aged ≥18 with advanced solid tumors were enrolled in n=3-6 cohorts. Measurable disease was not required. Rucaparib was taken once or twice daily until disease progression.

Results
Of 33 patients enrolled, 10 had high grade serous ovarian or primary peritoneal tumors (median age 54 yrs [range 46-71]; median prior regimens 3 [1-9]; 3 ECOG PS=0; dose levels 40 mg/day to 360 mg twice/day). One pt at 360 mg twice/day experienced a DLT of Gr 3 nausea. Treatment-related adverse events reported in >1 pt include nausea (n=2) and diarrhoea (n=2). No myelosuppression has been observed. One OC pt (BRCA1 mut) treated with 300 mg/day achieved a durable PR. Current overall disease control rate (CR+PR+SD>12 wks) in evaluable OC pts (5 BRCA mut, 1 BRCA wt, 1 BRCA unk) is 86% (6/7). Three pts (all BRCA mut) are ongoing in wks 27, 28, 40. 2 pts enrolled <12 weeks ago are also ongoing.

Conclusions
Continuous oral rucaparib is well tolerated, with encouraging clinical activity observed during dose-escalation. Once confirmed, the RP2D will be evaluated in platinum-sensitive OC pts with a deleterious gBRCA mutation. The phase 2/3 program will open in 2013.
THE IMPACT OF ITGBL1 PROTEIN ON OVARIAN CANCER CELL MIGRATION RATE

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Objectives
In our previous microarray study identified two molecular subtypes of serous ovarian cancers, with distinct gene expression profile. These subtypes are correlated with different survival of the patients. One of the genes that were differentially expressed between two subtypes of ovarian cancer was Integrin, beta-like 1 gene (ITGBL1). Our aim was to study whether and how ITGBL1 can influence adhesion and motility of cancer cells.

Methods
ITGBL1 expression in 5 ovarian cancer cell lines (OAW42, SKOV3, OVCAR-3, OVP-10, ES2) was assayed using semi-quantitative RT-PCR. ITGBL1 coding sequence was amplified from cDNA and cloned in pLNCX2 vector. Retroviral system was used to obtain cell lines with ITGBL1 overexpression. Wild type and ITGBL1-expressing isogenics cell lines were then used in scratch assay.

Results
We successfully obtained SKOV3, OAW42 and OVCAR-3 cell lines overexpressing ITGBL1. Than SKOV3/ITGBL1(+) and OAW42/ITGBL1(+) cell lines were assayed for cell proliferation and migration rate. The results were analyzed in comparison to the non-modified SKOV3 and OAW42 cell lines. We found the scratch area was faster covered with the cells overexpressing ITGBL1 than with the cells that do not express ITGBL1.

Conclusions
Our results indicate that ITGBL1 protein may enhance ovarian cancer cell proliferation and motility. This suggests that ITGBL1 may affect the aggressiveness of cancer cells and play an important role in ovarian cancer progression.

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LYMPH NODE DISSECTION CAN BE OMITTED IN PATIENTS WITH CLINICAL STAGE I MUCINOUS EPITHELIAL OVARIAN CARCINOMA

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Objectives
To evaluate the clinical efficacy of lymph node dissection in patients with clinical stage I mucinous epithelial ovarian carcinomas (mEOCs)

Methods
A total of 196 patients received surgery and were confirmed pathologically to have mEOCs at Asan Medical Center between 1990 and 2012. Among them, 155 patients whose tumor was apparently confined to the ovary were enrolled in this retrospective study. Patients with mucinous borderline tumors or ovarian metastatic mucinous carcinoma from other primary site were excluded.

Results
In the median follow-up of 65.8 months, 13 patients (8.4%) died from the cancer and 21 patients (13.5%) recurred (Table 1). 70 patients underwent lymphadenectomy during surgery and 85 patients did not. Among 70 patients who received lymphadenectomy, only 1 patients (1.4%) were upstaged due to the metastatic carcinoma in lymph node, 9 patients (87.1%) recurred and 8 patients (88.6%) died. While, 11 patients (86.1%) recurred and 4 patients (94.9%) died among 79 patients who did not received lymphadenectomy. There was no significant difference of 3-year PFS between patients with or without lymphadenectomy (90.7% vs. 86.1%, p=0.75). Also, 5-year OS was not significantly different between patients with or without lymphadenectomy (86.6% vs. 93.4%, p=0.13).
Conclusions
Patients with clinical stage I mEOCs has extremely low rate of lymph node involvement. In addition, there was no better clinical gain or survival gain in patients who had lymphadenectomy than in patients who did not. Therefore, it might be reasonable to omit LND in patients with mEOCs who seems to be clinically early stage.
THE VACCINATION TARGETED WITH CANCER STEM-LIKE CELLS EXPRESSING ALPHA-GAL EPITOPES INDUCE EFFECTIVE IMMUNE RESPONSES AGAINST OVARIAN CANCER

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Objectives
Cancer stem cells (CSCs) are a subset of highly tumorigenic cells with stem cell properties. Thus, processing and presentation of tumor associated antigen (TAA) of CSCs in the vaccine could be a suitable strategy. In this study, we hypothesized that IgG-mediated targeting of ovarian cancer stem-like cells could enhance presentation to APC by exploiting the natural anti-gal epitope in human ovarian cancer cells.

Methods
The expression vector of α(1,3) galactosyltransferase [α(1,3)GT] with GFP was constructed by using lentivirus plasmid packaging system and were transfected to human ovarian cancer cell line SKOV3. Ovarian cancer stem–like cells were enriched by serum-free stem cell culture system. Cell apoptosis was assayed by flow cytometry. α1,3GT knockout (KO) mice were immunized by tumor cell vaccination and the presence of anti-Gal in their serum was confirmed by ELISA.

Results
High expression levels of α-gal epitopes were observed on the SKOV3 cell surface after α1,3GT transfectants. The apoptosis rate of α1,3GT transfected cells were significantly increased after co-cultured with human peripheral blood mononuclear lymphocytes of ovarian cancer patients (p<0.05). The expression of α-gal epitopes did not affect the characteristics of cancer stem-like cells. Furthermore, vaccination with α-gal cancer stem-like cells or differentiated cells resulted in increase production of anti-Gal IgG compared with control. Vaccination with ovarian cancer cells expressing α-gal epitopes induced immune responses against not only differentiated cancer cells but also cancer stem-like cells.

Conclusions
We suggested that vaccination using cancer stem-like cells engineered to express α-gal epitopes is a novel strategy for treatment of ovarian cancer.
Poster Presentations: Ovarian Cancer

KINETICS OF HE4 AND CA125 IN METASTATIC OVARIAN CANCER: AN INTERMEDIATE ANALYSIS OF THE META-FOUR STUDY
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Objectives
The Meta-Four study (ClinicalTrials.gov Identifier: NCT01768156) was designed to compare the prognostic and predictive value of HE4 and CA125 during the follow-up of metastatic ovarian cancer patients.

Methods
Serums were collected before the 1st chemotherapy, during chemotherapy and every 3 months until treatment failure for 40 patients (mean = 7 samples/patient). We studied different biomarkers criteria linked to kinetics.

Results
Initially, 37/40 (92.5%) and 35/40 (87.5%) patients presented with an elevated value of CA125 (>35 UI/mL) and HE4 (>70 pg/mL), respectively. One patient had low values of both markers, 2 had low CA125 only and 4 patients had low HE4 only. 6/37 and 6/35 patients had during chemotherapy both initial elevation of CA125 and HE4, respectively. Five patients had the same profile for the both biomarkers. Among biological responders, the median of CA125 nadir was 29 UI/mL ([5-887; n=31]) and the median of HE4 nadir was 73 pg/mL [38-1430; n=29]. Time to nadir was 14 [4-37] and 16 [4-105] weeks for CA125 and HE4, respectively. 26/37 for CA125 and 20/35 patients had a doubling value from the nadir (biological recurrence, BR). Among the 11 patients without BR with CA125, 2 had BR with HE4. Among the 15 patients without BR with HE4, 6 had a BR with CA125. CA125 and HE4 doubling time were 17 [4-65] and 16.5 [3-39] weeks, respectively.

Conclusions
The baseline values and kinetics of HE4 and CA125 are similar. HE4 could be particularly helpful for monitoring metastatic ovarian patients presenting no changes in CA125.
Role of Lymph Node Positive Rate in Predicting the Overall Survival for Ovarian Cancer IIIc Patients

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Objectives
To investigate the clinical usefulness of the lymph node positive rate (LNPR) in predicting the overall survival for ovarian cancer IIIc patients.

Methods
73 patients with ovarian cancer IIIc underwent primary surgery followed by combination chemotherapy from 1997 to 2010 were included. Tumor size before initial surgery, optimality of surgery (cut off=1.0 cm), age, cell type, and histological grade were considered as risk factors of overall survival. We defined LNPR as the proportion of positive LN among total LN removed and proceeded following steps: (1) Find the risk factors of the overall survival using univariate analysis, (2) Determine the optimal cut-off value for LNPR, and (3) Evaluate the usefulness of LNPR in the multivariate model.

Results
Median survival time was 79 months with 55.9% of 5 year survival rate. Optimality of surgery (p=0.0435) and LNPR (p=0.0398) were statistically significant risk factors in univariate analysis. An optimal cut-off value was 35% of LNPR (p=0.0198). We divided patients into high/low LN risk group according to cut-off value. Multivariate Cox proportional hazard regression model showed that the sub-optimality of surgery (HR=2.262, 95% CI=1.040-4.918, p=0.0394) and high LNPR (HR=2.870, 95% CI=1.178-6.989, p=0.0203) were significant risk factors in predicting overall survival. Five year survival rates of high/low LN group were 31.3% and 62.0%, respectively.

Conclusions
LNPR (35% of cut-off) could be used as an important risk factor in predicting overall survival for ovarian cancer IIIc patients.
Poster Presentations: Ovarian Cancer

VACCINATION WITH EMBRYONIC STEM CELLS GENERATES EFFECTIVE ANTITUMOR IMMUNITY AGAINST OVARIAN CANCER

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Objectives
The purpose of this study was to investigate the therapeutic potential of hESCs as a vaccine to induce widespread antitumor effects in different animal models and various types of cancer.

Methods
C57BL/6 mice with ID8 ovarian cancer cell and Fischer 344 rats with NuTu-19 ovarian cancer cell models were used. Fifty-four mice were divided into six groups with nine mice in each group. Each mouse was immunized with pre-inactivated hESCs (H9) or mouse embryonic stem cells (mESCs; IVP-ES1) or ID8 or phosphate-buffered saline (PBS). Twenty-four rats were divided into four groups with six rats in each group, each rat immunized with pre-inactivated hESCs (H9) or NuTu-19 or PBS. After the vaccination, each mouse was challenged with live ID8 cells subcutaneously, and each rat was challenged with live NuTu-19 cells intraperitoneally.

Results
We discovered that vaccination of mice with the hESC line H9 and the mESC line IVP-ES1 generated consistent cellular and humoral immune responses against ID8 ovarian cancer. H9 and IVP-ES1 vaccinated mice obtained antitumor immune protection, and H9 vaccinated rats had the longest survival time and least distant metastases. No evidence of side-effects was observed.

Conclusions
hESC vaccines can induce antitumor effects in two animal models and in ovarian cancer.
THE ROLE OF P-GLYCOPROTEIN-EXPOSING EXTRACELLULAR VESICLES IN MULTIDRUG RESISTANCE IN EPITHELIAL OVARIAN CARCINOMA

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Objectives
Multidrug resistance (MDR) is a major problem in the treatment of epithelial ovarian carcinoma (EOC). Altered exposure of the multidrug transporter P-glycoprotein (P-gp) is associated with development of MDR. P-gp transports paclitaxel and doxorubicin, both used in the treatment of EOC. In vitro, P-gp is transferred from resistant to non-resistant cancer cells by extracellular vesicles (EV). Our aim was to determine whether this P-gp transfer occurs in EOC cells and contributes to MDR in ovarian carcinoma.

Methods
P-gp exposure was measured in EOC cell lines IGROV-1 (MDR−) and IGROVCDPP (MDR+) and patient samples. EV were isolated by differential centrifugation and visualized by flow cytometry and transmission electron microscopy. Both exposure and transfer of P-gp by EV were analysed by flow cytometry.

Results
MDR+ cells expose increased levels of P-gp compared to non-resistant cells (n = 3; p < 0.05). In contrast, P-gp was not detectable on EV, also not when cells were undergoing apoptosis. Incubation of MDR− cells with EV from MDR+ cells did not increase the exposure of P-gp on MDR− cells. Finally, P-gp was not detectable on EV in ascites from ovarian carcinoma patients.

Conclusions
P-gp is either absent or present in only low amounts on EV released by EOC cells. P-gp is not transferred to non-resistant EOC cells by EV. We hypothesize that retaining P-gp may be a selective mechanism to promote tumor-cell survival.
PHASE II TRIAL OF WEEKLY TRABECTEDIN PLUS WEEKLY PEGYLATED LIPOSOMAL DOXORUBICIN FOR TREATMENT OF ADVANCED, PERSISTENT OR RECURRENT OVARIAN CARCINOMA
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Objectives
The objective of this study was to determine safety, feasibility and efficacy of weekly Trabectedin (T) 0.4 mg/mq iv in combination with weekly Pegylated Liposomal Doxorubicin (PLD) 10 mg/mq in patients with recurrent ovarian cancer.

Methods
We carried out a single Institute Phase II trial in patients with advanced recurrent ovarian cancer. Inclusion criteria included: age 18-75; recurrent and measurable disease; acceptable organ function; normal blood chemistry parameters; ≤3 prior chemotherapeutic regimens; ECOG performance status 0-1; life expectancy > 3 months; signed informed consent. Trabectedin (0.4 mg/mq) was administered weekly via a central line, after premedication with dexamethasone, as a 3-h infusion weekly for 3 weeks followed by weekly infusion of Caelyx 10 mg/mq. Therapy continued until disease progression, unacceptable toxicity or patient refusal.

Results
Between March 2010 and October 2012, 26 patients were recruited; median age was 53 years (range: 36-75). The median number of cycles was 5 (137 total cycles, range 2-13). In 7 patients (27%) an objective response rate with measurable disease was achieved. The median progression-free survival was 5.1 months. No unexpected toxicities were found. The most frequent treatment-related grade 3/4 adverse events included neutropenia (27%), thrombocytopenia (11%), nausea/vomiting (15%), fatigue (11%) and reversible AST/ALT elevation (19%). No drug related cardiotoxicity was observed. There were no treatment-related deaths nor cases of liver failure.

Conclusions
Weekly administration of T and PLD is a safe and feasible therapeutic option for recurrent ovarian carcinoma. Further studies are needed in order to confirm these data.
A PHASE II STUDY OF TRABECTEDIN IN THE TREATMENT OF PATIENTS WITH RECURRENT OVARIAN CANCER (ROC)

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Objectives
The prognosis of patients with ROC is extremely poor, particularly after several re-treatments with platinum-based chemotherapy. Since ROC is not a curable disease, the principal objectives of treatment are to prolong survival, quality of life and alleviate cancer-related symptoms. In this open-label, non-randomized, phase II study we aimed to evaluate efficacy and safety of trabectedin (Yondelis®) as a single-agent in ROC.

Methods
Sixteen patients (median age 51 years, range: 44-71) with ROC who progressed after 2 (n=3), 3 (n=9) or 4 (n=4) previous chemotherapy lines were included. Patients were pre-treated with dexamethasone followed by trabectedin 1.1 mg/m² given as a 3-hour infusion every 3 weeks until disease progression, unacceptable toxicity or clinical benefits. The primary endpoint was the objective response rate as per RECIST v.1.1. Adverse events (AEs) were graded according to the NCI-CTC v.2.0.

Results
A median of 5 cycles per patient (range: 2-9) were administrated with no dosage reductions. Nine patients had partial response (PR; 56.2%), 4 had stable disease (SD, 25.0%) maintained for a median time of 12 weeks, and 3 patients (18.8%) progressed. In patients with PR the median PFS was 18 weeks. Common AEs were anemia (20.9%), leucopenia (15.0%), thrombocytopenia (4.5%) and asthenia (22.2%). No drug-related deaths were reported.

Conclusions
Trabectedin given as a single agent is an active treatment in heavily pretreated patients with ROC, which favourably compares with other active treatments. Trabectedin has a manageable and non-cumulative safety profile to be safely administered to patients with very limited therapeutic options for ROC.
Immune-phenotype assessment of ovarian cancer stem cells.

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Objectives
Current evidence suggests the presence of cancer stem cells (CSC) in epithelial ovarian cancer (EOC) and their role in chemoresistance and relapse. CD44+/CD24-, CD117+ and CD133+ expression have been reported as potential markers for CSC. The aim of this study was to assess the immune-phenotype of Ovarian CSC, and to compare it with ovarian cancer cells (non stem) and with healthy controls.

Methods
Tumor cells from 5 patients with chemo-naïve EOC and cells of ovarian and tubal epithelium from 5 healthy menopausal women undergoing surgery for benign pathology were cultured in standard medium (mediumA) and medium for embrionic cells (mediumB). Cells forming non-adherent spheres were considered CSC-like, and adherent cells as non-CSC-like. The percentages of CD24+, CD44+, CD117+, CD133+ and VEGF-R+ cells were determined by flow-cytometry.

Results
After 1-7 week sphere formation was observed in all EOC-cells cultured in mediumB but in none of the healthy controls. Mean percentages of markers expression are shown below.

<table>
<thead>
<tr>
<th>Marker</th>
<th>Non-CSClike mean(95% CI)</th>
<th>CSClike mean(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD24</td>
<td>17.78(1.0-34.6)</td>
<td>35.26(16.6-53.9)</td>
<td>0.089</td>
</tr>
<tr>
<td>CD44</td>
<td>59.92(27.3-92.6)</td>
<td>24.18(7.4-41.0)</td>
<td>0.036</td>
</tr>
<tr>
<td>CD117</td>
<td>16.98(1.8-32.1)</td>
<td>12.18(2.0-22.4)</td>
<td>0.489</td>
</tr>
<tr>
<td>CD133</td>
<td>36.84(23.7-50.0)</td>
<td>35.46(15.7-55.2)</td>
<td>0.876</td>
</tr>
<tr>
<td>CD309</td>
<td>0.64(0.0-1.4)</td>
<td>0.38(0.1-0.7)</td>
<td>0.430</td>
</tr>
</tbody>
</table>

Table2.- Non-CSClike

<table>
<thead>
<tr>
<th>Marker</th>
<th>Healthy controls mean(95% CI)</th>
<th>EOC cells mean(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD24</td>
<td>25.80(8.3-43.3)</td>
<td>17.78(1.0-34.6)</td>
<td>0.419</td>
</tr>
<tr>
<td>CD44</td>
<td>35.08(9.8-60.4)</td>
<td>59.92(27.3-92.6)</td>
<td>0.151</td>
</tr>
<tr>
<td>CD117</td>
<td>4.97(2.6-7.4)</td>
<td>16.98(1.8-32.1)</td>
<td>0.092</td>
</tr>
<tr>
<td>CD133</td>
<td>5.59(0.3-10.9)</td>
<td>36.4(23.7-49.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
**Conclusions**
Contrary to published data, expression of CD44+/CD24- was lower in CSClike; in Non-CSClike CD133+ was higher in EOC-cells compared to controls. Immunophenotype of CSClike is still lacking and further investigation is warranted for this goal.

| CD309 | 3.9 (0.28-7.5) | 0.64 (0.0-1.43) | 0.072 |
Poster Presentations: Ovarian Cancer

INHIBITING DOUBLE STRAND BREAK (DSB) REPAIR PATHWAYS AND PTEN SENSITISES OVARIAN CLEAR CELL CARCINOMA (OCCC) TO CYTOTOXIC AGENTS

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Objectives
DSB repair pathway function and PTEN are frequently lost in ovarian cancer. There are conflicting data on their contribution to cytotoxic agent sensitivity. This study aimed to determine the contribution of PTEN and the two DSB repair pathways' (homologous recombination (HR) and non-homologous end joining (NHEJ)) to treatment sensitivity in a chemo-resistant Ovarian Clear Cell Carcinoma (OCCC).

Methods
PTEN, HR and NHEJ were inhibited by viral transduction of shRNA to PTEN, ATR and DNA-PK respectively in a normal ovarian epithelial and an OCCC cell line. Cytotoxicity of cisplatin, paclitaxel, doxorubicin, camptothecin and irradiation was assessed using the Sulforhodamine-B colorimetric assay. The mechanism of cell growth inhibition was investigated using FACS at GI₅₀ of each agent.

Results
In normal ovarian epithelial cells, HR knock-down did not improve sensitivity, but NHEJ and PTEN knock-down sensitized to camptothecin and doxorubicin. In OCCC cells, PTEN, HR and NHEJ knock-down enhanced sensitivity to all agents. HR and NHEJ knock-down caused G1 and G2 cell-cycle arrest respectively and all agents caused cell-cycle arrest except paclitaxel.

Conclusions
These data suggest normal cells repairs DNA damage through alternative competent DNA repair pathways which are lacking in OCCC. Intrinsic OCCC molecular defects combined with DSB repair pathway inhibition causes chemo and radiosensitisation, supporting the concept of synthetic lethality, which will be cancer cell specific. Our results show PTEN knockdown causes chemo and radiosensitisation, which is in contrast to reports in PTEN mutated cancers, but is in keeping with previous reports in knockdown models.
MULLERIAN PRECURSOR LESIONS IN SEROUS OVARIAN CANCER PATIENTS AND CONTROLS; USING THE SEE-FIM AND SEE-END PROTOCOL

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Objectives
Accumulating evidence suggests that serous ovarian cancer develops from epithelium embryologically derived from the Müllerian ducts. A plausible precursor lesion has been found in the fallopian tubes, but in one-half of women no tubal precursor lesion has been identified. The aim of the current study is to improve insight into pathology of epithelium derived from the Müllerian ducts in ovarian cancer patients.

Methods
Sixty women diagnosed with serous ovarian carcinoma and 68 asymptomatic women were included in this multicentre study. Tissues were embedded completely for histological assessment, in accordance with the SEE-Fim and SEE-End protocol (Sectioning and Extensively Examining of the Fimbriated end; – Endometrium) for ovarian cancers and the SEE-End for controls.

Results
In 31 (52%) ovarian cancer cases premalignancies were identified, of which in sixteen (27%) multiple premalignancies were identified. In nine (15%) cases endometrial intraepithelial carcinoma (EIC), in nineteen (32%) cases atypical hyperplasia, and in 23 (43%) serous tubal intraepithelial carcinoma (STIC). The STIC occurred significantly more often concurrent to an endometrial premalignancy compared to benign endometrium (64% vs 28%; p=0.01). In asymptomatic women both atypical hyperplasia and a focus of intramucosal endometrial carcinoma were found in the endometrium in two cases (3%).

Conclusions
Histological assessment of epithelium derived from Müllerian ducts resulted in the identification of premalignancies in more than half of serous ovarian cancer patients, located in both the endometrium and fallopian tubes. Coexistence of premalignancies was common, and might represent an effect of field carcinogenesis or tumor implantation of migrating cells.
QUANTITATIVE ANALYSIS OF KISS-1, GPR54 AND DOK1 IN EPITHELIAL OVARIAN CANCER WOMEN

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Objectives
To ascertain the potential role of KISS-1, its receptor GPR54 and DOK1 as metastasis suppressor genes by evaluating whether their expression is decreased in peritoneal and epiploon tissue from women affected by epithelial ovarian cancer (EOC).

Methods
Pathological and non-pathologically affected peritoneal and epiploon biopsies from women with EOC (N=54) as well as related healthy tissue from control patients affected with benign ovarian pathologies (N=28) were obtained during prophylactic oophorectomy. Total mRNA was extracted and the relative expression of each candidate gene was determined by ΔΔCt method after QF-PCR. Gene expression between pathological versus non pathological biopsies from EOC women and between non-pathological tissues from healthy compared to EOC women was analyzed.

Results
In pathological epiploon biopsies a statistically decreased expression of KISS-1 (15.53±5.44, p=0.047) and a significant increased expression of GPR54 (11.80±8.33, p=0.039) were obtained when compared to non-pathologic tissues from EOC women (17.93±7.32 and 12.03±7.56, for KISS-1 and GPR54, respectively) and healthy tissues from healthy women (20.14±2.14 and 9.04±5.43). A significant diminished expression of KISS-1(15.07±6.73, p=0.047) and a significant increased expression of GPR54 (16.25±7.76, p=0.00) were detected when peritoneal biopsies from pathological conditions were compared to control conditions (17.92±8.26 and 8.74±9.34). No other significant differences were found.

Conclusions
Downregulation of expression KISS-1, but not GPR54 and DOK1 in pathological biopsies suggests its involvement as tumoral suppressor gene in EOC women.
LYMPHOCELE AND OVARIAN CANCER. RISK FACTORS AND IMPACT ON SURVIVAL
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Objectives
The aim of this study is to describe the incidence, the impact of survival and the risks factors of symptomatic lymphoceles in ovarian cancer.

Methods
Retrospective study of ovarian cancer with complete cytoreduction surgery and para-aortic and pelvic lymphadenectomy performed in our institute from 2005 to 2011. Patients were classified into two groups: the symptomatic lymphoceles and the control groups.

Results
During the study period, 194 patients with epithelial ovarian cancer had a cytoreductive surgery with lymphadenectomy without macroscopic residual disease.

Fifty four patients had symptomatic lymphoceles (28%). In multivariate analysis only supraradical surgery was significantly and independently associated to the risk of symptomatic lymphocele occurrence (OR=2.04, 95% CI [1.04-4.01], p=0.04).

Median follow-up was 24.8 months [1- 74]. Survivals were not significantly different in symptomatic lymphoceles group and control group. The two-year disease free survival was 54% for the group with lymphocele and 48% for the control group (p log Rank= 0.65). The two-year overall survival was 90% for the group with lymphoceles and 88% for the control group (p log Rank= 0.70).

Conclusions
Symptomatic lymphoceles are frequent after cytoreduction surgery in ovarian cancer. Supraradical surgery is an independent risk factor. Occurrence of symptomatic lymphoceles doesn’t decrease survival. Nevertheless further studies are needed to reduce the risk of lymphocele in such patients.
MALIGNANT OVARIAN TUMOR WITH PREGNANCY: PATHOLOGICAL ANALYSIS OF 41 CASES IN JAPAN

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Objectives
The aim of this study was to review the malignant ovarian tumors in Japanese pregnant women and to investigate maternal and perinatal management in relation to histological findings.

Methods
Retrospective study from 41 patients diagnosed and treated for ovarian malignancy during pregnancy from 1985 to 2010.

Results
Median age was 30 years old with the age bracket of 20 to 41. Thirty-eight (92 %) patients were diagnosed with stage I, and one (2 %) for each stage II, III and IV. Twenty-three (56 %) were borderline malignancy (BLM) and 10 (24 %) were epithelial ovarian cancer (EOC). Seven (17 %) were germ cell tumor and one was sex cord stromal tumor. All patients received primary surgery; 6 (14 %) patients were cystectomy, 32 (78 %) were unilateral salpingo-oophorectomy and 3 (7 %) were hysterectomy with bilateral salpingo-oophorectomy. Twenty-nine (70 %) cases raised live newborn; 21 BLM (91 %), 2 EOC (20 %) and 6 non-epithelial tumor (NET) (75 %). Eight cases were terminated to perform the standard treatment for ovarian malignancy and 2 cases aborted spontaneously.

Conclusions
In pregnant women, EOC was remarkably less frequent compared with non-pregnant, age-matched, statistically-corrected control based on Japanese annual report (10/33 (30 %) vs. control (60 %); EOC/(EOC + BLM), P = 0.001). Pregnant women with EOC preferred to prioritize the treatment of ovarian cancer at the sacrifice of their babies while those with BLM or NET could successfully raised the live newborn.
Poster Presentations: Ovarian Cancer

SHOULD HIGH-GR ADE SEROUS OVARIAN, TUBAL AND PRIMARY PERITONEAL CARCINOMA BE CLASSED AS A SINGLE DISEASE?

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Objectives
The dualistic theory of ovarian cancer proposes that epithelial 'ovarian' cancer is not one entity with several histological subtypes but a variety of different diseases arising from different cells of origin, which may not originate in the ovarian epithelium.

Methods
Cases were classified according to the dualistic theory into type 1 (low-grade endometrioid (LGE)/clear cell (CC)/mucinous (Mu)/low-grade serous (LGS)) and type 2 (high-grade serous (HGS)/high-grade endometrioid (HE)/carcinosarcomas (CS)/undifferentiated (U)) cancers.

Results
648 women were diagnosed with an ovarian (85.0%), tubal (3.9%) or peritoneal carcinoma (11.1%). Type 1 tumours accounted for 139 (25.2%) of ovarian, 1 (4.0%) of tubal and 6 (8.3%) of peritoneal cancers, whereas 328 (59.5%) of ovarian, 24 (96.0%) of tubal and 65 (90.3%) of peritoneal cancers were type 2 tumours. Only 16 (5.7%) of ovarian HGS cases were stage I at diagnosis whereas 242 (86.7%) were stage III+. Overall survival differed between the subtypes when matched for stage. Stage III LGS and HGS cancers had a significantly better survival compared to CC and Mu cancers, p=0.0194. There was no significant difference in overall survival between the HGS ovarian, tubal or primary peritoneal cancers when matched for stage (stage III p=0.754, stage IV p=0.739).

Conclusions
Type 2 ovarian cancers are more common than type 1 and account for the majority of tubal and peritoneal cancers. Histological subtype is a significant prognostic indicator independent of stage. HGS cancers, whether classified as ovarian, tubal or primary peritoneal, behave as one disease with no significant difference in survival outcomes.
Poster Presentations: Ovarian Cancer

SEQUENTIAL MAINTENANCE CHEMOTHERAPY WITH TAXANE AND ORAL ETOPOSIDE FOR ADVANCED OVARIAN CANCER AND PERITONEAL CANCER

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Objectives
To demonstrate preliminary results of sequential maintenance chemotherapy with taxane and oral etoposide (SMCTE) for patients with advanced ovarian cancer or peritoneal cancer.

Methods
Patients with Stage III ovarian cancer or peritoneal cancer who started initial treatment at our institute between January 2008 and December 2011 were enrolled. Eligible criteria were as follows: 1) patients with dissemination in multiple sites beyond the pelvis at the initial surgery, 2) patients with no evidence of disease after initial treatment had completed, and 3) patients obtained informed consent in a documented form. As SMCTE, we scheduled to administer them with paclitaxel (175mg/m²) or docetaxel (70 mg/m²) monthly for 10 to 12 cycles, followed by oral etoposide (50 mg/ day x 21 days) monthly for three or four cycles. The adverse effects, feasibility, and progression-free survival (PFS) were examined.

Results
Fourteen patients were enrolled in this study. Adverse effects were mostly moderate except for two patients who experienced angina and interstitial pneumonia, respectively, and discontinued treatment. Both of them had severe complications before the initial treatment. Except them, actual given cycles of monthly taxane varied six to 12 according to patients' conditions. In four cases, serum CEA level had increased during taxane administration, but decreased after oral etoposide administration. The median PFS was 45 months with median follow-up period of 39 months (range, 17 to 65 months).

Conclusions
Although patients with severe complications should be excluded, SMCTE is feasible and may improve prognoses of the patients with advanced ovarian or peritoneal cancer. Further prospective studies are warranted.
Poster Presentations: Ovarian Cancer

MESENTERIC LYMPH NODE INVOLVEMENT IN ADVANCED OVARIAN CANCER PATIENTS UNDERGOING RECTOSIGMOID RESECTION: PROGNOSTIC ROLE AND CLINICAL CONSIDERATIONS

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Objectives
The aim of this study was to retrospectively investigate the incidence of mesenteric lymph node (MLFN) involvement, and its prognostic role in advanced ovarian cancer (OC).

Methods
OC patients undergoing rectosigmoid resection during primary debulking (PDS) or interval debulking surgery (IDS) were recorded. Progression free survival (PFS) and overall survival (OS) were calculated from the date of diagnosis to the date of relapse/progression or death of disease or the date of last follow-up.

Results
MLFN were detected in 102/148 cases (68.9%); the rate of MLFN involvement was 47.0%. The percentage of metastatic MLFN was higher in cases with >5 MLFN removed compared to cases with ≤5 MLFN removed (62.7% versus 31.3%; p value=0.0027). A progressive increase in the rate of metastatic MLFNs was documented with depth of bowel infiltration (p value=0.026). Cases with metastatic MLFNs experienced more frequently isolated celiac trunk or aortic lymph node recurrences than patients without MLFN involvement (44.8% versus 10.7%, p value= 0.0008). Median PFS did not differ between positive versus negative MLFN involvement (1-yr PFS= 69% versus 85%; p value=0.58). In patients experiencing isolated lymph node recurrences, patients with positive MLFN showed a worse PFS than cases without MLFN involvement (2-yr OS= 89% versus 53%, respectively; p value=0.041).

Conclusions
OC patients undergoing rectosigmoid resection showed a not negligible rate of metastatic MLFN involvement. Metastatic MLFN status is associated with a high rate of isolated aortic and celiac trunk lymph node recurrence, and with a worse PFS in this subset of patients.
THE ASSOCIATION BETWEEN THE SERUM HE4 CONCENTRATION AND THE MENSTRUAL CYCLE PHASE

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Objectives

HE4 (human epididymis protein 4) is a new and promising ovarian tumor marker. The purpose of this study was to investigate whether serum HE4 concentration varies significantly within the normal menstrual cycle.

Methods

Our study population consisted of 21 premenopausal women without adnexal pathology on ultrasound scan. No one of the recruited women reported a history of any ovarian disease or intervention. We measured their serum HE4 concentrations and evaluated the influence of the menstrual cycle phase on the tumor marker concentration.

Results

No significant variation in serum HE4 concentrations in samples taken at different phases of the menstrual cycle. The median HE4 concentrations in proliferative, secretory and menstrual phase were 37.1, 40.2 and 34.3 pM in the recruited group of women.

Conclusions

The present study shows that the HE4 measurement in healthy premenopausal women can be performed at any phase of the menstrual cycle.
A COMPARISON OF HE4 WITH CA 125 AS TUMOR MARKERS IN PATIENTS WITH OVARIAN CANCER

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Objectives
Human epididymis protein 4 (HE4) has been proposed as a tumor marker for ovarian cancer. In this trial we evaluated HE4 in comparison with cancer antigen 125 (CA 125) in healthy individuals and preoperatively in patients with benign and malignant ovarian diseases.

Methods
The CA 125 and HE4 serum concentrations were determined in 23 healthy individuals and in 100 cases with ovarian tumors. For CA 125 and HE4 we took cutoffs of 35 kU/L and 140 pmol/L, respectively.

Results
In the recruited healthy individuals was not detected any abnormal result for HE4. CA 125 was above its cutoff value in 4.3% of the cases. HE4 resulted with a higher specificity than CA 125 in patients with benign gynecologic diseases. HE4 had an abnormal concentration in 1.5% and CA125 in 37.4% of the patients with benign pathology. A significantly higher area under the ROC curve was obtained with HE4 than with CA 125 for differentiating benign from malignant diseases (0.851 vs 0.511) and in the differential diagnosis of gynecologic diseases (0.950 vs 0.632).

Conclusions
HE4 showed significantly higher diagnostic specificity than CA 125, but their combination may improve the detection of ovarian cancer in all stages.
Poster Presentations: Ovarian Cancer

PROSPECTIVE VALIDATION OF THE IOTA LOGISTIC REGRESSION MODELS (LR1/LR2) BY A LEVEL-2 ULTRASOUND OPERATOR AND COMPARISON TO PATTERN RECOGNITION FOR THE DIAGNOSIS OF OVARIAN CANCER

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Objectives

Many ultrasound models exist to aid pre-operative diagnoses of ovarian tumours. This study aims to validate and assess the accuracy of the IOTA Logistic Regression Models (LR1 and LR2) by a level II operator and that of subjective pattern recognition.

Methods

This was a prospective single-centre study in a general gynaecology unit of a tertiary hospital over 33 months. Included were 292 consecutive women who underwent surgery following an ultrasound diagnosis of an adnexal tumour. All examinations by the single Level II operator were according to IOTA guidelines. The malignancy likelihood was calculated using the IOTA LR/LR2. An expert operator using subjective pattern recognition then examined women separately. These were compared to operative findings and histology.

Results

The AUCs for LR1 and LR2 were 0.94 (95%CI, 0.92-0.97) and 0.93 (95%CI, 0.90-0.96) respectively. Subjective pattern recognition gave an LR+ve of 13.9 (95%CI, 7.84-24.6) and LR-ve of 0.049 (95%CI, 0.022-0.107). The corresponding LR+ve and LR-ve for LR1 were 3.33 (95%CI, 2.85-3.55) and 0.03 (95%CI, 0.01-0.10), and for LR2 3.58 (95%CI, 2.77-4.63) and 0.052 (95%CI, 0.022-0.123). The accuracy of pattern recognition was 0.942 (95%CI, 0.908 to 0.966) significantly higher compared with 0.829(95%CI, 0.781 to 0.870) for LR1 and 0.836 (95%CI, 0.788 to 0.872) for LR2 (p<0.001).

Conclusions

The AUC of the IOTA LR1 and LR2 were similar in non-expert's hands when compared to the original and validation IOTA studies. Pattern recognition method was the more accurate test to diagnose ovarian cancer than either of the IOTA models.
ROMA INDEX IMPROVES SPECIFICITY OF OVARIAN CANCER DIAGNOSIS COMPARED TO CA125 ALONE

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Objectives

Ovarian cancer is the fifth most common cancer in women and the most frequent cause of gynaecologic malignancy-related mortality in women. Clinical outcome and survival may be improved if the disease is identified in the early stages. Recently a novel biomarker Human epididymis protein 4 (HE4) has been demonstrated to be a sensitive and specific serum biomarker for ovarian cancer that is elevated less frequently by benign conditions that occur in premenopausal women. The aim of the study was to evaluate the utility of HE4 as a diagnostic and prognostic marker of ovarian cancer in premenopausal and postmenopausal women.

Methods

Serum was collected from 386 women of various histological subtypes prior to surgery for invasive, borderline and benign ovarian disease. HE4 EIA protocol and CanAg CA125 EIA protocols were carried out according to manufacturer’s instructions (FUJIREBIO Diagnostics). Risk of Ovarian Malignancy Algorithm (ROMA), which combines the result of HE4 and CA125, was calculated for premenopausal and postmenopausal women. Kruskal-Wallis Test and Mann-Whitney test were used for statistical analysis.

Results

The combination of HE4 and CA125 in the ROMA index showed increased specificity with a decreased sensitivity for detecting ovarian cancer compared to Roche CA125 in premenopausal women. An increase in specificity with similar sensitivity was observed in postmenopausal women when using the ROMA index. HE4 alone is more specific than CA125. Significant decreases in HE4 were observed in the majority of patients in the post operative setting and throughout chemotherapy.

Conclusions

HE4 improves the specificity of ovarian cancer detection and holds promise as a prognostic marker.
Poster Presentations: Ovarian Cancer

PRIMARY DEBULKING SURGERY (PDS) VERSUS NEOADJUVANT CHEMOTHERAPY FOLLOWED BY INTERVAL DEBULKING SURGERY (IDS) FOR PATIENTS WITH ADVANCED OVARIAN CANCER
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Objectives
Compare the survival between PDS and IDS in treating patients with advanced ovarian cancer (stage III and IV)

Methods
We retrospectively reviewed 92 patients with advanced ovarian cancer and primary peritoneal cancer (PPC) in the period between 01/01/2006 and 31/12/2006 where the majority of patients were treated with PDS and we compare them with 89 patients in the period between 01/01/2010 to 31/12/2010 where more patients with advanced disease were treated with IDS

Results
In 2006, 92 patients with advanced ovarian cancer and PPC were treated with both surgery and chemotherapy. 77.2% were ovarian cancer, 20.7% were PPC and 2.2% were fallopian tube cancer. 82.6% were stage III and 17.4% were stage IV. 66.3% were treated with PDS and 33.7% were treated with IDS. In the second group (89 patients), 68.5% were ovarian cancer and 31.5% were PPC. 82% were stage III and 18% were stage IV. 59.6% were treated with IDS and 40.4% were treated with PDS. The survival of the second group was higher at year 1 (89.9% vs. 83.7%) but it was lower at year 2 (58.5% vs. 62%). The survival for patients with ovarian cancer only was higher in the second group at year 1 (91.8% vs. 83.1%) and similar at year 2 (63.9% vs. 62%). The rate of resection to no residual disease or <1cm was higher in the second group (75.3% vs. 67.2%)

Conclusions
The data suggest a better resection rate, a better survival at year 1 and a non inferior survival at year 2 with IDS.
Poster Presentations: Ovarian Cancer

CHEMOSENSITIVITY TESTING OF CIRCULATING EPITHELIAL TUMOR CELLS (CETC) IN OVARIAN CANCER IN VITRO: CORRELATION TO CLINICAL OUTCOME

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Objectives
Chemotherapy is one of the pillars of ovarian cancer therapy, however, it is predominantly applied according to empirically developed recommendations derived from statistical relapse rates and from progression-free interval data, without any possibility of determining the efficacy in the individual patient. Time and quality of life are lost if the drugs are not effective. Here, we present a method to determine the efficiency of chemotherapeutic drugs using tumor cells circulating in blood as the part of the tumor actually available in the patient’s body for chemosensitivity testing.

Methods
After only red blood cell lysis, omitting any enrichment (analogous to other blood cell enumeration methods, including rare CD34 cells), the white cells comprising the circulating epithelial tumor cells (CETC) from 56 patients with ovarian cancer were exposed to carboplatin, paclitaxel, topotecan and doxorubicine in three different concentrations for 3-9hrs. Staining with a fluorescence-labeled anti-epithelial antibody and nuclear staining with propidium iodide through membrane permeability distinguished vital from dying tumor cells.

Results
Increasing percentages of dying tumor cells were seen dependent on time and concentration. The sensitivity of the tumor cells to the drugs was shown to vary between patients during therapy and was correlated with decrease or increase in CETC and clinical outcome.

Conclusions
Thus, we are able to show that chemosensitivity testing of circulating tumor cells in ovarian cancer provides real-time information about the sensitivity of the tumor present in the patient, even at different times during therapy, and correlates with treatment success.
EFFICACY OF CARBOPLATIN/PACLITAXEL SCHEDULES TAILORED TO AGE AND COMORBIDITIES IN ADVANCED OVARIAN CANCER

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Objectives

Different Carboplatin/Paclitaxel schedules were retrospectively evaluated in advanced ovarian cancer (OC).

Methods

Three schedules were planned according to age and Comorbidity Illness Rating Scale (CIRS): Carboplatin AUC 1.7-Paclitaxel 60 mg/mq weekly (ARM A); Carboplatin AUC 5-Paclitaxel 175 mg/mq d1q21 (ARM B); Carboplatin AUC 6-Paclitaxel 175 mg/mq d1q21 (ARM C).

Results

46 patients with stage IIIC-IV were treated; median age 67 (33-85); old-elderly (≥75y) 10 (22%), young-elderly (≥65/<75) 16 (35%), non-elderly (<65y) 20 (43%); PS 0, 2%; 1, 76%; 2, 22%. CIRS: primary, 5 (11%); intermediate, 23 (50%); secondary, 18 (39%). Metastatic sites: peritoneum (91%), lymph-nodes (30%), pleura (26%). Schedules: ARM A, 20 (43%), median age 74.5, 5 (25%) intermediate, 15 (75%) secondary CIRS; ARM B, 16 (35%), median age 61, 14 (88%) Primary/Intermediate, 2 (12%) secondary CIRS; ARM C, 10 (22%), median age 55.5, 9 (90%) Primary/Intermediate, 1 (10%) secondary CIRS. Among 42 evaluable pts, ORR 75% (pathological complete response 7%). At 13 months median follow up, PFS and OS were 15 and 42 months respectively. ARM A, B, C, respectively: ORR 76%, 81%, 67%; PFS 29, 15, 15 months; OS 88, 43, 27 months. PFS and OS were not significantly different, even if ARM A seems trendly favourable. Toxicity profiles were not different according to arms.

Conclusions

Tailored Carboplatin/Paclitaxel schedules can be suggested in clinical practice, based on age/comorbidity, with similar benefit/toxicity ratio: weekly schedule for elderly/CIRS Intemediate and Secondary and non-elderly/CIRS Secondary; three-weekly schedule for non-elderly/CIRS Primary and Intermediate and elderly/CIRS Primary.
CHEMOTHERAPY FOR OVARIAN CANCER INDUCES PD-L1 OVEREXPRESSION VIA NF-KB SIGNAL PATHWAY

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Objectives
Ovarian cancer is leading cause of gynecological malignancies, and new treatment strategy for this cancer is urgent. Recently, growing evidences have shown response to chemotherapy is modulated by host immune system. The aim of this study was to analyze the relationship between chemotherapy and immune function in ovarian cancer.

Methods
After mouse or human ovarian cancer cell lines cultured with carboplatin or paclitaxel or gemcitabine, the expression of PD-L1 and upstream transcription factors of PD-L1 were analyzed by Western blot, qRT-PCR or flow cytometry. Following intraperitoneal injection of PD-L1 overexpressed (ID8-PDL1) or PD-L1 depleted (ID8-mirPDL1) into syngeneic mice, we administered paclitaxel or PBS into mice abdominal cavities and analyzed survival time.

Results
Firstly, we analyzed a public microarray dataset and found PD-L1, an immunosuppressive co-factor, and NF-kB upregulated after carboplatin treatment. Both PD-L1 and NF-kB protein expression was upregulated when carboplatin or paclitaxel or gemcitabine was added to mouse or human ovarian cancer cell lines. PD-L1 expression was decreased when NK-kB was knocked down by siRNA in mouse cell lines. Next, The ID8-PD-L1 mice without paclitaxel showed the worst prognosis, while ID8-mirPDL1 mice with paclitaxel showed the best prognosis (p<0.01).

Conclusions
As chemotherapy causes upregulation of PD-L1, a negative regulator of immune system, combination of chemotherapy with PD-1/PD-L1 signal blockade could be a promising treatment modality against ovarian cancer.
Poster Presentations: Ovarian Cancer

BRAIN METASTASES IN EPITHELIAL OVARIAN CANCER- MULTIMODAL TREATMENT INCLUDING SURGERY OR GAMMA-KNIFE RADIATION ASSOCIATED WITH PROLONGED SURVIVAL

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Objectives
To explore the influence of different treatment modalities on survival in patients with brain metastases from epithelium ovarian cancer

Methods
Retrospective chart review from all patients with ovarian cancer and brain metastases treated at 3 different hospitals (Canada, India, and China). Medline search was performed to extract data from published reports which detailed survival related to treatment modality

Results
Twelve patients with sufficient details were included, with mean age was 56, including 5 patients from China, 4 patients from Canada, and 3 patients from India. The median time from the diagnosis of ovarian cancer to brain metastasis was 19 months (range 10-37 months), and the overall survival from the diagnosis of ovarian cancer was 35 months (range 13-75 months). In patients who had multimodal treatment including gamma knife or surgery, the survival after the onset of brain metastasis was 24.5 months compared to the 4.5 months in patients whose treatment did not include targeted treatment. Analysis of the literature also indicated that use of Gamma-knife radio surgery and surgery in multi-modal treatment resulted in improved survival interval

Conclusions
Prolonged survival may be obtained by multidisciplinary therapy in patients with brain metastases from ovarian cancer, especially gamma knife and surgery.
Poster Presentations: Ovarian Cancer

TOLL-LIKE RECEPTOR SIGNALING: IMPACT ON PROGRESSION AND CHEMoresistance IN EPITHELIAL OVARIAN CANCER

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Objectives
Recent data suggest that tumor cells have adapted toll-like receptor (TLR) signaling. Exosomes, extracellular membrane vesicles sized 40-100nm, have been shown to activate TLR signaling, leading to NF-κB and STAT3 activation and subsequent release of pro-inflammatory molecules, changing the tumor microenvironment in a way that supports their own proliferation and survival. We aimed to identify the functional significance of TLRs on tumor cells and its requirements for cancer progression. We hypothesized that in ovarian cancer cell lines chemoresistance is, at least in part, induced by TLR-activation.

Methods
THP-1, OVMz and SKOV3 cell lines were examined for the expression of TLR-2,-4,-7,-8. We studied cytokine production following TLR stimulation and analyzed the effects of exosomes on TLR activation in tumor cells using exosomes from ovarian carcinoma cell lines, amniotic fluid and malignant ascites from ovarian cancer patients isolated by ultracentrifugation.

Results
We observed TLR2 and TLR4 expression in THP-1 cells. Knock-down of TLR2, but not TLR4 by lentiviral-shRNA blocked NF-κB and STAT3 activation. OVMz cells expressed TLR4, whereas SKOV3 cells showed predominantly TLR2 expression. Consistent with the literature, no expression of TLR7 and TLR8 was observed in OVMz or SKOV3 cells. THP-1 cell stimulation with ascites-derived exosomes showed upregulation of IL-6, IL-1β, TNFα, IL-23A, and RANTES after 24h. TLR-ligand stimulation of OVMz and SKOV3 is presently investigated and will be reported.

Conclusions
We demonstrated that exosomes trigger cytokine release in monocyctic cells suggesting that exosomes can induce an inflammatory and prometastatic state in a TLR-dependent manner. These inflammatory conditions could promote tumor progression and chemoresistance.
Poster Presentations: Ovarian Cancer

DETECTION OF NON-OVARIAN CANCERS ON PHASE 2 OF THE UK FAMILIAL OVARIAN CANCER SCREENING STUDY (UKFOCSS)

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Objectives
Ovarian cancer (OC) screening in high-risk women on UKFOCSS involved annual pelvic sonography and 4-monthly serum CA125. These can be abnormal in non-ovarian/tubal/peritoneal cancers, which this population is at increased risk of. We assessed how many of these other cancers were screen-detected.

Methods
Women were followed 1 yr post final screen. Only asymptomatic cancers referred with abnormal results were classified 'screen-positive'.

Results
4329 women aged 35-85 yrs without OC were evaluated. 674/4329 (15.6%) were referred with abnormal results: 292 (6.7%) for possible OC and 382 (8.8%) for thickened/abnormal endometrium or non-gynaecological scan abnormalities. 173 cancers were diagnosed (152 non-gynaecological cancer, 21 endometrial cancer (EC)/atypical endometrial hyperplasia (AEH)). 24/674 referrals (3.6%) had screen-positive pre-cancer/cancer: 2 AEH, 9 EC, 9 metastatic breast cancer (BC), 4 other non-gynaecological cancers (2 metastatic). 13/152 (8.8%) non-gynaecological cancers were screen-positive (mostly BC) (PPV 4.5%, 2.5%-7.7%). 11/21 (52.4%) EC/AEH were screen-positive (PPV 3.1%, 1.5%-5.6%). 7/8 postmenopausal women (87.5%) with EC/AEH were screen-positive (PPV 3.8%, 1.7%-7.9%). 6/13 (46%) women with screen-positive non-gynaecological cancers died vs. 8/120 (7%) in the screen-negative group (HR 8.98, 3.5%-23.9, p<0.001). Median survival was 11.1 and 19.4 months respectively (p<0.001).

Conclusions
OC screening using ROCA and annual pelvic sonography detected EC/AEH mostly in postmenopausal women. A proportion of non-gynaecological cancers were also detected. These results highlight the need to rule out other malignancies in this population when CA125 levels rise in the absence of primary ovarian/tubal/peritoneal cancer. If a non-gynaecological cancer is found, survival is poor, which may reflect detection of metastatic disease.
Poster Presentations: Ovarian Cancer

ANALYSIS OF BRCA-1 AND BRCA-2 MUTATIONS IN PLATINUM-RESISTANT AND PLATINUM-REFRACTORY PATIENTS WITH OVARIAN CANCER
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Objectives
The aim of investigation was the comparative analysis of the sensitivity of patients with ovarian cancer stage IC-IIIC to adjuvant therapy with platinum, depending on the presence or absence of mutations in the genes BRCA 1 and BRCA 2.

Methods
We investigated 74 patients with ovarian cancer stage IC-IIIC, who underwent optimal or suboptimal cytoreductive surgery followed by adjuvant chemotherapy with platinum. The criterion for dividing the patients into groups was selected ovarian sensitivity to platinum drugs.

Results
Mutation-1 of gene BRCA1 (polymorphism 185delAG) was detected in 56 (76.7%) patients of the main group and 12 (36.4%) patients of the control group. Mutation -2 of gene BRCA1 (5382 polymorphism insC) was detected in 53 (72.6%) patients of the first group and 6 (18.2%) female control group. Mutation-1 gene BRCA2 (polymorphism 6174delT) was detected in 45 (61.4%) patients in the first group and in 12 (36.4%) patients of the control group.

Conclusions
We have identified a variety of options for BRCA gene mutations in patients with ovarian cancer: BRCA 1 (185delAG) - 64.2%, BRCA 1 (5382 insC) - 55.7%, and BRCA 2 (6174delT) - 53.8%
It was shown no significant correlation between the stage of the disease, clinical and anamnestic characteristics of patients with ovarian cancer and tumor sensitivity to platinum drugs.
We found a significant positive correlation between carriage of mutations in the BRCA genes half and malignant ovarian tumors refractory to platinum-based chemotherapy. Mutations in these genes occurred significantly more often in patients with platinum-resistant and platinum-refractory ovarian cancer.
TREATMENT PATTERNS IN THE ADVANCED OVARIAN CANCER POPULATION: DATA FROM AGO QS-OVAR 2008 PROSPECTIVE COHORT
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Objectives
To describe platinum versus non-platinum based treatment patterns observed in a prospective cohort of women diagnosed with ovarian cancer.

Methods
QS-OVAR is a national quality assurance program including this prospective cohort of patients newly diagnosed with invasive epithelial ovarian cancer in Germany. Patients were enrolled in the third quarter of 2008 and followed for 4 years. Number of recurrences and use of platinum and non-platinum based regimens was evaluated in 700 patients diagnosed with advanced disease (FIGO stage IIB-IV) for each line of therapy.

Results
Two thirds of the study population (511/ 700) had at least one recurrence, 191 patients had at least two, and 76 patients had at least three recurrences. Out of the 611 patients who underwent chemotherapy, majority received platinum based regimen as initial treatment (97.2%), while 54.8%, 21% and 24.6% of the patients received platinum based treatment in the 2nd, 3rd, and 4th line, respectively. More than half of the patients (60%) had recurrence < 12 months since 1st line treatment, 31% had recurrence > 12 months after 1st line and 8% relapsed during initial treatment.

Conclusions
Non-platinum based regimens are frequently used in recurrent ovarian cancer. The proportion of patients receiving non-platinum based regimens rises with each subsequent line of therapy. More research is needed to understand the factors associated with the decision to use non-platinum based regimens in recurrent ovarian cancer.
Poster Presentations: Ovarian Cancer

NESTED STROMAL EPITHELIAL TUMOR (NSET ) OF THE LIVER WITH BILATERAL OVARIAN METASTASIS
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Objectives
Nested stromal epithelial tumor (NSET ) is a recently described primary neoplasm of the liver. This is predominantly a tumour of young women. This tumor is characterized by nests of epithelial and spindle cells, an associated desmoplastic stroma, as well as variable calcifications and ossifications.

Methods
Only 24 cases have been reported in the english-language literature whereas none of them has related ovarian metastasis. Herein we report a case of a nested stromal epithelial tumor of the liver in a 16-year-old female with bilateral ovarian metastasis.

Results
This case is the first case with ovarian metastasis and 4th case of NSET associated with genitourinary system abnormalities. Most patients are doing well with no tumor recurrence in 6 months to 14 years. Tumor recurrence has been observed in two of twenty four patients.

Conclusions
Our patient had liver transplantation for the treatement of primary NSET of liver. One year after succesful liver transplantation patient admitted to hospital with abdominopelvic pain. A magnetic resonas imaging(MRI) scan revailed bilateral giant over masses. She underwent bilateral oofectomy. Pathology of ovarian masses were revealed metastasis from nested stromal epithelial tumor of the liver. The patient is currently alive and well with no evidence of disease.
IN EPITHELIAL OVARIAN CANCER CELLS: 5T4 PROMOTES CELL MOTILITY, INDUCES EPITHELIAL MESENCHYMAL TRANSITION AND SWITCHES WNT SIGNALLING TO NON-CANONICAL PATHWAY

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Objectives
Metastasisation is clinically detrimental to Epithelial Ovarian Cancer (EOC) patients' survival who generally present with advanced stages. EOC has been previously found to express 5T4, an oncofetal glycoprotein not usually expressed by healthy adult tissues. The aim of this study was to investigate a functional role for 5T4 in EOC spread.

Methods
Flow cytometry and Immunostaining were used to determine surface expression of 5T4 and selected epithelial/mesenchymal markers (cadherins, vimentin and cytokeratins), cell motility was investigated by Fluorblok transwell assays while immunostaining of β-catenin was used to determine Wnt response.

Results
SKOV-3 (EOC cell line) was found to express 5T4 and showed a mesenchymal phenotype. 5T4 knockdown produced cells (KD-SKOV-3) which were broad, expressed epithelial markers and showed re-arrangement of actin 'stress fibres' to thin cortical bundles; all indicators of Mesenchymal Epithelial Transition (MET).

In addition, in comparison to controls KD-SKOV-3 manifested reduced cell motility to fetal calf serum and Wnt5a, and showed increased β-catenin nuclear translocation when treated with Wnt3a; indicative of a switch in Wnt response. Interestingly, 5T4 overexpression in Hoc-8, a 5T4-negative EOC cell line, promoted EMT and cell motility.

Analysis of 11 paired (primary & metastatic) human EOC samples showed higher 5T4 expression in the metastatic samples (17%, p=0.004), accompanied by reduced expression in cytokeratins (-54%, p=0.035), and correlated conversely with E-cadherin expression (Rho=-0.63, p=0.038).

Conclusions
This study found 5T4 to be upregulated in metastatic lesions, and changes in its expression in vitro supported a metastatic phenotype making 5T4 a potential marker and therapeutic target in metastatic ovarian disease.
**Poster Presentations: Ovarian Cancer**

**INTRATUMORAL PEAK SYSTOLIC VELOCITY – PSV AND INTENSITY OF VASCULARITY IN PREDICTING DRUG RESISTANT IN EPITHELIAL OVARIAN CANCER**

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**Objectives**
To evaluate the prognostic significance of ultrasound derived type of vascularity in predicting drug resistance in EOC

**Methods**
Data from 68 relapsed cases, stage III primary EOC were reviewed. PSV and intensity of vascularity were assessed immediately before cytoreductive laparotomy followed by adjuvant platinum and paclitaxel based chemotherapy. Type of vascularity according to the drug-sensitive and drug-resistant relapses was analyzed.

**Results**
Intensity of vascularization in primary tumors was as followed: no flow in 2 cases (2.9%), slight flow in 18 cases (26.5%), moderate flow in 14 cases (20.6%), and intense flow in 34 cases (50%). In platinum-sensitive cases moderate and intense flow were recorded in 8 (19%) and 34 (81%) respectively. There were no cases with no or slight flow. In platinum-resistant cases no flow was detected in 2 (7.7%), slight flow in 18 (69.3%), moderate flow in 6 (23%) cases. In this group any intense flow was detected. Mean PSV in platinum-sensitive relapses were 27.5 cm/s while in platinum-resistant were 9.25 cm/s and was significantly higher (p<0.0001). In suboptimal cytoreductive platinum-sensitive cases the mean PSV was 27.58 cm/s while in suboptimal cytoreductive platinum-resistant cases was 9 cm/s – p<0.0001. Similarly in optimal cytoreductive platinum-sensitive and platinum-resistant cases these data were 30.72 cm/s and 9.5 cm/s respectively – p<0.0001

**Conclusions**
Platinum sensitive tumors revealed significantly more intense vasculature and significantly higher peak systolic velocity as compared to platinum resistant cases both in optimal and suboptimal cytoreductive patients. Thus type of vascularity can predict drug resistance in relapsed EOC and can be the additional prognostic factor of response.
DIFFERENCE IN LINE-1 METHYLATION BETWEEN SOLITARY AND OVARIAN CANCER ASSOCIATED ENDOMETRIOSIS

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Objectives
Endometriosis in endometriosis-associated ovarian cancer (EAOC) is a lesion derived from the endometrium that may transform into ovarian cancer. Hypomethylation of Long Interspersed Element-1 (LINE-1 or L1) is a common epigenomic change in cancer and is strongly associated with ovarian cancer progression. This study evaluated alterations in LINE-1 methylation in endometriosis and EAOC.

Methods
First LINE-1 methylation levels in 19 normal endometrium, 29 solitary ovarian endometriosis (SOE), 35 ovarian clear cell carcinoma (OCC) and 22 ovarian endometrioid adenocarcinoma (OEA) tissues from unrelated samples were compared. Then, the eutopic endometrium, contiguous endometriosis and cancer from 16 EAOCs were collected by laser capture microdissection, and the LINE-1 methylation status was analyzed.

Results
The total LINE-1 methylation levels were significantly different among the endometrium, endometriosis and ovarian cancer (P<0.001). A stepwise decrease in LINE-1 methylation was observed in the following order: normal endometrium, SOE, OEA and OCC. Interestingly, endometriosis in EAOC of both OEA (P=0.016) and OCC (P=0.003) possessed a higher percentage of LINE-1 unmethylated loci than SOE.

Conclusions
LINE-1 hypomethylation is an early molecular event involved in OEA and OCC malignant transformation. Precise measurements of LINE-1 methylation may help to distinguishing SOE and endometriosis in EAOC.
SOE : Solitary Ovarian Endometriosis, OCC: Ovarian Clear Cell carcinoma, OEA : Ovarian Endometrioid Adenocarcinoma, EAOC : Endometriosis-Associated Ovarian Cancer, \textsuperscript{m}C\textsuperscript{u}C : partial methylation, \textsuperscript{u}C\textsuperscript{u}C : unmethylated.
THE TOXICITY OF CHEMOTHERAPY IN OLDER OVARIAN CANCER PATIENTS

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Objectives

Ovarian cancer confers a poorer prognosis in older patients, even after adjustment for life expectancy. Factors which have been shown to contribute to this difference include late presentation and less frequent use of chemotherapy. The optimal strategy for the use of chemotherapy in these patients remains the subject of debate.

Aim: To explore the feasibility of chemotherapy administration in older patients with advanced ovarian cancer.

Methods

Data were gathered from the notes of a random sample of 250 patients with advanced ovarian or primary peritoneal cancer. All patients presented via the regional Specialist Gynaec-Oncology MDT between January 2006 and July 2009. The data included patient characteristics, management strategies and survival.

Results

Ninety-nine of the 250 patients studied were aged 70 or older (40%). Sixty-three of these older patients received chemotherapy (64%). There were thirteen dose reductions during first line treatment (21% of patients) and thirty-three dose delays due to toxicity (9% of planned chemotherapy cycles). Twenty patients (32%) stopped 1st line chemotherapy earlier than expected; ten due to treatment toxicity, five due to progressive disease and five patients died prior to completion of chemotherapy.

Conclusions

Older women make up around forty percent of our ovarian cancer patient population. A significant group of these patients experienced toxicities; frequently leading to dose reductions and delays as well as cessation of treatment. Further work is needed to ascertain a method by which to assess suitability for chemotherapy, to allow selection of the optimal treatment strategy for these older women.
Poster Presentations: Ovarian Cancer

USE OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY AND COMPUTED TOMOGRAPHY BASED NOMOGRAMS TO PREDICT INCOMPLETE CYTOREDUCTION IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Objectives
To develop a preoperative PET/CT based nomogram to predict incomplete cytoreduction (macroscopic residual disease) in patients with advanced-stage epithelial ovarian cancer (AEOC).

Methods
Between 2004 and 2009 159 AEOC patients with preoperative PET/CT were retrospectively reviewed. The ratio between the highest SUVmax in the upper abdomen and lower abdomen divided at the level of the umbilicus was expressed as the UA/LA SUVmax. Possible predictors of incomplete cytoreduction (including 10 PET/CT features) were analyzed using a logistic regression model, from which a nomogram was developed and internally validated.

Results
The median age was 55 (27–80) years; 133 and 26 patients had stage III and IV disease, respectively. Complete cytoreduction was achieved in 44 (27.7%) patients. Multivariate analysis revealed that four PET/CT features including diaphragm disease (P=0.027, OR 3.699, 95% CI 1.164–11.760), peritoneal carcinomatosis (P=0.033, OR 6.554, 95% CI 1.163–36.923), lymph node outside abdomen (P=0.029, OR 3.580, 95% CI 1.140–11.247), and UA/LA SUVmax (P=0.016, OR 4.798, 95% CI 1.338–17.206) were independent predictors of incomplete cytoreduction. A nomogram predictive of an incomplete cytoreduction incorporating these four significant variables was constructed (concordance index = 0.80). The predictive ability of this nomogram proved to be superior to that of traditional predictors (CA125 and albumin) (P<0.05).

Conclusions
A nomogram based on four preoperative PET/CT features can accurately predict incomplete cytoreduction in patients with AEOC. If externally validated, it could be used in patients with AEOC to establish a more meticulous preoperative plan or determine whether neoadjuvant chemotherapy should be considered.
Fig. Constructed nomogram based on four preoperative PET/CT feature to predict incomplete cytoreduction in patients with AEOC.

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EPIDERMAL GROWTH FACTOR RECEPTOR GENE STATUS IN BORDERLINE OVARIAN TUMORS AND LOW GRADE SEROUS CARCINOMA

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Objectives
Borderline ovarian tumours (BOT) comprise 15-20% of ovarian epithelial neoplasms. The majority of BOT behave in a benign fashion, while few recur or progress as low grade carcinoma. To date there are no predictive biomarkers for the behaviour of BOT and no effective therapy for recurrent/progressive tumours. Somatic mutations and polymorphisms in epidermal growth factor receptor (EGFR) have been correlated with treatment responses and prognosis in some epithelial cancers. The aim of this study was to investigate EGFR gene status in BOT and low grade serous carcinoma (LGSC).

Methods
DNA was extracted from formalin fixed paraffin embedded tissue of 59 BOTs (45 serous and 14 mucinous) and 9 LGSC. Using bi-directional Sanger sequencing, we studied the sequence in 4 mutation hot spots (exons 18-21) in the tyrosine kinase domain of the EGFR gene.

Results
No functional mutations were detected in any of the tumours. Sequence analysis revealed the presence of c.2361 G>A polymorphism in exon 20 (rs1050171). The genotypes GG, GA and AA were detected respectively in 15 (25.4%), 29 (49.2%) and 15 (25.4%) of BOT and in 0 (0%), 8 (88.9%) and 1 (11.1%) in LGSC. Regarding exon 21, rs17290559, rs41420046 (in heterozygocity) were detected in BOT in 5(8.2%), 1 (1.6%), while one case of LGSC showed the rs17290559. COSM26129, a rare silent substitution was identified in one BOT.

Conclusions
EGFR mutations do not appear to be a molecular event in BOT and LGSC. However, there are gene polymorphisms, some of which are reported to be predictive of response to anti-EGFR agents.
SYSTEMATIC LYMPHADENECTOMY AT SECOND LOOK SURGERY IN APPARENT EARLY STAGE OVARIAN CANCER AFTER INADEQUATE SURGERY AND CHEMOTHERAPY: A RETROSPECTIVE STUDY
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Objectives
Systematic aortic and pelvic lymphadenectomy (SAPL) is a milestone procedure in the treatment of early stage ovarian cancer. It defines staging and prognosis and helps in tailoring adjuvant chemotherapy. Only limited data are available about SAPL at second look surgery in patients with apparent early stage ovarian cancer who underwent inadequate surgical staging and adjuvant platinum based chemotherapy.

Methods
From January 1991 through January 2013, 66 patients with International Federation of Gynecology and Obstetrics (FIGO) stage IA-IIA epithelial ovarian carcinoma unoptimally staged at primary surgery and treated with adjuvant chemotherapy, were referred to our centre and underwent a second look surgery including SAPL.

Results
Twenty- two women underwent bilateral and 44 monolateral SAPL. A total of 2168 nodes were removed and analysed. The median number of lymph nodes sampled was 29 (range 14-73); in particular it was 29 (range 14-60) in case of unilateral and 37 (range 17-73) in case of bilateral lymphadenectomy. Only one woman had nodal metastasis (1.5%). After a median follow up of 78 months, 10 women relapsed and 5 died of progressive disease. The 5-year disease-free survival and overall survival were 91.7% and 96%.

Conclusions
The risk of nodal metastases in stage I-IIA unstaged ovarian cancer after adjuvant chemotherapy is negligible. Our study suggest that SAPL at second look in the retroperitoneum is not indicated in this subset of women.
VORINOSTAT INDUCES ARID1A SPlicinG VARIANT EXPRESSION WHICH MAY REGULATE HNF1B AND CELL SURVIVAL, IN OVARIAN CLEAR CELL CARCINOMA (CCC)

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Objectives
Clear cell carcinoma (CCC) is a rare type of ovarian cancer known to be highly chemoresistant and having a very poor prognosis. Unique histology, de novo expression of HNF1β (responsible for cell survival and glycogen metabolism), molecular changes in tumor suppressor ARID1A gene, and overexpression of histone deacetylases (HDAC) are also associated with CCC.

Aims: To evaluate the action of vorinostat, a HDAC inhibitor, in the regulation of HNF1β, ARID1A and cell survival.

Methods
We used a CCC cell line- ES2,- cultured with and without vorinostat (5µM). Cell death was evaluated by flow cytometry, Annexin V-FITC and 7AAD-PE. HNF1β and ARID1A expression was evaluated by RQ-PCR, immunofluorescence and western blotting. HNF1β promoter activity was evaluated by luciferase reporter gene assay. ARID1A binding to HNF1β promoter was evaluated by chromatin immunoprecipitation.

Results
Vorinostat only induced cell death in ES2 during the first 30h, after this time, cells were able to recover and proliferate. Vorinostat increased HNF1β promoter activity as well as HNF1β and a splicing variant of ARID1A expression. This ARID1A variant (20KDa) was supposed to be destroyed by NMD (Non-sense Mutation Decay) system. Vorinostat also highly increased the relative occupancy of ARID1A in HNF1β promoter.

Conclusions
Vorinostat is not an appropriate therapy in ovarian CCC, since it induces the expression of HNF1β, responsible for these cells survival. CCC cell line exposure to vorinostat pointed out a regulation mechanism of HNF1β expression, mediated by a splicing variant of ARID1A. This mechanism can be used to define more effective therapeutic strategies.
Poster Presentations: Ovarian Cancer

QUANTITATIVE NUCLEAR EXPRESSION OF H2AX AND P53 IN OVARIAN AND FALLOPIAN TUBE EPITHELIUM FROM RISK-REDUCING SALPINGOO- OOPHORECTOMIES IN BRCA1/2 MUTATION CARRIERS

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Objectives

Mutations in BRCA1 and BRCA2 confer an increased lifetime risk for breast and ovarian cancer. Increased lifetime ovarian cancer risk among BRCA1/2 mutation carriers can be substantially decreased by risk-reducing salpingo-oophorectomy (RRSO), which also provides tools for molecular research focusing on early pathogenesis of serous ovarian cancer. RRSO studies have suggested fallopian tube as primary site of serous high-grade ovarian cancer.

Methods

The nuclear expression of γ-H2AX and p53 by immunohistochemistry was quantitatively assessed in ovarian and fallopian tube epithelium from RRSOs in 30 BRCA1/2 mutation carriers compared to controls. An individual multi-tissue block was made for each BRCA1/2 mutation positive patient. Two control tissue microarray blocks were constructed using ovarian and fallopian tube tissue blocks from mutation-negative and Lynch syndrome patients.

Results

Both p53 and γ-H2AX nuclear staining was significantly higher in BRCA1/2 mutation positive fallopian tube epithelium compared to controls (p=0.006 and p=0.011, respectively). p53 and γ-H2AX nuclear expression levels were similar in BRCA1/2 mutation positive ovarian epithelium and controls. Both γ-H2AX and p53 showed significantly higher nuclear expression in fallopian tube epithelium compared to ovarian epithelium in BRCA1/2 mutation carriers (p<0.0001 and p<0.0001, respectively). Nuclear expression of γ-H2AX and p53 in fallopian tube epithelium showed a positive correlation in BRCA1/2 mutation carriers (Pearson r=0.508, p=0.003).

Conclusions

Our results of quantitative p53 and γ-H2AX nuclear expression analysis in ovarian and fallopian tube epithelium from RRSO in BRCA1/2 mutation carriers support the previously suggested role of fallopian tube epithelium serving as an initial site of serous ovarian carcinogenesis.
**BETTER PROGNOSIS WITH POSITIVE SUPRACLAVICULAR LYMPH NODE: DO WE NEED SUBSTAGE IN FIGO STAGE IV OVARIAN CANCER?**

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**Objectives**

To evaluate the validity of recently proposed new FIGO staging system for ovarian carcinoma.

**Methods**

Survival outcomes were compared between the two staging allocations after restaging according to the forthcoming staging system.

**Results**

A total of 870 patients were analyzed. Mean age at diagnosis was 51.7 years. Median follow-up was 45 months. The 5-year survival rates (5YSR) according to the current staging system were 93.5% (Ia), 82.5% (Ic), 75.0% (IIb), 74.5% (Iic), 57.5% (IIla), 54.0% (IIlb), 38.1% (IIlc), and 33.0% (IV). For the new staging system, patients with current FIGO stage Ic disease were restaged into Ic1, Ic2, and Ic3, of which 5YSR were 92.0%, 85.0%, and 71.0%, respectively (p = 0.004). Patients allocated to current FIGO stage IIIc only due to retroperitoneal LN metastasis were reassigned to stage IIIa2, of which 5YSR was 66.3%, better than that of the remaining stage IIIc, 35.8% (p = 0.005). Patients allocated to stage IV due to supraclavicular LN metastasis had significant better 5YSR than those with other indications for stage IV disease (40% versus 28%, p = 0.022).

**Conclusions**

Our findings suggest that the forthcoming FIGO staging system for ovarian carcinoma seems to be superior to the current system in discriminating survival outcomes of patients who have surgical spillage or isolated retroperitoneal LN metastasis. Better prognosis of stage IV with supraclavicular LN metastasis should be confirmed in large scale-validation studies.
COMBINATION THERAPY WITH BEVACIZUMAB AND GEMOX FOR PATIENTS WITH RECURRENT OVARIAN CANCERS: A PHASE II STUDY.

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Objectives: Combination therapy using gemcitabine with oxaliplatin (GEMOX) showed moderate activity in recurrent ovarian cancers (ROC), however, severe toxicities have been frequently observed. On the other hand, bevacizumab enhances chemotherapeutic efficacy in various cancers. Here we conducted a phase II study to evaluate the effect of weekly low-dose administration of GEMOX in combination with bevacizumab (B-GEMOX) for patients with platinum-resistant ROC.

Methods: Simon’s two-stage design was used, and a total number of 25 cases were enrolled in the study. This design yielded a type I error rate of 0.05 and power of 0.8 when the true response rate was 40%. B-GEMOX therapy consisted of 2mg/kg of bevacizumab, 300mg/m² of gemcitabine, and 30mg/m² of oxaliplatin, three weeks on and one week off, q4weeks. The treatment was continued until development of severe toxicities or progressive disease. Tumor responses were assessed using the Response Evaluation Criteria In Solid Tumors (RECIST) and Gynecologic Cancer Intergroup (GCIG) criteria.

Results: Median number of the B-GEMOX therapy was five cycles. Response was observed in seven cases (41%) by RECIST, and in 2 cases (29%) by GCIG criteria, resulting in overall response rate of 36%. Clinical benefit including stable disease was obtained in 84% of the patients. Median progression-free survival was 4.5 months (range: 2–18+ months). Toxicities were mild and mainly consisted of hematologic, gastrointestinal, and neuropathy, however, there were no non-hematologic toxicities more than grade 1.

Conclusions: Weekly administration of B-GEMOX was active for patients with ROC, and showed mild toxicities. These results warrant further prospective studies for patients with ROC.
INVESTIGATION OF MOLECULAR HETEROGENEITY IN OVARIAN CLEAR CELL CARCINOMA IS A STEP TOWARD INDIVIDUALIZED CLINICAL THERAPY

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Objectives
Ovarian clear cell carcinomas (CCCs) have been thought to represent a lethal histological subtype of epithelial ovarian carcinomas (EOCs), and one of their precursors has been clinicopathologically showed to be endometriosis. Besides, CCCs occasionally exhibited independence of endometriosis or better clinical behavior, implying that CCCs might not been in a single category.

Methods
Focusing on CCCs mixed with other histological subtypes of EOCs, we re-evaluated the pathology of 46 CCCs and divided these into two subgroups, 35 CCCs alone as 'pure type' and 11 CCCs with other histological subtypes, endometrioid carcinomas (ECs) or/and serous carcinomas (SCs) as 'mixed type'. Immunohistochemical analysis for expression of ARID1A, p53, PTEN, Annexin-4, hepatocyte nuclear factor-1β (HNF-1β) and WT-1 was employed.

Results
Consequently, there was a significant association between endometriosis and age in pure-type, but not in mixed-type. In mixed type, the immunohistochemical-staining patterns revealed that each component of CCCs, ECs and, SCs predominantly had altered expressions of ARID1A/Annexin-4/HNF-1β, PTEN, and p53/WT-1, respectively, due to possible internal transition of each histological component. In pure-type, expressions of ARID1A and p53 were mutually altered, and altered expression of ARID1A and p53 were associated with better and worse prognosis, respectively.

Conclusions
The present results provide clinicopathological evidence in support of the hypothesis that CCCs would often have molecular and pathological heterogeneity, of which component determines the patient's prognosis. And the immunohistochemical analysis in CCCs plays an indispensable role in determining the prognosis, and may shed light on the selections for the individualized cancer-therapy.
FEASIBILITY AND SURVIVAL EFFECT OF LIVER RESECTION IN PATIENTS WITH GYNECOLOGICAL CANCER

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Objectives
Although it is rare liver is also involved in patients with epithelial ovarian cancer. It may be seen at primary or recurrent setting, and sometimes together with other metastases. To achieve complete cytoreduction liver resection may be performed in several forms including metastasectomy, segmentectomy or lobectomy/r-l hepatectomy. The purpose of this study is to evaluate the patients treated with liver resection at tertiary referral center.

Methods
The patients treated for liver resection between 2003 and 2012 were included for this study. The patients having superficial subcapsular metastasis were not included.

Results
Overall twenty-five patients were included. Of these patients 13 underwent liver resection at primary debulking, 9 were operated at secondary and the remaining 3 were at tertiary cytoreductive surgery. Several different surgical techniques were used including kelly-klemp, harmonics, argon-beam, and radiofrequency assisted parenchymal resection. Many additional procedures were also performed besides liver resection especially for patients treated at primary debulking. Metastasectomy was the most common procedure (n=16) after segmentectomy (n=6), and right or left hepatectomy (n=3). No intraoperative major complication was seen including bleeding. In the postoperative period one patient had subhepatic abscess treated with drainage and antibiotics. No surgical mortality was seen.

Conclusions
Liver resection is feasible operation in the treatment of epithelial ovarian cancer in several settings including primary, secondary, and tertiary. Since the maximal cytoreduction is the main purpose of surgical treatment the patients having liver resection should be referred to experienced centers to achieve debulking with acceptable morbidity rates.
**Poster Presentations: Ovarian Cancer**

**EXPRESSION PATTERN AND MOLECULAR FUNCTION OF TRANSCRIPTION FACTOR FOXM1 (FORKHEAD BOX PROTEIN M1) IN EPITHELIAL OVARIAN CANCER CLINICAL SPECIMENS AND CELL LINES**

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**Objectives**

This study identified the genetic fingerprint of endometrioid ovarian carcinomas (END-EOC) and analyzed the role of the transcription factor Forkhead box protein M1 (FOXM1) in ovarian tumorigenesis.

**Methods**

The gene expression patterns of 24 snap-frozen END-EOCs and 15 normal endometrium (NE) biopsies were determined by microarray technology. FOXM1 expression was tested in 100 clinical tissue specimens with different histology and in a panel of EOC cell-lines by quantitative real-time-PCR (qRT-PCR) and immunohistochemistry. A siRNA approach was used to knock-down FoxM1 expression in vitro in three EOC cell-lines; proliferation, cell cycle and colony formation were assayed. The mRNA expression level of FOXM1 transcriptional targets was assayed by qRT-PCR.

**Results**

Hierarchical cluster analysis identified FOXM1 as one of the top differentially expressed gene among 463 up-regulated genes in END-EOCs, when compared with NE. FOXM1 gene expression levels, analyzed by qRT-PCR, significantly correlated with gene-chip results (rs=0.78, p<0.005). The relative expression levels of FOXM1 mRNA were significantly higher in EOC tissues than in normal ovarian samples (P<0.01). Nuclear positive immunostaining of FOXM1 was observed in 100% (95/95) EOC specimens. Compared with control, FoxM1 small interfering RNA-transfected cells showed decreased cell proliferation rate, inhibition of colony formation and deregulation of genes involved in cell cycle progression (cyclin B1, cyclin D1, Cdk2, cdc25B, p21 and p27), in the degradation of extra cellular matrix (mmp-2, mmp-7, mmp-11) and in angiogenesis (VEGF-A).

**Conclusions**

FOXM1 is overexpressed in EOCs and this study provides new insights in its oncogenic mechanisms associated with cancer onset and progression.
SYNCHRONOUS GENITAL CANCERS

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Objectives
A clinical and histopathologic review of synchronous primary gynecologic
malignancies is presented.

Methods
Between January 2002 - December 2011, 17 patients suffering from
synchronous primary gynecologic cancers were treated by surgery in the first
Clinic of Obstetrics and Gynecology Iasi. Clinical and pathologic information
were obtained from medical records.

Results
The most frequently observed synchronous neoplasm was ovarian cancer
coexistent with endometrial cancer – 12 cases. The mean age of these
patients was 54 years. Both types of tumor were stage I. In 10 situations we
had endometrioid histology for both endometrium and ovary, and from these
we had 4 situations for which was demonstrated the development on ovarian
endometrioma. For two others the ovarian tumor was mucinous borderline type
and granulosa cell tumor. All these women underwent total hysterectomy with
bilateral salpingo-oophorectomy and infracolic omentectomy followed by
adjuvant therapy. For 5 patients with more than 50% myometrial invasion it
was made lymphadenectomy. We also had 3 patients with ovarian cancer
synchronous with cervical cancer, one case synchronous with breast cancer,
and other one synchronous with tube cancer.

Conclusions
Patients suffering from primary genital malignancies are sometimes co-afflicted
with others primary cancers. Synchronous ovarian and endometrial cancer
constitutes the most common of these cases, and is detected at a relatively
early age than that with endometrial cancer alone, with generally favorable
prognoses. The differential diagnosis between a primary ovarian cancer and
ovarian metastasis from endometrial cancer can be histological difficult and
than we need an inmunohistochemical exam.
EFFECT OF SURGICAL STAGING ON 539 PATIENTS WITH BORDERLINE OVARIAN TUMORS: A TURKISH GYNECOLOGIC ONCOLOGY GROUP STUDY

Turkish Gynecologic Oncology Group

Objectives
The objective of this study was to examine demographic and clinicopathologic characteristics and to determine the effects of primary surgery, surgical staging and the extensiveness of staging.

Methods
In a retrospective Turkish multicenter study, 539 patients, from 14 institutions, with borderline ovarian tumors were investigated. Some of the demographic, clinical and surgical characteristics of the cases were evaluated. The effect of type of surgery, surgical staging; complete or incomplete staging on survival rates were calculated by using Kaplan-Meier method.

Results
The median age at diagnosis was 40 years (range 15-84) and 71.1% of patients were premenopausal. The most common histologic types were serous and mucinous. Majority of the staged cases were in Stage IA (73.5%). 242 patients underwent conservative surgery. Recurrence rates were significantly higher in conservative surgery group (8.3% vs. 3%). Of all patients in this study, 294 (54.5%) have undergone surgical staging procedures. Of the patients who underwent surgical staging, 228 (77.6%) had comprehensive staging including lymphadectomy. Appendectomy was performed on 204 (37.8%) of the patients. The median follow-up time was 36 months (range 1-120 months). Five-year survival rate was 100% and median survival time was 120 months. Surgical staging, lymph node sampling or dissection and appendectomy didn't cause any difference on survival.

Conclusions
Comprehensive surgical staging, lymph node sampling or dissection and appendectomy are not beneficial in borderline ovarian tumors surgical management.
THE ROLE OF SURGERY IN THE MANAGEMENT OF PATIENTS WITH PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER: SURVEY AMONG DUTCH GYNAECOLOGISTS AND MEDICAL ONCOLOGISTS.

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Objectives
Evidence of randomized comparative clinical trials on surgery in recurrent platinum-sensitive ovarian cancer is non-existing. Three randomized phase 3 trials are ongoing. The aim of this study is to evaluate the current opinion of Dutch gynecologists and medical oncologists awaiting the results of these three trials.

Methods
A 16-item questionnaire was sent to all gynecologists (N=124) and medical oncologists (N=195) with special interest in gynecologic oncology in the Netherlands. The data were collected and analyzed using descriptive statistics.

Results
In total, 80 (65.0%) gynecologists and 67 (34.0%) medical oncologists responded. Among the respondents, 11.3% and 26.9% were not convinced of the benefit of secondary cytoreductive surgery, respectively. Completeness of primary surgery and performance status were important factors to consider surgery for 75.0% and 99.0%, of all respondents, respectively. For only 17.5% of all respondents diagnostic laparoscopy before surgery is a prerequisite. In general medical oncologists settle for a smaller gain in both progression free as well as overall survival than gynecologists.

Conclusions
Although most gynecologists and medical oncologists are convinced of the usefulness of secondary cytoreductive surgery in certain patients, a better understanding of the real benefits and patients selection criteria for secondary cytoreductive surgery will be achieved after the completion of three ongoing randomized controlled trials (DESKTOP III, GOG 213 and the SOCcERe).
Poster Presentations: Ovarian Cancer

EXTERNAL VALIDATION OF THREE PROGNOSTIC MODELS PREDICTING OVERALL SURVIVAL IN PATIENTS WITH ADVANCED STAGE EPITHELIAL OVARIAN CANCER

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Objectives
For various malignancies, prognostic models have shown to be superior to traditional staging systems in predicting overall survival. The purpose of this study was to validate and compare the performance of three prognostic models and the International Federation of Gynecology and Obstetrics (FIGO) stage in the prediction of overall survival in patients with advanced stage epithelial ovarian cancer.

Methods
An external multi-institutional epithelial ovarian cancer database was used to identify patients and to evaluate the predictive performance of two nomograms, a prognostic index and FIGO stage. All patients were treated for advanced stage epithelial ovarian cancer between January 1996 and January 2009 in 11 hospitals in the eastern part of the Netherlands.

Results
In total, 542 patients were found to be eligible. Overall performance did not differ between the three prognostic models and FIGO stage. The discriminative performance for Chi’s model was moderately good (c indices 0.65 and 0.68) and for the models of Gerestein and Teramukai reasonable (c indices between 0.60 and 0.62). The c indices of FIGO stage ranged between 0.54 and 0.62. After re-calibration the three models showed almost perfect calibration whereas calibration of FIGO stage was reasonable.

Conclusions
The three prediction models show a general applicability and a reasonably well predictive performance especially in comparison to FIGO stage. However, to date there are no studies available that analyze the impact of these prognostic models on decision-making and patient outcome. Therefore, the usefulness of these models in daily clinical practice remains to be investigated.
CHEMOTHERAPY IN MEASURABLE GRANULOSA CELL TUMOURS: A RETROSPECTIVE STUDY AND REVIEW OF LITERATURE
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Objectives
Patients with irresectable granulosa cell tumours (GCT) often receive platinum-based chemotherapy (Bleomycin, Etoposide and Platinum (BEP) in most patients). The effectiveness of this approach, however, is uncertain. Aim of our study was to assess the response rate to platinum-based chemotherapy for residual and recurrent inoperable GCT.

Methods
All consecutive patients in three referral hospitals who were treated with first-line platinum-based chemotherapy for residual or recurrent GCT (1968-2011) were included. Response according to RECIST criteria was the main outcome. A literature search in MEDLINE through PubMed was performed.

Results
Twenty-seven patients with GCT who received first-line platinum-based chemotherapy were identified. Nine were available for RECIST evaluation. One patient (11%) had a complete response and one patient (11%) had a partial response, resulting in a response rate of 22% (95%CI, 0-49%). Seven patients (78%) had stable disease (range 2-50 months) and none had progressive disease. Sixteen studies that assessed response rates to first-line chemotherapy on measurable disease in a total of 224 patients showed a response rate of 50% (95%CI, 44-57%). Strict criteria of response, however, were not uniformly applied in the majority of these published series.

Conclusions
In contrast to literature data we could not confirm a substantial beneficial effect of chemotherapy in patients with irresectable GCT with measurable disease. Comparison with previous studies is hampered by lack of standardized response evaluation in many studies. Given the toxicity of BEP chemotherapy and the relatively low clinical benefit, prospective studies to assess the therapeutic ratio of other chemotherapy, hormonal or targeted therapy regimens, are needed.
WHOLE ABDOMINOPELVIC RADIOTHERAPY AS PALLIATION FOR CHEMOTHERAPY-RESISTANT OVARIAN CANCER.

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Objectives
Asses the effect of WAPRT using Intensity Modulated Arc Therapy for chemotherapy-resistant ovarian cancer.

Methods
Forty-two patients were treated with WAPRT (33Gy in 22 fractions). Median Karnofsky performance scale (KPS) was 80 (range: 40-90). All patients had symptoms: intestinal (sub)-obstruction (n=22), masses (n=7), pain (n=20), ascites (n=11), and vaginal bleeding (n=2). Median CA125 level was 421 U/ml [6-13796 U/ml]. All patients were heavily pre-treated with surgery, chemotherapy, HIPEC and hormonal therapy. Symptom response rates were classified according to the best response obtained. A partial response required at least 50% resolution of these symptoms. The actuarial overall survival (OS) and abdominal progression free survival (aPFS) was calculated from the start of radiation therapy, symptom response duration from the end of radiation therapy.

Results
Patients with KPS≥70 ended the treatment more (p<0.001). Response rates for patients who completed treatment (n=30): table. The median response duration (all symptoms) was 16 [0-139] weeks. Multivariate analysis showed a significant influence of KPS on OS. For the whole population, median OS and aPFS was 4 months [0-32] and 11 weeks [0-142] respectively. For the patients who completed treatment, median OS and aPFS was 8 months [2-32] and 17 weeks [4-142] respectively. Univariate analysis showed a significant increase in median OS, aPFS and response of symptom palliation when KPS≥70: 8 vs. 1 month; 18 vs 3 weeks and 22 vs 5 weeks respectively.

Conclusions
WAPRT can resolve symptoms (specifically intestinal obstruction) for a substantial period and should be presented to patients with KPS≥70.
Poster Presentations: Prevention of Gynaecologic Cancer

OUTCOME OF MANAGEMENT OF GLANDULAR NEOPLASIA
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Objectives
Cervical Glandular Intraepithelial Neoplasia (CGIN) is rare and difficult to diagnose due to non-specific cytological and colposcopic features. Treatment can be also challenging and recurrence rate is up to 30%.

Aims: To review the management and outcome of cGIN over 9 years at Colposcopy Department of UHL (January 2002 to November 2011).

Methods
We analysed 43 cases of CGIN, which were confirmed by histology after initial treatment for abnormal smear/CIN2+.

Results
Of women with confirmed CGIN (n=43), 36% were referred with suspected glandular neoplasia, 35% with high grade smears and 29% low grade smears. At colposcopy, 70% had changes suggestive of high grade disease and 30% low grade. Punch biopsies was performed in 56% with 70.5% confirmed CGIN, with the remaining showing high or low grade disease. Early invasive cancers were diagnosed in 4 cases after initial treatment. The depth of excised samples was adequate in 72% of cases after first treatment and 88% after second treatment which took place in 33% of cases. Follow up smears were normal in 61% at 6 months and 63% at 1 year, low grade was 16% at 6 months and 21% at 2 years. There was 1 case of recurrent high grade lesion and 1 case of borderline smear in endocervical cells at 6 month follow up.

Conclusions
Treatment of CGIN remains challenging with 1/3 of women needing repeated treatment. There was relatively high rate of recurrence despite of adequate and timely treatment.
COST AND EFFECTIVENESS COMPARISON OF IMMEDIATE COLPOSCOPY VERSUS HUMAN PAPILLOMAVIRUS DNA TESTING IN MANAGEMENT OF ATYPICAL SQUAMOUS CELLS OF UNDETERMINED SIGNIFICANCE (ASCUS) IN TURKISH WOMEN

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Objectives
Although immediate colposcopy, HPV-DNA testing or expectant management are three recommended options in ASCUS triage, a consensus does not currently exist on which one of these approaches is the most efficient. In this study, we aimed to compare the performance and cost of the immediate colposcopy and colposcopy based on the human papillomavirus (HPV) testing for detecting histologically confirmed high-grade cervical intraepithelial neoplasia (CIN) in women with atypical squamous cells of undetermined significance (ASCUS).

Methods
Records of 594 women with an index Papanicolaou (Pap) smear showing ASCUS were retrospectively analyzed. Women in the immediate colposcopy arm were referred directly to colposcopy (immediate colposcopy group, n=255) and those in the HPV triage arm were proceeded to colposcopy if the high-risk HPV (hrHPV) test was positive (HPV triage group, n=339). High grade CIN (CIN2+) detection rate and treatment costs were compared between the groups.

Results
The detected rate of CIN2+ was higher in the HPV triage group compared to immediate colposcopy group (8% vs. 1.6%, p=0.011). The total cost (€ 87,952 vs. € 26,608), cost per patient (€ 259.1 vs € 104.3) , and the cost per one HGSIL diagnosis (€ 14,654 vs. € 6,652) were significantly higher in the HPV triage group (p<0.001).

Conclusions
In women with ASCUS cytology, HPV DNA testing followed by colposcopy was more costly than immediate colposcopy, but this approach was associated with higher rate of CIN2+ detection. This findings suggest that HPV DNA testing combined with cervical cytology could reduce the referral rate to colposcopy.
Poster Presentations: Prevention of Gynaecologic Cancer

OVERTREATMENT IN A SEE-AND-TREAT APPROACH TO CERVICAL INTRAEPITHELIAL LESIONS
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Objectives
Advantages of a see-and-treat approach to cervical intraepithelial lesions (CIN) include a single visit to the hospital, less emotional stress, and low complication rates. However, its main concern is overtreatment. Aim of this study is to determine the overtreatment rate at colposcopy in women who underwent a see-and-treat approach.

Methods
We identified 3,192 patients in RUNMC between 1981–2010. Overtreatment, defined as ≤CIN1 at final histopathological analysis, was investigated in relation to the age, time of referral, smear result, colposcopic impression, and histopathology result.

Results
A total of 579 women (18.1%) were overtreated. The lowest overtreatment rate (4.5%) was seen in women with both a high-grade cervical smear, and a high-grade colposcopic impression. Women with either a high-grade cervical smear, and a low-grade colposcopic impression or a low-grade cervical smear, and a high-grade colposcopic impression were overtreated in 29.2% and 28.6% respectively. Women aged <40 years were less likely to be overtreated (13.1%) than women aged 40–49 years (24.2%) and aged ≥50 years (42.2%).

Conclusions
The overtreatment rate is low for patients with both a high-grade smear result and a high-grade colposcopic impression, justifying a see-and-treat approach these patients. In women with either a high-grade smear or a high-grade impression on colposcopy, a see-and-treat approach may still be preferable but has higher overtreatment rates. Given the side effects of cervical surgery on pregnancy outcome, young women, in particular those who have either a low-grade smear, or low-grade impression on colposcopy, are better served by biopsies. Further treatment is based on the biopsy results during a second visit.
Poster Presentations: Prevention of Gynaecologic Cancer

PREVALENCE AND GENOTYPE DISTRIBUTION OF HUMAN PAPILLOMAVIRUS TYPES IN EGYPTIAN WOMEN WITH CERVICAL CARCINOMA AND PRE-INVASIVE LESION

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Objectives

Having scarce Data on HPV genotype distribution, To our knowledge, this is considered the first published study in Egypt to identify HPV types in cervical carcinoma and pre-invasive cervical lesions from a population of Egyptian women guiding the introduction of prophylactic vaccines.

Methods

After pathological review 165 primary invasive cervical carcinoma and 49 precancerous lesion specimens were recruited from The Early Cancer Detection Unit of Ain Shams university hospital during the period from 2006 to 2011. HPV detection was performed by PCR using L1 consensus primer (GP5+/GP6+) and Genotyping by Sanger sequencing using forward primer(GP5+). For samples with sequencing pattern suggesting multiple infections, PCR with type specific primers assay was done.

Results

HPV genotypes detected in our studied population were: HPV-16 (64.6%), HPV-33 (36.87%), HPV-31 (23.9%), HPV-18 (12.4%), HPV-45 (4.8%), HPV-59 (3.8%) and HPV-6 (0.5%) and 1.4% harbored undetermined genotypes. Single infection was detected in 70.3% of the samples, 75.5% of them was attributed to HPV-16. Multiple infections were detected in 28.2%. The most prevalent genotypes in cervical carcinoma were HPV-16 (62.4%) and of importance that the most prevalent genotypes in low grade cervical lesion (CINI) was HPV-16 detected in 72.9% of cases.

Conclusions

The prevalence of vaccinal HPV genotypes (16, 18) is high in Egypt assuming that implementing HPV vaccination could reduce the burden of cervical carcinoma. Moreover, as most precancerous lesions harbored high risk genotypes, it may be useful to apply HPV testing for triaging women with low grade cervical lesions (CINI) for early referral to colposcopy and offering treatment or returning to routine screening.
SCREENING FOR CERVICAL CANCER IN HIV INFECTED WOMEN IN A LARGE ITALIAN COHORT: A DIFFICULT RELATIONSHIP

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Objective

Improve adhesion to screening and prevention for cervical cancer (CC) in HIV infected women.

Methods

We collected HIV infected women referred to our gynecological center since 2002. Because many were lost to follow-up, we organized an active call to plan a pap test and colposcopy at the same time if necessary.

Results

HIV infected women referred to our center since 2002 are 354. Median age is 46 years (range = 26-74 y) and the median of last pap smear was 4 years (range = 0-12 y). Forty-four patient never had a pap smear in our center (12%), 184 were negative (51%), 29 had low grade dysplasia (8%) and 20 had high grade dysplasia (6%).

Eight patients were treated with local excision in our hospital, 17 patients had a hysterectomy (5%) of these 10 for benign causes.

We lost 164 (46%) women to follow up (2) while 89 patients underwent regular gynecological control of these only 17 (19%) have had alteration in the previous pap test.

Conclusions

All the patients called for consultation came to receive screening.

HIV positive women have a low adherence to screening and follow up for cervical cancer prevention but answer to active call.

For these reasons all the HIV women carers must work together to support screening and follow up to prevent CC.
NON-RESPONDERS OF THE CERVICAL SCREENING PROGRAMME: QUESTIONNAIRE RESULTS ABOUT NON-ATTENDANCE AND HPV SELF-SAMPLING IN THE NETHERLANDS

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Objectives
High levels of participation in population based cervical screening are essential for effective cervical cancer prevention because half of all carcinomas is found in the non-attendees. Offering a self-sampling device for HPV testing to these non-attendees has proven to increase participation rates. The objectives of this study were to determine why women do not attend cervical screening, and why non-attending women do, or do not participate when offered a self-sampling device.

Methods
A questionnaire study was conducted in a group of 30,130 Dutch women who did not attend regular cervical cancer screening, and thereafter were offered a self-sampling device.

Results
Results are based on the analysis of 10,166 (33.7%) returned questionnaires. Of these questionnaires, 9,484 (93.3%) were returned together with a self-sample specimen. The main reason for non-attendance to the regular screening programme was that 3,068 women (32.9%) did not, or forgot to schedule an appointment. Important reasons why women did choose to use the self-sampling device were that they could use the test in their own time (4,763; 50.7%), they could do it themselves (3,478; 37.0%), and that it took less effort than having a cervical smear taken (3,982; 42.4%).

Conclusions
Organisational barriers are the main reasons for non-attendance in regular cervical screening. Important reasons for non-attendees of the screening programme to use a self-sampling device are convenience and self control.
Routine Use of a Screening Questionnaire Improves Detection of Individuals at Possible Risk of Hereditary Gynecologic Cancer

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Objectives
A positive family history for cancer is an important risk factor for hereditary cancer syndromes. Guidelines exist for appropriate referral of individuals to Cancer Genetic Services (CGS), based on personal and family history. However, only a minority of individuals at risk is recognized by health care providers, possibly due to suboptimal family history recording and lack of knowledge on referral guidelines.

This pilot study aims to evaluate whether using a family history questionnaire improves identification of patients who warrant referral to CGS, compared to their identification in usual care, at a gynecology outpatient clinic.

Methods
We conducted a prospective intervention study with historic control group, with focus on hereditary breast and ovarian cancer and Lynch syndrome. A questionnaire based on established CGS referral criteria was completed for new outpatients between June 1 and August 1, 2011. Individuals with increased risk were scheduled for a telephone consultation for further evaluation. The referral rate in routine consultation was determined retrospectively for the period between May 1, 2009 and April 30, 2010. Differences and proportions between groups were tested by the chi-square test.

Results
In the routine consultation arm, 8 of 3036 patients (0.26%) were referred to CGS. In the prospective arm, 209 (42%) of 500 screening questionnaires were completed. Twenty four women (11.5%) received a telephone consultation. Five (2.4%) were referred. Referral rates differed significantly (p<0.001) between the two arms.

Conclusions
The routine use of a screening questionnaire may improve referral rate to CGS of individuals at risk for hereditary cancer.
THE IMPACT OF PERIMENOPAUSAL METABOLIC DISORDERS ON THE ENDOMETRIAL TRANSFORMATION.
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Objectives
Perimenopausal period is conducive to android obesity (AO) which predisposes to derangement of cell division and apoptosis. Relationship between metabolic disorders and predilection for neoplastic endometrial transformation was studied in order to improve management of perimenopausal-age women (PW) with endometrial hyperplasia (EH).

Methods
149 PW were allotted respective of AO and endometrial state. The targets were serum insulin, lipoproteins, apoptosis markers (sFas, Fas-ligand, TNF-ALPHA). Endometrial samples underwent immunohistochemical investigation including to Ki-67 and p16INK4a. Then women with AO were administered metformin.

Results
The lowest sFas was in group without AO and EH (Ia) - 0,86±0,31 ng/ml. It was almost the same in groups: Ib — AO with quiescent endometrium (4,08±0,37), II — simple EH without AO (4,14±0,39). In III group with AO and non-atypical EH more significant sFas was noticed (13,78±1,27) with vast range and two distinctive peaks. Considering that group was divided: IIIa — range 8-11 ng/ml, IIIb — 13-17 ng/ml. The highest sFas was in IV group of atypical EH (73% women with AO) - 19,86±1,92. Immunohistochemical investigation confirmed incremental frequency of apoptosis abnormalities depending on EH, AO, especially atypical EH. That pattern was consistent with sFas fluctuations. Follow-up showed trend towards improvement in Ib, IIIa and IIIb with regard to weight loss, insulin susceptibility, lipoprotein spectrum, except sFas: in IIIb it was unyielding and went with worse clinical outcomes.

Conclusions
the study elicited trend towards high incidence of prospective atypical EH if sFas >13 ng/ml irrespective of metabolic treatment.
DIAGNOSTIC ACCURACY OF LIQUID-BASED ENDOMETRIAL CYTOLOGY IN ENDOMETRIAL CANCER DETECTION

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Objectives
The objectives of this study were to assess the diagnostic accuracy in endometrial cancer (EC) detection (1) of liquid-based endometrial cytology (LBC) and (2) of transvaginal ultrasound (TVS) combined with LBC.

Methods
The patient included in this study were 206 women with postmenopausal bleeding. Patients underwent sequentially hysteroscopy, TVS, LBC and endometrial biopsy. The cutoff value of endometrial thickness to exclude EC was 4 mm.

Cytological sampling was obtained using the Endoflower device. Histological sampling was performed using the Endoram device. Cases with definitive histological diagnosis of EC and atypical hyperplasia (AH) were identified and used to evaluate sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of TVS and LBC.

Results
Twenty-eight cases (13.6%) of positive histology were detected in the study group (EC = 24; AH = 4). TVS and LBC identified 25 of 28 and 26 of 28 pathological cases, respectively. The sensitivity, specificity, NPV and PPV were 89.3%, 14.2%, 98.3% and 15.5%, respectively, for TVS and 92.8%, 100%, 98.9% and 100%, respectively, for LBC. TVS was combined with LBC identified all pathological cases (sensitivity, 100%; specificity, 15.6%; NPV, 100%; PPV, 15.6%).

Conclusions
Our data shown that LBC has a high diagnostic accuracy in the identification of EC whereas the specificity of TVS with a cutoff value of 4 mm is low. By combining the two tests, we obtained a 100% sensitivity.

Our experience suggest LBC and TVS could be used as first diagnostic step in evaluation of symptomatic postmenopausal women to exclude EC.
THE ALTERATIONS OF HPV-RELATED BIOMARKERS AND THE USEFULNESS ROLE OF SCORING SYSTEM FOR THE SURVEILLANCE OF CERVICAL PATHOLOGY DURING PREGNANCY: PRELIMINARY RESULTS

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Objectives
To assess the alterations of HPV-related biomarkers during pregnancy, in order to determine the role of Scoring System.

Methods
Design: Prospective observational pragmatic study
Setting: University Hospital of Ioannina, Greece
Period: September 2010 till September 2013
Population: Pregnant women with cervical intraepithelial lesions classified in three subgroups for further evaluation, as follow:
Group A: Pregnant women who were in close surveillance prior to pregnancy
Group B: Pregnant women with an initial referral for colposcopy evaluation at pregnancy.
Group C: Women who have been scheduled for treatment but in meanwhile conceived
Group D: Pregnant women with high grade squamous intraepithelial lesions (HgSIL) who have scheduled in previous pregnancy for treatment
Interventions: All pregnant women had cytology and colposcopy every 3-4 months during pregnancy in order to rule out invasion. A liquid-based cytology sample was taken pre- and during pregnancy and was tested for HPV-related biomarkers.
Outcomes: Positivity rates for various HPV-related biomarkers pre-, intra- and post-pregnancy.

Results
A total of 54 women were included (30 in 1st group and 24 in 2nd group). A total of 15/24 (62.5%) women tested positive for HPV-DNA pre-pregnancy and the rate was similar during pregnancy (p>0.05). Conversely, NASBA test was positive in 9/24 (37.5%) women pre-pregnancy and it appeared to be reduced (12.5%) during pregnancy (p>0.05).

Conclusions
This preliminary data shows pre- and intra-pregnancy positivity rates for different HPV-related biomarkers that appear to remain stable pre- and during pregnancy.

**Poster Presentations: Prevention of Gynaecologic Cancer**

**PROPHYLACTIC SALPINGECTOMY IN PREMENOPAUSAL LOW-RISK WOMEN FOR OVARIAN CANCER: PRIMUM NON NOCERE**

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**Objectives**

The objective of this study is to compare ovarian function and surgical outcomes between patients affected by benign uterine pathologies submitted to total laparoscopic hysterectomy (TLH) plus salpingectomy and women in which standard TLH with adnexal preservation was performed.

**Methods**

We retrospectively compared clinical data of 79 patients who underwent TLH plus bilateral salpingectomy (group A) with those of 79 women treated by standard TLH without adnexectomy (sTLH)(group B). Ovarian reserve modification, defined as the difference (expressed as Δ) between 3 months postoperative and preoperative values of AMH, FSH, AFC, mean ovarian diameters and PSV, was recorded for each patients. For each surgical procedure, moreover, operative time, variation of Hb, postoperative hospital stay, postoperative return to normal activity, and complication rate were recorded as secondary outcomes.

**Results**

According to our post-hoc analysis this equivalence study resulted in a statistical power of 96.8%. No significant difference was found between groups in term of Δ AMH ($p = 0.35$), Δ FSH ($p = 0.15$), Δ AFC ($p = 0.09$), Δ Mean ovarian diameters ($p = 0.57$), and Δ PSV ($p = 0.61$). No significant difference between groups was also observed in terms of operative time ($p = 0.79$), Δ Hb ($p = 0.41$), postoperative hospital stay ($p = 0.16$), postoperative return to normal activity ($p = 0.11$) and complication rate.

**Conclusions**

Adding bilateral salpingectomy to TLH for prevention of ovarian cancer in low risk women has no negative effects in term of ovarian function. In addition, no perioperative complications are related to the salpingectomy step in TLH.
Objective

The over-expression of thymidylate synthase (TS) and of the other folate cycle enzymes, is one of the mechanisms of resistance to cisplatin (cDDP) encountered in most of resistant human ovarian cancer cell lines, accounting for the more efficient DNA repair and synthesis. Oligopeptides were designed to inhibit TS activity by interfering with its dimerization. Among these, the LR octapeptide showed cell growth inhibitory activity against two cisplatin-sensitive human ovarian cancer cell lines.

To improve the intracellular delivery of LR, we designed a bioconjugate with folic acid (FA-LR), which enters cell by exploiting the folate receptor alpha (FRα)-mediated endocytosis.

Methods

-Cell lines. The human ovarian cancer cell lines OAW28, COV504, IGROV-1, TOV112D, 2008, C13*, A2780 and A2780/CP.
-Real Time PCR of FRα mRNA.
-Flow cytometric analysis of FRα cell surface expression
-Folic acid surface binding studies. -Uptake studies

Results

Real Time PCR, western blot analysis and folic acid surface binding assay indicate that IGROV-1 and OAW28 cells show high expression levels of FRα, while TOV112D, 2008 and 2008/C13* almost don't express FRα on their cell surface.

The folate bioconjugate FA-LR blocked competitively the binding of [3H]Folic acid to FR and consequently its cellular uptake. FA-LR is detected in the cell and its stability evaluated.

Conclusions

The chemical modification of the folate with the LR drug motif only minimally altered the intrinsic affinity the bioconjugate for FR and suggest that the pteroate-peptide conjugate exploits FR as a substrate for its internalization. Cytotoxicity of the bioconjugate will be presented.
ENDOXIFEN AND FULVESTRANT REGULATE GENE EXPRESSION OF ESTROGEN RECEPTOR ALPHA AND ITS CO-ACTIVATORS DEADBOX5 AND 17

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Objectives
Tamoxifen, with its active metabolite endoxifen, acts as a selective receptor down-modulator by inhibition of ERα-activating function 1 (AF-1). Fulvestrant is a selective receptor down-regulator via increased ERα degradation by inhibition of both ERα-activating functions (AF-1, AF-2). DDX5 and DDX17 act as ERα-co-activators. Overexpression of both factors could be demonstrated in various malignancies. Here we investigated potential regulatory effects of endoxifen and fulvestrant on the expression of ERα and its co-activators DDX5 and 17.

Methods
ERα-positive and -negative in vitro-models underwent treatment with endoxifen or fulvestrant vs. control. mRNA and protein levels of ERα, DDX5 and DDX17 were analyzed by RT-PCR and Western blot.

Results
Both ERα antagonists created a significant decrease of mRNA and protein expression levels of all target genes. DDX5 and 17 expression levels generally decreased, whereas endoxifen treatment triggered a stronger effect than fulvestrant. While both ERα antagonists caused a uniform decrease in ERα protein levels, DDX protein levels were differentially affected. Fulvestrant triggered a uniform downregulation of DDX5 and 17. In contrast, endoxifen stimulation resulted in an up-regulation of DDX5 and 17 protein levels in some ERα-positive cell lines.

Conclusions
Both ERα antagonists show regulatory effects on ERα, DDX5 and 17 mRNA and protein expression. However, differing effects could be observed on protein levels in different in vitro-models. These data might explain individual therapeutic efficacy or occurrence of endocrine therapy resistance dependent on cellular context. Furthermore, the elucidation of DDX status might serve as a useful prognostic tool to estimate efficacy of anti-estrogen treatment in breast cancer therapy.
POSTER PRESENTATIONS: TRANSLATIONAL RESEARCH

ENDOXIFEN AND HTRA2-BETA1 REGULATE ESTROGEN RECEPTOR ALPHA ALTERNATIVE SPlicing PATTERN IN BREAST CANCER CELLS

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Objectives
Endoxifen is the major metabolite of tamoxifen and acts by blocking estrogen receptor alpha (ER\(\alpha\)) transcriptional activity. Alternatively spliced ER\(\alpha\) mRNA variants are present in normal and malignant breast tissues. These ER\(\alpha\) variants possess the potential for increased estrogen activities. Human Tra2-beta1 is a splicing factor. Its intracellular localization may vary during cancer progression or is changed by exogenic stimuli. Here we analyzed the potential impacts of endoxifen and hTra2-beta1 on ER\(\alpha\) expression. Additionally, we examined effects of endoxifen on hTra2-beta1’s alternative splicing.

Methods
Breast cancer cell lines were subjected to functional experiments. Estrogen-stimulated cells received endoxifen vs. control. Transient hTra2-beta1-knockdown was performed. PCR, immunocytochemistry and Western blot were applied for expression analysis on mRNA and protein level.

Results
Endoxifen induced a significant reduction of ER\(\alpha\) protein expression in ER\(\alpha\)-positive cells. Endoxifen triggered a shift in ER\(\alpha\) splicing toward the ER\(\alpha\)Δ7 variant. hTra2-beta knock-down created a similar impact on ER\(\alpha\) splicing. In addition, a novel isoform of hTra2-beta1 occurred under endoxifen treatment. Interestingly, endoxifen also triggers an intracellular translocation of hTra2-beta1 characterized by decreased nuclear protein expression and increased accumulation in cytoplasm.

Conclusions
We hypothesize that endoxifen exerts a regulatory impact on hTra2-beta1 alternative mRNA splicing pattern and intracellular protein localization. hTra2-beta1 is most likely involved in ER\(\alpha\)-dependent regulation of breast cancer by triggering aberrant ER\(\alpha\) alternative splicing. Different ER\(\alpha\) variants exerts different functions in controlling ER\(\alpha\) signaling. ER\(\alpha\) Δ7 might be of auspicious clinical significance to potentially serve as a prognostic indicator for evaluation of human breast cancer endocrine therapy efficacy.
Poster Presentations: Translational Research

PREOPERATIVE HE4 AND CA125 LEVELS IN THE PREOPERATIVE ASSESSMENT OF ENDOMETRIAL CANCER PATIENTS: A DANISH PROSPECTIVE MULTICENTER STUDY (ENDOMET)

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Objectives
To evaluate whether HE4 and CA125 correlate to known prognostic factors for endometrial cancer (EC)

Methods
Pre-operative blood samples were obtained from 371 patients with EC and atypical endometrial hyperplasia. Biomarker levels were correlated to pathological characteristics of hysterectomy specimens

Results
Both HE4 and CA125 were significantly positively correlated with histological grade (HE4: p<0.0001 and CA125: p=0.001), lymph node metastases (p<0.0001), myometrial invasion (p<0.0001) and cervical involvement (p<0.0001). Furthermore, a significant increase was found with increasing FIGO stage for both markers (p<0.0001). In a combined index including age, the diagnostic value increases. Area under the receiver operating characteristics curves were higher for the index compared to the markers individually for all our end-points. The calculated plots for the combined index may assist gynecologists predicting the risk of deep myometrial invasion, cervical involvement and lymph node metastases. The analyses emphasize that the combined markers should be used in the prediction of prognostic factors.

Conclusions
This study confirmed that the markers are significantly elevated in patients characterized by clinical high-risk factors and may, therefore, be used as an additional tool in combination with imaging and clinical information when planning the treatment of EC patients.
INHIBITION OF UTERINE SARCOMA CELL GROWTH THROUGH SUPPRESSION OF ENDOGENOUS TYROSINE KINASE B SIGNALING

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Objectives
Uterine leiomyosarcoma is an aggressive tumor typically found at advanced stages due to difficulties with early diagnosis. Because uterine leiomyosarcoma is resistant to conventional radiation and chemotherapy, the development of more potent medical therapeutics is anticipated. We found brain-derived neurotrophic factor (BDNF) and receptor tyrosine kinase B (TrkB) is expressed in uterine sarcoma and investigated the role of endogenous TrkB signaling to establish a novel medical therapy.

Methods
We investigated the expression level of TrkB and its ligands in different uterine sarcoma cell lines and compared the levels among human leiomyosarcoma, leiomyoma and myometrium using quantitative real-time RT-PCR. To determine the effects of endogenous TrkB signaling, human uterine sarcoma cells were cultured with or without Trk inhibitor. We also examined the effect of Trk inhibitor on in vivo tumor growth of human uterine sarcoma xenografts in athymic nude mice.

Results
The expression of TrkB and its ligands was elevated in a multidrug-resistant cell line and leiomyosarcoma tissue. Suppression of endogenous TrkB signaling leads to inhibition of uterine sarcoma cell growth in both in vitro and in vivo studies.

Conclusions
Our findings indicated that endogenous signaling of the TrkB pathway contributed to uterine sarcoma cell growth, and inhibition of TrkB signaling in these tumors could provide a novel medical therapy for patients with uterine sarcomas.
BIOMARKER PROFILING REFLECTS CARBOPLATIN RESISTANCE IN PRIMARY OVARIAN CANCER

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Objective

Carboplatin based combination therapies are the first choice of chemotherapy in primary ovarian cancer. Initial response rates are high. However, most of the tumors develop drug resistance resulting in poor prognosis. The present study aims to explain the molecular basis of platin based resistance by a comprehensive biomarker profile.

Methods

Fresh tumor samples obtained from 20 primary ovarian cancer patients were snap frozen in liquid nitrogen. Cryo sections were characterized by immunohistochemistry and molecular biology. RNA was isolated using the Maxwell16 simply RNA tissue kit. cDNA was generated with the MMLV Rnase H minus and analyzed with qPCR. Biomarker profiling was correlated with chemotherapeutic response in multicellular spheroids and patients.

Results

Protein biomarker profiling on primary ovarian cancers revealed a heterogeneous proliferation activity reflected by Ki67 expression (mean 36\%, range 15-80\% Ki67 positive cells) and growth factor receptor expression. EGFR was detected in 80\% of the primary tumors and a high fraction of cancer cells (mean: 60\%, range 20-09\% EGFR positive cells). Contrary, ER- and PgR positive tumors were rare (ER+: 30\%, PgR+: 10\%). The uPA protease system was strongly expressed (uPAR+tumors: 90\%, uPA+tumors: 60\%) indicating the aggressiveness of primary ovarian cancer. The molecular biomarker profiling strongly reflected carboplatin resistance showing high expression levels of BRCA1, BRCA2 and FANCF and reduced expression levels of CCND1 and RPL32.

Conclusions

Primary ovarian tumours reveal striking differences in biomarker expression reflecting differences in the carboplatin response pattern. Biomarker profiling elucidating drug resistance has a substantial impact on individualized cancer therapy selecting the most effective drugs for the individual patient.
DETECTING HYPERCOAGULABILITY IN GYNAECOLOGICAL CANCER PATIENTS UNDERGOING SURGERY—THE ROLE OF THROMBOELASTOGRAPHY

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Objectives
Gynecological malignancies are associated with an increased risk of venous thromboembolism (VTE). The treatment and prevention of VTE in gynaecological cancer is challenging particularly after major surgery. Thromboelastography (TEG) is a technique which allows rapid global assessment of haemostatic/fibrinolytic function and has been proposed as a marker of hypercoagulability in a variety of clinical settings. The aim of this pilot study is to determine the level of hypercoagulability using TEG in patients undergoing major gynecological surgery for suspected cancer, and to determine the potential of the TEG as a predictor of VTE.

Methods
Patients undergoing surgery or suspected or confirmed gynecological cancer had TEG analysis on venous blood samples. D Dimer was measured by central pathology laboratory according to standard procedures.

Results
Clot formation time (K) was significantly shorter in the malignant group compared with benign (P<0.05). Ovarian cancer patients had a shorter clot formation time (k) compared with patients with benign disease (p<0.05). The maximum amplitude (MA) was significantly greater in the ovarian and endometrial malignant groups compared with benign controls (P<0.05). Clot strength (g) was slightly greater in the malignant group as a whole compared with the benign. K, g and MA values correlated significantly with D-dimer levels in the malignant group (P<0.001).

Conclusions
The results of this pilot study show that TEG may have potential as a screening tool for hypercoagulability in gynecological cancer patients. Larger prospective studies are required to determine the ability of TEG to predict VTE in this population.
THE CHARACTERISATION AND FUNCTIONAL ASSESSMENT OF EPITHELIAL OVARIAN CANCER CELLS DERIVED FROM ASCITIC FLUID USING IMAGESTREAM

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Objectives
Ovarian cancer is a heterogeneous disease, yet currently is treated as one single entity. Reliable biomarkers predicting response to novel cytotoxic agents are essential if stratification of treatment is to result in improved outcome. A functional assay to assess homologous recombination (HR) DNA repair of cultured primary ovarian cancers has been described and correlates with response to PARP-inhibitors ex-vivo and platinum in-vivo. The process however requires viable cells and is not currently easily clinically reproducible. This project aimed to explore the feasibility of characterizing the cellular components of ascitic fluid whilst simultaneously determining HR status using ImageStream® technology.

Methods
Ten ml of ascitic fluid taken directly from patients with ovarian malignancy was enriched, labeled with a panel of antibodies and processed using Imagestream®. Results were compared to parallel cultured ascitic samples characterized using established techniques.

Results
All ascitic samples were characterized and results available within 72 hours of collection using ImageStream® technology. Epithelial cancer cells were identified in all ascitic samples (n=10). Subpopulations of cancer cells were identified based upon EpCAM, pan-cytokeratin and CA-125 expression demonstrating possible intra-tumour heterogeneity. Imagestream® was also used to identify and quantify γH2AX and RAD51 nuclear foci, following induction of DNA damage, in cell lines with known HR status and this has been applied to the primary cells.

Conclusions
The use of Imagestream® technology allows for the morphological and functional characterization of ovarian cancer within 72 hours of collection potentially enabling rapid stratification of treatment following a single minimally invasive test.
TWO CASES OF UTERINE GESTATIONAL TROPHOBLASTIC NEOPLASIA IN PERI MENOPAUSAL WOMEN DEVELOPING AFTER A LONG LATENT PERIOD- A LITERATURE REVIEW

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Objectives
Review of two cases of Gestational trophoblastic neoplasia and literature review

Methods
Retrospective study of clinical records and histology and literature review

Results
Both our women were of perimenopausal age group (44-48 yrs) at the time of presentation and their main symptom was menorrhagia. None of them had known to have a molar pregnancy in the past. Precedent pregnancies were 9 yrs and 21 yrs ago. One of them had a very high level of beta HCG, hence the diagnosis was easier. The other lady was only found to have epithelioid gestational trophoblastic tumour (ETT) after hysterectomy. Both these women underwent further investigations for metastatic disease, one of them had lung metastases. The lady with metastatic choriocarcinoma underwent chemotherapy and the women with ETT was deemed cured due to the surgical treatment.

Conclusions
Incidence of choriocarcinoma, most aggressive form, is around 1 case in 50,000 live births in the UK and curable with chemotherapy. Metastases is common with choriocarcinoma and responds to chemotherapy well. To the best of our knowledge, there are nearing 100 cases of ETT have been identified. ETT is a rare trophoblastic tumor that simulates carcinoma and can behave in a malignant fashion. It appears to be less aggressive than choriocarcinoma and appears that ETT develops from neoplastic transformation of chorionic-type intermediate trophoblast. ETT is thought to be relatively chemoresistant. We conclude the importance of maintaining a high level of suspicion of GTD in women with abnormal PV bleeding even in context of a long latency period from last pregnancy.
Poster Presentations: Trophoblastic Diseases

OUTCOME OF LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA (GTN) TREATED WITH METHOTREXATE

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Objectives
To evaluate the response to Methotrexate treatment protocol that we use in our institute. Review the treatment complications and side effects.

Methods
We retrospectively reviewed the records of all patients with gestational trophoblastic neoplasia (GTN) treated at a tertiary care referral center from 2008 till 2012. The treatment protocol used was methotrexate 0.4 mg/kg daily IM injection for 5 days, which was repeated every two weeks till the beta human chorionic antigen (BhCG) becomes negative; two maintenance cycles were then given.

Results
The diagnosis of low-risk GTN was made by both histological and clinical criteria. Scoring was done according to the International Federation of Gynecology and Obstetrics (FIGO) Oncology Committee. Complete response was diagnosed when three weekly BhCG levels were within normal range (less than 2 mIU/mL).

A total of 59 patients with GTN were reviewed. 44 patients had low risk disease (FIGO score 6 or less). 37 patients received methotrexate. There were 34 (92%) complete response and 3 treatment failures (8%). The median FIGO score for patients who failed methotrexate was 5 (3-5), while it was 2 (0-6) for those who responded. 4 patients had transient neutropenia (grade 2-3), 6 patients had mouth ulcerations (all were grade 1-2). There were no hepatic toxicities.

<table>
<thead>
<tr>
<th></th>
<th>complete response</th>
<th>resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of patients</td>
<td>37</td>
<td>3</td>
</tr>
<tr>
<td>median age (range)</td>
<td>35 (23-51)</td>
<td>41 (22-50)</td>
</tr>
<tr>
<td>Median FIGO score</td>
<td>2 (0-6)</td>
<td>5 (3-5)</td>
</tr>
<tr>
<td>Median interval (months)</td>
<td>1.25 (1.10)</td>
<td>3.5 (1.5-11)</td>
</tr>
</tbody>
</table>

Conclusions
We report a complete response of 92% to initial Methotrexate therapy. The treatment was well tolerated with no major complications.
Poster Presentations: Trophoblastic Diseases

HYDATIDIFORM MOLE: AGE-RELATED DIFFERENT CLINICAL PRESENTATION AND HIGH RATE OF SEVERE COMPLICATIONS IN OLDER WOMEN (> 50 YEARS)

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Objectives
The purpose of this study was to evaluate differences in clinical presentation of Hydatidiform Mole (HM) between patients ≥ 40 years and younger.

Methods
365 patients with HM were enrolled and divided into Group A (< 40 years, 318 cases) and Group B (≥ 40 years, 47 cases). A Pearson c² test was performed in order to detect statistically significant differences in clinical presentation. The same analysis was performed for each age-group considering partial HM (PHM) and complete HM (CHM). Particular attention was focused on patients ≥ 50 years.

Results
In Group B the diagnosis of HM at ≥ 12 gestational weeks was more frequent (P 0.001) and the prevalence of ultrasound features was higher (P 0.012) than in Group A. Vaginal bleeding before (P 0.005) and after evacuation (P 0.001), increased uterine volume (P 0.0001), hyperemesis (P 0.033) occurred more frequently in Group B. Among CHM, Group B presented a higher prevalence of vaginal bleeding before (P 0.05) and after evacuation (P 0.015), increased uterine volume (P 0.003) and hyperemesis (P 0.04) than Group A. Furthermore, CHM diagnosis performed after 12 weeks of gestation was higher in Group B (P 0.0001). In patients ≥ 50 years an increased rate of disease-related complications has been detected.

Conclusions
Clinical features of HM in patients ≥ 40 years are different from those of younger patients. Failures in the early detection of HM in older women, in particular ≥ 50 years, may expose them to a higher rate of severe complications, nowadays increasingly rare in clinical practice.
Poster Presentations: Trophoblastic Diseases

SIX MONTHS FOLLOW UP AFTER MOLE EVACUATION: IS IT NECESSARY?

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Objectives
To determine if ongoing follow up of uncomplicated molar pregnancy beyond achieving undetectable hCG levels is necessary for detecting relapse of gestational trophoblastic disease.

Study design
A total number of 279 women treated at two referral university-hospitals in Tehran were analyzed. Only 86 patients (31%) had completed their follow-up period.

Results
All these 86 patients achieved at least one undetectable hCG level, and none had any evidence of relapse.

Conclusion
We found that in patients with uncomplicated hydatidiform mole, relapse is unlikely after achieving undetectable serum hCG levels. Although further checkups on monthly basis are recommended, but it seems that the probability of recurrence is very low.
RESISTANCE TO SINGLE-AGENT CHEMOTHERAPY AND ITS RISK FACTORS IN THE LOW-RISK GESTATIONAL TROPHOBLASTIC NEOPLASM AMONG IRANIAN PATIENTS

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Objectives
We studied resistance to the single agent chemotherapy and its risk factors in the low risk gestational trophoblastic neoplasm (GTN).

Methods
We followed 168 GTN patients who were treated in ValiAsr Hospital, Tehran, Iran in 2001-2011 and were classified as low risk based on the International Federation of Gynecology and Obstetrics (FIGO) new scoring system. We used case-control design and studied odds ratio (OR) and 95% confidence interval (CI) and studied the risk of different variables on the drug resistance. In addition, we compared the rate of resistance by different chemotherapy drugs.

Results
We found 19% resistance to the sequential single agent chemotherapy, although all patients had complete remission after combination chemotherapy and surgery. Patients who had FIGO score higher than 4 had 14 time higher resistance compared to the low score patients (OR=14.28, 95% CI:5.54-36.81, \emph{P} value: 0.000). In addition, we found significant high odds ratio among patients who were presented with a metastasis (OR=8.42, 95% CI:2.44-29.07, \emph{p}:0.001), had large tumor size (>3 cm) (OR:7.73, 95% CI:1.93-30.91,\emph{p}:0.004), their beta human chorionic gonadotropin (βhCG) level was higher than 100,000 (OR=5.86, 95% CI:1.07-32.02, \emph{p} values:0.041) and were diagnosed more than four months after index pregnancy (OR=3.30, 95% CI:1.08-10.02, \emph{p} value:0.035) compared to their corresponding reference group. There was no statistical significant priority by different chemotherapy regimens.

Conclusions
Although all patients with low-risk disease ultimately achieved remission regardless of their initial response, clinical trial and cost-effectiveness studies are needed to suggest a better choice of treatment in the intermediate risk groups(score>4).
e-Posters: Breast Cancer

INNOVATION FOR BREAST CANCER PREVENTION ACTIONS IN DEVELOPING COUNTRIES
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Introduction
Community participation does not mean involvement in an action designed by health professionals in a top-down approach. Meanwhile, community participation and health education toward breast cancer prevention are not similar to other activities included in primary health care in Iran.

Method
More than 200 articles published from the year of 1985 through 2009 were reviewed mostly by following electronic databases such as Science Direct, Pub Med, MEDLINE, and ISI’s Web of Sciences. An assessment framework was developed based on the literature review to offer a model which would be applicable to increase women’s participation in breast cancer prevention programs. This framework incorporated a typology of community participation approaches in health proposed by Rifkin (1985 & 1991) and three theories to identify factors influencing breast health behaviors.

Result
We have demonstrated that more positive belief, greater social influence, and lower barriers toward preventive behaviours (e.g. mammography use) can motivate women to be involved in breast cancer prevention activities. In addition to this, the specific psycho-social factors influence the levels of community participation in prevention programs.

Conclusion
We believed that specific psycho-social factors are likely to empower women to protect themselves against breast cancer. Drawing attention to the continuing need for breast health-seeking behaviors prior to community participation in breast cancer prevention will help to reduce delayed diagnosis of breast cancer, to improve treatment, and to develop health promotion strategies in a variety of context. This could be accomplished by combining the individual and community concerns in the breast intervention programs.
HOMOCYSTEINE LEVEL, MTHFR POLYMORPHISMS AND RISK OF BREAST CANCER

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Objectives
To evaluate the C677T and A1298C functional polymorphisms in the MTHFR gene and their associations with breast cancer risk, as well as effect of the plasma levels of total homocysteine (tHcy) on the MTHFR-associated risk, a case–control study was conducted on a Kazakhstan population consisting of 315 histologically confirmed incident breast cancer cases and 604 age-matched controls without a history of cancer. Commercial TaqMan SNP Genotyping assays was used for MTHFR polymorphism genotyping and HPLC was used to measure the plasma tHcy. Statistical evaluations were performed using SPSS 19.0, Japan. The MTHFR 677T variant allele was associated with increased risk for breast cancer [adjusted ORs were 1.71 (95% CI: 1.21–2.43) and 1.55 (95% CI: 1.11–2.16) under codominant and dominant models, respectively]. The MTHFR 1298C variant allele was associated with decreased risk for breast cancer [adjusted ORs were 0.68 (95% CI: 0.49–0.95), dominant model]. The tHcy levels were higher in the cancer patients (p=0.001), who were also characterized by folate deficiency (p=0.019) compared with controls. tHcy levels were not associated with either MTHFRC677T (p=0.67) or A1298C (p=0.36) but they were inversely correlated to the folate status of the patients(p<0.0001) and were higher in patients with MTHFR 677TT genotype. Multivariate analysis showed that folate (p=0.019) were independent predictor of elevated Hcy levels in the cancer patients. These results provide support for the important role of homocysteine metabolism in breast tumorigenesis. Further mechanistic studies are warranted to investigate how MTHFR combined genotypes exert their effect on cancer susceptibility.
e-Posters: Breast Cancer

PIONEER EXPERIENCE OF THE REGIONAL HOSPITAL OF JENDOUBA: ABOUT 56 CASES OF BREAST CANCER. \\
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>Introduction:
Detection and treatment of breast cancer in Tunisia are experiencing disparities between regions. In fact, there are only three centers of oncology (Tunis, Sousse and Sfax) across the coastal region. Thus, cases of breast cancer in the inland areas are often under-diagnosed or diagnosed at an advanced stage, making the possibility of conservative treatment difficult. Jendouba region, north-west of the country was devoid of structures for the treatment of breast cancer. Since April 2010, there was the installation in the Regional Hospital of Jendouba of a university team of gynecologists, a surgeon oncologist and a chemotherapist.

Material and Methods
We conducted a retrospective study of 56 patients operated on for breast cancer. The study period is from April 2010 to September 2012. Sensitization of the population was conducted in collaboration with the local family planning, including posters, training of midwives and days of screening in peripheral hospitals.

Results
- The average age is 55.5 years operated patients; extremes of 25 and 72 years.
- The average clinical size at diagnosis was 3.4 centimeters.
- The average tumor diameter 2.51 cm.
- Conservative treatment was performed in 42.8% of cases.

Discussion
Histological size at treatment of breast cancer is lower than the national average to make it easier for conservative treatment. It is important to note the difficulties regarding the implementation of radiotherapy.
e-Poster: Breast Cancer

REPEAT USE OF CHEMOTHERAPY IN METASTATIC BREAST CANCER
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²Medical Oncology, cpmc, algiers, Algeria

Objectives
Novel strategies for the use of chemotherapy in metastatic breast cancer (MBC) are needed. Patients are treated with sequential cytotoxic agents, using different drug classes to avoid cross resistance. Both anthracyclines and taxanes have shown activity when reused in MBC after initial use in the adjuvant setting. Our aim was to determine response with repeat use of chemotherapy during treatment for MBC.

Methods
Patients were recruited from 2000 through 2010. Subjects were women with MBC who had at least one repeat use of a drug or class of drugs during treatment for metastatic disease only. A retrospective analysis was performed to determine response rates (RR) with initial and repeat uses, time interval between initial and repeat use, and time to progression (TTP) and overall survival (OS) after repeat use.

Results
Of 1600 patients with breast cancer, 320 women had MBC, 110 had at least one repeat use of a chemotherapeutic agent. The most frequently reused agents were docetaxel (D), vinorelbine (Navelbine [N]), gemcitabine (G), capecitabine (C), and combination docetaxel/carboplatin/trastuzumab (DCT). Overall, there was a RR of 15 % and stable disease (SD) in 33 % for repeat use of any chemotherapy. Median interval between first and second use was 547 days (1 year and half). Median TTP was 100 days, and median OS was 215 days after repeat use. There was no association between time interval and response.

Conclusions
Chemotherapy resistance may be variable over time or between different metastatic deposits. Our study describes the response after repeat use of chemotherapeutic agents during treatment for MBC.
PREGNANCY ASSOCIATED BREAST CANCER: A REPORT OF OUTCOMES OF PREGNANCY AND BREAST CANCER FROM AN ARAB COUNTRY

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Objectives
We report on the outcomes of pregnancy and the breast cancer of women treated for pregnancy associated breast cancer (PABC) from an Arab country.

Methods
Consecutive patient diagnosed to have PABC between 2005 and 2012 at the Sultan Qaboos University Hospital in Oman were the subjects.

Results
There were a total of 16 patients. Median age at diagnosis: 31 (26-40) years. Nine (56%) patients were multiparous with > 5 previous pregnancies. Mean gestational age at diagnosis: 19.7±7.4 weeks. Mean tumor size: 6 cm. Nuclear grade (GI=2, GII=6, and GIII=7). Immunophenotype: ER/PgR positive, HER-2 negative 3; ER/PgR positive, HER-2 positive 4; ER/PgR negative, HER-2 positive 4; triple negative 5 (31.3%). Eleven (68.8%) patients received chemotherapy during pregnancy [5 AC > Docetaxel, 8 AC, (Docetaxel±Trastuzumab was delivered after delivery) 1 FEC, one patient received chemotherapy in palliative setting, and one refused further treatment after mastectomy]. Response to chemotherapy: pCR 1; CR 0; PR 5; SD 5 (ORR 55%). Mean gestational age at delivery: 35.6±1.6 (33-38) weeks. Mean APGAR score at 5 minutes: 8.7±0.9; at 10 minutes: 9.5±0.9. One baby (6%) had low birth weight. Post delivery, CT scan revealed 2 further patients to have metastatic disease. Clinical stage after delivery: 0 = 1, II = 6; III = 6; IV = 3. 5-year PFS = 55%; and 5 year OS = 67.9%.

Conclusions
Administration of multiple agent chemotherapy during the second and third trimester was safe. The PFS and OS were comparable to what has been reported in the literature.
e-Posters: Breast Cancer

CLINICAL EFFECTS OF A4889G AND T6235C POLYMORPHISMS IN CYTOCHROME P-450 CYP1A1 FOR BREAST CANCER PATIENTS TREATED WITH TAMOXIFEN: IMPLICATIONS FOR TUMOR AGGRESSIVENESS AND PATIENT SURVIVAL.

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Objectives
To evaluate whether T6235C and A4889G gene polymorphisms are related to pathological presentations and clinical outcomes of ER+/PR+ breast cancer in women using tamoxifen.

Methods
We included 405 women with ER+/PR+ tumors, who used tamoxifen as their primary therapy, and for whom 5 year follow-up data were available. We evaluated associations within clinicopathologic features, including overall 5-year survival, with CYP1A1 gene status.

Results
Univariate analysis showed that a slightly higher proportion of women with AG/GG genotypes were of European descent (P = 0.05), and that TC/CC genotype was significantly associated with premenopausal status (P = 0.01); however, no significant association remained after multivariate adjustment. Women with CYP1A1 genotypes other than AA and TT were more prone to develop low-grade tumors; 85.9% of tumors in AA and TT genotype groups were grade III, but only 76.1% of tumors in carriers of the polymorphisms were grade III (adjusted P = 0.02; OR = 0.51 for grade III disease; 95% CI: 0.28–0.93). After 60 months of follow-up, ~75% of the women were alive. There was no significant difference in survival related to the CYP1A1 gene status.

Conclusions
Breast cancer patients carrying CYP1A1 gene polymorphisms developed less aggressive tumors, but showed no evidence of better prognoses.
e-Posters: Breast Cancer

CHEMOTHERAPY RELATED CARDIOTOXICITY: PREVENTION AND DETECTION
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Background
Chemotherapy related cardiotoxicity has to be considered and prevented.

Methods
Gynaecologists and cardiologists developed a score to assess treatment related risk and monitor cardiac function in breast cancer patients. Between March 2011 and March 2013, 85 women were treated at the Department of Gynaecologic Oncology, Mauriziano Hospital of Turin, Italy. Clinical data, blood and cardiologic tests were used to classify patients and monitor them.

Results
Women were treated with anthracyclines (83%), taxanes (71%) or both (61%). Trastuzumab was administered in 24.7% of cases. Most of patients received their first line of chemotherapy (93%) with an average of 5 courses administered. Individual cardiovascular risk was calculated considering age (mean 54 years), BMI (mean 24.4), total and HDL cholesterol (mean 194 and 51 respectively), diabetes (4%), hypertension (29%), smoking habit (9.4%). Global cardiovascular risk was low in 21%, mild in 77% and high in 2% of patients. Patients were submitted to ECG and echocardiography every three months during treatment and then followed up by cardiologists. Mild and high risk women underwent also BNP and troponine dosage every three months. Low or mild diastolic heart failure was recognized in 15 patients (17%), but no treatment was discontinued. Most of patient belonged to mild global cardiovascular risk (87%) and were treated with regimens containing anthracyclines and taxanes (66%). Half of them received also Trastuzumab.

Conclusions
Mild cardiovascular risk patients represent the majority of women affected by breast cancer. Their identification and monitoring is vital to prevent cardiac toxicity.
e-Posters: Breast Cancer

PHARMACOGENETIC STUDIES ON CHEMOTHERAPEUTIC AGENTS THAT HAVE THE POTENTIAL TO REVOLUTIONIZE THE WAY CLINICIANS DETERMINE A PATIENT’S OPTIMAL TREATMENT REGIMEN

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Objectives

Although there has been relatively little progress to date in using genetics to improve the treatment of common diseases, there are some encouraging signs of progress in basic research. Our aim was to use genetics involved in pharmacogenetics, which seeks to identify the genetic factors that influence responses to medicines in breast cancer cases.

Methods

Seven Polymorphisms in five specific candidate genes were analyzed in DNA obtained from biopsy samples of 280 Breast Cancer patients and compared to 150 healthy age matched women volunteers using PCR and SNP analysis. Statistical analysis determined the significance of the results.

Results

The role of genes like CYPs, TS, MTHFR, SULT1A1, and DPD in Breast cancer seen in this study, represents a test for an ADR when the drug is administered and the proportion of people with a negative test who will not have an ADR, respectively. This is the first report from India analyzing the association of polymorphisms in several drug metabolizing genes, showing the drug-gene interactions which are associated with breast cancer.

Conclusions

These findings suggest that changes modulated at the molecular biologic level supervene earlier than histologic changes, and that molecular interventions are an early diagnosis in the process of cancer therapy or cancer progression. In addition, impaired body image decreased sexual functioning and sexual enjoyment in patients, must be seriously considered in long-term survivors of breast and cervical cancer, to improve their overall quality of life.
e-Posters: Breast Cancer

THE RESISTANCE OF MAMMARY BREAST ADENOCARCINOMA TO PHOTODYNAMIC THERAPY WITH HYPERICIN IS ASSOCIATED WITH INCREASED SOD-2 ACTIVITY.

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Objectives
Photodynamic therapy (PDT) is currently one of the alternative therapeutic methods used in the treatment of solid tumours and non-malignant lesions. Under physiological conditions, antioxidant defence systems overcome toxic effect of reactive oxygen species (ROS) produced by PDT through the intracellular superoxide dismutase (SOD), catalase and glutathione peroxidase. However, tumour cells are deficient in antioxidant defence systems, what reflects their high sensitivity to ROS.

Methods
The production of ROS was monitored by flow cytometry short time after PDT with hypericin (PDT-HY) in MCF-7 and MDA-MB-231 cells and the activity of SOD-2 was measured at the same time by ELISA assay. Furthermore, the effect of PDT-HY on the expression of SOD-2 was investigated by Real-Time PCR.

Results
ROS production in MCF-7 and MDA-MB-231 cells increased 1 hour after PDT-HY, but at 3 hour time point decreased in MCF-7 cells, whereas in MDA-MB-231 remained elevated. This phenomenon correlated well with increased activity of SOD-2, which in MCF-7 cells is more prominent already within an hour after PDT, whereas in the case of MDA-MB-231 cells, only modest increase in SOD-2 activity was observed. Interestingly, in the case of MCF-7 cells the increased activity of SOD-2 was associated with an increase in SOD-2 gene expression. Role of SOD-2 in resistance of MCF-7 cells to PDT-HY was also confirmed by 2-methoxyestradiol - SOD-2 inhibitor.

Conclusions
Higher activity as well as the expression of SOD-2 are probably responsible for the rapid reduction of ROS after PDT and can be a cause of the resistance of MCF-7 cells to PDT-HY.
e-Posters: Breast Cancer

**CYTOTOXICITY OF SATUREJA KITAIBELLI AND S. MONTANA SUBSP. PISIDICA**

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**Objectives**
The cytotoxicity of methanol extract of *Satureja kitaibelii* from mountain Rtanj and essential oils of *S. montana* subsp. *pisidica* from two localities (mountains Korab and Galicica) was tested against MDA-MB-361 (estrogen-dependant), MDA-MB-453 (estrogen-nondependant)-breast cancer cell lines, and healthy MRC-5-a human fetal lung fibroblasts.

**Methods**
Cell lines were treated with extract and essential oils for 72 hours, and cell survival was determined using the MTT assay.

**Results**
Forty nine components were identified in the each sample of essential oils with the major compounds carvacrol, thymol, *p*-cymene and ß-linalool.

The major compound in the methanol extract was rosmarinic acid.

The methanol extract of *S. kitaibelii* exhibited moderate activity against MDA-MB-361 and MDA-MB-453 cell lines (IC50 from 138.06±0.16 µg/ml to 172.25±1.28 µg/ml).

The antiproliferative activity of rosmarinic acid was almost double IC50 71.77 ± 1.45 µg/ml then the cytotoxicity of methanolic extract. Both, rosmarinic acid and tested extract showed no cytotoxicity against healthy MRC-5-a human fetal lung fibroblasts (IC50 >200 µg/ml). Treatment of cells to high concentrations (200 µg/ml) led to a decrease in cell survival by 20% in normal cells.

Interestingly, as carvacrol was recognized as a major and lipophilic compound, the essential oil *S. montana* subsp. *pisidaca* with less carvacrol (Korab) possessed higher cytotoxic activity against tested cell lines (IC50 72.26±0.11 – 108.99±0.21 µg/mg), as well against MRC-5 cells (IC50 102.82±0.11).

**Conclusions**
The methanol extract exhibited lower antiproliferative activity, but also lower cytotoxicity against tested healthy cell line then the essential oils. Rosmarinic acid was active against tested breast cancer cell lines with no cytotoxicity against MRC-5.
e-Posters: Breast Cancer

SOCIAL SUPPORT AND QUALITY OF LIFE IN WOMEN WITH BREAST CANCER AFTER TREATMENT IN UNIVERSITY HOSPITAL: A COMPARATIVE STUDY

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Objectives

Purpose of this research was to study the comparison of social support and quality of life in different factors of women with breast cancer after treatment in university hospital.

Methods

This cross-sectional research was studied in 132 women with breast cancer after treatment at least 1 year. Data were collected during January - April 2013. The instruments were (1) the personal disease and treatment, (2) social support questionnaires developed by Toljamo and Hentinen (2001), and (3) quality of life for breast cancer questionnaires (FACT_B) Thai version developed by Cella et al. (1997). Alpha Cronbach's coefficients for both instruments were .88. Data were analyzed by descriptive, independent t-test and Mann-Whitney test if data were not normal distribution.

Results

Results found that there were significant different between social support separated by illness distress and partner status group at .05 level. Meanwhile, there were significant different between quality of life separated by illness distress and financial status at .05 level. Another factors such as age group, time after treatment, and stage of cancer were not significant different with social and quality of life in women with breast cancer after treatment.

Conclusions

Results from the study could provide basic data to promote social support and quality of life in these women.
MALE BREAST CANCER. OUR EXPERIENCE

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Objectives
Breast cancer in men is rare (1/100 women with breast cancer). Our objective was to analyze the clinicopathological features and therapeutic management of 28 patients diagnosed and treated in our department.

Methods
Treatment plan: Radical mastectomy (RM) vs neoadjuvant chemotherapy (NQT) with ADR/FEC +/- Paclitaxel, Tumorectomy + SLND (TL), radiotherapy, Tamoxifen if positive receptors +/- Herceptin if HER2 positive.

Results
The 28 patients were evaluable for statistical analysis. RM: 10/28 (35%); Tumorectomy + SLND: 9/28 (32%). Simple Mastectomy: 4/28 (14.2%), Lumpectomy: 1/28 (3.5%) and exclusive QT: 4/28 (14.2%). Pathology: ypT1pN0: 7/24 (29%), ypT1N2:7 (25%); ypT2pN0:4 (14%); ypT2pN1:2 (7%); ypT2pN2:2 (7%); ypT3pN3:1(3.5%). There were 6/28 distant recurrences (bone/5 and liver/2) and 5/6 died. With the mean of 147 months, at 60 and 100 months, 73.9% and 61% of patients remained free of relapse respectively. Toxicity. The procedures were generally well tolerated and there were no toxic death related to the procedures.

Conclusions
In our series, breast palpation was the most common form of detection and clinical stage IIA (35%) the most frequent. The conservative surgery + SLND increased in recent years, reaching 32%.
Objectives

Pregnancy-associated breast cancer is rare (0.2 and 3.8% of all malignant tumors of the breast). Objective: To analyze the clinicopathological characteristics and therapeutic management of 17 consecutive patients diagnosed and treated at two hospitals in the city.

Methods

Data from 17 patients treated between 2002 to 2013.

Treatment: Surgery (S) vs neoadjuvant chemotherapy (NCT) with FEC-Paclitaxel followed by S, radiotherapy, Hormonotherapy if + receptors +/- trastuzumab if HER2 +.

Results

All 17 patients were evaluable. The median age was 35 years (range 21-42y). Stage crIIA: 5; crII B: 5; crIIIA: 3; IV: 3. Diagnosed in the first, second, third quarter and postpartum (2, 3, 2 and 10). Histology: IDC: 17. G3:9. Triple negative: 3

Treatment: Modified radical mastectomy: 2/17 (11%); Tumorectomy + linphadenectomy: 11/17 (64%); NCT : (2 with Herceptin): 8/17 (41%), ypRC: 2 (11%) treated with trastuzumab; ypT1 <1 cm: 2 (11%); ypT1 (1-2 cm):3 (17%); ypT> 2 cm: 1 (5%). The 17 births were to live fetus and none had congenital malformations. There were 5/17 (29%) recurrences (2 local and 3 distance) and 2/5 (40%) deaths. The most frequent sites of relapse were: Bone: 3 and Liver: 2.

With a median follow up of 94 months (CI: 9.7-178m), at 36 and 120 months, 77% and 50% remained alive without relapse. Toxicity. Procedures were well tolerated and there were no toxic death related treatments.

Conclusions

In our series confirms that patients diagnosed with breast cancer during pregnancy can be treated with anthracycline chemotherapy schemes +/- Trastuzumab. The administration of chemotherapy after 14 weeks of pregnancy was safe.
**e-Posters: Breast Cancer**

**BREAST MRI FOR EVALUATING PATIENTES WITH METASTATIC AXILLARY LYMPH NODE AND INITIALLY NEGATIVE MAMMOGRAPHY AND SONOGRAPHY**

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**Objectives**
We wished to investigate the ability of breast MR imaging to identify the primary malignancy in patients with metastatic axillary lymph node and initially negative mammography and sonography, and we correlated those results with the conventional imaging.

**Methods**
From January to December 2012, two patients with axillary lymph node metastases and initially negative mammography and sonography underwent breast MR imaging to identify occult breast carcinoma. We analyzed the findings of the MR imaging, the MR-correlated mammography and the second look sonography.

**Results**
MR imaging detected occult breast carcinoma in both cases. The MR-correlated mammography and second-look sonography localized lesions that were not detected on the initial exam.

**Conclusions**
Breast MR imaging can identify otherwise occult breast cancer in patients with metastatic axillary lymph nodes. Localization of the lesions through MR-correlated mammography and second-look sonography is, in practice, practically feasible in most cases.
e-Posters: Breast Cancer

70-Gene Signature (MammaPrint®): Assessment Using Samples Fixed in Formalin and Embedded in Paraffin, Obtained Via Diagnostic Core-Needle Biopsies

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Objectives
To establish the possibility of obtaining a valid analysis of the tumor genetic fingerprint, using paraffin blocks containing samples obtained during the diagnostic procedure, via echo-guided large needle biopsy.

Methods
5 cases, with samples obtained via echo-guided biopsy with a 12 G needle (3 to 5 samples) through malignant solid masses during the diagnostic procedure. The samples used for examination by MammaPrint® came from the paraffin blocks used for the conventional histological diagnosis, following assessment by a pathologist. A review was performed of the available literature on the subject.

Results
The number of samples varied from 3 to 5. In all five cases, we were able to obtain valid samples for MammaPrint® assessment. The results was ‘High Risk’ (three cases) and ‘Low Risk’ (two cases).

Conclusions
The same samples obtained via percutaneous biopsy for assessment of suspicious lesions, with a result of malignancy, can be used for assessment of 70-gene signature (Mammaprint®).
e-Posters: Breast Cancer

BREAST CANCER AND ABLATIVE CHEMOTHERAPY WITH CON STAMP-V. OUR EXPERIENCE

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Objectives
To show the results of a group of breast cancer with stage II-III high-risk, treated with AQT + auto transplantation-Stem-cell

Methods
Conservative surgery + lymphadenectomy (CC) or MRM was planned. Chemotherapy (CT): FEC/75 (5FU: 600mg/m²; 4Epi: 75mg/m² and Genoxal 600mg/m²) and STAMP-V (QTA): (1.5 Gr/m² Genoxal day 4; Carboplatin 200mg/m² day Thiotepa 125mg/m² by 4 and day 4) and reinfusion of stem cells.

Results
Came to surgery-FEC75/6-QTA stage IIB and IIIB to FEC/3-surgery-FEC/3-QTA. All received radiotherapy and TMX
18 were evaluable for statistical analysis. MRM: 10 CC: 8. IIB: ypT2pN3 9 ypT3pN3 2. IIIB ypT1pN3 3, ypT2pN3 2 ypT3pN3:1. IIIC: ypRC: 1
Relapse: IIB:6/11 (54%); Died:5/11 (45%). IIIB:5/6 (83%); Died:5/6 (83%);
IIIA:1/1(100%) died from TB
The median overall survival from surgery was 98 months (CI: 49-179m) and median relapse of 43meses (CI: 28-57m). The more common recurence were: SNC + Bone: 3; SNC: 2; Bone: 2. Toxicity. There was no toxic death related to the procedure.

Conclusions
After 19 years of follow up 7/18p remain alive without disease (38%)

There were no transplant-related deaths.

The most common recurrences were located in the CNS and in the skeletal system.
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PREDICTIVE FACTORS OF ADDITIONAL LYMPH NODE INVOLVEMENT IN BREAST CANCER PATIENTS SUITABLE FOR CONSERVATIVE SURGERY WITH UP TO TWO MACROMETASTATIC SENTINEL NODES

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Objectives
To analyze predictive factors for additional nodes in breast cancer treated with conservative surgery (BCS) and 1-2 macrometastatic sentinel nodes (SN).

Methods
Retrospective study between July 2006-March 2012.

Inclusion criteria: 1-2 macrometastatic SN and subsequent axillary lymphadenectomy (AL), radiotherapy and systemic treatment. Exclusion criteria: neoadjuvant chemotherapy, clinical/sonographic suspicion of lymph node involvement and micrometastases/isolated tumor cells in SN.

Results
Fifty-six patients (age 58.8 years (±12.1); tumor size 17.2mm (±6.7)).
Histology: IDC 81.7 %; ILC 8.3%; others 10%. Positive hormonal receptors in 90%, positive Her2neu in 10% and 1 triple-negative case.

After AL, 78.6% had non-additional positive nodes. Among patients with additional nodes (n=12; 21.4%) there was one more metastatic node in 66.6% (n=8) and 2/more involved nodes in 4 cases.

When only one macrometastatic SN (n=35), additional involvement depended on number of harvested SN: 40% if 1/1; 6.6% if 1/2 and 0 if 1/3; there was not >2 additional nodes.

When 2 positive SN (n=9), additional involved nodes were in 9 cases without any dependence on the number of excised SN. There were not >2 additional involved nodes.

In univariate analysis, predictive factors for additional involved nodes were: tumor size >5mm [OR 4.6(1.057-20.160)], involved SN ratio>0.5 [OR 9.5(1.132-79.696)] and the presence of 2/more macrometastases [OR 4.41(1.134-17.143)]. In multivariate analysis, significant factors were: macrometastasis size [OR 6.419(1.192-34.551)] and percentage of involved SN [OR 7.718(1.251-47.630)].

Conclusions
If AL was omitted, residual metastatic nodes would remain in nearly one third. There were no >2 additional involved nodes. Significant predictors were macrometastasis size and percentage of SN affected.
e-Posters: Breast Cancer

BREAST-CONSERVING SURGERY: HOW CAN WE IMPROVE OUR OUTCOMES?

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Objectives
To determine the most accurate method of guiding breast-conserving surgery (BCS) to guarantee a complete removal of affected tissue and acceptable aesthetics.

Methods
Retrospective study in 81 patients treated by BCS during 2011. Exclusion criteria: ductal carcinoma in situ, multifocality-multicentricity or neoadjuvant chemotherapy. Non-palpable tumor surgery was guided by metallic dispositive (MD) or radioguided occult lesion localization (ROLL). Intraoperative re-excision was performed if insufficient margins. The real resection volume (RRV) was the ellipsoid volume of the specimen adding ampliations. The optimal resection volume (ORV) was the spheric tumor volume adding 1cm margin. The ratio RRV/ORV was calculated and in best conditions should be 1. We calculated tumoral volume by ultrasound (UV) and ratio UV/histological tumor volume. Indeed we calculated ratio UV+1cm (OUV)/ORV.

Results
There was a 37% of palpable; a 28.4% of MD-guided and a 34.6% of ROLL-guided tumors. Intraoperative re-excision was required in 55.6%, 55.2% and 52.2% of cases [p=0.994]. There were insufficient margins in 10.7%, 10.3% and 13%, respectively [p=0.948]. Median RRV/ORV was 2.7, 1.6 and 2.8, respectively [MD vs ROLL p=0.01]. Median ratio UV-histological volume was 0.82. Median ratio OUV/ORV was 0.91 (0.04-2.86), with 35% overestimated cases, 55.7% underestimated cases and 8.9% cases with ratio=1.

Conclusions
There is a similar insufficient margin percentage with BCS conventional guiding methods. With all them, we excise an excess of healthy tissue affecting aesthetics. Ultrasound (US) underestimates the real histological tumour volume, but adding 1cm margin to US gives a more accurate ratio. Intraoperative US-guiding surgery accuracy should be studied prospectively.
THE EFFECTIVENESS OF DEAD SPACE CLOSURE WITH QUILTING SUTURE IN THE PREVENTION OF SEROMA FORMATION WITH THE USE OF PROPENSITY SCORE MATCHING ANALYSIS.

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Objectives
The study aimed to assess if quilting suture decreases seroma formation without complications in consecutive patients in comparison to conventional closure with drainage. The effectiveness of quilting suture was tested by using propensity score matching analysis.

Methods
Between January 2009 and April 2012, we studied a subset of patients with breast cancer that were scheduled for modified radical mastectomy or simple mastectomy by two surgeons: a senior and a junior.

Patients were divided into two groups according to their closure technique: quilting suture and closure in the standard fashion with drainage.

Propensity score matching was performed based on preoperative risk variables to correct for selection bias.

Results
119 patients were studied, with 60 undergoing quilting sutures and 59 with conventional closure. In the Quilting group, seroma overall incidence was significantly reduced (OR) 0.19; 95% confidence interval 0.08 to 0.45; p<0.001. Quilting did not affect back pain or compromise wound healing: There were no significant differences in early pain scores between the two groups. At day 15-21 there was a significant reduction of pain score in group 1 (OR) 0.27; 95% confidence interval 0.13 to 0.59; p<0.001. Hospitalization length was significantly decreased in group 1 ((OR) 0.18; 95% confidence interval 0.07 to 0.45; p<0.001. A propensity score analysis confirmed the benefit of quilting for seroma incidence (p=0.002), length of hospital stay >5 days (p=0.01), and pain at the first postoperative follow-up visit (p=0.01).

Conclusions
Our results show evident benefit in term of complications (seroma formation), hospital stay and pain at the first postoperative visit.
LOBULAR CARCINOMA OF BREAST UNUSUAL PRESENTATION OF RECURRENCE, MIMICKING OVARIAN CARCINOMA

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Objectives
Metastases to the female genital tract from extragenital cancers are rare. On the other hand, most common metastasis sites of breast cancer are the lungs, bones, liver, and brain, whereas genital involvement by metastatic breast disease is rare.

Methods
59 years old patient was admitted to our clinic with a complaint of vaginal bleeding. Medical history was normal except the diagnosis and treatment of lobular breast carcinoma 10 years ago. Her ultrasonographic examination revealed 4x4 cm solid mass in the right adnexial region. CA 125:44, 2 CA 19-9: 55, 9.

Results
The patient underwent laparatomy with a pre-diagnosis of ovarian malignancy. Intraoperatively an adnexial mass of 5 cm in diameter was detected. Frozen section investigation revealed malignant epithelial tumor without origin. Total Abdominal Hysterectomy+ Bilateral salpingooofrectomy+ Omentectomy+ Appendectomy+ Bilateral Pelvic Paraaortic lymph node dissection were performed. Final pathological result revealed metastasis of lobular carcinoma of breast+ 61 metastatic lymph node in both pelvic and paraaortic region.

Conclusions
Breast carcinoma is the most common malignancy among female population. Genital recurrence of breast carcinoma especially lobular in histology is rare but possible. It should be kept in mind that, routine gynecological follow-up examination should be carried out in breast cancer patients even if the patient is disease free for 10 years.
RADIONUCLIDE 99MTC-MDP IMAGING IS EXTREMELY SENSITIVE AND SUPERIOR TO CONVENTIONAL RADIOGRAPHY IN THE DETECTION OF BONE METASTASIS IN BREAST CANCER

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Objectives
To determine the potential role of 99mTc-MDP bone scintigraphy for the evaluation of bone metastases in carcinoma breast.

Methods
This study was performed in the division of nuclear medicine, department of radiation oncology, Kamla Nehru Hospital, Gandhi Medical College, Bhopal, India. A total of 53 patients, all females, in the range of 25 to 72 years old. 50 out of 53 patients was histopathologically diagnosed as cancer breast referred to nuclear medicine for bone scan and two patients came directly with the history of lump in breast with pain in joints. All were scanned before and, after surgery, radiotherapy, chemotherapy and during follow-up. 22 to 25 mCi of 99mTc-MDP was injected IV, static anterior and posterior views of entire skeleton was taken under the ECIL gamma camera.

Results
Total 53 patients were investigated. On visual analysis there was positive scan findings (bone metastases) in 17 patients (33.4%) and negative scan findings (normal bone scan) in 34 patients (66.6%). Survival was lower in patients with Osteoblastic and osteolytic disease compared with the other sites of bone mets.

Conclusions
It is a very sensitive and specific method, cheaper than C.T, MRI, PET-CT procedures. 99mTc-MDP bone scintigraphy measures the extent of bone metastasis & bone scintigraphy elucidates tumour characteristics and shows prognosis and response to chemotherapy, hormonal treatment. Quality of life will be good, If diagnosed early, accurately and managed properly. Finding bone metastases is frequently important for clinical decisions affecting quality of life. Detection of such bone metastatic lesions allows radiation therapy or surgical interventions to prevent pathologic fractures.
e-Posters: Breast Cancer

CLINICAL VALUE OF 18(F)FDG-PET/CT FUSION IMAGING IN BREAST CANCER MANAGEMENT.
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Objectives
Clinical roles of 18(F)FDG-PET/CT imaging in staging and treatment evaluation of breast cancer and detection of recurrence.

Methods
A total of 46 patients, were seen in the department of nuclear medicine and PET/CT, AIIMS, New Delhi, India, from October, 2010 to April, 2011. A standard dose of 18(F) FDG of 10 mCi (370 MBq), was injected and imaging was performed with CT and PET.

Results
Out of 46 cases n=1 (2.17%) had bilateral breast cancer. Positive lymph nodes were found more often in larger tumors > 2 cm. Lymph nodes metastasis was seen in n=20 (43.47%), n=10 (21.73%) had lung metastasis, n=11 (23.93%) had bone metastasis and recurrent disease was noticed in n=11 (23.93%) patients. No evidence of disease was observed in n=11 (23.93%) patients during follow-up evaluation. Eight (17.39%) patients had progressive disease. Residual disease was observed in n=8 (17.39%) patients in 3rd follow-up with PET-CT. Pleural effusion was found in n=5 (10.86%) patients. Metastasis were noticed in liver in n=4 (8.69%), in adrenal gland in n=3 (6.52%), in thyroid gland in n=3 (6.52%) and in brain in n=2 (4.32%). One (2.17%) patient showed partial response to treatment. We had observed SUVmax values from 31-39.

Conclusions
18(F) FDG-PET/CT is a superior and an adjunct to USG, mammography, CT, and MRI for staging patients of breast cancers with distant metastasis, helps in monitoring tumour response to treatment and recurrence.
ASSOCIATION BETWEEN INTAKE LEVELS OF FOLATE, PYRIDOXINE, AND COBALAMIN AND PLASMA TOTAL HOMOCYSTEINE STATUS AMONG IRANIAN PRIMARY BREAST CANCER PATIENTS

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Objectives
Recently an elevated plasma total homocysteine (tHcy) concentration is suggested as a notable characteristics of proliferation. The objective was to describe the association between dietary intakes of folate, riboflavin, vitamin B-6, and vitamin B-12 and plasma tHcy concentration among primary breast cancer patients.

Methods
In this prospective consecutive case series study, 148 Iranian women newly diagnosed with histopathologically confirmed malignant BC within the range of 30-69y old were recruited. A validated 136 food items FFQ was used to estimate the certain nutrients during a year ago. The plasma measurements of tHcy and pyridoxal-5-phosphate were undertaken using HPLC with fluorescence detection. Plasma folate and cobalamin were measured using automated electrochemiluminescence immunoassay.

Results
The level of plasma tHcy was observed significantly higher among BC participants with stage III where the plasma concentration of folate was also comparably lower (P<0.05) vs. lower stags. The plasma concentration of tHcy was correlated inversely with plasma folate concentration (β=-0.26, P<0.05), daily dietary folate (β=-0.32, P<0.01), and residual folate intakes levels (β=-0.30, P<0.01) after adjustment for confounders. Daily dietary intake of cobalamin was also negatively associated with plasma level of tHcy, after adjustment for effective confounders (β=-0.27, P<0.05). The multivariable ORs of comparing the highest tertiles of plasma cobalamin (>394pmol/l) and folate levels (>11.4ng/ml) vs. the lowest categories were associated with reducing the likelihood of manifesting high tHcy status at ORs of 0.20 (95%CI: 0.04-0.98) and 0.14 (95%CI: 0.03-0.64), respectively.

Conclusions
In conclusion, nutrition-related methyl-group insufficiency could harbour the immense outbalance in tHcy metabolism as the secondary manifestation of cancer.
e-Posters: Breast Cancer

DIETARY METHYL INTAKES AND RETINOIC ACID RECEPTOR-BETA2 PROMOTER HYPERMETHYLATION STATUS IN PRIMARY BREAST CANCER

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Objectives
Intake of dietary methyl group donors might selectively influence the hypermethylation status of some putative genes in carcinogenesis and therapeutic approaches, i.e., retinoic acid receptor-beta2 (RARbeta2), which is speculated to be tissue dependent. We aimed to explore the association of dietary intake of methyl groups with hypermethylation status and expressional level of RARβ2 gene among Iranian breast cancer patients.

Methods
The hypermethylation status of RARbeta2 gene was investigated in 146 dissected tissues from primary breast cancer patients thorough methylation-specific PCR (MSP). The expression level was evaluated by real-time RT-PCR. Dietary intake of nutrients was estimated using validated 136 items FFQ.

Results
There was inverse association between either crude-dietary folate or adjusted-cobalamin intake and methylated RARbeta2 gene with OR at 0.44 (95%CI: 0.22-0.87), or 0.16 (95%CI: 0.04-0.75), respectively. The later associations were notable in ages younger than 48y. However, high dietary riboflavin or pyridoxine intake versus less intake strata was also revealed to associate with increasing tumors harboring RARbeta2 methylation, just after adjusting for independent covariates.

Conclusions
In conclusion, our findings may suggest new insights into the contribution of methyl group donors which seem differently react on methylation of RARbeta2 gene. The insufficient daily dietary intake of folate or cobalamin, and adequate riboflavin or pyridoxine intake were associated with increased prevalence of developing breast tumors with promoter methylation at RARbeta2 gene as putative tumor-specific gene, where methylated largely in BC subjects.
PROGNOSTIC SIGNIFICANCE OF HISTOLOGICAL GRADE 2 IN PATIENTS WITH BREAST CANCER

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Objectives
One of the best established prognostic factors in breast cancer is histological grade. Grade 2 tumors show an intermediate outcome during the early years of follow-up and an obvious trend for continued recurrence and impaired outcome in the long term follow-up. In order to study the association of G2 tumors with other prognostic and predictive factors of breast cancer and its relation to G1 and G3 tumors, we analyzed tissue samples from 177 patients surgically treated for invasive ductal carcinoma.

Methods
Correlation of the tumor size (T), degree of tumor differentiation (G), vascular invasion (VI), axillary node status (N), steroid hormone receptors (SR), HER-2 and Ki-67 status with patient age and with G2 and G3 was evaluated. We also analyzed survival outcomes according to histological grade.

Results
G2 was associated with negative VI (p<0.001), patient age >50 years (p=0.001), T≤2 cm (p<0.001), T2-5cm (p<0.001), Ki-67≤15% (p<0.001) and negative N (p<0.003, p<0.006). G3 was associated with negative SR (p<0.001), negative VI (p<0.002), patient age >50 years (p=0.005), T≤2 cm (p<0.003), T2-5cm (p<0.015) and Ki-67≤15% (p<0.001). After 5 years, 175 patients were available for the follow-up examination. The 5-year cumulative survival rate among patients with G1 was 93%, with G2 75% and with G3 63%. Histological grade was significantly correlated to the 5-year survival rate (p<0.002).

Conclusions
Concerning the difference in the 5-year survival rate according histological grade, regardless of the similarity of G2 and G3, it is necessary to apply a different therapeutic approach in the treatment of breast cancer.
CLINICOPATHOLOGICAL FEATURES OF BREAST CANCER MOLECULAR SUBTYPES IN BRAZILIAN WOMEN.
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Objectives
There are few series related to the proportion of each molecular subtype in Brazilian women with breast carcinoma. The objective of the present study was to assess the relationship between molecular subtypes and clinical characteristics in a subset of Brazilian women with invasive breast carcinomas.

Methods
Expressions of estrogen receptor (ER), progesterone receptor (PR) and Ki67 were assessed by immunohistochemistry in TMA (tissue microarray) in 211 patients. FISH were used to assess HER2 status. Molecular subtypes were classified as Luminal A (positive ER and/or PR, negative HER2 and low Ki67 rate), Luminal B (positive ER and/or PR, positive HER2 or high Ki67 expression), HER2 overexpressed (negative ER and PR and positive HER2) and Triple negative (negative ER, PR and HER2). Chi-square and Fisher’s exact test were used to calculate subtypes expression and clinical characteristics.

Results
Among the 211 tumors, 39.8% were classified as Luminal A, 32.7% as Luminal B, 10.4% as double negative HER2 overexpressed and 17.1% as Triple negative. Triple negatives tumors were associated with younger age and higher tumor size. There was a predominance of undifferentiated tumors in all molecular subtypes. Peritumoral vascular and lymphatic invasion (observed in 33.9% of the entire cohort), peritumoral neural invasion (detected in 12.6%) and dermal lymphatic invasion (present in 10.3%) were not associated with the molecular subtype.

Conclusions
In this series of Brazilian women with invasive breast carcinoma, more than 70% of the tumors were Luminal molecular type. Younger age and advanced stage were associated with triple negative tumors. Grant research from FAPESP 2009/17097-1.
EFFECT OF ACTIVE EXERCISE AND MANUAL LYMPHATIC DRAINAGE ON LYMPHATIC COMPENSATIONS FOLLOWING BREAST CANCER SURGERY

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Objectives
The lymphedema of the upper limb (UL) ipsilateral to surgery promotes substantial functional and psychological disturbance. More attention has been devoted to the physical complications and improvement in preventive and rehabilitation techniques. The objective was to evaluate the effect of active exercise and manual lymphatic drainage (MLD) on lymphatic compensations of the UL following breast cancer surgery.

Methods
A non-randomized controlled clinical trial was conducted, including 89 women undergoing radical breast cancer surgery, matched for staging, age and body mass index. In the postoperative, 46 women did active exercises for the UL and 43 received MLD, during one month. Perimetry and lymphoscintigraphy of the UL were performed preoperatively and 60 days postoperatively.

Results
After surgery, 34.8% of the exercise group and 48.8% of the MLD group had a worse rate of radiopharmaceutical uptake, while 19.6% of the exercise group and 18.6% of the MLD group showed an improved rate. Concerning intensity of uptake, 43.5% of the exercise group and 55.8% of the MLD group showed worsening and 13.0% of the exercise group and 14% of the MLD group, showed some improvement. UL perimetry, the presence of dermal backflow, liver absorption and collateral circulation were similar between groups in both time points evaluated. The exercise group had a significant increase in postoperative liver absorption.

Conclusions
Postoperative lymphatic compensations were similar between groups, suggesting that active exercise and/or MLD may be employed according to patient complaints or symptoms.
e-Posters: Breast Cancer

FNA BREAST TUMORS: THE RELIABILITY OF THE METHOD IN OUR MATERIAL
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Objectives
To compare the negative and positive fna with final diagnosis (histology), to assess the results and to evaluate the accuracy of the method.

Methods
The results were examined in 131 FNA that were effected during the period 2008 to 2012 in our hospital and evaluated in the cytology laboratory.

Results
32.1% were positive for malignancy FNA, 2.3% were suspicious for malignancy FNA, 61.1% were negative for malignancy FNA and 4.5% were not identified. Both positive and suspicious for malignancy FNA and negative FNA for malignancy were evaluated in relation to histological diagnosis. From these arose: 100% were confirmed (histologically) positive for malignancy FNA, 33.3% of the suspicious FNA had positive histological diagnosis, 25% of (-) FNA were confirmed in the laboratory and 2.5% of (-) FNA were false negative. It is worth to mention that the false negative FNA due to factors such as small tumor size, fibrous tissue, histological malignancy Grade 1, etc. The sensitivity of the method was 95, 55%.

Conclusions
The degree of agreement FNA (+)-final diagnosis is very high and 33.3% were confirmed histologically positively labeled as suspicious for malignancy FNA. The degree of agreement FNA (-) - final diagnosis varies due to lack of information for further development at a rate of 72.5%. We estimate that the sensitivity of the method used had high success rates compared with those of the literature (89-98%).
e-Posters: Breast Cancer

FACTOR PREDICTING QUALITY OF LIFE IN WOMEN WITH BREAST CANCER AFTER TREATMENT IN UNIVERSITY HOSPITAL

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Objectives
Purpose of this research was to study factors predicting the quality of life in women with breast cancer after treatment in university hospital.

Methods
This study was cross-sectional research. Samples included 132 women who completed their treatments since 1 year at university hospital during January - April 2013. Three instruments were used to collect data. They were the personal disease and treatment, sense of coherence-13 (short form) questionnaires developed by Antonovsky (1987), social support developed by Toljamo and Hentinen (2001), and quality of life questionnaires (FACT_B) Thai version developed by Cella et al. (1997). Alpha cronbach's coefficient for sense of coherence, social support, and quality of life questionnaires were .88, .88, and .75 respectively. Data were analyzed by multiple regression.

Results
Results found that the sense of coherence and social support, age group, and financial status could predict the quality of life at .05 level. Whereas partner status, distress illness, stage of cancer, education level, and time after treatment could not predict quality of life in women with breast cancer after treatment.

Conclusions
Results from the study can be used as an evidence-based to provide and improve quality of life in women with breast cancer after treatment.
CHARACTERIZATION OF A COHORT OF YOUNG PATIENTS (UNDER 35 YEARS) WITH BREAST CANCER
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Objectives
Determine the clinicopathological characteristics of breast cancer patients under 35 years old attended in the Breast Unit of Gynaecology and Obstetrics Department of the Canary Islands University Hospital between the years 2001-2011.

Methods
The study included a historical cohort of 68 patients with breast cancer under 35 years old at diagnosis who attended the Breast Unit. We excluded 20 patients who had been previously treated in other centers or with missing data. We collected and analyzed the following variables: demographic, genetic, clinical, tumor-related (histological type, size, grade, estrogen and progesterone receptors, HER2, Ki 67, and TNM), related to the treatment applied and follow-up until February 2013. Tumors were classified into subtypes based on the recommendations of the St Gallen International Expert Consensus 2011.

Results
The mean age was 32 years, 31 (46%) nulipara, 5 (7.35%) smokers. The 66% of patients (45) had an infiltrating ductal carcinoma (IDC). The average tumor size at the moment was 35 mm, 30 (44%) patients had a Luminal B subtype, 17 (25%) Basal Like, 12 (18%) Luminal B HER2 positive, 5 (7%), Erb-B2 overexpression and 4 (6%) Luminal A.

Conclusions
In this group of patients under 35 years old with breast cancer, large tumors with poor prognosis subtypes were more frequent. This data could be usefull for prospectives studies.
IMPACT OF SOCIO-DEMOGRAPHIC AND MEDICAL FACTORS ON QUALITY OF LIFE IN PATIENTS WITH BREAST CANCER
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Objectives
Breast cancer is the most prevalent malignancy type among women in world with quality of life (QOL) issue being of special importance. This study is aim to explore impact of socio-demographic and medical factors on QOL in patients with breast cancer.

Methods
The simplified Chinese version of the FACT-B was used to measure QOL in 233 patients with breast cancer at the time of their admission to the hospital and at discharge. Information was also collected regarding socio-demographic and clinical variables such as age, education, symptoms, treatments, etc. Spearman correlation analysis, ANOVA, t tests, and multiple linear regression were used to examine factors related to QOL.

Results
All domains had statistically significant changes after treatments with the standardized response mean (SRM) ranging from 0.14 to 0.31. Quality of Life in patients with breast cancer were influenced by age, perceived income, education, occupation, medical security level, symptoms, treatments, etc., with different domains of Physical Well-being (PWB), Social/Family Well-being(SFWB), Emotional Well-being (EWB), Functioning Well-being (FWB) and Additional Concerns (BCS) being different factors. However, in terms of explanatory power these associations displayed a relatively small Adjusted R Square from 0.047 to 0.21.

Conclusions
Our findings can be used for making decisions in clinical trials as well as in aiding individual management and preventive care of this cancer. In order to improve quality of life, some appropriate measures on these aspects should be taken.
e-Posters: Breast Cancer

BCL-6 IS A TARGET GENE OF MIR-339-5P IN BREAST CANCER CELL

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Objectives
To predict and verify the direct target gene of miR-339-5p in breast cancer cell.

Methods
1 Bioinformatics tools were used to analysis and predict the potential genes of miR-339-5p.
2 The 3' UTR region of target gene was cloned to the psiCHECK-2 vector which including luciferase reporter gene and then co-transfected with miR-339-5p mimics to T47D. MiR-339-5p target genes were confirmed by luciferase reported assay.
3 The protein expression of taget gene was detected by transfection of miR-339-5p mimics to T47D through western-blot.

Results
1 Bioinformatics tools analysis revealed that BCL-6 was one of the potential target genes of miR-339-5p.
2 The luciferase reporter assay indicated that miR-339-5p was directly bound to BCL-6 3' UTR.
3 Western-blot results showed that the expression level of BCL-6 protein was significantly decreased in T47D cell with forced expression of miR-339-5p.

Conclusions
MiR-339-5p could regulate the expression of downstream target gene BCL-6 in breast cancer cell.
e-Posters: Breast Cancer

DECREASED MIR-320 AND INCREASED AQP1 IN PATIENTS WITH BREAST CANCER AND THE CLINICAL SIGNIFICANCE
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Objectives
The aim of this study was to investigate the role of miR-320 and its target gene AQP1 in breast cancer and to assess their clinical significance.

Methods
QRT-PCR was used in the detection of miR-320 and AQP1 mRNA expression both in breast cancer tissue and in adjacent normal tissue. Immunohistochemistry and western blot were used in the detection of AQP1 protein expression. The clinicopathological implications of these molecules were analyzed statistically. Survival analysis was also performed to assess their prognostic significance.

Results
Down-regulation of miR-320 was associated with overexpression of AQP1 mRNA in breast cancer tissue with a negative correlation ($r = -0.698, P < 0.05$). MiR-320 expression was significantly associated with pathological stage ($P = 0.004$) and lymph node involvement ($P = 0.024$). Overexpression of AQP1 was associated with histological grade ($P = 0.033$). Survival analysis indicated that reduced expression of miR-320 versus overexpression of AQP1 is associated with a poorer prognosis ($P < 0.05$).

Conclusions
Our results suggest that down-regulation of miR-320 may result in enhanced expression of AQP1 in breast cancer, which consequently favored tumor progression. MiR-320 and AQP1 may play important roles as biomarkers for prognosis and therapeutic targets in breast cancer.
THE ASSESSMENT OF A SIMPLER COLD KNIFE CONIZATION TECHNIQUE FOR THE DIAGNOSIS AND TREATMENT OF CERVICAL DYSPLASIA OR MICROINVASIVE CARCINOMA.

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Objectives
The main goals of our study were to assess a simpler cold knife conisation technique (as described by Ostergard, Berman and Yee in Atlas of Gynecologic Surgery) as well as the sexual quality of life of our treated patients.

Methods
Our retrospective study enrolled 134 patients who required cold knife conisation for diagnosis and treatment of cervical dysplasia or microinvasive cervical carcinoma. 67 patients were operated by a single surgeon using the above mentioned technique, while the others 67 were operated by another single surgeon using the Green technique. Operation time, complications, blood loss, rate of lesion clearance, elements from the pathological report, therapeutic and obstetric outcomes as well as sexual quality outcomes of our patients were assessed.

Results
There were no statistically significant differences in the complication rate (one cervical stenosis in the first group) or the rate of lesion clearance between the 2 study groups. The operation time was significantly shorter for the new technique (p<0.01) as well as the amount of blood loss. The excision specimens were significantly larger in the first group, while the mean cervical stump was 2.04 cm. Out of the 67 patients that suffered the simpler technique 11 got pregnant and gave birth to 11 healthy babies. There were no significant differences in the sexual quality of life of the patients from the two groups.

Conclusions
The technique we have assessed seems feasible, significantly shorter as far as operation time is concerned, resulting in larger specimens due to the comfort of the surgeon in closing the cervical stump.
e-Posters: Cervical Cancer

CLINICAL SIGNIFICANCE OF LVSI: DOES IT PREDICT LYMPH NODE METASTASES?

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Objectives

The aim of this study is to point out clinical significance of LVSI and to identify its relationship with lymph node metastases and overall survival according to clinical stages and histologic subtypes.

Methods

We retrospectively analysed 222 clinical stage 1 patients who underwent surgery between the years 2007 and 2013. The statistical analyses are done by using spss16.

Results

Mean age was 50 (range 25 to 80). Clinical stages was 1a1(20/222), 1a2(4/222), 1b1 (145/222) and 1b2(53/222). Histologic subtypes was squamous cell (175), adeno cancer(36) and adenosquamous cancer (11). In squamous cell group 49 of 57 patients with metastatic LN had positive LVSI (p<0.002). In adeno cancer group 10 patients had LN metastases and all of them had positive LVSI (p<0.004). In AS group 3 of 4 patients with metastatic LN had LVSI (p<0.91). If we consider all stage 1 patients LVSI and LN metastases has significant correlation (P<0.001).

<table>
<thead>
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<td>17</td>
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<tr>
<td></td>
<td></td>
<td>poz</td>
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<td>2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
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<td>19</td>
</tr>
<tr>
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<td>LVSI</td>
<td>neg</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>poz</td>
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<td>4</td>
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<tr>
<td>Total</td>
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<td></td>
<td>4</td>
<td>4</td>
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<tr>
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<tr>
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<td>9</td>
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<tr>
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<td></td>
<td>poz</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>22</td>
<td>31</td>
</tr>
</tbody>
</table>

Conclusions

LVSI is not statistically significant factor for overall survival in stage 1 cervical cancer but it can predict lymph node metastases. Since lymph nodal involvement is a major risk factor for overall survival LVSI must be considered in treatment of stage 1 cervical carcinomas.
WHAT IS THE ROLE OF ADJUVANT RADIATION IN 1B1 CERVICAL CANCER PATIENTS WITH DEPTH OF STROMAL INVASION MORE THAN % 50 AND POSITIVE LYMOHOVASCULAR SPACE INVASION

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Objectives
The goal of the study is to evaluate the role of adjuvant radiation on overall survival in 1b1 squamous cell cervical cancer patients with depth of stromal invasion more than % 50 and positive Lymphovascular space invasion.

Methods
We partially retrospectively and prospectively analysed 35 patients(1b1) who were subjected to Radical Hysterectomy and Bilateral Pelvic Paraortic Lympadenectomy between the years 2007 an 2013 And the pathology reports are re-evaluated by co-author pathologist and reported as sq cell carcinoma ,positive LVSI and the depth of stromal invasion is more than 50 % The stastical analses are done by using SPSS 16.

Results
13 patients recieved adjuvant radiation therapy and 22 patients were observed .Mean follow up time was 23,4 months(range 4 to 69 months) 4 patients died (2 radiotherapy group,) during this follow up time .5 year overall survivals were 84,6 % and 90,9 % respectively and there was no statistical differance (p<0,83) between two groups

Conclusions
We could not find any superiority of radiation therapy .According to our study there is no role of radiation therapy in minor risk factors positive 1b1 sq cell cervical cancer patients But further prospective studies are needed.
CARBOPLATINUM IN NEOADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER: A PILOT STUDY.
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Objectives
Standard chemotherapy for cervical cancer is actually considered Cisplatin plus Paclitaxel and Ifosfamide (TIP), but it unfortunately is correlated with high toxicities rates. The Italian SNAP02 study indicated the two-drug combination of Cisplatin plus Paclitaxel (TP) as possible alternative to standard chemotherapy, reporting similar response rates (78-100%). Despite this toxicities are still very high. The primary endpoints of this study is to evaluate response rates to the combination of Carboplatin and Paclitaxel as neoadjuvant chemotherapy (NACT) in patients affected by locally advanced cervical cancer (LACC). Secondary endpoint was safety with toxicity profile.

Methods
Between June 2007 to May 2012, all patients with diagnosis of LACC (IB2-IIIB) were eligible for this protocol. They received 3 cycles of Carboplatin (AUC6) and Paclitaxel 175 mg/mq in neoadjuvant setting. Toxicities and response to treatment were evaluated according to WHO criteria.

Results
35 patients with LACC were considered. A total of 23 patients completed 3 cycles of NACT. The overall clinical response rate after NACT was 78.3% including: 43.5% (n=10) complete response, 34.8% (n=8) and partial response. 17.4% (n=4) had stable disease and 4.3% (n=1) suffered disease progression. The most common toxicity was haematologic, nausea/vomiting and neuropathy with grades 1 and 2 and occurred in 56.5%, 56.5% and 17.4% respectively. No renal toxicity was registered.

Conclusions
Our results suggest that Carboplatin is a well tolerated drug with a response rate similar to standard Cisplatin. Then, it may represents, in neoadjuvant setting, a valid alternative in patients affected by LACC.
UTERINE PERFORATION AND DOSIMETRIC IMPLICATIONS IN HDR BRACHYTHERAPY FOR CARCINOMA OF THE CERVIX

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Objectives
To assess the incidence of uterine perforation in cervical cancer intracavitary High-Dose-Rate (HDR) brachytherapy, and evaluate its effects on Computed-Tomography (CT)-based treatment planning.

Methods
Cervical cancer patients treated with HDR brachytherapy from February 2006 to December 2012 were retrospectively identified. All applications were performed without radiological guidance for uterine tandem insertion. CT-based treatment plans were reviewed for uterine perforation or near-perforation (sub-serosal insertion of tandem, i.e. within 5 mm from the uterine serosa). For each patient, the plans showing sub-optimal insertion of intra-uterine tandem were analysed and the dose coverage of clinical-target-volume (CTV) was compared to plans with adequate intra-uterine insertion.

Results
A total of 231 brachytherapy CT-based plans for 82 patients were reviewed. We identified 34 (14.7%) treatment plans with sub-optimal insertion of tandem: 14 applications (6%) with uterine perforation and 20 (8.6%) with sub-serosal insertion of tandem.

Dose distribution and dose-volume histograms analysis was performed for 17 sub-optimal implant plans, and showed decreased CTV dose coverage when compared to the plans with adequate intra-uterine insertion.

<table>
<thead>
<tr>
<th>Uterine perforation</th>
<th>Near-perforation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference* (%)</td>
<td>p</td>
</tr>
<tr>
<td>CTV D₉₀</td>
<td>-115.7±134.9</td>
</tr>
<tr>
<td>D₁₀₀</td>
<td>-102.8±132.3</td>
</tr>
</tbody>
</table>

* Percent difference (mean and standard deviation).

Percent differences between sub-optimal implant and adequate intra-uterine insertion for 14 patients.

Conclusions
We report a low incidence of uterine perforation in patients treated with intracavitary HDR brachytherapy for cervix carcinoma.
However, the effect on clinical-target-volume dose coverage is significantly detrimental.

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HYSTERECTOMY AFTER CERVICAL CONIZATION WITH POSITIVE SURGICAL MARGINS.
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Objectives
To evaluate final pathological results of hysterectomies which were done after the finding of positive cervical conization margin.

Methods
Thirty-five patients underwent hysterectomy after cervical conization revealing positive surgical margins among 252 patients who had undergone cervical conization between 2005 and 2013 were included in this study.

Results
Mean age of the patients were 38.79 ± 8.82. Hysterectomies were performed in 1.57 ± 1.24 months following conization. Dysplasia was revealed in only 9 hysterectomy specimens (9/35), 6 High grade CIN, 3 Low grade CIN.

Conclusions
A careful follow-up can be a good alternative to post-cone hysterectomy or reconization decision after the finding of positive cervical conization margin.
A SUCCESSFUL PREGNANCY DURING THE TREATMENT OF CERVICAL SARCOMA BOTRYOIDES AND ADVANTAGE OF COLPOSCOPIC FOLLOW-UP: A CASE REPORT

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Objectives
Sarcoma botryoides of cervix is an extremely rare variant of rhabdomyosarcomas of female genital tract which has a better prognosis comparing with rhabdomyosarcomas of uterine corpus and vagina. It is usually diagnosed in first or second decade of life presenting with cervical polyp or rarely infiltrative mass.

Methods
We report a 21 year-old nulligravid woman complaining about the feeling of a mass protruding from introitus which was represented with a 5x5x3 cm “grape-like” cervical polyp on speculum examination. She underwent a local excision of the polyp. The histopathologic examination revealed typical findings of sarcoma botryoides. She received three cycles of adjuvant chemotherapy. She refused to have a surgery because of a new unplanned and desired pregnancy at three months after the chemotherapy. And she was lost during the follow-up. After having an uneventful pregnancy period and a successful delivery, she reapplied to our clinic at postpartum 6th month. Colposcopic evaluation revealed a local polypoid area, the histopathologic examination of biopsy suggested recurrence even though positron emission tomography scans were unremarkable. Therefore complementary treatment was planned as simple trachelectomy subsequent to three cycles of chemotherapy.

Results
The aggressiveness in the surgical management of sarcoma botryoides has been declined since 1960s when pelvic exenteration was recommended for the treatment of this tumour. The median age of the patients with sarcoma botryoides obligates us to keep closer to fertility-sparing managements.

Conclusions
Thus, close follow-ups with colposcopy have utmost importance for early detection of recurrences. Fertility preserving can be a possible option in these cases.
e-Posters: Cervical Cancer

EVOLUTION OF CERVICAL CARCINOMA IN HIV POZITIVE PATIENT 49 YEARS OLD
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Objectives
A case of a HIV positive patient who was developing cervical and in same time neoplasia of vulvae, from CIN III, VIN III, with rapid evolution for one and half year.

Methods
Observation and clinical, and labaratorical evaluation of patient for two years

Results
Case report: The patient 49 years old, HIV positive from 1995, on HAART, came in the clinic with diagnostics PA III and condylomata acuminata vulvae and vagine in June 2010. After biopsy of PVU and vulvae HP result was CIN III, VIN III. Conisation and excision vulvae were done in September and HP result was Carcino PVU Ib1, G2Hg2, and VIN III.

Radical hysterectomy was performed in November without positive lymphatic nodes, and decision was follow up.

On the second control on the labia major was diagnosed tumor of vulvae and after first biopsy of vulvae HP result was VIN III. Vulvar excision was performed in July 2011 and HPP result was VIN III, And margins was in healthy tissue.

In February on next control was diagnosed suspected area in vulva again, and biopsy, and incision of vulvae was preformed again with HPP result VIN III.

From April 2012 to April 2013 patient has 2-3 month follow-up without new pathology on vulva and vagina

Conclusions
That case report indicate strong correlation between HIV and Cervical, intraepithelial neoplasia of vulvae, and carcinoma, and rapid transformation to carcinoma, with indicative parallel evolution of cervical and vulvae neoplasia also.
e-Posters: Cervical Cancer

COMPARATIVE STUDY OF CURRENTLY FDA-APPROVED HPV TESTS

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Objectives
The detection of high-risk HPV infection is essential to manage precancerous lesion of cervix. But the main concern has been its lower specificity, due to the fact that it cannot separate transient from persistent infections, and only the latter are associated with an increased risk of high-grade CIN and cancer, compared to Pap smear cytology. Recently new HPV tests having more clinical specificity and reproducibility has been developed from different company. APTIMA HPV test, Hybrid Capture 2 test, Cervista HR HPV test and Cobas4800 test was approved by U.S. Food and Drug Administration up to date.

In current study, we aimed to overview the HPV high risk type detection power, clinical implication and limitation of four FDA-approved HPV tests.

Methods
Using MEDLINE, we reviewed literatures from 2001 through to 2008 to compare between FDA-approved HPV tests in a same cohort.

Results
According to comparison studies of FDA-approved HPV tests demonstrated comparable clinical performance to detect CIN≥2 with HC2. But there are not enough evidences which one has the best clinical performance to detect CIN≥2. In one study, Aptima have higher specificity to detect CIN≥2 in all ages than HC2.

In an analytical performance, all HPV tests had fulfilled all the criteria issued by the US FDA. But HC2 test had cross reactivity with some low risk HPV type. Only Cobas 4800 test had no cross reactivity with low or undetermined risk HPV type.

Conclusions
This study can be used to guide the clinicians to choose the HPV test in clinical practice.
e-Posters: Cervical Cancer

RECURRENT SQUAMOUS CELL CARCINOMA OF THE CERVIX ON THE ABDOMINAL WALL; UNUSUAL PRESENTATION

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Objectives
To present an unusual case of recurrent cervical cancer.

Methods
Patient data reviewed retrospectively. Fifty-one years old woman was admitted to our clinic with the symptom of right upper-quadrant pain and palpable mass. She had the history of radical hysterectomy with pelvic-paraortic lymphadenectomy and postoperative radiation therapy due to cervical squamous cell cancer. Her diagnostic work-up was normal for gynecologic examination, vaginal cuff smear, chest X-ray and biochemical analysis. CT evaluation revealed an exophytic 57x46 mm solitary mass in the 7th liver segment reaching the abdominal wall. Fine needle aspiration revealed metastatic epithelial tumor. Explorative laparotomy was performed and 8 cm fixed dense tumor mass originated from abdominal wall with involvement of liver and diaphragm was inspected. Infero-lateral border of the liver and retroperitoneal space through Gerota’s fascia were also invaded by tumor. En block resection of 11th-12th ribs, abdominal wall, 7th liver segment, diaphragm and Gerota’s fascia was performed.

Results
Pathologic diagnosis was metastatic squamous cell carcinoma. Adjuvant chemotherapy with cisplatin and fluoropyrimidines was planned but patient refused therapy. Ten months later a recurrent intra-abdominal mass filling the half of the abdominal cavity with abscess formation due to tumor necrosis was diagnosed. Abscess drainage with antibiotic treatment was performed and patient was discharged from hospital. Unfortunately, she died after 3 months.

Conclusions
Cervical carcinoma is the second most common malignancy in women. Recurrence occurs about 30% within 2 years of primary treatment and vaginal cuff is usually the most common site. However unusual presentations like in our case might take place.
SYNCHRONOUS CERVICAL AND VAGINAL SQUAMOUS CELL CARCINOMA; A DISTURBING CASE REPORT

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Objectives
To attract attention to likelihood of synchronous cervical and vaginal carcinoma.

Methods
Forty-two years G2P2 woman with the symptom of chronic pelvic pain was admitted to our hospital. She had the history right salpingoophorectomy due to benign ovarian cystic mass. Transvaginal ultrasonography revealed a normal appearing uterus with left adnexa but Pap test result was ASC-H. According to patient requirements Colposcopy was performed. Cervical biopsy revealed HGSIL. Cold knife conization was planned to assess micro-invasive disease. Pathologic results were consistent with squamous cell cervical carcinoma. Tumor diameter was 10mm in horizontal plane and deepness of invasion was <7mm with lymphovascular involvement and positive surgical margins along the endocervical canal. Due to positive surgical margins and patient's status radical hysterectomy with pelvic-paraaortic lymphadenectomy was performed.

Results
Permanent pathology results revealed cervical epithelial cell changes due to HPV infection with no residual tumor and negative lymph nodes. Surprisingly well-differentiated keratinizing primary squamous cell vaginal carcinoma was diagnosed on posterior vaginal wall. Tumor was 1 cm apart from the cervix and had the diameter of 3x1.5 cm with no lymphovascular involvement.

Conclusions
During follow-up period patient had three times the opportunity to seek medical attention in which one of them was under sedation anesthesia. But the vaginal tumor did not draw enough attention. Numerous patients, strenuous radical operations, exhausting night shifts or personalized familial problems could not be the result of this kind of carelessness. As a textbook knowledge; patients who have cervical carcinoma, must be evaluated carefully against synchronous vaginal cancer.
e-Posters: Cervical Cancer

HAVE A REST AND GESTAGEN FOR CERVICAL CANCER' MORE ATTENTION TO PREGNANT WOMAN

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Objectives
To attract attention to cervical dysplasia and cancer probability instead of abortus in the presence of vaginal bleeding during pregnancy.

Methods
A 47-year-old G8P7 woman was evaluated for vaginal bleeding in the first trimester. She had no antenatal screening and was afraid of aborting her baby. Ultrasonographic examination showed 8 weeks fetus with positive cardiac activity and no intrauterine hematoma. During gynecological examination about 5 cm, fragile, partially necrotic, ulcerated mass was seen. Punch biopsy was done and patient followed for suspected cervical malignancy till the permanent pathology. Patient had clinical stage IIA disease and radical surgery was performed.

Results
Cervical cancer is the most common gynecologic cancer during pregnancy with the estimated incidence of 1.5-12 per 100,000 pregnancies. It is important to make cervical surveillance with routine Pap Test screening. In the presence of abnormalities colposcopic examination with biopsy is appropriate. Conization could be performed during second trimester to exclude invasive disease. Management of disease depends on gestational age and lesion severity.

Conclusions
Cervical precancerous and cancerous lesions tend to advance quickly in pregnancy due to rapid turn over of transformation zone. Women who don't have opportunity to have regular gynecologic examination must be checked against cervical pathology during pregnancy. Presence of vaginal bleeding in a pregnant woman must bring to mind the probability of cervical cancer. Prescription of gestagenic drugs or rest advice to prevent abortion without gynecologic examination is hazardous to patients especially in primary and secondary centers.
ELDERLY WOMEN BEYOND CERVICAL CANCER SCREENING RISK
ADVANCED STAGE CERVICAL CANCER
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Objectives
The Swedish organized cervical screening-program invites all women age 23-65 to a cervical smear.

Methods
The study aims to evaluate the cervical screening program of the region of southern Sweden, where all women (n=165) diagnosed with cervical cancer between January 2009 and December 2010 were analyzed for their previous cervical screening history.

Results
The histology in the diagnosed cervical cancer was squamous cell carcinoma in 71% and adenocarcinoma in 29% of the cases. Half of the women with cervical cancer (83/165) had not attended the regular screening program. The women above 65 year of age at diagnosis were 26%. The screening program detected 18 % of the cases whereas the majority of the cases (82%) were diagnosed due to symptoms taking the patient to doctor. 39% of the patients had an advanced stage of the disease (IIb-IV). Women above 65 years had significantly more often an advanced stage disease compared to those below 65 years of age (70 vs. 24% respectively, p<0.001). At median follow-up time (36 months) all patients diagnosed by cervical screening were still alive (30/30) having a significantly better overall survival compared to those who were discovered due to symptoms (91/135; p<0.001).

Conclusions
Women above age of 65 with cervical cancer are discovered at advanced stage of cervical cancer and have worse prognosis. Since cytology screening do worse in elderly, a possible benefit for this group could be an HPV exit test at age 60-65 to reduce the risk for cervical cancer and improve survival.
CERVICAL CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 1998-2012 PERIOD

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Objectives
Our study concerning the incidence of cervical cancer covers the 1998-2012 time span.

Methods
The data was collected from the Histopathology Exams (HPE) registers.

Results
Cervical cancer represented 58.22% (1020 cases) of the 1752 overall genital cancer cases. All but two patient had different type of carcinomas (99.80%), with the sole exception of a carcinoma-sarcoma combination and a neoplasia with neuroendocrine cells (each case representing 0.10% of all cervical cancers). There were 17 cases (1.67%) of microinvasive carcinomas combined with CIN lesions, two cases of invasive carcinoma combined with CIN lesions (0.20%), and four cases of CIN III combined with in situ carcinoma (0.39%). There was also a patient with endometrial carcinoma and CIN II (0.08%). The mean patients’ age in case of cervical cancer was 53.21±13.21 years (age range 22 to 87 years). One patient had a combination of carvical and uterine cancer. The mean age of the patients with cervical cancer was statistically highly significant (p<0.0001) from the mean age of the patients with cervical dysplasia (as a whole, as well as from every type of dysplasia taken separately).

Conclusions
Early detection of CIN lesions through adequate clinical and paraclinical exams is of utmost importance for preventing cervical cancer, which remains a serious and frequent health problem in Romania.
e-Posters: Cervical Cancer

CERVICAL INTRAEPITHELIAL NEOPLASIA IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 1998-2012 PERIOD
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Objectives
Our study concerning the incidence of Cervical Intraepithelial Neoplasia (CIN) covers the 1998-2012 time span.

Methods
The data was collected from the Histopathology Exams (HPE) registers.

Results
Early detection of CIN lesions through adequate clinical and paraclinical exams is of utmost importance for preventing cervical cancer, which remains a serious and frequent health problem in Romania.

Conclusions
Early detection of CIN lesions through adequate clinical and paraclinical exams is of utmost importance for preventing cervical cancer, which remains a serious and frequent health problem in Romania.
CERVICAL CARCINOMA WITH BONE METASTASES IN ASTRAGALUS. CASE REPORT AND REVIEW OF THE LITERATURE
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Objectives
Case report and review of literature published regarding a patient diagnosed of cervical esquamous carcinoma with an isolated bone metastases in astragalus.

Methods
66 year-old patient, diagnosed in 2009 of cervical esquamous carcinoma stage IIB (FIGO), treated with chemo-radiotherapy.

Results
After 2 years follow-upasymptomatic, she showed SCC elevation. Subsequently, she consulted Emergency Room with a bone fracture in right astragalous after getting off an autobus. The imaging tests showed an irregular lytic lesion suggestive of metastases with no abdomino-pelvic disease associated. Guided biopsy confirmed the diagnosis, and she started radical radiotherapy with poor response.

Finally, she underwent right leg infratuberositary amputation.

Conclusions
Advanced cervical carcinoma is a major cause of death among women of childbearing worldwide. Local spread to adjacent tissues as well as lymphatic dissemination of the tumor is frequent. However, haematogenous spread is uncommon, being lung, liver and bone, the most affected organs. The incidence rate for bone metastases varies from 1 to 29% affecting in most of cases lumbar spine, dorsal spine and pelvis. They have been described more frequently in advanced disease. The most common symptoms are pain and functional limitation. Because of the rarity of the entity, there are no clinical guidelines published for treatment. The prognosis of cases described in literature is bad, despite aggressive treatment, with a median survival of less than 1 year.
e-Posters: Cervical Cancer

ROBOTIC RADICAL HYSTERECTOMY: SYNCHRONOUS PRIMARY SQUAMOUS CARCINOMA OF THE CERVIX AND PSAMMOMATOUS CARCINOMA OF THE OVARY: A RARE ASSOCIATION

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Objectives
Among the rare simultaneous occurrence of cervical and ovarian cancers, there are superficial spreading squamous cancers involving the endometrium, tubes and ovaries and cervical adenocarcinomas metastasizing to the ovaries. Synchronous primary tumours of the female genital tract are rare, accounting for 0,7-1,8 % of all cases. Most commonly reported double primaries are ovarian and endometrial cancers. Synchronous endocervical adenocarcinoma and ovarian epithelial carcinomas are also reported although rarely. We are reporting an unusual occurrence of synchronous squamous carcinoma of the cervix and psammomatous carcinoma of the ovary.

Methods
A 60 year-old woman was referred to our clinic for detected cervical carcinoma. A robotic radical hysterectomy with bilateral pelvic lymphadenectomy was planned. During the operation tumoral tissue was observed on the right tube. The operation was completed as planned. Clinical implications of this case along with the preoperative work-up for the diagnosis of synchronous female genital tract malignancies and robotic surgical performance are discussed.

Results
Pathologic evaluation was reported as moderately differentiated squamous carcinoma of the cervix and psammomatous carcinoma of the right ovary, infiltrating the right paratubal region and focally the left ovary. Pelvic lymph nodes were bilaterally negative.

Conclusions
Robotic surgery is an excellent mode of surgery for most gynaecological pathologies, especially oncology. Not only it promises a safer and more ergonomic performance to the surgeon, but it provides a thorough visualisation of the whole internal genital tract. With increasingly performed robotic surgeries, synchronous tumours of the genital tract, which are not diagnosed preoperatively maybe suspected and/or diagnosed peroperatively.
CT-GUIDED INTRACAVITARY BRACHYTHERAPY FOR THE TREATMENT OF CERVICAL CANCER: A PROSPECTIVE STUDY

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Objectives
To assess the efficacy and toxicity of Computed tomography (CT)-guided high-dose-rate intracavitary brachytherapy (HDR-ICBT) for patients with advanced cervical cancer.

Methods
Sixty-four consecutive patients with stage?B2-?B cervical cancer were included in this prospective study. CT-guided intracavitary brachytherapy (CT-BT group) and conventional brachytherapy (c-BT group) were randomly performed in 31 and 33 patients, respectively. High-dose-rate source iridium-192 was used with standard intracavitary applicators. Treatment planning of CT-BT group was made using three-dimensional CT data. Postimplantation dosimetry was performed with the integrated afterloading treatment planning system, including calculation of dose to the Point A bilaterally, the rectum and bladder. External irradiation and concurrent chemotherapy were performed during brachytherapy. The tumor coverage and normal tissue avoidance were evaluated. Furthermore, treatment response and toxicities were assessed.

Results
The median follow-up was 30 months (range, 6-48 months). CT-BT plans yielded better dose conformity to the target and better sparing of the rectum and bladder than c-BT group (P=0.037, and P=0.022, respectively). Although no significant differences were found for 1- and 2-year overall survival, obviously higher 1- and 2-year local failure free survival (LFF) was observed in CT-BT group (1-year: 90.3% vs. 78.8%, P =0.017; 2-year: 87.1% vs. 72.7%, P =0.038). Moreover, significant lower incidence of acute and chronic toxicities was observed in CT-BT group (P<0.05).

Conclusions
CT-guided brachytherapy can be performed safely and accurately in the treatment of cervical cancer. This approach makes excellent dose distribution and lower toxicities.
THE EFFECT OF DELIVERY ON REGRESSION DEGREE OF ANTEPARTAL CERVICAL INTRAEPITHELIAL NEOPLASIA II AND III LESIONS

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Objectives
To evaluate the development of cervical intraepithelial neoplasia (CIN) II and III after delivery and the correlation among the regression or progression degree of CIN and the course of delivery.

Methods
The examination was conducted at the University Gynecology and Obstetrics Clinic in Skopje on 70 pregnant patients with satisfactory colposcopic examinations and biopsy-proven CIN II and III. We received the information for the course of delivery and following postpartum biopsy results by chart review.

Results
From the 70 patients who had satisfactory colposcopic examinations and biopsy-proven CIN II and III during pregnancy, 32 were excluded from the study (19 lost to follow-up and 13 with inadequate postpartum follow-up). The rest 38 patients that were included were divided into two groups: 21 with CIN II and 17 with CIN III. The regression degrees among these patients were 68% and 70%, respectively (P = 0.78). Progression degree from CINII to CIN III after delivery was 7%. 25%/30% from CINII/CINIII patients remained the same after delivery. There was no progression to invasive carcinoma, and no correlation between the regression or progression degree of CIN and the course of delivery, which was the following: 32 vaginal deliveries, 4 patients with labours and afterwards cesarean section, 2 with caesarean section without labouring.

Conclusions
The study demonstrated that the regression degree was high but there was no correlation to the course of delivery. The recommendation is conservative management during pregnancy with adequate postpartum follow-up apart from the course of delivery.
MOLECULAR DETECTION AND TYPING OF HUMAN PAPILLOMA VIRUS IN CERVICAL SPECIMENS AMONG EGYPTIAN FEMALES IN ALEXANDRIA AREA

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Background
Cervical cancer is ranked as the second among cancers affecting women. Most of cervical cancer cases are caused by infection with certain subtypes of human papilloma virus. Development of vaccines against HPV has major implications for both primary and secondary prevention of cervical cancer. The aim of this study: was to establish the prevalence of HPV among patients with cervical intraepithelial neoplasia, invasive cervical cancer. A control group with normal cervical appearance was included.

Methods
The study was performed on 85 patients with CIN II and III, 50 patients with invasive cervical cancer and 50 females as a control group. Cervical brush was performed to all groups for histopathological studies and molecular typing. Typing was performed using commercial kit for HPV molecular typing.

Results
Among CIN II and III, HPV DNA was detected in 61.1% (52/85). The subtypes were as follows: HPV16 46.1% (24/52), HPV33 19.2% (10/52), HPV18 17.3% (9/52), HPV33 9.6% (5/52) and HPV31 7.8% (4/52).

Among Invasive cervical cancer, HPV DNA was detected in 79% (35/50). The subtypes were as follows: HPV16 57.1% (20/35), HPV18 20% (7/35), HPV33 17.1% (6/35), HPV31 2.9% (1/35) and HPV45 2.9% (1/35).

In controls, HPV DNA was detected in 8% (4/50) HPV16 75% (3/4) and HPV 18 25% (1/4).

Conclusion
HPV infection was common with CIN II & III and invasive carcinomas in. It also has an important implication for the use of the vaccines as a tool to prevent cervical cancers.
VAGINAL-ASSISTED LAPAROSCOPIC RADICAL HYSTERECTOMY (VALRH): INITIAL EXPERIENCE OF A GYNECOLOGICAL CANCER CENTER IN BRAZIL.

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Objectives
Cervical cancer is one of the leading types of malignancies worldwide with 500,000 new cases annually. Particularly in Brazil, it is the second most diagnosed invasive neoplasm among women. In the last decade, several studies have demonstrated advantages of endoscopic approach in face of traditional surgery. The objective of the study was to evaluate operative and oncologic outcomes of a series of patients submitted to VALRH at instituto do Cancer do Estado de São Paulo.

Methods
We retrospectively analyzed data of 41 patients with histologically confirmed cervical cancer FIGO stages Ia2 to Ib2 who underwent to VALRH and laparoscopic lymphadenectomy between April 2011 and April 2013.

Results
The mean patient age was 50 (27 – 69) years. Histology revealed squamous-cell carcinoma in 65% of the cases, while 35% had adenocarcinomas. Mean operative time was 225 (180 – 315) minutes, and mean number of retrieved nodes 23 (10 – 38). All patients had free margins. Conversion to laparotomy occurred in one case (2.5%) due to technical difficulties. Median hospital stay was 2.5 days (1-5 days). One patient (2.5%) had excessive intraoperative bleeding and another woman developed a pelvic abscess (2.5%). No genitourinary fistula or symptomatic lymphocele were observed. After mean follow-up of 16 (2 – 24) months, disease-free survival and overall survival was 92.5% and 100%, respectively.

Conclusions
VALRH is a feasible alternative to abdominal radical hysterectomy in patients with early-stage cervical cancer. Potential advantages of the technique include the possibility to tailor vaginal cuff according to tumor size and to avoid tumor spread. Further studies are needed to attest oncological safety.
CERVICAL NECROSIS AFTER CHEMORADIATION FOR CERVICAL CANCER: CASE SERIES AND LITERATURE REVIEW

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Objectives
The aim of this study was to assess the management of cervical necrosis (CN) following radiotherapy (RT) and the impact of smoking status. This rare complication mimics a neoplastic recurrence, and causes concern among attending physicians.

Methods
Between July 2008 and March 2013, 5 women on 285 with localized cervical cancer had a CN following RT. Patients were treated with concomitant chemoradiation. The medical records were reviewed to abstract demographic and clinical information.

Results
1.75% (95% confidence interval: 0.23 to 3.28%) developed CN. All patients were smokers with a mean of 19.5 pack-years. All patients were treated with weekly Cisplatin chemotherapy and external beam radiation to the pelvis, 45 Gy in 25 fractions. Four patients received an extra boost with a median dose of 7.2 Gy. All patients had intracavitary brachytherapy. Clinical presentation was similar for all the cases: vaginal discharge associated with pain. Mean time for time post-radiation therapy to necrosis was 9.3 months (range: 2.2-20.5 months). Standard workup was done to exclude cancer recurrence: biopsies and radiologic imaging. Conservative treatment was performed with excellent results. Resolution of the necrosis was complete after a few months (range: 1 to 4 months). Median follow-up until March 2013 was 19 months. All the patients were alive with no clinical evidence of disease.

Conclusions
This study, the largest to date, shows that conservative management of CN after RT is effective, and should be attempted. This complication is more common in smokers, and counseling intervention should result in fewer complications of CN.
CONTINENT CUTANEOUS ILEOCECAL RESERVOIR USING THE SUBMUCOSALLY EMBEDDED APPENDIX AFTER ANTERIOR EXENTERATION FOR GYNAECOLOGICAL MALIGNANCIES: TECHNIQUE AND COMPLICATIONS

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Objectives
Patients with advanced gynecological malignancies or recurrences of gynecological malignancies (vaginal carcinoma, endometrial carcinoma and cervical carcinoma), who had to be treated by anterior exenteration and did not have an appendectomy, were reconstructed by continent cutaneous ileocecal reservoir using the submucosally embedded appendix. Data of 11 patients from the years 2008 and 2012 were analysed for intraoperative and early postoperative complication rate.

Methods
The appendix-pouch technique starts with the transsection of the terminal ileum about 12 cm away from the ileocecal valve and of the colon ascendens about 15 cm away from the hepatic flexure. In order to reduce the tension of the wall of the pouch a teniamyotomy of the colon is performed. The efferent segment of the pouch is built by the appendix and is passed out at the umbilicus.

Results
The mean operation time for the complete anterior exenteration was 280 (range 230 – 320) minutes, for the reconstruction by the appendix pouch 75 (range 60 – 90) minutes. The main complications were: problems with wound healing and retention of secretion in the small pelvis. Insufficiencies of the sutures were not observed.

Conclusions
Our experience shows, that the appendix-pouch-technique is a good alternative for continent reconstruction of the bladder after anterior exenteration. This technique is combined with a quite low complication rate.
AORTIC LYMPH NODE RECURRENCE AFTER NEGATIVE PRETHERAPEUTIC EXTRAPERITONEAL STAGING FOR LOCALLY ADVANCED CERVICAL CANCER: CASE REPORT

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Objectives
The value of pretherapeutic extraperitoneal laparoscopic staging of locally advanced cervical cancer has become recently accepted. Lymph node metastasis, particularly para-aortic lymph node involvement together with tumor stage, is the most important prognostic factor in cervical cancer. Surgical staging for the assessment of paraaortic involvement allows an adequate histological evaluation of retrieved lymph nodes, and additionally the resection of enlarged positive nodes provides therapeutic benefit.

Methods
A 29-years-old women with FIGO stage IB2 cervix adenocarcinoma underwent pretherapeutic robot-assisted laparoscopic extraperitoneal para-aortic lymphadenectomy. Pretherapeutic image staging with PET-Scan was also performed without any suspected nodes founded. No aortic lymph node involvement (0/18) was observed in the histological evaluation.

Results
The patient received chemoradiation and adjuvant brachytherapy.

Before brachytherapy and because of partial response after chemoradiation, adjuvant surgery (robot-assisted laparoscopic hysterectomy and anexectomy) was performed with no tumor residual found.

The patient was in complete remission with normal physical and image examinations.

Nine months after the surgical staging, in a control PET-Scan, hipermetabolic activity in interaortocaval region was seen and node recurrence was suspected. The patient underwent new robot-assisted transperitoneal node debulking with 12 nodes removed, 5 of them positive.

Conclusions
She is currently receiving extended chemoradiation and up to now, there is no evidence of tumor recurrence.
IS ROBOT-ASSISTED LAPAROSCOPY NEEDED IN PRETHERAPEUTIC EXTRAPERITONEAL STAGING FOR LOCALLY ADVANCED CERVICAL CANCER??

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Objectives
To compare the role of robot-assisted laparoscopy with conventional laparoscopy in pretherapeutic extraperitoneal paraaortic lymphadenectomy in locally advanced cervical cancer patients.

Methods
17 non-consecutive patients with locally advanced cervical cancer (FIGO stages IB2, IIA2 and IIB-IVA) who underwent robot-assisted laparoscopy with the Da Vinci S surgical system were compared with 83 patients who underwent conventional laparoscopy at the Unit of Gynecologic Oncology of Hospital Vall d’Hebron in Barcelona, Spain. The cephalic boundary of the aortic lymphadenectomy was the left renal vein and the caudal margin was the bifurcation of the common iliac artery bilaterally.

Results
No differences between robot-assisted laparoscopy and conventional laparoscopy were seen in terms of operation time, hospital stay, intra and post-operative complications and lymph nodes removed (however, it was significant when comparison of median, p<0.05). On the other hand, a significant difference was observed in intra-operative blood loss between robot-assisted laparoscopy and conventional laparoscopy (p<0.05).

Table 1. Comparison between conventional and robot-assisted laparoscopy.

<table>
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<tr>
<th></th>
<th>Conventional laparoscopy (n=83)</th>
<th>Robot-assisted laparoscopy (n=17)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Median operation time</td>
<td>150 (80-255)</td>
<td>150 (85-270)</td>
<td>0.59</td>
</tr>
<tr>
<td>(min)(range)</td>
<td></td>
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<tr>
<td>Intraoperative blood</td>
<td>90 (10-260)</td>
<td>20 (5-350)</td>
<td>&lt;0.05</td>
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<tr>
<td>loss (ml)(range)</td>
<td></td>
<td></td>
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<tr>
<td>Median hospital stay</td>
<td>2 (1-4)</td>
<td>2 (1-5)</td>
<td>0.22</td>
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<tr>
<td>(days)(range)</td>
<td></td>
<td></td>
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<tr>
<td>Median lymph node</td>
<td>14 (11-18)</td>
<td>17 (15.5-23)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>removed (interquatile</td>
<td></td>
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<td>range)</td>
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<tr>
<td>Mean lymph node removed</td>
<td>15.5 (8.2)</td>
<td>18.6 (5.5)</td>
<td>0.14</td>
</tr>
<tr>
<td>(SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-operative</td>
<td>7 (8.4%)</td>
<td>3 (17.6%)</td>
<td>0.23</td>
</tr>
<tr>
<td>complication rate (%)</td>
<td></td>
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Conclusions
Robot-assisted laparoscopy is a feasible approach for the pretherapeutic staging method in locally advanced cervical cancer which does not seem to improve conventional laparoscopic surgical outcomes.
MIR-99A INHIBITS THE PROLIFERATION OF CERVICAL CELLS BY THE NOVEL TARGET mTOR

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Objectives
microRNAs (miRNAs) are small noncoding RNAs that play a significant role in cancer development and progression by regulating the expression of proto-oncogenes or tumor suppressor genes. Previous studies revealed that mTOR is activated and contributes to survival of cervical cancer cells, and it is a predicted target of miR-99a in three algorithms Pictar, TargetScan and miranda. However, the role of miR-99a in human cervical cancer is still unclear.

Methods
The expression of miR-99a in cervical cancer was examined by quantitative RT-PCR. The effects of miR-99a overexpression and silencing on the cell proliferation, cell viability, cell cycle and tumor formation of cervical cancer cells were investigated. Dual luciferase assay was conducted to explore whether mTOR was a direct target of miR-99a in cervical carcinoma.

Results
miR-99a was down-regulated in cervical cancer tissues and cell lines. The ectopic expression of miR-99a suppressed the cell growth and significantly attenuated tumor formation. Consistently, miR-99a silencing promoted cell growth and tumor formation. Furthermore, miR-99a overexpression caused cell cycle arrest, along with the down-regulation of mTOR protein. Dual luciferase assay revealed that miR-99a inhibited the expression of mTOR through direct binding to the specific core sequences. Moreover, activation of mTOR signaling pathway by overexpression of AKT rescued the miR-99a-induced inhibition of cell proliferation.

Conclusions
Our findings suggest that miR-99a may serve as a therapeutic reagent for the treatment of cervical cancer.
ADENOMA MALIGNUM WITH OVARIAN MUCINOUS ADENOCARCINOMA
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Objectives
The term minimal deviation carcinoma (adenoma malignum) has been used to describe an extremely well-differentiated adenocarcinoma which is often misdiagnosed because of its benign looking histological features. These tumors are clinically highly malignant and sometimes associated with mucinous tumor of ovaries, also minority of the cases are component of Peutz-Jeghers syndrome.

Methods
A 43 year old patient with bloody vaginal discharge since last 4 months referred to hospital. She had an cervical mass and left ovarian cyst of 4cm. Cervical biopsy reported as malignant epithelial tumor with endocervical glandular atypia. She was regarded as clinically stage 2B cervical carcinoma and treated with primary concomittand radiochemotherapy. On her 4th year follow-up, ultrasonography revealed 9cm left ovarian cyst with suspicious cytology and cervical biopsy showed atypical squamous cells. Frozen section of left ovary was malignant, and she underwent hysterectomy, bilateral salphingoopherectomy and pelvic-paraaortic lymphadenectomy. Paraffin results reported cervical adenoma malignum (with endometrial stromal invasion), ovarian mucinous cystadenocarcinoma (without capsule invasion), reactive lymph nodes. Patient was examined for cafe-au-lait; and gastroscopy and colonoscopy performed for the suspicion of Peutz-Jeghers Syndrome was normal. As we consulted the first cervical biopsy specimen with pathologists, it was understood that the first diagnosis was adenoma malignum.

Results
There are difficulties in histological differentiation with adenoma malignum from common cervical adenocarcinomas.

Conclusions
In women with coexistence of ovarian cysts and cervical adenocarcinomas possibility of adenoma malignum should be considered because of the differences in treatment and prognosis from other cervical carcinomas.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

**e-Posters: Cervical Cancer**

**CASE REPORT : ADENOID BASAL CARCINOMA OF THE CERVIX**

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²gynecologic oncology, tepecik research & training hospital, Izmir, Turkey

**Objectives**

Adenoid basal carcinoma (ABC) of the cervix is a rare tumor which is often seen in postmenopausal women. ABC constitutes less than 1% of cervical adenocarcinomas. ABC is often detected with other cervical tumors. Pure forms of ABC are rare. In this report, we present a case of pure ABC which is quite rare.

**Methods**

69 year-old postmenopausal woman with vaginal bleeding and pelvic pain symptoms was admitted to gynecology clinic. In gynecological examination the size of uterus was similar to twelve weeks pregnant uterus and polypoid mass was seen in the cervix. TAH+BSO was performed and materials were evaluated in the pathology unit.

**Results**

At macroscopic observation, 1.5x1x0.5 cm polypoid lesion was seen in cervix. Histological examination shown, islands and cords formed by small, narrow cytoplasmic cells in the cervical stroma. Nuclei of the cells that are surrounding cystic spaces around the necrotic debris shown peripheric palisading. The maximum sizes of the basal carcinoma areas was 0.4 cm and vertical depth of invasion was 0.4 cm. Lymphovascular invasion areas was positive. Tumor cells immunohistochemical staining features, were positive for CEA, CK7 and negative for HMWCK, vimentine and CD34.

**Conclusions**

ABC and adenoid cystic carcinoma have similar histological features and these two entities are often mixed with each other. ABC was described firstly in 1966. Absence of hyaline material in the cystic spaces, less pleomorphism and mitosis are important features in distinction of these entities. It is important to keep in mind this rare entity because of its prognosis and different treatment options.
HYDRONEPHROSIS AS A PROGNOSTIC FACTOR IN ADVANCED SERVIS CANCER
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Objectives
To determine if hydronephrosis is an independent prognostic factor of survival among patient with advanced cervical carcinoma.

Methods
Retrospective analysis of patient with FIGO stage IIIB or higher cervical carcinoma between 1990 and 2011 at our departman. Inclusion criteria were clinical staging according to FIGO criteria, standardized radiation treatment and cisplatin-based chemsensitization regimens. Associations between hydronephrosis and covariates-age, histopathology, pelvic sideinvolvement, stage.

Results
Of 165 included patient, 91 patients had no hydronephrosis, 41 had unilateral and 33 had bilateral. Median time to death was significantly shorter for patient with unilateral hydronephrosis (42 months) and bilateral hydronephrosis (30 months) versus patients without hydronephrosis (71 months).

Conclusions
Hydronephrosisis an independent poor prognostic indicator of survival in patient with advanced cervical cancer.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

**e-Posters: Cervical Cancer**

**LAPAROSCOPIC PELVIC EXENTERATION FOR CERVICAL CANCER: INITIAL EXPERIENCE OF 3 CASES.**

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**Objectives**

Pelvic exenteration has both palliative and curative role in the management of cervical cancer. This procedure remains one of the most difficult with high postoperative morbidity. Laparoscopic approach has been proposed in an attempt to reduce postoperative complications. We want to represent our experience in performing laparoscopic pelvic exenteration (LPE).

**Methods**

From July 2012 to April 2013 three patients with advanced cervical cancer underwent LPE in our clinic. In two cases – total LPE, in one – anterior LPE. Five ports technique was used. Pelvic organs were resected en-bloc and extracted through vagina. In case of total LPE the terminal colostoma was done. For urinary diversion an ileal-loop conduit (the Bricker technique) was used in all patients. Uretero-ileostomy and stenting were performed intracorporally in one case and extracorporally in two.

**Results**

All three patients had centro-pelvic recurrence of cervical cancer within 8-13 months after combined chemo-radiotherapy (associated with surgery in two cases), complicated with different fistulas in pelvis. The mean age was 43.7 (38-52) years. The average operative time was 410 (350-520) minutes. Median blood loss was 400 ml (350-500). All patients tolerated the procedure well. Mean length of hospital stay was 9 days (6-14). In all cases R0 margins were obtained. Postoperative complications were: paresis of the intestine (1) and positional fibular neuritis (1) with conservative treatment.

**Conclusions**

LPE is technically feasible and can be offered to carefully selected patients with advanced carcinoma of cervix. Potential postoperative advantages of laparoscopic approach are faster recovery, low morbidity and better cosmetic results.
RADICAL HYSTERECTOMY WITH PRESERVATION OF PELVIC PLEXUS NERVE IN PATIENTS WITH INFILTRATIVE CERVICAL CARCINOMA
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²oncurology, National Cancer Institution, Kyiv, Ukraine

Objectives
To estimate the contractile function of urinary bladder in patients with infiltrative cervical carcinoma (CC) after radical hysterectomy (RH) with preservation of pelvic plexus nerve.

Methods
To study the effect on the contractile function of the urinary bladder (UB) preservation of the pelvic plexus in the performance of the RH in 2012 year in Department oncogynecology National Cancer Institute conducted study in which 30 patients with infiltrative cervical cancer (mean age patients 32.7 ± 4.9 years) completed the RH: of these 15 patients (I group) RH performed with preservation of the pelvic plexus and 15 patients RH performed by standard methods, without saving the pelvic nerve plexus (II group control). Predictors were identical to the research groups. Method of cystometry: Cystometry was carried out on urodynamic rack URO-missile according to standard technique.

Results
According to cytomanometric of patients in group I contractile UB function was restored in full at 2-3 days after surgery in 80% of the control group only 20% of cases. The patients in group II function of the lower urinary tract restored within 7 days after the RH, 20% of patients in this group long lasting paresis detrusor UB, who partially restored after 7 days and 21 days, indicating that the deep neurological violations contractility UB in the surgical trauma pelvic plexus part of the standard RH II patients group.

Conclusions
THE ROLE OF HPV TEST IN THE FOLLOW-UP OF HIGH-GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA TREATED WITH EXCISIONAL PROCEDURES
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2Pathology, IRO Iasi, Iasi, Romania
3Imunology, UMF “Gr.T.Popa” Iasi, Iasi, Romania
4Pathology, UMF “Gr.T.Popa” Iasi, Iasi, Romania

Objectives
To evaluate the frequency of HPV infection in patients during the follow-up period, after treatment for cervical intraepithelial neoplasia and to examine the role of high-risk HPV as prediction of recurrent or residual CIN.

Methods
We analyzed 34 women treated with conization or LLETZ (large loop excision of the transformation zone) for high-grade intraepithelial lesion. The cases were followed-up by HR-HPV DNA test 4 months after the excision procedure and further followed by colposcopy and cytology every 6-month intervals for 24 months.

Results
During the follow-up period we had 3 cases (8.8%) with residual or recurrent CIN. All three had HR-HPV test positive, two had a positive follow-up smear and one had positive margins at excision. From 34 treated women, 7 were HR-HPV positive, 3 had an abnormal smear and 6 had positive section margins. Women with HR-HPV DNA at 4 months showed recurrent or residual CIN in 14% (1/7) if they had normal follow-up Pap smears and in 50% (2/4) if they had abnormal Pap smears. Margin status was not statistically significant associated with Human Papillomavirus status. The absence of HR-HPV DNA has a 100% negative predictive value.

Conclusions
On the basis of the study results it seems recommendable that the HPV test should be used as a method of detection of residual HPV infection after conization. Data suggest that HPV testing should be integrated in a follow-up algorithm after conization for CIN.
ENDOCRINAL GLANDULAR INVOLVEMENT, MULTICENTRICITY AND EXTENT OF THE DISEASE ARE FEATURES OF HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

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²Pathology, Istanbul Bilim University, Istanbul, Turkey

Objectives
To evaluate the rate of endocervical glandular involvement, positive surgical margins, multicentricity and disease extent between low-grade and high-grade cervical intraepithelial lesions after loop electrosurgical excision procedure (LEEP)

Methods
Pathology charts of patients that underwent LEEP were reviewed retrospectively. Patients with negative LEEP results were excluded. LEEP reports of patients with CIN 1, 2 and 3 were compared.

Results
There was no statistically significant difference between patients with CIN 1 (n=24), CIN 2 (n=27) and CIN 3 (n=64) when age and surgical margin positivity were considered. Endocervical glandular involvement, multicentricity and disease extent were higher in patients with CIN 3 (p=0.001, p=0.002, p=0.001 respectively).

Conclusions
In conclusion we recommend patients with endocervical glandular involvement, lesions involving more than 2/3 of the LEEP specimen and multicentricity to be followed up more closely.
DETECTION OF HPV E6/E7 MRNA USING NUCLISENS EASYQ HPV™ IN ABNORMAL CYTOLOGY SPECIMENS

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²Microbiology, Celal Bayar University, Manisa, Turkey
³Pathology, Celal Bayar University, Manisa, Turkey

Objectives
To analyze HPV E6/E7 mRNA (16, 18, 31, 33, 45) ratios in patients with abnormal smear cytology and to evaluate its efficiency in detecting CIN lesions.

Methods
Nuclisens EasyQ HPV E6/E7 mRNA (16, 18, 31, 33, 45) test is applied in all patients with abnormal cytologies. The demographic and clinical features of the cases with HPV E6/E7 mRNA positivity and negativity are recorded. The sensitivity, specificity, positive and negative predictive values of HPV E6/E7 mRNA test are calculated after the diagnosis of CIN.

Results
HPV E6/E7 mRNA was positive in 55.3% of the abnormal cytologies. Furthermore, it was positive in 92.8% of HGSIL, 100% of ASC-H, 100% of AGC-NOS and 27.6% of ASC-US cases. In cases with abnormal cytology, HPV type 16 (%38.6) is isolated most commonly, HPV type 18 being the second (%24.6). Age, parity, number of sexual partners and contraceptive methods, there was no significant difference between HPV E6/E7 mRNA positive and negative cases, whereas positive HPV E6/E7 mRNA was significantly higher in smokers. Sensitivity was found to be 100%, specificity 27%, positive predictive value 27% and negative predictive value 100%. Any case with CIN was established if there was negative result of HPV type E6/E7 mRNA test with abnormal smear cytology.

Conclusions
Approximately in half of cases with abnormal cytology, HPV E6/E7 mRNA was positive. Furthermore, it was more prominent with cases except ASC-US. The high sensitivity and low false negative ratios make the HPV E6/E7 mRNA test to become efficient in clinical use.
e-Posters: Cervical Cancer

THE EPIDEMIOLOGY OF CERVICAL CANCER IN MOROCCO
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2, Al Azhar Oncology Center, Rabat, Morocco

Objectives
Cervical cancer is one of the most common neoplastic diseases in women. It is the second most common cancer, after breast cancer and the fourth leading cause of cancer death among women in Northern Africa, with an estimated 5278 new cancer cases and 3101 deaths from cancer in 2008, the most recent year for which international estimates are available (GLOBOCAN 2008). The aim of this study is to determine the frequency and the epidemiological characteristics of cervical cancer in Morocco.

Methods
This is a retrospective study of cervical cancer cases, diagnosed and treated at Al Azhar Oncology Center in Rabat between 1994 and 2004.

Results
There were 710 new cases of cervical cancer diagnosed at Al Azhar Oncology Center, accounting for 17.7% of all new cases of cancer in women reported during the study period. The average age at diagnosis was 51.8±11.2 years. The risk of developing cervical cancer is associated with age, 86.8% of cases were diagnosed in women aged 40 years and older, with 80% of new cancer cases occurring among those aged 40-69 years. Among all detected cases, 2.1% were diagnosed with metastatic disease and 8.2% died during the study period.

Conclusions
Cervical cancer is a preventable disease, and a significant decrease in incidence and mortality can be expected as a result of population-based screening programs, which rely on regular preventive examinations to search for precancerous changes and to prevent the development of malignant tumors.
e-Posters: Cervical Cancer

ACUTE UTERO-CERVICAL ANGLE: A CHALLENGE IN HIGH DOSE RATE (HDR) BRACHYTHERAPY FOR CERVICAL CANCER PATIENTS

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Background

Cervical cancer patients with a uterus having acute utero-cervical angle is a challenge in HDR brachytherapy. The hard uterine tandem cannot be introduced through this acute angle into the uterine canal to reach the fundus. Incidence of uterine perforation or suboptimal application is high in this situation.

Aim

To describe a new technique facilitating insertion of uterine tandem through acute utero-cervical angle.

Patients and Methods

MRI pelvis was done to evaluate the patient before brachytherapy. The uterine length was measured from MRI sagittal image. Under general anesthesia, the cervix was dilated without introducing the sound or dilators into the uterine cavity to prevent uterine perforation. The distal part of a large size Foley catheter was cut (length equal to the distal thinner part of the uterine tandem) and a marker (one silk suture) was put on it denoting uterine length. The Foley-catheter-cut was introduced through the dilated cervical canal and it can pass the acute utero-cervical angle smoothly into the uterine cavity to reach the fundus (the silk suture marker touch the cervix). The uterine tandem was introduced to the uterus through the Foley-catheter-cut without risk of uterine perforation. Two ovoids were inserted and the whole system was fixed as usual. CT-scan pelvis was done to evaluate the application.

Results and Conclusion

We introduced a new simple method facilitating uterine tandem insertion in a uterus with acute utero-cervical angle decreasing the risk of uterine perforation and suboptimal application.
e-Posters: Cervical Cancer

SOCIOECONOMIC CHARACTERISTICS, HOUSING CONDITIONS AND CRIMINAL BEHAVIOR IN WOMEN WITH CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) BETWEEN 1960 AND 2006.

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3Pathology, Uppsala University, Uppsala, Sweden

Objectives
Cervical neoplasia has historically been associated with social disadvantages. It is unclear if the sexual revolution and the introduction of modern contraceptives have equalized these differences. This study includes a number of socioeconomic variables. For the first time criminal behavior is also studied.

Methods
1331 women with cervical biopsies showing cervical intraepithelial neoplasia (CIN) or cancer were compared with age- and geographically matched controls. Registers used were the Population and Housing Censuses (PHC) in 1970, 1980 and 1990, including questions about civil status, education, housing conditions, housing equipment, employment, socioeconomic status (SES), occupation, income etc. The National Register of Conviction Decisions was used to withheld information on criminal offences.

Results
Women with a diagnosis of cervical neoplasia were more likely to be divorced, less likely to have a university education, and high SES, and less likely to own their own house or apartment than their age-matched controls. Severe criminal activity was increased in the study group compared to the control group. When two generations of women were studied separately, we saw more marked differences compared with controls in the younger women compared to the older regarding university education, owning one’s residence, and size of living area.

Conclusions
The results of this study indicate that women with cervical dysplasia is a socioeconomically more disadvantaged group and an increase of criminal offences persists after adjusting for socioeconomic status. Surprisingly, these differences had not equalized in the younger, compared to older age groups.
DIRECT COMPARISON ON DIAGNOSTIC ACCURACY OF 9 FREQUENTLY INVESTIGATED SERUM BIOMARKERS IN CERVICAL CANCER

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Objectives
To assess the diagnostic accuracy and model the optimal combination of a literature derived set of commonly studied serum biomarkers aimed at identifying recurrence in cervical cancer patients.

Methods
From a systematic literature search, 9 biomarkers (CEA, VEGF, TNF-α, CYFRA 21-1, IL-6, CA-125, CA-15.3, hsCRP and SCC-Ag) were selected for our prospective serum analysis. Samples were derived from a biobanked historical cervical cancer cohort. Subjects were included when sample quality criteria were met and when one preceding and minimally one sample following primary treatment was available. In case of recurrence, two additional post-recurrence samples were analyzed. Biomarker serum levels were quantified by enzyme linked or chemiluminescence microparticle immunoassays. Logistic regression and receiver operating curve analysis were employed for selection, modeling and comparison on the diagnostic accuracy of the tested biomarkers.

Results
205 samples were analyzed from 75 subjects, of whom 19 (25.3%) had a recurrence. The area under the curve (AUC) of CEA, VEGF, TNF-α, CYFRA 21-1, IL-6, CA-125 and CA-15.3 were all <0.750. Only SCC-Ag and hsCRP were included in the final model with an AUC of 0.822 (95%CI: 0.744-0.900) and 0.831 (95%CI: 0.758-0.905) respectively. Combined AUC was 0.870 (95%CI: 0.805-0.935). Rises in SCC-Ag and hsCRP significantly increased the odds for recurrence. Each µg/l of SCC-Ag increase, related to an odds ratio (OR) of 1.117 (95%CI: 1.039-1.200). Comparably, the OR for hsCRP (in mg/ml) was 1.025 (95%CI: 1.012-1.038).

Conclusions
Combined testing of SCC-Ag and hsCRP yields the highest detection rate of disease recurrence during cervical cancer follow up.
METHYLATION OF LIQUID BASED CERVICAL CYTOLOGY INFECTED WITH HUMAN PAPILLOMAVIRUS TYPE 16 DNA ACCORDING TO THE DEGREE OF CERVICAL PATHOLOGY.

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Objectives
Detection of hypermethylated genes in cervical scrapings has been suggested as a promising tool for identification of cervical intraepithelial neoplasia and cancer. The aim of this study was to evaluate the presence of hypermethylated genes according to the degree of cervical disease.

Methods
Study subjects with HPV 16 DNA positive were 122 women attending Seoul St. Mary’s Hospital from January 2009 to July 2011. Cervical cytology positive for HPV 16 were normal, CIN1, CIN2, CIN3, and cancer. Using quantitative bisulfite-pyrosequencing, we measured the methylation of PAX1, CADM1, ADCYAP1 and MAL genes of cervical scrapings.

Results
Cervical scrapings were used for detection of the methylation in normal (n=29), CIN 1 (n=29), CIN2 (n=4), CIN3 (n=42), and cervical cancer (n=18). We observed that 4 genes (PAX1, CADM1, ADCYAP1, MAL) were more frequently methylated in cervical cancer (83.3, 77.8, 88.9 and 72.2 %) than in normal cytology (0, 3.4, 3.4 and 6.9%). ROC curve demonstrated that methylation of the 4 genes discriminated between ≥ CIN3 and <CIN3. The estimated specificities of these 4 genes for detecting high grade lesion were 100, 96.6, 96.6 and 93.1% (p=0.0001). And the estimated sensitivities of that were 83.3, 77.8, 88.9 and 93.1% (p=0.0001). Additional ADCYAP1/PAX1 methylation analysis on the HPV16-positive women increased the sensitivity to 88% with a specificity to 96.7%( P<0.001).

Conclusions
Methylation of the PAX1, CADM1, ADCYAP1 and MAL is significantly associated with the development of ≥ CIN3. Hence, testing for methylation may provide a diagnostic marker for the triage of high risk HPV-positive women at risk of ≥ CIN3.
e-Posters: Cervical Cancer

CLINICAL AND MORPHOLOGICAL EFFECTIVENESS EVALUATION OF PREOPERATIVE CHEMORADIOThERAPY FOR CERVICAL CARCINOMA WITH THE INCLUSION OF TEGAFUR

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Objectives
The aims and objectives of the work should provide clinical and morphological study of squamous cell cervical carcinoma of Ib2-III clinical stages using this preoperative chemoradiotherapy for evaluation of the immediate effect of therapy.

Methods
41 patients with cell cervical carcinoma of T₁b₂-T₃N₀-₁M₀ (Ib2-III stages) have been included in a pilot study. Scheme of the treatment was falling: weekly administration of Cisplatin (30mg/m²), 3; a daily taking of Tegafur 1200 mg/day from 1-st to 21-st day, distant gamma therapy with SFD 2 Gray and TFD 30 Gray 5 times a week from 1-st day of the treatment.

Results
In 9 patients (22%) a complete clinical response was marked, in 28 cases (68%) – partial and in 4 cases (10%) – stabilization. At the end of the chemoradiation phase 37 patients were operated on - radical hysterectomy with bilateral iliac lymphadenectomy (Wertheim-Meigs method). Operating material was subjected to histological and morphometric study to determine the next treatment outcome and the grade of mass damage. The advantages of the method: presence of large areas of necrosis, a larger number of necrotized cells and elements with irreversible forms of dystrophy, more severe inhibition of mitotic activity in this group of carcinomas compared with tumours which had undergone radiation.

Conclusions
The use of chemoradiation with Tegafur method contributes to development of damage in squamous cell cervical carcinoma of any histological structure. It did not affect patients’ life quality, has good tolerability and proved to have high curative effect.
ADVANCED CERVIX CANCER IN PREGNANCY


**Ginecology, Hospital Universitario de Torrejón, Madrid, Spain**

**Objectives**
Management of cervix cancer stage T2b (TNM) or IIB (FIGO) in 14 weeks pregnant with heavy bleeding which required tamponade and transfusion.

**Methods**
43 year old woman 14 weeks pregnant who presented with severe vaginal bleeding. Five previous normal deliveries

Exploration: Cervix necrotic more than 4 cm. Heavy bleeding. Free Vagina. Digital rectal examination left parametrial involvement

Fetal Ultrasound: 14 weeks. Heartbeat present.


MRI PELVIS: Heterogeneous mass cervix 5.5 x 6 cm caudally and extending towards the left anterior portion of the vagina without clear infiltration of its wall. The mass appears to extend affecting left parametrial fat.

Toracoabdominopelvic CT: Focal liver lesions compatible with cysts. Probably nonspecific millimetric liver nodule in segment VII solid.

During hospitalization needed taponade in two occasions with hemostatic agents. Two red cell concentrates were transfused and four doses of intravenous iron administrated.

**Results**
The clinical situation was discussed with the family and the management agreed in multidisciplinary session. The patient informed consent gave accept all diagnostic tests knowing abortion that would occur as a result of treatment with radiotherapy and chemotherapy.

**Conclusions**
The treatment of locally advanced disease is radiotherapy and concomitant chemotherapy. Treatment guidelines for pregnant patient with invasive cervical cancer are the same as for nonpregnant patients. In early pregnancy, external radiation therapy can be started with the fetus in situ. After miscarriage, radiation treatment is completed with intracavitary brachytherapy.
e-Posters: Cervical Cancer

FERTILITY SPARING RADICAL ABDOMINAL TRACHELECTOMY – A CHANCE FOR YOUNG PATIENTS WITH EARLY STAGES CERVICAL CANCER

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Objectives
This study aimed to report on a series of patients with early-stage cervical cancer who underwent abdominal radical trachelectomy to preserve their fertility or menstrual function.

Methods
This is a retrospective study of all patients who underwent radical abdominal trachelectomy in 2 centers of gynecologic oncology in Romania, between 2010-2013. Data collected included age, stage, histologic subtype, tumor grade, tumor size, evidence of lymphovascular space invasion, number of lymph nodes removed, perioperative complications, as well as oncologic and obstetrical outcomes.

Results
Twenty-one patients underwent this procedure. Median age was 31 years. 11 patients had stage IA2, 9 stage IB1 and 1 stage IB2. Median tumor size was 1.8 cm (range = 0.3-4.2 cm). Histologic subtypes were: 12 squamous, 3 adenosquamous, 6 adenocarcinoma. Median number of pelvic lymph nodes removed was 28 (range = 16-60). There were 5 postoperative complications (1 pelviperitonitis, 4 secondary amenorrhoea). No adjuvant therapy was instituted. 3 patients were able to get pregnant spontaneously; 2 spontaneous miscarriages and 1 live birth by cesarean delivery. No recurrences were reported.

Conclusions
Abdominal radical trachelectomy is a feasible procedure and a viable option for women wishing to preserve their fertility or menstrual function.
COMPLICATIONS AFTER COMBINED RADIOSURGICAL TREATMENT OF CERVICAL CANCER

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Objectives
To present the incidence and types of postoperative complications after combined radiosurgical treatment of patients in IB1, IB2, IIB stage of cervical cancer

Methods
Between 11. 2002- 11. 2011, 294 patients (stage IB1-110, IIB-86, IB2-98) with cervical cancer underwent surgery in the Gynaecological clinic of MBAL ‘St. Anna’ – Varna. The patients’ average age was 48 years (ranged from 27 to 84 years). The main surgical intervention was Class III radical hysterectomy with adnexa, including pelvic lymph node dissection. The patients in stages IB2 and IIB are divided into 4 groups:

Group 1 – IB2 stage with primary surgery (n = 83)
Group 2 – IB2 stage with radiotherapy prior to surgery (n = 11)
Group 3 – IIB stage with primary surgery (n = 31)
Group 4 – IIB stage with radiotherapy prior to (n = 50)

Radiotherapy is TGT at a preoperative dose of 30Gy and 52Gy adjuvant or complementary.

Results
Late complications after combined radiosurgical treatment for all operated are 25,5% (75/294): fistula (vesico-ureterovaginal) 3,4% (10/294); urinary incontinence 1.7% (5/294); hydronephrosis II-III degree 9.5% (28/294); ileus 4.4% (13/294); lymphoedema5.4% (16/294); lymphocele1,2% (3/294).

Conclusions
Late postoperative complications occur in ¼ of the patients with cervical cancer, who received combined radiosurgical treatment. The bimodal treatment (surgery and irradiation) potentiate their side effects and lead to increased late morbidity and worsened quality of life.
COMPLICATIONS AFTER SURGICAL TREATMENT OF PATIENTS WITH CERVICAL CANCER

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Objectives
To present the incidence and types of the intraoperative complications, as well as the types of early postoperative complications in the surgical treatment of patients in IB1, IB2, IIB stage of CC, who have undergone primary surgery or radiotherapy prior to surgery.

Methods
Between 2002-2011, 294 patients (stage IB1-110, IIB-86, IB2-98) with CC underwent surgery in the Gynaecological clinic. The patients median age was 48 years (ranged from 27 to 84 years). The main surgical intervention was Class III RH with adnexa, including pelvic LND. The patients in stages IB2 and IIB are divided into 4 groups:

Group 1 – IB2 stage with primary surgery (n = 83)
Group 2 – IB2 stage with radiotherapy prior to surgery (n = 11)
Group 3 – IIB stage with primary surgery (n = 31)
Group 4 – IIB stage with radiotherapy prior to (n = 50)

Radiotherapy at a preoperative 30Gy and 52Gy adjuvant or complementary.

Results
The intraoperative complications are 2.7%: including lesion of ureters, lesion of the bladder, lesion of a large vessel, lesion of n. obturatorius.

Early postoperative complications for all operated are 12.9%: suppurative, thrombophlebitis, hydronephrosis, ileus, urinary infection, atonic bladder, incontinence, lymphocele, fistula. Early postoperative complications in stage IB1 are 10.1%; for the 4 groups in stages IB2-IIB respectively 20.5%, 18.2%, 6.5% and 14%.

Conclusions
Early postoperative complications are more common for LACC (IB2-IIB) compared to early invasive CC (IB1 stage). In stage IB2, preoperative radiotherapy does not increase these complications, while in stage IIB it leads to their significant increase.
AN INVESTIGATION OF VESICAL BRANCHES IN THE VESICOOUTERINE LIGAMENT USING CADavers EMBALMED BY THIEL'S METHOD
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Objectives
Nerve-sparing radical hysterectomy has been included in type C1 of new classification of radical hysterectomy. Although this method was established in 1961, it has still some unclear points, especially as to preservation of vesical branches. Accordingly, the course and distribution of vesical branches was investigated using human cadavers embalmed by Thiel's method.

Methods
Two female cadavers were dissected according to the same procedure as nerve-sparing radical hysterectomy. We separated ureterohypogastric fascia including the ureter and the hypogastric nerves from the peritonuem. After deroofing the ureter tunnel and rolling the ureter laterally, the anterior layer of the vesicouterine ligament was dissected with keeping this fascia. The running and distribution of nerves at the ureterovesical junction was studied.

Results
Some visceral branches are running down along the paracolpium. Then they branch, and run into the two sides of the ureterovesical junction. Lateral fibers run over the ureterohypogastric fascia in a fan shape, and are distributed to the bladder body over the distal most the ureter. Medial fibers run along the outside of the paracolpium and distributed to the the trigone.

Conclusions
These fibers are corresponded to the vesicovaginal ligament. These nerves are prone to injury during the procedure of the radical hysterectomy. Lateral fibers suffer damage when the ureter is rolled laterally, especially close to Waldeyer's fascia. Medial fibers are cut by further separation of the bladder from the vagina wall followed by dividing the paracolpium. This injury may have an association with the urinary incontinence after radical hysterectomy.
e-Posters: Cervical Cancer

Extended Field Concurrent Chemoradiation or Pelvic Field Concurrent Chemoradiation for Radiologic Negative Para-aortic Lymph Nodes Locally Advanced Cervical Cancer

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Purpose

Our aim was to evaluate whether extended field concurrent chemoradiation (EF-CCRT) leads to results better to those obtained by standard whole pelvic (W P-CCRT) in locally advanced cervical cancer with radiologic negative para-aortic lymph nodes (PALN).

Methods and Materials

Patient eligibility included histopathologically proven squamous cell carcinoma, adenocarcinoma or adeno-squamous cell carcinoma; radiologic negative PALN locally advanced cervical cancer stages IIB-IVA with normal hematologic, renal, and liver functions. Between July 2007 and April 2008, 82 were accrued. Patients were randomly assigned to WP-CCRT (40 patients) and EF-CCRT (42 patients) followed by high dose rate brachytherapy. Data regarding the safety profile, response rates and occurrence of local, para-aortic or distant failure were recorded.

Results

With a median follow-up time of 60 months (18-66), overall PALN control rates were 97.1% and 82.4% in EF-CCRT arm (38 patients) and WP-CCRT arm (36 patients) withp value 0.02. Distant metastasis (DM) control rates were better in EF-CCRT than WP-CCRT (86.9% vs. 74.7%, p =0.4). Disease-free survival (DFS) and overall survival (OS) rates were also better in EF-CCRT arm (80.3% and 72.4%) than WP-CCRT arm (69.1% and 60.4%, p = 0.04). Radiologic positive pelvic lymph nodes and FIGO stages were found important prognostic factors for PALN and DM control rates. No difference in acute toxicity profile was seen in both groups and late toxicities were mild and minimal.

Conclusion

Prophylactic EF-CCRT can be considered in patients with locally advanced cervical cancer with radiologic positive pelvic lymphadenopathy, however further multicenter prospective trial is warranted.
RAPIDLY RECURRENT SMALL CELL NEUROENDOCRINE CARCINOMA OF THE UTERINE CERVIX PRESENTING WITH SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION (SIADH)

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Abstract: Small cell carcinoma of the uterine cervix is rare. Generally, 10% of small cell lung cancer have SIADH. A proportion of small cell carcinoma of the uterine cervix exhibit neuroendocrine characteristics by immunohistochemistry. However, case presenting typical symptom due to SIADH are extremely rare. Here, we report a case of ADH producing cervical small cell carcinoma who showed rapidly progression with hyponatremia.

Methods:
A 41-years-old Korean women, para 3, referred bloody discharge. Pre-operative investigation diagnosed a small cell carcinoma over 4Cm in diameter. She had hyponatremia (124mEq/liter), decreased serum osmolality (252mOsm/L) and elevated urine osmolality (384mOsm/L). After operation, i.e. radical hysterectomy with both salpingectomy, pelvic and para-aortic lymphadenectomy, her serum sodium level increased to 135mEq/L.

Results:
The tumor was immunoreactive for neuroendocrine specific enolase as well as for chromogranin A. Final diagnosis was small cell neuroendocrine tumor, FIGO stage Ib2 cervical cancer with lymph node metastasis on both external iliac lymph nodes. Adjuvant chemo-radiotherapy was done. Four month after surgery, she was admitted due to anorexia and fatigue. She also have hyponatremia (133mEq/L) and the recurrence at multiple para-aortic lymph nodes. The patient was treated with combined chemotherapy and surgical resection of enlarged lymph nodes. Three month after second operation, she also showed hyponatremia and recurrence at subclavain lymph node.

Conclusions:
This report of the small cell carcinoma of the uterine cervix with symptomatic SIADH. It is extremely rare case. These rapidly recurrent cervical cancer also showed tumor-associated para-neoplastic syndrome in every recurrence.
THE DIFFERENCE OF MICRONNA EXPRESSION BETWEEN HIGH GRADE CERVICAL NEOPLASIA AND NORMAL UTERINE CERVIX TISSUE

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Objectives
microRNA has been reported to be involved in tumor suppression or progression in some cancers, the association has been reported in some studies in cervical cancer. However, until now of cervical cancer, precancerous lesions, cervical dysplasia, especially in high-grade lesions for microRNA expression patterns in cervical tissue and distinguish in normal uterine cervix is not well known.
In this study, we analysed the comparative patterns of microRNA between high-grade intraepithelial neoplasia and normal uterine cervix to evaluate the difference of two groups.

Methods
microRNA expression was assessed in high-grade cervical dysplasia and normal cervical tissues. mirVana miRNA isolation kit(AMBION) was used for microRNA based on commercial protocol. Western blot, real time PCR were used for the identification and the difference of functional role of the specific microRNA in high-grade cervical dysplasia.

Results
Some up-regulated and down-regulated microRNAs were consistently found in high-grade cervical dysplasia compared with normal cervical epithelium cells including miR-34, 183, 142

Conclusions
Our findings indicate that some microRNAs plays a role in precancerous progression in uterine cervical tissue and its alteration is associated with the possibility of cervical cancer pathogenesis.
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OVEREXPRESSION OF SOCS 1/3 MAY INHIBIT INVASION AND METASTASIS OF CERVICAL CANCER

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Objectives
To investigate whether the overexpression of SOCS-1/3 affects the radiosensitivity and to find the association between the radiosensitivity and COX-2, p21, MMP-2.

Methods
We established stable SOCS-overexpressing HeLa cell line with pLNCX2-mSOCS1-Myc and pLNCX2-mSOCS3-FLAG. Also we established xenograft nude mouse model for tumor growth delay experiment. FACS and immunohistochemistry were employed to elucidate the pattern of expression of COX-2, MMP-2, p21, and tunnel staining for apoptosis evaluation in SOCS-1/3 overexpressing HeLa cells. Migration inhibition assay was performed to find whether SOCS overexpression affected cell migration.

Results
SOCS-1/3 overexpression induced p21 protein and affected cell cycle regulation. We observed SOCS-1/3 overexpression caused G2/M arrest after 5 Gy irradiation. Also we found that SOCS-1/3 overexpression inhibited cell migration. In xenograft mouse model, tumor growth delay was observed in SOCS overexpressing tumor compared to wild type tumor (HeLa). Immunohistochemistry showed that COX-2 expression had no difference while MMP-2 expression was decreased in SOCS-1 overexpressing tumor. Also p21 expression increased strongly in SOCS-1 overexpressing tumor. Also increased apoptotic activity was observed in SOCS-1 overexpressing tumor through tunnel staining.

Conclusions
SOCS-1/3 overexpression may inhibit invasion and metastasis of cervical cancer.
INTERIM REPORT: 5-YEAR PROSPECTIVE MULTICENTER STUDY OF KOREAN HPV COHORT

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Objectives
To evaluate the natural change of HPV infection and abnormal Pap with time and to determine related factors for progression, we constructed a 5-year Korean HPV cohort study. This study aimed to provide its 3-year interim results.

Methods
Patients who met the inclusion criteria of having both HPV positivity and abnormal Pap (ASCUS or LSIL) were recruited from the five institutions. Patients received blood sampling and questionnaire study every year, and cervical cytology and HPV DNA testing every six months.

Results
497 women who received a follow-up at least once were used for analysis. Most of the patients were non-smokers, drinkers, and highly educated. Logistic regression analysis failed to find a significant epidemiologic factor such as obstetric or sexual history, related with change on Pap or HPV infection. The result of Pap was progressed in 16.9%, unchanged in 22.1%, and regressed in 61%, and the result of HPV DNA was persistent in 2.8%, incidental infection in 58.6%, clearance of infection in 33.6%. The rate of progression on Pap smear was decreasing according to HPV consistency. On the other hand, the rate of regression on Pap smear was increasing.

Conclusions
Our findings show that progression from ASCUS/LSIL is intimately related with consistency of HPV infection. Although our interim data still do not demonstrate any significant epidemiologic risk factor, it could show natural change in cytology and HPV infection with six-month interval, and serve as a reference for Korean-specific cohort.
TOLERANCE OF MULTIMODALITY THERAPY FOR LOCALLY ADVANCED UTERINE CERVIX CANCER PATIENTS
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Objectives
Assessing the tolerance of combined radiotherapy (CRT) with systemic photodynamic therapy (PDT), whole-body hyperthermia with induced hyperglycemia and cisplatin chemotherapy (WBHT with IHG and ChT) for locally advanced uterine cervix cancer (UCC).

Methods
Thirty-four stage IIB-IV UCC patients were randomly assigned to two groups. Study group was administered two procedures of PDT with Photolon (1.2 mg/m²) and intravenous laser irradiation of blood (3 procedures), and also 2 sessions of controlled WBHT with IHG and ChT with cisplatin (40 mg/m²) in the setting of standard CRT.

Results
Ten patients of the control group and 9 of the study group completed the whole treatment course. The rest are still in the process of the planned therapy implementation. The patients of the control group presented with grade I-II enterocolitis (3 cases) and grade II-III cystitis (4 cases). Grade I-II burn of gluteal skin (4 cases), grade II anemia (1 case), grade I enterocolitis (2 cases), grade I leukopenia (1 case), occurred in the study group. All 17 patients of the study group received 2 PDT treatments but two of them underwent only one session of WBHT with IHG and ChT because of skin reaction and refusal to accept treatment (one case each).

Conclusions
PDT was found to be fairly tolerated and to produce no side effects. The combination of PDT and WBHT with IHG and ChT, the pause after PDT being 3 to 14 days, does not cause severe morbidity, nor does it impair the patient’s condition.
RADICAL ABDOMINAL TRACHELECTOMY FOR CLEAR CELL ADENOCARCINOMA OF CERVIX IN A 4 AND HALF YEAR OLD GIRL: A CASE REPORT.

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Objectives
Clear cell adenocarcinoma of cervix is a very rare tumor in paediatric population. Historically the recommended treatment is Radical Hysterectomy + Bilateral pelvic node dissection, which would result in permanent infertility. Radical Trachelectomy is an established technique in adult women with early cervical carcinoma, who wish to preserve fertility. This approach has been used to treat young girls with carcinoma cervix and there are few case reports describing the outcomes. We used this fertility preserving option in a very young girl (4 1/2 yrs) with clear cell adenocarcinoma of cervix.

Methods
A four and half year old girl presented in emergency with pervaginal bleeding. During evaluation was found to have a mass 2 x 2 cms arising from cervix. Biopsy revealed clear cell adenocarcinoma of cervix. MRI showed no parametrial/vaginal involvement and no lymphadenopathy. She was staged as Clear Cell Adenocarcinoma of Cervix IB1. After parental counseling and preoperative evaluation the child underwent Radical Abdominal Trachelectomy with Bilateral Pelvic Node Dissection. Intraoperative frozen section showed no lymph nodal involvement, also the proxal/vaginal/parametrial cut margins were free. After evaluating the final histopathology report, she was advised close observation.

Results
Four years on regular follow-up the patient is disease free.

Conclusions
Clear Cell adenocarinoma of cervix is very rare tumor seen in young girls. Fertility preservation in the form of Radical Trachelectomy is possible in these young girls. This approach appears feasible and safe.
NEOADJUVANT CHEMOTHERAPY OF LOCALLY ADVANCED CERVICAL CANCER
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Objectives
Traditional chemo-radiation therapy IIB-stage can be efficacive in 50%. In this regard, the study of the new schemes of combined and complex treatment with the possibility of surgical intervention is urgent.

Methods
The study included 35 patients with cervical cancer IIB-IIIB. The average age of patients was 45.33±1.57 year (32-61 year). In 24 patients (68.5%) was diagnosed with squamous cell carcinoma, in 9 patients (25.7 %) - adenocarcinoma, in 2 patients (5.7 %) – low differentiated cancer. Patients received at first 3 cycles of neoadjuvant chemotherapy with an interval of 10 days of the scheme BOP: Vincristine 1 mg/m2 day 1, Bleomycin 25 mg/m2 days 1-3, Cisplatin 50 mg/m2 day 1.

Results
Radical hysterectomy was completed in 28 patients (80%) after neoadjuvant chemotherapy BOP. 7 patients (20%) failed to perform the operation, and they had been appointed in the subsequent combination of radiation therapy. Frequency of recurrence after combined treatment was 15.7%. Period of monitoring of patients is now 120 months. Three-year overall survival of patients subjected to surgical treatment was higher than that of non operable: 77.1% and 42.8%, respectively.

Conclusions
Adjuvant chemotherapy BOP in patients with LACC shows a fairly high efficiency with a high frequency of objective response and allows to perform radical surgical treatment in the majority of patients.
**e-Posters: Cervical Cancer**

**CASE-CONTROLLED COMPARISON OF ADJUVANT CHEMOTHERAPY VERSUS RT/CCRT AFTER RADICAL HISTERECTOMY IN PATIENTS WITH FIGO STAGE IB-IIA CERVICAL CANCER**

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**Objectives**  
To verify the therapeutic efficacy of adjuvant chemotherapy (AC) in FIGO stage IB-IIA cervical cancer

**Methods**  
In this case-controlled study, 276 cervical cancer patients were enrolled, who received radical hysterectomy (RH) and adjuvant therapy at Asan Medical Center between 1991 and 2012; 94 patients received AC and 182 received adjuvant RT/CCRT (AR). The weighted Cox proportional-hazards regression models using the inverse-probability-of-treatment weighting (IPTW) was used to reduce the impact of treatment selection bias and potential confounding factors such as lymph node metastasis (LNM), parametrial invasion (PI), positive resection margin, deep stromal invasion (>50%), bulky tumor (>4cm), or lymphovascular space invasion.

**Results**  
During 45.5 months of median follow-up duration, 41 patients (14.9%) had recurred and 18 patients (6.5%) died of disease. In multivariable analysis, PI and LNM significantly affected recurrence (PI HR 2.479, 95% CI 1.211-5.074, p=0.01; LNM 1.97, 95% CI 1.045-3.712, p=0.04), however, only LNM significantly affected death (HR 3.007, 95% CI 1.111-8.137, p=0.03). After IPTW matching, HR of recurrence did not significantly differ between both arms (p=0.49), however, HR of death was significantly higher in patients with AR (HR 4.82, 95% CI 1.254-18.524, p=0.02).

**Conclusions**  
AC has equivalent therapeutic effect as AR in patients with FIGO stage IB-IIA cervical cancer. Regarding recurrent cases, patients with AC have more treatment options than those with AR. In addition, AC has much lower prevalence of long-term complication. Therefore, AC can also be an adjuvant treatment option especially in younger patients.
Predictors of Mortality in Patients with Cervical Cancer - A Hospital Admissions Study: 2000-2012

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Objectives

Cervical Cancer is a common condition that has been well studied. However, the predictors of mortality in patients with Cervical Cancer have not been well studied in a large hospital population in the UK. We investigated the predictors of mortality in patients with Cervical Cancer from a large sample of hospital admissions.

Methods

Anonymous information on patients with Cervical Cancer, co-morbidities and procedures attending large multi-ethnic general hospitals in Manchester, United Kingdom in the period 2000-2012 was obtained from the local health authority computerised hospital activity analysis register using ICD-10 and OPCS coding systems. Statistical analysis was performed using SPSS version 20.

Results

Out of 458410 patients admitted, there were 1208 (0.3%) patients with Cervical Cancer; mean age 36.9 years ± 13.8 (S.D); Female (100%). The main co-morbidities were Hypertension (91; 7.5%), Depression (41; 3.4%), Type 2 Diabetes (26; 2.2%), Ischemic Heart Disease (22; 1.8%) and Breast Cancer (10; 0.8%). A multi-nominal logistic regression model accounting for variations in age, sex and ethnic group showed Age (RR 1.07; C.I 1.05-1.09), Disease Duration (RR 0.99; C.I 0.99-0.99) and Hypertension (RR 0.37; C.I 0.14-0.97) as significant predictors of mortality (p <0.05).

Conclusions

We have shown that Age, Disease Duration and Hypertension are the only significant predictors of mortality in patients with Cervical Cancer from a large hospital based sample in the UK. Our improved understanding of these predictors will guide clinicians to focus on these high risk groups to improve clinical practice and outcomes in patients with Cervical Cancer.
THE CORRELATION OF DIAGNOSTIC MRI IMAGING IN FIGO STAGING SYSTEM AND HISTOPATHOLOGY FINDINGS IN PRIMARY CERVICAL CANCER

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Objectives
The aim of this study was to assess the diagnostic accuracy of preoperative MRI and clinical FIGO staging in patients with cervical cancer by confirmation pTNM histopathology.

Methods
Retrospectively, our study enrolled 187 patients with surgical-pathological proven FIGO IA-IIB cervical cancer who underwent an MRI investigation before start of surgical treatment between January 2004 and December 2011. At the Department of Obstetrics and Gynecology, Ulsan University (UUH, Ulsan, Korea).

Results
187 patients with cervical cancer are consisted of IA1 25(13.3%), IA2 8(4.4 %), Ib1 99(52.9%), Ib2 23(12.3%), IIa1 2(1.1%), IIa2 2(1.1%), and IIb 28(14.9%) of AJCC tumor-node-metastases (pTNM).

By comparison of Postoperative histopathological staging(pTNM), the accuracy rate of MRI-FIGO clinical staging was 62.6% (62/99) and under-staging rate was 20.2% (20/99), over-staging rate was 17.2%(17/99) in pTNM stage Ib1. In pTNM stage Ib2 accurate staging rate of preoperative MRI was 60.9%(14/23), under-staging rate was 4.3%(1/23), over-staging rate was 34.8%(8/23). Under-staging rate was 50%(1/2) and over-staging rate was 50%(1/2) in pTNM stage IIa1. Accurate staging rate was 50 %( 1/2) and under-staging rate was 50 %( 1/1) in pTNM stage IIa2. Accurate staging rate was 60.7 %( 17/28), under-staging rate was 39.3 % ( 11/28) pTNM stage IIb.

Conclusions
In despite of usefulness of diagnostic modality of MRI in estimation of cancer volume and distant metastasis, there were limitations of preoperative diagnostic accuracy of MRI in FIGO staging the patients with cervical cancer.
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ASSESSMENT OF TUMOR VOLUME REGRESSION AND SERUM SQUAMOUS CELL CARCINOMA ANTIGEN DURING CHEMORADIATION THERAPY FOR CERVIX CANCER
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Objectives
To evaluate the changes in primary tumor volumes (pTV) and serum squamous cell antigen (sSCC) levels during chemoradiation therapy (CCRT) in patients with cervical cancer.

Methods
We retrospectively reviewed 29 cervical cancer patients who were treated with CCRT from August of 2009 till February of 2013. All patients were received the External beam radiation therapy (EBRT) and intracavitary brachytherapy (ICR). The changes of pTV and the levels of SCC-ag between preradiotherapy (pre-RT) and midradiotherapy (mid-RT) were evaluated. The measurement of pTV was performed by magnetic resonance imaging (MRI). Pre-RT MRIs were obtained within 4 weeks before EBRT was begun and Mid-RT MRIs were obtained before the start of ICR. The SCC-ag levels were also measured at pre-RT and mid-RT.

Results
The median age of all patients was 58 (40-82) years. The median follow-up duration between pre-MRI and mid-MRI was 44 days (28-64 days). The pre- and mid-RT pTV were 98.0 ± 92.3 cm³ and 16.2 ± 21.5 cm³, respectively. Complete remission was noted in 11 patients (38%). The pTV reduction rate was 80.5% ± 22.1 % (p=0.001). The pre- and mid-RT SCC-ag levels were 26.3 ± 34.0 ng/ml and 3.9 ± 4.9 ng/ml, respectively. The SCC-ag levels reduction rate was 64.4% ± 34.4 % (p=0.001). The correlation coefficient between pTV reduction rates and SCC-ag levels reduction rates was 0.389 (p=0.037).

Conclusions
During CCRT for cervix cancer, the pTV and SCC-ag levels were significantly reduced. Furthermore, a significant correlation was observed between the pTV and SCC-ag levels.
RISK FACTORS OF DIAGNOSTIC DISCREPANCY BETWEEN COLPOSCOPICALLY-DIRECTED BIOPSIES AND LOOP ELECTROSURGICAL EXCISION PROCEDURE CONIZATION OF THE UTERINE CERVIX

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Objectives
The goal of current study was to determine the clinical factors independently associated with diagnostic discrepancy of patients were performed colposcopically directed biopsy and conization by Loop Electrosurgical Excisional Procedure (LEEP).

Methods
Two hundred and fifty eight patients who were diagnosed with abnormal uterine cervical histopathology on colposcopically directed biopsy were underwent LEEP. Usually two types of discrepancies in histopathologic finding between colposcopically directed biopsy and conization were observed.: (1) Diagnosed with CIN2, 3 or CIS in the colposcopically directed biopsy, however diagnosed with CIN1 or chronic cervicitis in the subsequent conization (overdiagnosis), (2) Diagnosed with CIN2, 3 or CIS in the colposcopically directed biopsy, however diagnosed with invasive squamous cell carcinoma in the subsequent conization (under diagnosis), and (3) Diagnosed with CIN1 or chronic cervicitis with koilocytotic atypia in the colposcopically directed biopsy, however diagnosed with CIN2, 3 or invasive squamous cell carcinoma in the subsequent conization (under diagnosis).

Results
The probability of (1) (n=52, 20.2%) was inversely related to severity of cervical cytology and infection with HPV type 16. The probability of (2) (n=17, 6.6%) was positively related to severity of cervical cytology. The probability of (3) (n=13, 5.0%) was only related to the severity of cervical cytology.

Conclusions
The present study couldn’t confirm previous observations regarding the positive association of patient’s age and visibility of active squamo-columnar junction with the probability of missing the diagnosis of high grade CIN or carcinoma. Cervical cytology and infection with HPV type 16 were shown to be related to the diagnostic discrepancies between colposcopically directed biopsy and conization.
TOTAL LAPAROSCOPIC (WERTHEIM’S) RADICAL HYSTERECTOMY VERSUS ABDOMINAL RADICAL HYSTERECTOMY IN THE MANAGEMENT OF STAGE I CERVICAL CANCER IN SINGAPORE: A PILOT STUDY.  
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Objectives
To compare Total Laparoscopic Radical Hysterectomy (TLRH) versus Abdominal Wertheim’s Radical Hysterectomy (RAH) in the management of early cervical cancer in Singapore.

Methods
This is a prospective study in a single tertiary institution. Inclusion criteria included surgically fit patients with early cervical cancer without radiological evidence of regional or distant metastases.

Results
From November 2009 to February 2011, we performed a total of 18 cases of TLRH and bilateral pelvic lymphadenectomy and 30 cases of RAH. There was no statistical difference regarding age, parity, BMI, FIGO stage and tumour size between the TLRH and RAH groups.

The median blood loss in the RAH group was significantly more than the TLRH group. (300ml vs 500ml; P=0.04) The median operative time for the TLRH group was 268 minutes appears to be longer than the RAH group (240 min) but this did not reach statistical significance. (P=0.44) A total of 10 patients in the TLRH group (55.6%) received adjuvant treatment compared to 16 (53.3%) in the RAH group. (P=0.8)

There was no intra-operative bladder, ureteric or bowel complications in both groups. Postoperative complications occurred in two TLRH patients (11.1%) and four RAH patients (13%). With a median follow up of 37.3 weeks (10 to 68 weeks), the recurrence was 5.6% for the TLRH group and 10% for the RAH group.

Conclusions
The results suggest that TLRH is a safe and effective procedure in the management of early cervical cancer in Singapore.
PROGNOSTIC SIGNIFICANCE OF ENDOGLIN EXPRESSION IN VASCULAR ENDOTHELIAL CELL AND TUMOR CELL IN CERVICAL CANCER

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Objectives
Endoglin, a co-receptor for TGF-β, is up-regulated in tumor vessels. We attempted to investigate whether endoglin expression in vascular endothelial cells or tumor cells can be used as a prognostic marker for cervical cancer patients. We also investigated the functional role of endoglin in vitro models.

Methods
We retrospectively analyzed endoglin immunohistochemical expression of tissue samples from 80 patients with different FIGO stages cervical cancer before treatment. Clinicopathological variables including endoglin expression were analyzed for treatment outcomes. In vitro model, cervical cancer cells with different endoglin expression were established. The expressions of downstream proteins were determined by Western blotting. Proliferation, migration/metastasis assay were also performed to determine the functional role of endoglin in tumor progression.

Results
Endoglin was expressed exclusively in endothelial cells but not tumor cells. Cox regression analysis showed that FIGO stage and endoglin MVD were independent factors to predict survival. In vitro, we successfully established cervical cancer cell lines with different endoglin expression. The expressions of downstream proteins of TGF-β signaling pathway p-Smad 1, 5, 8 and Smad 1 were positively correlated with endoglin expression while proteins p-ERK and p-p38 were negatively correlated with endoglin expression. The results indicating that endoglin modulate tumor progression might be via Smad-mediated TGF-β signaling pathway. Proliferation, migration/metastasis assay showed that endoglin expression paradoxically attenuated cervical cancer cell proliferation, migration, and invasion.

Conclusions
Different endoglin expression patterns may correlate with distinct clinical prognosis. Patients with more endoglin expression in endothelial cells harbored poor clinical outcome. However, presence of endoglin expression in tumor cells might inhibit tumor growth.
RESTRICTIONS ON THE ACTIVITIES OF DAILY LIVING IN INVASIVE CERVICAL CANCER SURVIVORS

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Objectives
There is not in literature an assessment tool of the activities of daily living (ADL) for patients with invasive cervical cancer (ICC). The objective of this study was the development and validation of an instrument for assessing ADL’s for patients with cervical cancer the following phases: planning, construction, content validation, validation of reliability.

Methods
Participated in these evaluation 45 women (15 cases and 30 controls). (Figure 1) The intra and inter-examiner was rated as very good (k = 1.00) with p <0.001. The result of the index of ADL (Table 1) was analyzed by chi-square p <0.001.

Results
In group 1, 73.7% had score 0. The score 1 was more prevalent in case groups: group 2 (59.4%), group 3 (53.5%) and group 4 (50%). The score 2 was more representative in groups 3 (20%) and 4 (23.3%). No patient presented scores 3 and 4.

<table>
<thead>
<tr>
<th>Score</th>
<th>Significance</th>
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<tbody>
<tr>
<td>0</td>
<td>full independence</td>
</tr>
<tr>
<td>1</td>
<td>minimum dependence</td>
</tr>
<tr>
<td>2</td>
<td>low dependency</td>
</tr>
<tr>
<td>3</td>
<td>moderate dependence</td>
</tr>
<tr>
<td>4</td>
<td>maximum dependence</td>
</tr>
</tbody>
</table>

Table 1: Instrument for assessing activities of daily living ADL’s for patients with cervical cancer.

Conclusions
The presentation of assessment tools on the ADL's patients for cervical cancer could help the health care professional approach, as it allows measuring their level of independence in daily tasks and occupational
FUNCTIONAL ASSESSMENT OF PATIENTS TREATED FOR INVASIVE CERVICAL CANCER


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Objectives
The objective of this study was to evaluate the functional capacity (CF) in patients with invasive cervical cancer using the Functional Capacity Index (FCI) method Veronesi.

Methods
Have been selected 45 women (15 cases and 30 controls) to verify the reliability of the instrument with the questionnaires by 2 examiners. (Table 1) The groups were categorized: group 1 (control, n = 57), group 2 (surgery alone, n = 32), group 3 (surgery and chemoradiation, n = 30) and group 4 (chemoradiation, n = 30). The evaluation inter-and intra-observer concordance rated as very good (k = 1.00) with p <0.001. The result of the ICF - cervical cancer between groups was compared using the chi-square p <0.001.

Results
The score 0 was more prevalent in group 1 (40.4%). The score 1 (25) was highest in group 3 (77.3%). The score 2 had higher value in group 4 (30%). None of the patients had scores 3 and 4.

<table>
<thead>
<tr>
<th>Score</th>
<th>Significance</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>100% functional capacity</td>
</tr>
<tr>
<td>1</td>
<td>25% disability</td>
</tr>
<tr>
<td>2</td>
<td>50% disability</td>
</tr>
<tr>
<td>3</td>
<td>75% disability</td>
</tr>
<tr>
<td>4</td>
<td>100% disability</td>
</tr>
</tbody>
</table>

Table 1: Instrument to evaluate functional capacity in patients with cervical cancer.

Conclusions
ICF could help many health professionals to assess CF in these patients to direct guidance on returning to work activities in accordance with the appropriate classification of CF presenting the final evaluation.
e-Posters: Cervical Cancer

PRIMARY SIGNET-RING CELL CARCINOMA OF THE CERVIX – CASE REPORT
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²Pathology, IPO Porto, Porto, Portugal
³Gynecology, IPO Porto, Porto, Portugal

Objectives
Primary signet-ring cell carcinoma of the uterine cervix is a rare pathology, with only 14 cases published in the literature. The pathological and molecular characterization, as well as the therapeutic options available for these patients remains a challenge for the clinician.

Methods
Case Report

Results
The authors present the case of a 60 year old woman, diagnosed with an invasive carcinoma of the uterine cervix, with signet-ring cells, stage IVB FIGO (lymph node, lung, liver, muscle, bone and adrenal metastases, the latter confirmed histologically). Immunohistochemistry revealed reactivity for AE1AE3, CK7, GCDFP-15, CDX2 and estrogen receptors. Primary malignant disease of the breast and digestive tract was ruled out. The patient developed bilateral hydronephrosis with acute kidney injury which motivated a percutaneous nephrostomy. After renal function normalization, chemotherapy with carboplatin and paclitaxel was instituted. The patient completed 4 cycles of this regimen, with progression of the disease (increase in numbers and dimensions of bone metastases and de novo skin metastization in the right inguinal region). She started second-line chemotherapy with cisplatin and etoposide, stopped after one cycle due to clinical deterioration. The patient was afterwards proposed for best supportive care.

Conclusions
Although rare, primary signet-ring cell carcinoma of the uterine cervix can exist as a primary malignancy which must be distinguished from a setting of metastization as this implies important differences in therapeutic approach and prognosis.
e-Posters: Cervical Cancer

PRESERVATION OF OVARIAN FUNCTION PRIOR TO PELVIC RADIOTHERAPY

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Objectives
Radiotherapy to the pelvis in pre-menopausal women results in premature ovarian failure. Anatomical relocation of the ovaries from their location in the pelvis to the abdomen is known as ovarian transposition. It is undertaken to prevent premature menopause as well as offer the option of assisted reproductive capacity.

We report our experience of ovarian transposition in women with cervical and colorectal malignancies and their hormonal status.

Methods
Retrospective data collection from medical records and laboratory databases in a tertiary oncology centre under the auspices of two surgeons. Patient demographics, intra and post-operative data collected. Type of malignancy and management also recorded.

Results
The procedure was undertaken in 11 patients. The procedure was performed in a day case setting. 2/11 were performed robotically and the remaining 9/11 laparoscopically. In 2/11 the procedure was performed for colorectal cancer while cervical cancer was the commonest indication. The blood loss was minimal (5-25 mls). In 3/11 women with cervical cancer, the procedure was complicated due to previous pelvic lymph node dissection and fibrosed sidewalls.

Hormonal levels were checked in the post-operative period 6 weeks later for levels of FSH, LH and oestradiol.

Ovarian Failure noted in 2/11 cases with elevated FSH levels. No pregnancies reported during the period of data collection.

Conclusions
Use of robotics ensures greater efficiency when performing complex surgical tasks. Ovarian transposition is a safe procedure and is feasible with minimally invasive surgery and offers a method of preservation of ovarian function in younger women at risk of radiotherapy induced menopause.
PROGNOSTIC VALUE OF LYMPHANGIOGENESIS RELATED FACTORS IN SQUAMOUS CELL CERVICAL CANCER

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²Department of Pathology, Medical Faculty University of Rijeka, Rijeka, Croatia

Objectives
Potential role of the Lens Epithelium Derived Growth Factor (LEDGF) – VEGF-C axis in tumor induced lymphangiogenesis and metastatic spread of squamous cell cervical cancer was tested.

Methods
The clinical outcome from 99 patients diagnosed with squamous cell cervical carcinoma and formalin-fixed, paraffin-embedded specimens by immunohistochemistry for LEDGF, VEGF-C expression and Lymphatic Vessel Density (LVD) of primary tumors were examined.

Results
The expressions of LEDGF and VEGF-C were significantly higher in the lymph node positive group. VEGF-C expression was independent prognostic factor for lymph node metastasis, while LSI was an independent prognostic factor for recurrent disease and survival in cervical cancer.

Conclusions
VEGF-C expression was independent prognostic factor for lymph node metastasis while, LSI was an independent prognostic factor for recurrent disease and survival in cervical cancer.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK

e-Posters: Cervical Cancer

CERVICAL CANCER PARAMETRIAL SPREAD ASSESSMENT: GIANT SECTION VS STANDARD TECHNIQUE.
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4Pathology, "Santa Maria Goretti" Hospital, Latina, Italy

Objectives
To compare diagnostic accuracy of two different pathologic techniques aimed to evaluate parametrial spread of cervical cancer.

Methods
Parametrial spread of 120 pts with cervical cancer which underwent type 3-4 radical hysterectomy was evaluated with two pathologic techniques. In 72 patients [stage IB1: 37(52%), IB2: 18(25%), IIA: 3(4%), IIB: 14 (19%); median age 50 yrs, range 26-71] the cervix and parametria were processed with the giant section technique, whereas in 48 patients [Stage IB1: 23(48%), IB2: 10(21%) , IIA 2(4%), IIB 15(31%); median age 53 yrs, range 35-77] the cervix and parametria were placed on a cork mold and processed according to the standard of College of American Pathologist (CAP). Locally advanced cervical cancer patients (IB2-IIB) were treated with neoadjuvant chemotherapy.

Results
Parametrial nodes were observed in 59 (82%) giant section pts [with the uterus 46 (64%), lateral distal 47 (65%)], and in 40 (83%) CAP pts [with the uterus 24 (50%), lateral distal 25 (52%)], p=NS (χ²). Median number of parametrial nodes was 4 (0-20) and 3 (0-12), respectively. Type of parametrial invasion according to the pathologic technique is reported in table 1.

<table>
<thead>
<tr>
<th>Type of parametrial invasion by stage and pathologic technique</th>
<th>Type of parametrial invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>GIANT SECTION</td>
</tr>
<tr>
<td>IB1</td>
<td>Giant Section</td>
</tr>
<tr>
<td>CAP mod</td>
<td>23</td>
</tr>
<tr>
<td>IB2-IIB</td>
<td>Giant Section</td>
</tr>
<tr>
<td>CAP mod</td>
<td>27</td>
</tr>
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</table>

Conclusions
The most diffused technique of CAP processing seems to be equivalent to the more complex and time consuming giant section technique in terms of parametral node and tumor spread detection.
e-Posters: Cervical Cancer

TISSUE PROTEIN MARKERS OF THE RELAPSE OF SQUAMOUS CERVICAL CANCER

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2Oncology and Pathology, Karolinska Institute, Stockholm, Sweden
3Gynaecologic Oncology, Örebro University Hospital, Örebro, Sweden

Objectives
Cervical cancer is yearly diagnosed in 0.5 mln women world-wide. It remains the major malignancy in developing countries. Treatment of cervical cancer is combinatory and comprises of surgery, contact and distant radiotherapy with "sensitising" chemotherapy. Radiochemotherapy is the basis for the treatment of cervical cancer at the stage IB2-IVA.

Prognosis for the patients after relapse of cervical cancer is poor because of the development of radiochemoresistance in the tissues. In 40% of the cases relapse of cervical cancer localises outside pelvis.

We used the methods of proteomics to analyse the tissue of cervical cancer and to identify proteins that are possibly related to the development of radiochemoresistance.

Methods
The methods comprised of the two-dimensional gel (2-D) electrophoresis of cervical cancer tissue proteins, analysis of gels by SameSpot (Nonlinear) software and MALDI-TOF MS-assisted identification of proteins. Tissue biopsies were collected at the Örebro University Hospital prior to any treatment.

Results
- 2-D gels were generated from 32 biopsies of cervical cancer.
- Protein expression was compared between the cases that remained relapse-free and those that developed local relapse (1) and distant relapse (2) (Figure 1).
- 123 differentially expressed spots were subjected to protein identification by mass spectrometry.

Figure 1. Principal component analysis of 2-D gels.

Conclusions
Analysis of 2-D gels of cervical cancer tissue proteins suggests existeance of protein markers that are related to future local and distant relapses of the disease, and poor overall survival.
BLOOD LOSS DURING RADICAL HYSTERECTOMY – OUR CLINICAL EXPERIENCE

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Objectives
In spite of applied preventive measures, there is still a high incidence of cervical cancer in Serbia. Institute of Oncology Vojvodina is referential centre for treating women with cervical cancer for Region of Vojvodina. The incidence rate of cervical cancer is very high in Serbia, 27.4/100 000. In Vojvodina region, incidence rate is similar. Lot of patientes at the time of diagnosis have local advanced disease. A size of primary tumor is important prognostic factor to choose primary therapy. All patients had radical hysterectomy Piver class III with pelvic lymphadenectomy

Methods
We have processed 354 patients who had radical histerectomy with pelvic lymphadenectomy, because of early cervical cancer stage Ib1, Ib2, IIa and IIb. The aim of the work is evaluate blood loss during radical hysterectomy.

Results
In consideration with the blood loss during a radical hysterectomy, patients are divided into three groups: blood loss to 500 ml, blood loss from 500 to 1000 ml and blood loss over 1000 ml. Largest number of patientes had blood loss to 500 ml, 20% of patientes had blood loss to 1000 ml and 20 patientes had blood loss over 1000 ml. Correlation of patientes with blood loss over 1000 ml did not show any significante compared to previous operations and the age of patientes.

Conclusions
Massive blood loss was notice with patientes in the stages Ib2 and II b of disease, with massive tumor and parametrial invasion, so pathological vascularisation can be considered as predictive factor. Careful selection of patientes is very important for operative treatment.
RADICAL TRACHELECTOMY IN A PATIENT WITH UTERINE MULFORMATION

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Objectives
The most effective surgical treatment for early stages of cervical cancer (IA2–IB1) is a total radical abdominal or vaginal hysterectomy and pelvic lymphadenectomy. This operation results in infertility. We attempted this approach in a 31 year old patient with uterine malformation of the vagina who opted for a fertility sparing treatment.

Methods
Thirty one-year-old female (para 0+0) with uneventful medical and surgical history presented with recent history of vaginal bleeding. Preliminary biopsy of the cervix revealed high grade squamous cell carcinoma (SCC). We performed partial organ resection via abdominal radical trachelectomy and pelvic lymph node dissection.

Results
MRI of the pelvis revealed complete bicornuate uterus (type IV uterine malformation) and concomitant urinary tract anomalies. We performed surgical separation of the uterus in low uterine segment, ovary sparing radical hysterectomy of the «right» uterus and radical abdominal trachelectomy of the «left» uterus. This procedure was followed by pelvic lymph node dissection.

Conclusions
There were no complications after surgery. The histology confirmed SCC of the cervix uteri Ib1 stage (pT1b1N0M0G1) with negative lymph nodes. No additional treatment was required. Menstrual cycles were preserved. Potential for pregnancy was preserved, however feasibility of this procedure remains questionable.
HPV TRIAGE: COLPOSCOPIC AND BIOPSY OUTCOME

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¹Northern Institute for cancer research, Newcastle University, Newcastle upon Tyne, United Kingdom
²Obstetrics and Gynaecology, Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom

Objectives
HPV triage for borderline cytology and mild dyskaryosis has been applied nationwide. The aim of this study was to assess the rates of attendance and outcomes of colposcopy in HPV positive women at Newcastle Royal Victoria Infirmary.

Methods
Retrospective audit of the HPV triaged patients with borderline cytology and mild dyskaryosis referred between 01/04/2012 and 30/03/2013.

Results
In the study period 373 (31%) new patients were referred with borderline cytology (62%) or mild dyskaryosis (38%) triaged for high risk HPV. 86% of HPV positive women attended colposcopy. 65% of women who attended had a punch biopsy and 1 patient an excisional biopsy at first visit; 30% of these had a negative histology, 52% CIN1, 12% CIN2 and 3% CIN3. No cases of cervical cancer were found in this cohort. The positive predictive value (PPV) of HPV triage for CIN2+ in our unit was 10.4%. 9.5% of HPV positive women who attended colposcopy had an excision biopsy, of which 3% showed no CIN, 24% CIN1, 45% CIN2, 21% CIN3 and 7% CGI.

Conclusions
From this study it appears that the PPV of HPV in our unit (10.4%) is lower that that reported in sentinel sites (16.3%) and pilot studies (18.7%). All except one, excisional biopsies were performed for CIN2+ diagnosis on punch biopsy; therefore the rate of negative histology for excisional biopsy was low (3%). However, larger studies are needed to explore the finding of CIN1 in 24% of excisional biopsies, which were performed for CIN2+ histology on punch biopsy.
THE ASSOCIATION BETWEEN PAP SMEAR AND COLPOSCOPY FINDINGS AND LLETZ RESULTS IN AN AUSTRALIAN DISTRICT HOSPITAL SETTING

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Objectives
Aim: To investigate the reasons that LLETZ or cone biopsy may be performed in cases where no histologically significant lesion is found on excision.

Methods
A retrospective observational study was performed involving 63 cervical excisions in a single centre. Relationships between variables in patient history and course of treatment were assessed using ANOVA.

Results
The false positive rate for smears to colposcopy was 11.50% and for colposcopy to excision was 27.40%. However, the PPV for colposcopy was 71%. There were 14 cases of not performed/normal/LSIL biopsies proceeding to excision. Of these, 4 had evidence of HSIL on referral and an unsatisfactory colposcopy. The other cases were referred with either LSIL on referral or HSIL on smears taken at colposcopy. There was a significant association between unsatisfactory colposcopy and a lower degree of dysplasia at excision (0.32 p < 0.05). The figure shows that CIN3 at colposcopy was strongly predictive of a high degree of dysplasia at excision but CIN2 was not.

Conclusions
Although this PPV is acceptable, it is clear that there is much room for improvement. Most inappropriate referrals were made on the basis either of LSIL on referral and an unsatisfactory colposcopy or on the basis of HSIL on cytology performed at the the time of referral.
EMBRYONAL RHABDOMYOSARCOMA OF THE CERVIX WITH PLEOMORPHIC SUBTYPE IN A 17 YEAR OLD FILIPINA: A CASE REPORT

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Objectives
Introduction: Embryonal rhabdomyosarcoma is a rare disease that usually occurs in the vagina and peaks at 3 years old. It is even rarer if it arise in the uterine cervix of the female genital tract with an incidence peak in women in their late teens and early 20s.

Methods
Case Report: Presenting a case of a 17 year old, nulligravid Filipina who had history of soft, grape-like, non-tender cervical mass protruding from the introitus. The mass gradually enlarged in size for over a year and was accompanied by several months of amenorrhea and weight loss. CT scan, immunostaining and excision of the cervical mass were performed.

Results
Histopathologic evidence showed embryonal type of rhabdomyosarcoma, but the unusual feature, and the key reason of reporting this case, was the focal presence of pleomorphic cells which are also found in pleomorphic type. There were anaplastic cells with large, lobate, hyperchromatic nuclei noted. Radical hysterectomy with bilateral salpingo-oophorectomy followed by Doxorubicin-Cisplatin-Etoposide combination chemotherapy were done but patient succumbed to death after her 4th cycle. Hence, there is no definitive conclusion about the effectiveness of this regimen.

Conclusions
This type of condition has never been reported in our local literature and the existence of highly pleomorphic cells were previously described only in two cases of cervical embryonal rhabdomyosarcoma, documented abroad, in U.K. and Italy. The rarity of the condition, its diagnostic approach and management is worth documenting for future reference.
SURGICALLY TREATED EARLY SQUAMOUS AND NON-SQUAMOUS CANCER OF THE CERVIX - IS THERE A DIFFERENCE?

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Objectives
In 2000, Peters et al. reported that the addition of concurrent cisplatin-based chemotherapy (CT) to radiation therapy (RT) significantly improves PFS and OS of high-risk patients with early cervical carcinoma after radical hysterectomy (RH). At present, CCRT is the gold standard for high-risk patients after RH regardless of histological types. Our aim was that to evaluate adjuvant therapy for SCC and non-SCC after RH.

Methods
By December 2010, 194 patients (SCC:138, adenocarcinoma (AD):48, adenosquamous cell carcinoma (ADSCC):8, except neoadjuvant CT and RT) with stage I-II disease and pelvic lymph node (PLN) metastasis underwent RH at four university hospitals and were also enrolled. We analysed prognostic factors. The one-sided log-rank test (p≤0.05 for significance) was used to assess PFS and OS, and Cox regression analysis was performed.

Results
The following prognostic factors were identified: histological type (p=0.012) and metastasis to more than two lymph nodes (p=0.002). Among patients with more than 2 metastatic lymph nodes, the following prognostic factors were identified: adjuvant therapy (p=0.03) and histological type (p=0.002). Compared with operation plus chemotherapy (OC) and operation, chemotherapy plus radiation therapy (OCR) cases of non-SCC, OC patients had significantly better OS (p=0.011). In OC patients, more PLNs were dissected (p=0.023) and para-aortic lymph node (PAN) dissection (p=0.077) was also performed more often.

Conclusions
We suggest that the combination of adjuvant chemotherapy and RH with PLN and PAN dissection is very useful for operable patients with metastasis to more than 2 lymph nodes in early (stage I-II) non-SCC.
CHEMOTHERAPY IN THE TREATMENT OF ADVANCED/RECURRENT CERVICAL CANCER (CC). THE EXPERIENCE OF SLOVAK NATIONAL CANCER INSTITUTE, BRATISLAVA

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Objectives
In several randomised phase 3 trials investigated the activity of chemotherapy (CHT) in advanced/recurrent CC, most of the patients achieved stable disease, with progression free survival (PFS) and overall survival (OS) till 4, 6 months (M) and 9.9 M. The aim of the study was to evaluate the response and survival benefit of CHT in advanced/recurrent CC in our institute.

Methods
This retrospective study analysed 89 patients with advanced/recurrent CC from 2005 to 2012 treated by chemotherapy alone. Survival analysis was performed by Kaplan-Meyer method, differences between subgroups by log-rank test, toxicity according to CTCAE 4.0

Results
Median age of pts. was 49.1 years, 25(28.1%) pts had primary metastatic disease, 64(71.9%) recurrent disease, 75(84.3%) had squamous cell carcinoma, 60(67.4%) had nodal mts. Topotecan with cisplatin (Topo/cis) received 46(51.7%) pts. in the first line CHT, 15(16.9%) paclitaxel with carboplatin and 14(15.7%) ifosfamide (IFO). 34(38.2%) pts. received vinorelbine and gemcitabine in the other lines of CHT. Topo/cis achieved 8% of CR, 5% of PR, IFO 6% of PR, other drugs only SD (43-62%). Main toxicity, neutropenia, occurred mainly after Topo/cis (Grade 3, 4: 59% of lines). Median of follow up was 13.8 M. Median PFS was 6.5 M and median OS 14.8 M in all patients. There were no significant differences in survival between histologic subtypes and type of combined CHT. Only statistical difference of survival we observed between CHT with IFO and other types of CHT (OS 7.1 M vs. 15.8 M, p 0.006).

Conclusions
In our institute chemotherapy of advanced/recurrent CC has moderate impact on survival. Topo/cis is the standard first line treatment, but with measurable toxicity. Paclitaxel/Karbo is efficient alternative.
CERVIX CARCINOMA AND SARCOIDOSIS

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Objectives

The gynecologic malignancies and sarcoidosis are uncommon. For proper diagnosis biopsy is required (1).

Methods

Review of a case diagnosed in our service and treatment received

Results

Fifty-eight years female was diagnosed in February 2005 of cervix carcinoma stage IIA and treated with radiotherapy+brachytherapy achieving CR. In January/2009 CT scan showed para-aortic and mediastinal nodes, two right pulmonary nodules and mass in the psoas. Right segmentectomy was performed with pathological report of a pulmonary parenchyma necrotizing granulomatous inflammation compatible with sarcoidosis. Follow up was made with CT and three years later (January 2013) the CT showed a group of nodes with necrotic features at the celiac trunk (4.7x6.2x5.1cm), mediastinum (3.1x3.1x5cm) and mass in the psoas (4.5x4.8cm.) The lymph nodes biopsy showed a positive metastatic carcinoma from primary cervical carcinoma similar to the patient.

PET showed hypermetabolic lymphadenopathy above and infradiaphragmatic, in the right lower lobe three hypermetabolic cavitary nodules and bilateral mass in the psoas. Clinically the patient had a left supraclavicular lymph node of 1.0cm. With the diagnosis of metastatic cervix carcinoma she started in February 2013 Cisplatin-Topotecan every 3 weeks. So far two cycles have been given reaching almost complete clinical response at the supraclavicular lymph node.

Conclusions

The reported case emphasizes that in case of doubt, biopsies are mandatory (lymph node or visceral soft tissue) to rule out the coexistence of gynecological malignancy and sarcoidosis

GENOME ANALYSIS OF CERVICAL CARCINOMA USING ARRAY-BASED COMPARATIVE GENOMIC HYBRIDIZATION (ARRAY-CGH)

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Objectives
Chromosome abnormalities are frequent genetic alterations in malignancies. It is assumed that recurrent changes in copy number of DNA sequences (amplification or deletion) of specific genes might be initiating factor in the process of malignant transformation.

Methods
We analyzed genome-wide profile of genetic abnormalities in tissue samples of cervical cancer using array-CGH to DNA oligonucleotide microarrays using newly introduced platforms 4 x 180 K Agilent CGH + SNP (oligo array-based comparative genome hybridization). Our effort was detecting of differences between patients with and without metastatic lymph node involvement and mapping the genome of the tumor.

Results
In the group of 13 women with proven squamous cell carcinoma of the uterine cervix we have found regional changes in the number of copies of DNA sequences. We detected multiplication in 3q22qter (6/13 women), 20q11q13.3 (5/13 women), 8q21.3qter (4/13 women) and loss in 13q11q21.2 (4/13 women), 3q (3/13 women), 4q (3/13 women). In 5 women with metastatic involvement of lymph nodes we proved duplication in 2p and 5p regions of the chromosome and deletion of 3p compared with patients without metastatic lymph nodes (8 women).

Conclusions
Array-CGH represents a perspective method of whole-genome screening and identification of potential DNA markers. It could allow the patients selection and risk specification of lymph node involvement in cervical cancer.

The pilot project was rising by support of Experimental intention Ministry of Health FUNDIN MZ0 MOU2005 and IGA Research Grant Project NT 11089-4/2010.
NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

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Objectives
The purpose of this study was to evaluate the efficacy and toxicity of paclitaxel and cisplatin as neoadjuvant chemotherapy for patients with stage IB2 to IIB cervical cancer and determine factors responsible for response.

Methods
From Nov. 2009 to Jan. 2011, a total of 19 patients with stage IB2 to IIB cervical cancer were treated with three 10-day courses of paclitaxel 60 mg/m² and cisplatin 80 mg/m² followed by type III radical hysterectomy and adjuvant therapy if indicated, or chemoradiation in non-resectable patients.

Results
Clinical response occurred in 79% (15/19) of patients, including 10.5% (2/19) with complete response and 68.5% (13/19) with partial response. 4 (21%) patients were nonresponders including 16% (3/19) with stable and 5.2% (1/19) with progressive disease. Resectability rate was 68.5% (13/19). Pathological optimal response rate was 46% (6/13). Suboptimal response (PR2) (residual disease with >3mm stromal invasion) was 54% (7/13). It seems that both clinical and pathological response were correlated with tumor stage and size. Clinical response was seen in 87.5% of tumors sized = < 8cm versus 33.3% of tumors sized > 8cm (P=0.166) and optimal pathological response was seen in 66.7% of tumors sized <4cm versus 28.6% of tumors sized 4-8cm, (P=0.286), although because of small number of patients the difference is not statistically significant. Adjuvant therapy was necessary for 38.5%( 5/13) of patients. Toxicities were not lifethreatening and all manageable.

Conclusions
Our results suggest that NAC with paclitaxel and cisplatin is a highly active and well-tolerated regimen. Best candidates are patients with stages IB2/IIA bulky and IIB nonbulky than IIB bulky groups.
RETROPERITONEAL VARIANTS OF VESSELS IN PATIENTS WITH CERVICAL CANCER EARLY STAGE, UNDERGOING SYSTEMATIC PARA-AORTIC AND BILATERAL PELVIC LYMPHADENECTOMY

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Objectives
To identify variants of retroperitoneal vascular structure during systematic para-aortic lymphadenectomy in patients with cervical cancer early stage and to investigate the effects of these anomalies in surgical procedures.

Methods
Seventy nine patients who underwent systematic para-aortic lymph node dissection with or without nerves preservation and bilateral pelvic lymph node dissection between 2006 and 2013 were included. Normal architecture and structural anomalies of inferior vena cava (IVC), renal arteries and veins, common iliac vein and ovarian vessels were studied.

Results
Variants of major retroperitoneal vascular structure were present in 10 patients (12.7%). Variants of renal vessels were identified in 8 patients (10.1%): supernumerary renal arteries and veins observed in 5 patients (6.3%); retroaortic left renal vein type I and II – in 3 patients (3.8%). So rare variants, as double IVC detected in 1 patient (1.3%) and duplication common iliac left vein - in 1 patient (1.3%). Variants of ovarian veins were detected in 3 patients (3.8%). Vessel injury was present no one case in patients with variants of vascular structures and in 1 of 69 (1.4%) patients without variants of retroperitoneal vascular structure. There was no difference in intraoperative hemorrhage, transfusion red blood cell and rate of intraoperative hemoglobin between the groups.

Conclusions
Rate of vessel variants by retroperitoneal surgery discovered in 10 patients (12.7%) with cervical cancer early stage. Acquisition of knowledge and visualization of vascular variations decrease complications during systematic para-aortic and bilateral pelvic lymphadenectomy.
KNOWLEDGE, ATTITUDES AND ACCEPTABILITY OF HUMAN PAPILLOMA VACCINATION AMONGST PRIMARY SCHOOL GIRLS (9 YEARS AND ABOVE) IN MINAKULU SUB-COUNTY OYAM DISTRICT

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Objectives
To determine the knowledge, attitudes and acceptability of cervical cancer vaccination among primary school girls aged 9 and above years in Minakulu sub-county, Oyam district, Lango sub region in Northern Uganda.

Methods
This descriptive analytical study determines knowledge, attitudes and acceptability of HPV vaccination amongst primary school girls aged ≥ 9 years in Minakulu Sub County, Oyam district-Northern Uganda. Systematic sampling of 415 pupils and 5 purposively selected key informants was conducted using semi structured questionnaires. Quantitative data was analyzed using SPSS 16.0. Directed content analysis of themes of transcribed qualitative data was conducted manually.

Results
Of the 415 respondents, majority 82.9% (n = 344) would accept and recommend an HPV vaccine, majority 57.6% (n = 239) had not been vaccinated. 39.5% (n = 164) were not sure of the site where the HPV vaccine is administered, 45.3% (n = 188) believed it is harmful to the body, 29.9% (n = 124) had never had of HPV vaccine. 9.6% (n = 40) disagreed when asked whether cervical cancer affects only females while 9.2% (n = 38) were not sure.

Conclusions
There was generally limited knowledge about cervical cancer and HPV vaccine that requires massive community sensitization to improve on vaccine uptake amongst the targeted population.
e-Posters: Cervical Cancer

ROBOTIC NERVE-SPARING VERSUS LAPAROSCOPIC NERVE-SPARING RADICAL HISTERECTOMY IN EARLY CERVICAL CANCER : URINARY DISEASES

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Objectives
Radical hysterectomy in early cervical cancer less than 2 cm is associated with specific morbidity. Urinary disorders are often noticed and can depend on pelvic plexus nerve injuries. The purpose was to compare surgical and short-term outcomes, as well as urinary disorders between robotic-assisted and laparoscopic nerve sparing radical hysterectomy.

Methods
This is a prospective study realized between 2005 and 2013. We compared 25 cases of robotically assisted nerve-sparing radical hysterectomy for early cervical cancer less than 2 cm, with 45 cases of open-laparoscopy nerve-sparing radical hysterectomy.

Results
The 2 groups were comparable in terms of age, BMI and tumor size.

There was no significant difference with median of blood loss.

Robotic hysterectomy was associated with a shorter hospital stay median (4 vs 5 days, p<0.01). The median operating time was longer in the robotic group but the difference was no significant (290 vs 270 min).

We constated one complication in robotic group with 1500ml of blood loss and no conversion to laparotomy. In laparoscopic group, we notified one conversion and one baldder injury.

Urinary post-operative complications occurred in 2 patients in laparoscopic group with one ureteral fistula and one ureteral stenosis but no in robotic group.

We noticed more post-operative urinary retention (7 vs 2), more patients needed catheterization (7 vs 0) in the laparoscopic group.

Conclusions
Robotic-assisted nerve-sparing radical hysterectomy can be considered as a feasible and safe procedure.

Using the robotic system can help to preserve the autonomic nerve and therefore, can decrease the bladder dysfunction and improve the quality of life of these young patients.
A CASE OF TEENAGE VIRGIN WITH MUCINOUS ADENOCARCINOMA IN UTERINE CERVIX

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Objectives
The prognosis of adenocarcinoma of cervix is poorer than that of squamous carcinoma. The ratio of adenocarcinoma, especially invasive carcinoma in adolescence, increases year by year. We report the case of mucinous adenocarcinoma in teenage virgin.

Results
This case is a 16-years-old Japanese virgin with atypical genital bleeding. She was evaluated with ultrasound and hormonal examination. Without abnormal findings, she was received hemostatics in the other clinic. After six months later, she was transported by ambulance with sudden severe hemorrhage. The patient had a bleeding soft mass of cervix approximately 6cm diameter. The CT scan showed left internal iliac lymphnode swelling. Pap smear showed mucinous adenocarcinoma cells and negative HPV-DNA. In an attempt for FIGOstage?B2, radical hysterectomy with pelvic lymphadenectomy was performed after blood transfusion and embolization. Pathology was read out as mucinous adenocarcinoma with multiple metastasis of left common/internal iliac lymphnodes, CK20(-), CK7/CEA/CA125(+), Muc-2(-)Muc-6(+), MIB-1>90% and tumor emboli. The patient underwent adjuvant chemotherapy with Taxol/CBDCA. She had multiple lung metastasis on CT scan after two months from the six cycles and underwent the second-line with THP/CDDP. She had progression of disease after four cycles, and CPT-11/CDDP was chosen for the third-line. After 4 cycles, she had more progression and therefore further chemotherapy was terminated. She died at 16 months after initial treatment.

Conclusions
HPV infection has been detected in up to 80% of women with adenocarcinoma, similar to squamous carcinoma. Nevertheless gastric-typed mucinous adenocarcinoma with poor prognosis is independent of HPV infection.
CERVICAL CANCER SCREENING IN NIGERIA; A TOOL FOR IMPROVED WELLBEING.
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Objectives
To present the findings of a free cervical cancer screening activity in an oil company in Nigeria.

Methods
A prospective survey of cervical cancer screening (Pap smear) done for 582 women in an oil company in Nigeria as part of the company's routine fitness to work exercise from November 2008 to September 2012.

Results
A total of 582 women have been screened. 21.82% had abnormal results. Of the abnormal results, 41.73% had squamous intraepithelial lesions while 52.76% revealed inflammatory changes. All women with abnormal results were adequately treated. There were no cervical cancer related deaths amongst this cohort of women.

Conclusions
Cervical cancer is the commonest genital malignancy in Nigeria. It is associated with very high mortality. Nigeria has a population of 160 million and access to basic healthcare is a huge challenge. Poor access to healthcare and lack of screening facilities has contributed to the high mortality associated with cervical cancer in Nigeria. The provision of comprehensive Medicare for staff and staff dependants are important engine of growth and development for the region. In this study cervical cancer screening was incorporated into the fitness to work exercise organized once in two years for all staff of an oil company. We conclude that free cervical cancer screening enhances access to health and improves wellbeing. There has been no cervical cancer related deaths since this screening exercise started.
THE ROLE OF USER FEES IN THE UTILIZATION OF CERVICAL CANCER SCREENING SERVICES

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Objectives
To present the correlation between the introduction of user fees and clients utilization of a new cervical cancer screening facility.

Methods
A prospective survey of clinic records at a new cervical cancer screening facility in Port Harcourt, South South Nigeria. Socio-demographic data and total number utilizing the screening facility before and after the introduction of user fees were collated for the months of March and April 2013.

Results
Before the introduction of user fees, in March 2013, 77 clients assessed the new cervical cancer screening facility and had their pap smear done. After the introduction of user fees in April 2013, only 31 clients assessed the cervical cancer screening facility. The sociodemographic characteristics of the clients utilizing the screening facility before and after the introduction of user fees as well as the results of the screening exercise are presented.

Conclusions
The introduction of user fees at the cervical cancer screening facility negatively impacted on clients utilization of the facility.
LOCAL CONTROL IN PATIENTS WITH CERVICAL CANCER TREATED WITH 3D CONFORMAL BRACHYTHERAPY

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Objectives
Treatment options in locally advanced cervical cancer unfit for surgery has evolved with the introduction of brachytherapy (BT). Improvements in BT reflect on treatment results in cervical cancer, reaching 90% 5 year local control rates. Sophisticated techniques like 3D conformal BT are promising better tumor coverage while higher normal tissue sparing. We analysed our results in cervical cancer patients treated with 3D conformal BT (CBT).

Methods
Between January 2008 and May 2011, 55 patients diagnosed with stage IB-IVA cervical cancer have been retrospectively analyzed. 23 patients (%41.8) were stage ≥III. All underwent 50.4 Gy ERT with weekly concurrent cisplatin followed by computed tomography (CT) based 3D CBT consisting of 4 fractions of 7 Gy.

Results
Median follow up period was 25 months (ranged 5 – 61 months). Physical examination and imaging techniques including magnetic resonance imaging (MRI) or positron emission tomography (PET) were performed for each patient after the completion of the treatment. 2 year local control rate was 84.8%. On multivariate analysis, tumor size >5cm, age ≤40 and initial SUVmax values ≥15.6 showed significantly lower local control.

Conclusions
3D CBT is an effective option for local control of cervical cancer. Our results are comparable with the literature. Patients with bulky tumors and high SUVmax values at presentation fare worse in terms of local control. Further studies are necessary to evaluate recurrence patterns and dose escalation.
e-Posters: Cervical Cancer

TOXICITY RESULTS IN PATIENTS WITH CERVICAL CANCER TREATED WITH 3D CONFORMAL BRACHYTHERAPY

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Objectives
Improvements in brachytherapy (BT) reflect on treatment results in cervical cancer. The importance of treatment related toxicity is emerging. 3D conformal BT (CBT) techniques are promising better tumor coverage while higher normal tissue sparing. We analysed our gastrointestinal (GI) toxicity results in patients treated with 3D CBT.

Methods
Between January 2008 and May 2011, 55 patients diagnosed with stage IB-IVA cervical cancer have been retrospectively analyzed. All underwent 50.4 Gy ERT with weekly concurrent cisplatin followed by computed tomography (CT) based 3D CBT consisting of 4 fractions of 7 Gy. At least 95% of CTV received 100% of prescribed dose.

Results
Median follow up period was 24 months (5-60). Physical examination and imaging were performed for each patient after the completion of treatment. GI toxicity was evaluated according to the RTOG CTCAE v3.0. Genitourinary toxicity could not be evaluated due to the low number of events (2 grade 3, 1 grade 4). Grade ≥3 GI toxicity was seen in 11 (1 grade 3, 10 grade 4) patients (20%). On multivariate analysis, CTV, RD1 and RD2 (minimum doses of 1cc and 2cc of rectum) were statistically significant for grade ≥3 GI toxicity.

Conclusions
Our 3D CBT toxicity results are comparable with the literature. The effect of “learning curve” as well as lack of magnetic resonance imaging (MRI) based BT planning explains the toxicity rates.
MULLERIAN ADENOSARCOMA (PRIMER UNKNOWN; UTERUS OR CERVIX) WITH SARCOMATOUS OVERGROWTH: A CASE REPORT

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Objectives
Mullerian adenosarcoma (MA) which is a rare malignant neoplasm of the uterus and an aggressive variant of MA with sarcomatous overgrowth (MASO) is extremely rare.

Methods
We report the case of a 33-year-old woman referred to our department with abdominal mass. The patient underwent laparotomy and frozen investigation after clinical examination. Frozen examination revealed malignancy and staging surgery was also performed. On the pathological examination; tumor kept all cervical and endometrial tissues and the primary localization was not established. The tumor was composed of benign epithelial and malignant stromal components. The malignant stromal component was consisted of high-grade stromal endometrial stromal sarcoma, leiomyosarcoma, rhabdomyosarcoma, and chondrosarcoma. All of the cervical and endometrial tissue was kept and fullest extent of the myometrium was invaded until the serosa by the tumor. Surgical treatment was associated with adjuvant whole-pelvis radiation (45 Gy) and adjuvant chemotherapy (cisplatin/ifosfamide).

Results
MA which usually has low malignant potential is a rare malignant tumor of the uterus. MASO is separated from MA due to the having malignant behavior. The management of patient with MASO is similar with uterine sarcoma. Adjuvant radiotherapy can be successful with pelvic control and decrease the local recurrence of the tumor. The results of adjuvant chemotherapy are unclear.

Conclusions
The insufficient number of patients causes to lead to difficulty in finding the most appropriate treatment for MASO and attentive pathological investigation is necessary for the variety of the prognosis and treatment options of MA and MASO.
e-Posters: Cervical Cancer

OVARIAN ACTINOMYCOSIS ASSOCIATED WITH HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION

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Objectives
Pelvic actinomycosis is uncommon accounting for %3 of all human actinomycotic infections. It is well known that intrauterine device use is a risk factor for genital actinomycosis. Non-specific symptoms and sneaky progression make the diagnosis challenging. Ovarian actinomycosis is rarer because the structure of an ovary is resistant to surrounding inflammatory disease. Formation of a solid mass in the nature of disease gives the impression of gynecological malignancies.

Methods
A 48 years old women was admitted to hospital with lower abdominal pain. Transvaginal ultrasonography revealed a nodular mass 6 cm in diameter in left adnexial region.

Results
Laboratory findings demonstrated marked leukocytosis (WBC: 20400/mm³) and elevated C-reactive protein concentration. (176mg/dl) The patient had been an IUD user for 5 years. During pre-operative preparation HGSIL was detected in her Pap smear. Combined antibiotic treatment was started and conisation was performed. The pathology revealed margin positive HGSIL. Control USG revealed normal ultrasonographic findings. In the hysterectomy that performed secondary to her conisation showed dense adhesions in the left adnexial region with no abscess formation. Adhesions were also present between the intestines in the pelvic wall.

Conclusions
Actinomycosis is a insidious infection that diagnosis can be difficult preoperatively. It has been reported pelvic actinomycosis mimicking ovarian and cervical carcinomas. HGSIL+ pelvic mass in this case makes the diagnosis more challenging. Resolution of mass with antibiotic treatment during conization gives us important information that on contrary to well known antibiotic treatment only can be adequate in some cases and clarify the diagnosis.
THE INFLUENCE OF NUMBER OF HIGH RISK FACTORS ON CLINICAL OUTCOMES IN PATIENTS WITH EARLY-STAGE CERVICAL CANCER AFTER RADICAL HYSTERECTOMY

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Objectives
To evaluate the prognosis according to the number of high risk factor in patients with high risk factors after radical hysterectomy for early stage cervical cancer

Methods
Patients with early-stage cervical cancer who had high risk factors after radical hysterectomy were retrospectively analyzed.

Results
135 out of 404 patients had more than one high risk factor. 82 out of 135 (60.8%) had single high risk factor, 40 (29.6%) had two high risk factors, and 13 (9.6%) had all three high risk factors. The probability of cancer recurrence and death were higher according to the number of high risk factors. Non-SCC histology, corpus involvement, vaginal involvement, parametrial involvement and ≥2 risk factors were associated with recurrence-free survival (RFS) and non-SCC histology, corpus involvement, and ≥2 risk factors were associated with overall survival (OS) in univariate analysis. Multivariate analysis showed non-SCC histology and ≥2 high risk factors were associated with RFS (p<0.05). Relative to the single risk group, the probability of cancer recurrence was significantly higher in the multiple risk group (OR=4.329, 95%CI=2.127-8.808, p<0.001). The probability of cancer death was also significantly higher in the multiple risk group (OR=3.586, 95%CI=1.075-11.956, p=0.038).

Conclusions
Patients with ≥2 high risk factors had more poor prognosis and clinical outcomes in early stage cervical cancer. For patients with ≥2 high risk factors, it may be worthwhile to consider new strategies to improve survival.
e-Posters: Cervical Cancer

PREVALENCE OF HUMAN PAPILLOMAVIRUS INFECTIONS IN CERVICAL AND BLOOD SAMPLES OF PREGNANT AND NON-PREGNANT WOMEN IN A DEVELOPING COUNTRY

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Objectives
Some studies suggest that the physiological process of pregnancy changes the behavior of HPV. However, the results regarding the prevalence of HPV during pregnancy are conflicting. The objective was to investigate the presence of Human papillomavirus (HPV) in cervical samples and in blood samples of pregnant and non-pregnant women from South-Brazil by polymerase chain reaction (PCR).

Methods
Ninety-one pregnant and ninety-two non-pregnant women were prospectively enrolled in the study. They were initially interviewed and submitted to cytopathological exam and colposcopy. In addition, blood and cervical samples were collected in each trimester and in the puerperium. All samples were analyzed through PCR with consensus primers GP5+/GP6+. Genotyping was performed using specific primers.

Results
HPV DNA was detected in 23/91 (25.3%) cervical samples from the pregnant women and in 12/92 (13%) cervical samples from non-pregnant women (P=0.035). There was a significant association among cervical HPV infection and young age, number of sexual partners in lifetime and the presence of abnormal cervical cytology. HPV16 and HPV18 were the viral types more frequently detected. Out of the 23 HPV-positive pregnant women, 17 (73.9%) had normal cervical cytology. No HPV DNA was detected in blood samples.

Conclusions
There is a significant higher prevalence of HPV infection during pregnancy. This finding might be related to the relative immunosuppression observed in pregnant women, outlining the importance of the early diagnosis of the viral infection in this specific population.
e-Posters: Cervical Cancer

IMPROVED CONTROL OF CERVICAL CANCER WITH RT+CT AND HDR BRACHYTHERAPY

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Objectives
To assess the efficacy radio-chemotherapy (RT+CT) and high-dose-rate brachytherapy (HDR-BT) in cervical carcinoma stage IIB-IIIIB.

Methods
Between January-02 and August-09, 61 patients with cervical carcinoma (55 squamous-cell), 46 stage IIB and 15 IIIB, were treated. The median age was 55 years (29-87). Radiotherapy was given to pelvis (50Gy) and paraaortic areas (45Gy) if pelvic lymph nodes were involved. Concomitant cisplatin 40mg/m2 was associated weekly. 4-5 HDR-BT applications were performed twice a week subsequently, giving 5.5-6.5 Gy to points A or target volume to achieve an equivalent dose of 85-90 Gy.

Results
With 60 months of median follow-up (4-111), there were 8 local recurrences. Actuarial local-regional control (LRC) at 5 years was 88.3% in stage IIB and 74.6% in IIIB. There were 10 relapses in para-aortic area, never after RT. The cause-specific survival at 5 years (CSS) was 81.3% in stage IIB, but 57.4% in stage IIIB (p <0.04), due to the incidence of distant metastases, with metastasis-free survival in stage IIB 88.1% vs. 46% in stage IIIB. Compared with a previous study in 68 patients treated with LDR without chemotherapy, the LRC was 60% in both stages, and the SSC was 54% and 59% respectively. The rate of complications with HDR-BT was 9.8% G3 and 4.9% G4.

Conclusions
The RT+CT and HDR-BT have improved LRC in stage IIB-IIIB cervical cancer, and SSC in stage IIB. Stages IIIB need a systemic treatment to decrease the rate of distant metastases. The para-aortic RT improves SSC when pelvic lymph nodes are involved.
HISTOPATHOLOGICAL PROGNOSTIC FACTORS IN STAGE IA-IIA CERVICAL CANCER SURGICALLY TREATED: A RETROSPECTIVE STUDY WITH FIVE YEARS FOLLOW UP.

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Objectives
The aim of the study is to determine the histopathological prognostic factors and treatment outcomes for surgically early stage cervical cancer.

Methods
Retrospective study of patients with consecutive FIGO stage IA1 - IIA cervical cancer with surgical treatment between 2001 – 2007, Hospital Sótero del Rio Santiago de Chile. The Kaplan-Meier and multiple regression analysis method was used to determine overall survival.

Results
There were 141 eligible patients, mean age 48 (range 25 – 78). For stage IA2 to IIA a radical hysterectomy and pelvic lymphadenectomy was performed. The histological type were squamous cell carcinoma 123 (86%), adenocarcinoma 22(16%), adenosquamous 2, others 4. According to FIGO stage there were 15 patients for stage IA1, IA2:5, IB1: 96, IB2: 18, IIA: 7. No significant difference was found in survival when the analysis of histological factors such as histological type, tumor grade, tumor size, depth invasion, lymphovascular space invasion and surgical margin were evaluated. The only prognostic factor was the presence of lymph node metastases (p =0.0056). The 5 year overall survival was 100% for stage IA1 and IA2, 85% IB1, 80% IB2 and 83% for IIA. There were 35 patients with adjuvant radiotherapy 23% of IB1, 61% IB2 and 29% for IIA. Only one patient had positive para aortic lymph node.

Conclusions
The most prevalent prognostic factors were the presence of lymph node involvement. Our survival data is similar to internationals publications.
SORTING AND IDENTIFICATION OF SIDE POPULATION CELLS IN THE HUMAN CERVICAL CANCER CELL LINE HELA

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**Objectives**
Studies have demonstrated that side population (SP) cells isolated from diverse cancer lines harbor cancer stem-like properties, but there are few reports examining the role of SP cells in human cervical cancer. The aim of this study is to detect properties of the SP cells from Hela cells.

**Methods**
Isolated SP and non-SP cells from Hela cell lines by Hoechst33342 dying method. Observing morphology of SP and non-SP cells. The expression of various biomarkers of cancer stem cells were investigated by immucytotoxicity of sorted cells. We also analyzed cell cycle and cell apoptosis for sorted cells. The oncogenicity of the SP and non-SP cells were analyzed by tumor formation in NOD/SCID mice. The drug-resistant and radiation-resistant index between SP, non-SP and Hela cells was estimated.

**Results**
The fraction of SP cells in Hela cell was 1.07±0.32%. SP cells were smaller and rounder in sharp than non-SP cells. Immunocytochemistry showed that stem cell markers (Oct3/4, CD133, and BCRP) were highly expressed in SP cells. Moreover, the number of apoptotic cells among non-SP cells (17.6±3.7%) was higher compared with SP cells (4.4±1.2%). There no significant differences between SP and non-SP cells in NOD/SCID mice tumorigenicity. But the HE staining of tumor result from SP cells showed more poor differentiation. SP cells demonstrated a higher degree of drug resistance against trichostatin A (TSA) compared with non-SP Hela cells. SP cells were also found to be more resistant against radiotherapy.

**Conclusions**
SP cells possess the characteristics of CSCs, namely high proliferation ability, chemoresistance and radioresistance, which may be helpful to elucidate novel target for clinical treatments of cervical cancer.
PTEN INHIBITS PROLIFERATION OF CERVICAL CANCER CELLS BY AKT MEDIATED CELL METABOLISM

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Objectives
To explore the relationship between PTEN and cell proliferation in cervical cancer cells, and further analyze the role of PTEN and underlying mechanisms in cervical cancer cells

Methods
The expression of PTEN was detected in different kinds of cervical cancer cell lines by western blotting. Then the overexpression vector of PTEN was constructed and transfected into cervical cancer cells. The proliferative index was estimated by cell counting and MTT. The contents of glucose, glutamine and lactic acid was detected by the BioProfile FLEX analyzer to evaluate the effect of PTEN on the cell metabolism. The proteins related to cell metabolism were measured by western blotting.

Results
PTEN was down-regulated in cervical cancer cell lines relative to normal cervical epithelium cells. The overexpressing PTEN vector was transfected into HeLa and C-33 A cells, resulting in the up-regulation of PTEN. Enforced expression of PTEN inhibits the proliferation of cervical cancer cells confirmed by cell counting and MTT (P<0.05). We also found that glucose and glutamine in extracellular were increased, but lactic acid was decreased. Moreover, PTEN suppressed the expression of pAKT, PFKFB3?PKM2 and GLS in these cells.

Conclusions
PTEN inhibits proliferation of cervical cancer cells by AKT mediated cell metabolism, providing new insight into novel molecular target for diagnosis and therapy.
e-Posters: Cervical Cancer

EXPRESSION OF CANCEROUS INHIBITOR OF PP2A IN HUMAN CERVICAL CARCINOGENESIS

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Objectives

CIP2A is an endogenous inhibitor of PP2A with oncogenic activity. In this study, we aimed to investigate the role of CIP2A in cervical carcinogenesis.

Methods

In the present study, immunochemistry and western blot analysis were performed to examine the expression of CIP2A and CDC42 in cervical cancer tissues and cell lines. The proliferation and tumorigenicity were determined by cell counts, colony formation, tumorsphere formation, and xenograft assay. Pull-Down and mass spectra assay were used to analyze the endogenous interacting proteins with CIP2A.

Results

Expression of CIP2A was observed in a significantly higher frequency in high-grade squamous intraepithelial lesions (HSIL) and cervical cancers compared with normal cervixes. Particularly, CIP2A staining was associated with the progression of cervical cancer. In addition, CIP2A was abundant expressed in HeLa, SiHa, C33A, Caski and HT-3 cell lines. Silencing CIP2A deduced the tumorsphere formation ability in vitro and tumorigenicity in vivo. Flag-HA-CIP2A overexpression system was established in HeLa cells and the Pull-Down purifications were undergone with mass spectra assay. CDC42 was selected as a potential CIP2A binding protein and IHC showed their expressions were in a positive correlation in cervical tissues. Otherwise, datasets analysis showed CIP2A and CDC42 were correlated with survival of patients suffered with cancers.

Conclusions

These results suggested that CIP2A participated in cervical carcinogenesis and CIP2A and CDC42 may be potential prognosis markers for cancers.
EXPRESSION OF HIWI IN HUMAN CERVICAL CARCINOGENESIS
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Objectives
HIWI, also named PIWIL1, is a human homologue of the PIWI family which related in stem cells and overexpressed in several cancers. In this study, we aimed to investigate the role of HIWI in cervical carcinogenesis.

Methods
In the present study, immunochemistry and western blot analysis were performed to examine the expression of HIWI in cervical cancer tissues and cell lines. The proliferation and tumorigenicity were determined by cell counts, colony formation, tumorsphere formation, xenograft assay and cell cycle analysis. The chemoresistance ability of fluorouracil (5-FU) and cisplatin (DDP) was determined by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay.

Results
Compared with normal cervixes, a significantly higher frequency of HIWI staining was observed in high-grade squamous intraepithelial lesions (HSIL) and cervical cancers. Particularly, HIWI staining was restricted in basal cells of normal cervix and associated with the progression of cervical cancer and chemical resistance. In addition, HIWI was promoted the proliferation, clonogenicity, tumorsphere formation in vitro and tumorigenicity in vivo than control when overexpressed in C33A, while silenced in HeLa, it decreased these abilities related to the stemness. Otherwise, ectopic HIWI increased the chemical resistance in C33A and silencing HIWI in HeLa decreased the viability.

Conclusions
These results suggested that HIWI may participate in carcinogenesis of cervical cancers and may be a potential therapeutic target molecule for cervical cancers.
e-Posters: Cervical Cancer

EPHB2 PROMOTES CERVICAL CANCER PROGRESSION BY INDUCING EPITHELIAL-MESENCHYMAL TRANSITION

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Objectives
To investigate the expression and functions of EphB2 in cervical cancer.

Methods
In this study, we performed immunohistochemistry/immunocytochemistry in clinical cervical specimens and cervical cancer cell lines. Western-blotting and real time PCR were used to analyze the expression of EphB2 in different cervical cancer cell lines. Then, EphB2 was overexpressed in HeLa cells and silenced in C33 A. The invasion and migration abilities of cells were determined by transwell assay. Then the expression of epithelial and mesenchymal related markers such as E-cadherin, Fibronectin and Vimentin were measured by immunocytochemistry, western blotting and Real time PCR. Tumorsphere-formation assay and tumor xenotransplantation were employed to test the function of EphB2 to induce stem cell phenotypes. R-Ras activation was detected by immunoprecipitation.

Results
We found that EphB2 was abnormally overexpressed in cervical cancer and correlated with the cancer progression, and found that exogenous EphB2 promoted cell migration, invasion and an epithelial–mesenchymal transition (EMT) signature, while silencing EphB2 led to opposite results. Furthermore, HeLa cells with exogenous EphB2 exhibited a stem cell state that promoted the tumorsphere formation ability in vitro and tumorigenesis potential in vivo, and C33 A cells with EphB2 silencing inhibited the stem properties. In addition, we investigated the intracellular signaling pathways in cervical cancers and found that R-Ras expression was positively correlated with EphB2 in clinical samples and its activity was regulated by EphB2 in cervical cancers.

Conclusions
These findings define an important function for EpbB2 in the progression of cervical cancer by orchestrating an EMT program through activating R-Ras.
e-Posters: Cervical Cancer

THE SIGNIFICANCE OF LA PROTEIN EXPRESSION IN CERVICAL CANCER TISSUE

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Objectives
To investigate the expression of La protein in cervical cancer tissue and to investigate its role in the initiation and progression of cervical cancer.

Methods
The expression of La protein in cervical cancer and normal cervix were detected by immunohistochemical staining. Using RNAi technology to silence the La protein in Hela cell, a cell line of cervical cancer, then screen by G418, finally the stable expressed Hela-shLa cell line was constructed and the cell proliferation assay and tumorsphere formation assay were performed.

Results
The expression of La protein in cervical cancer tissue was significantly higher than those in normal cervical tissue (p<0.05), however, after La protein expression was silenced by RNAi, the capability of proliferation and tumorsphere formation were decreased significantly compared to the control (p<0.05).

Conclusions
RNA binding protein La promote the formation of cervical cancer, and maybe play a critical role in carcinogenesis and progress of cervical cancer.
CHEMORADIATION WITH CONCOMITANT BOOST FOLLOWED BY RADICAL HYSTERECTOMY IN BULKY STAGE IB2,IIA2 AND IIB CERVICAL CANCERS

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Objectives
To assess the pathologic response rates of bulky cervical cancers treated with chemoradiation with concomitant boost followed by radical hysterectomy

Methods
Between January 2012 and October 2012, 30 patients with bulky cervical cancers were treated with concomitant boost irradiation 180cGy/22# to whole pelvis and 90cGy thrice weekly boost to primary to a total dose of 50.4gy along with weekly cisplatin 40mg/sq.m. Patients were taken up for radical hysterectomy 6 weeks after completion of chemoradiation.

Results
Majority (63%) of patients had stage IIB disease, 30% had stage IB2 and 7% had stage IIA2 disease. Gastrointestinal toxicity was the most common toxicity observed. All 30 patients underwent radical hysterectomy and were available for final evaluation of pathologic response. Totally 22 patients in the study attained complete response (73.3% of the total patients in the arm). 6 patients had gross residual disease in the cervix. 2 patients had lymph node positivity [microscopic partial response].

Conclusions
Despite the significant improvement achieved with the combination of chemotherapy and radiation in locally advanced cervical cancers, the therapeutic results are far from optimal. The main objective of delivering a neoadjuvant treatment with concomitant boost is to increase the pathologic response rates which has been shown to be of prognostic significance in several studies. The pathologic complete response rates obtained with the above treatment modality are really encouraging. However the prognostic significance of the pathologic response rates needs to be evaluated during further follow up.
e-Posters: Cervical Cancer

CERVICAL LEIOMYOSARCOMA: A CASE REPORT
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Objectives
Cervical leiomyosarcoma are exceedingly rare neoplasms associated with a poor prognosis and very difficult management. The objective of this case report was to show the alternative surgical treatment.

Methods
50 years old, obese - 41 Body Mass Index, patient, presenting vaginal bleeding requiring blood transfusion and bulky cervical mass. The preoperative biopsy revealed atypical mesenchymal neoplasia. The Magnetic Resonance Image showed a 9.0 cm cervical mass without lymphnode involvement or ascitis.

Results
Due to high, surgical and anaesthesic, risk, we performed an extensive vascular embolization followed of the conization without cervical vessels clamp. After the cervical mass excision, an abdominal hysterectomy with adnexectomy was carried out. The patient was discharged in the first postoperative day and no, early or late, complications were observed. The histopathological and immunohistochemical analysis revealed a leiomyosarcoma with very low mitosis rates and both, parametrial and cervical, free margins. No adjuvant therapy was performed and patient is asymptomatic without any evidence of tumour recurrence after 03 months of follow-up.

Conclusions
Leiomyosarcoma of uterine cervix is one of the rarest of the cervical sarcomas. The still cornerstone of this disease treatment is the surgery. Unfortunately, this disease, that commonly presenting as a very large cervical mass, provide high number of surgical complications by thecnical difficulties due a poor lateral
access to perform a hysterectomy. While the optimal management of these
tumors is uncertain and the aggressive primary surgery could promote a high
rate of complications, we described an alternative schedule to avoid it.
e-Posters: Cervical Cancer

HIGH RISK HPV, REASON OF SCREENING AND PROGRESSION.
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Objectives
To evaluate the progression of HR-HPV to precancer lesions (L-SIL, H-SIL) depending on the reason of testing HPV: inadequate screening, ASC-US, previous positive HPV, after conization, and other reasons (HIV-positive, genital warts-low risk coinfection and promiscuous women).
Inadequate screening: women over 40 years old not screened within the past five years.

Methods
HR-HPV DNA testing using hybrid capture II system (genotypes 16,18,31,33,35,39,45,51,52,56,58,59 and 68) to all candidates patients period October 2006-October 2011 in the gynecology outpatient public health department in the city of Hospitalet de Llobregat (Barcelona).

We evaluated the progression to precursor lesions of cervical cancer by cytology or colposcopy and biopsy during the 18 months following the realization of the HPV test.

Prospective, descriptive study about the positive cases in the following 18 months after HPV testing.

We introduce the results in a computer database.

Results
View graphs

Conclusions
The progression to precancer lesions is lower in inadequate screened patients and after conization.

In previous positive HPV and ASC-US 40% of the women will progress.

The progression to pre-cancer lesions is much higher in HIV positives patients, genital warts-low risk virus coinfection or promiscuous women.

The progression to pre-cancer lesions in HR-HPV positives patients depends on the screening reason.
**CRITICAL VIEW ON NEOADJUVANT CHEMOTHERAPY FOLLOWED BY FERTILITY-SPARING SURGERY. EXPERIENCES WITH 25 PATIENTS**

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**Objectives**  
25 women with early stage cervical cancer that do not fulfill standard criteria for fertility-sparing surgery (tumor more than 2 cm in the biggest diameter or infiltrating more than half of stroma) were included into study. All women had strong desire of pregnancy.

**Methods**  
All patients received three cycles of dose-density neoadjuvant chemotherapy (NAC) at a 10-day interval: cisplatin plus ifosfamide in squamous cell cancer or plus doxorubicin in adenocarcinoma. No cycle of chemotherapy was postponed for toxicity. Patients underwent laparoscopic pelvic lymphadenectomy and vaginal simple trachelectomy after NAC. Sentinel lymph node (SLN) mapping was performed in all cases.

**Results**  
Six patients had no residual tumor, 8 had only microscopic residual disease and 11 had macroscopic residual disease. Seven women lost fertility. Ten women wanted to be pregnant, 8 of them became pregnant (1 miscarriage in 1st trimester, 1 in 2nd trimester). Six women delivered 8 babies (two premature-24th and 34th week and six term deliveries). Three women had recurrence (two local and one distant). Radical hysterectomy was recommended to one them after trachelectomy, she didn't agree. One of them is after radical hysterectomy without evidence of disease, two died of disease (recurrence rate was 16.7%, mortality was 11.1%).

**Conclusions**  
NAC followed by fertility-sparing surgery could be treatment for women with tumor bigger than 2 cm or infiltrated more than half of stroma. Response for NAC and extension of residual disease is important. Based on these results would be necessary to reevaluate inclusion criteria for NAC followed by fertility-sparing surgery. This work is supported by grant MZCR-NT-13166
e-Posters: Cervical Cancer

PREGNANCY OUTCOME AFTER COLD-KNIFE CONIZATION AND MODIFIED PLASTIC PROCEDURE

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Objectives
To assess the pregnancy outcome after cold-knife conization and reconstructive procedures on the remaining uterine cervix.

Methods
A retrospective five years study has been performed. All patients having a birth after having had a conization in our service were included in the study. For each patient several aspects were followed: age, parity, gestational weeks at delivery, delivery route and also newborn parameters (weight, length, Apgar score). The data were analyzed using Microsoft Excel software.

Results
All patients have delivered at term, no premature ruptured of membranes or preterm labor being signaled in the study population.

Conclusions
The pregnancy outcome seems not to be affected in our group, but further studies are needed.
e-Posters: Cervical Cancer

12-YEAR EXPERIENCE IN LAPAROSCOPIC RADICAL HYSTERECTOMY WITH PELVIC LYMPHADENECTOMY FOR EARLY-STAGE CERVICAL CANCER IN HIGH-INCIDENCE COUNTRY.
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Objectives
To evaluate operative and oncologic outcomes of laparoscopic radical hysterectomy with pelvic lymphadenectomy in patients with early-stage cervical cancer.

Methods
Retrospective cohort study, reviewed from hospital records of early-stage cervical cancer patients who had intended to underwent laparoscopic hysterectomy with pelvic node dissection (LRHND) during 12-year period in Siriraj Hospital, Mahidol University, Thailand.

Results
All 52 patients, the mean age was 46.6 years and the mean body mass index was 23.6 kg/m². Seven patients had stage IA2, 44 patients had stage IB1, and one patient had stage IB2 of cervical cancer. Laparoscopic radical hysterectomy with pelvic lymphadenectomy were underwent in 50 patients. Two patients were abandoned hysterectomy. The mean tumor size was 1.46 cm. The mean operative time of 50 LRHND was 313.8±85.6 minutes (median 300 and range 195-607 minutes) and the mean blood loss was 363.6±324.1 mL (median 200 and range 50-1,300 mL). The mean of pelvic node number was 20.8±12.7 and 17.5 nodes. Overall of 52 patients achieved complete response. The median length of follow-up period was 19.6 months (range 0-78 months). Three patients had tumor recurrences, 1 had vaginal stump mass, 1 had carcinomatosis peritonei, and 1 had neck node metastasis.

Conclusions
Laparoscopic radical hysterectomy for primary treatment in early-stage cervical cancer patients delivered favorable surgical and oncologic outcomes.
LONG TERM OUTCOMES OF LOOP ELECTROSURGICAL EXCISION PROCEDURE FOR CERVICAL NEOPLASIA IN A HIGH-INCIDENCE COUNTRY.

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Objectives
To evaluate operative, oncologic and obstetrics outcomes of loop electrosurgical excision procedure (LEEP) in patients with cervical neoplasia.

Methods
Retrospective cohort study, reviewed from hospital records of patients who had underwent LEEP during 6-year period in Siriraj Hospital, Mahidol University, Thailand.

Results
All 407 patients, the mean age was 39.7±10.5 years. 61.4% of patient were multiparity. The three most common abnormal cytology were 69.5% of high-grade squamous intraepithelial neoplasia (HSIL), 16.5% of squamous cell carcinoma (SCCA) and 8.8% of low-grade squamous intraepithelial neoplasia (LSIL), respectively. Operative complications found in 70 patients (17.2%); 63 patients had bleeding, 7 patients had infection and 1 patient had cervical stenosis. 260 patients (63.9%) had free margin of conization specimens. LEEP pathology showed that 89 patients (21.9%) had lesion ≤ cervical intraepithelial neoplasia (CIN) I, 295 patients (72.4%) had CIN II or III, and 23 patients (5.6%) had invasive cervical lesions. After diagnostic LEEP, 133 patients had underwent hysterectomy. Overall of 407 patients achieved initial complete response with the median length of follow-up period was 36 months. For 274 patients who had LEEP only, 7 patients (2.5%) had recurrences, 1 patients had CIN I, 1 patients had CIN II, and 5 patients had CIN III. All of these recurrent patients achieved remission by surgical treatment, which are 6 patients had underwent re-LEEP, and 1 patient had simple hysterectomy. Twelve patients had pregnancy; 12 term pregnancy and 2 abortion.

Conclusions
LEEP for patients with cervical neoplasia delivered favorable surgical, oncologic and obstetrics outcomes.
e-Posters: Cervical Cancer

CLINICAL EVALUATION OF EARLY CERVICAL ADENOCARCINOMA AND ADENOSQUAMOUS CELL CARCINOMA TREATED BY RADICAL SURGERY. WHICH AS ADJUVANT THERAPY SHOULD BE SELECTED AFTER RADICAL SURGERY?

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Objectives
At present, concurrent chemoradiation therapy (CCRT) is the gold standard as adjuvant therapy for high-risk patients after radical hysterectomy (RH). According to JGOG 1069, non-SCC is distinguished from SCC in 70% of institutions, and paclitaxel plus carboplatin is selected as adjuvant chemotherapy. This approach to non-SCC is unique to Japan. Our aim was that to evaluate adjuvant therapy for SCC and non-SCC after RH.

Methods
362 patients (SCC: 251, adenocarcinoma (AD): 95, adenosquamous cell carcinoma (ADSCC): 16, except neoadjuvant CT and RT) in stage I-II underwent RH and were enrolled in this study.

Results
The following prognostic factors were identified.

We further analysed patients with stage II disease or tumor size >30 mm or lymph node metastasis (pN1) because OS for was 100% for stage I, tumor size <30 mm and no lymph node metastasis (pN0).

Histological type was not associated with OS. In non-SCC patients with stage II disease or tumor size >30 mm or lymph node metastasis (pN1), operation (O) and operation plus chemotherapy (OC) were associated with OS (p=0.011). In the operation plus radiation therapy (OR) group, the prognosis was rather poor.

Conclusions
We suggest that the combination of adjuvant chemotherapy and RH is very useful for early non-SCC. Choosing more effective chemotherapy will need further consideration in the future.
RADICAL SURGERY WITH RESECTION OF THE LOWER URINARY TRACT IN THE SURGICAL MANAGEMENT OF LOCALLY ADVANCED CERVICAL CANCER

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Objectives
The purpose of this study is to evaluate the benefits of radical surgery involving resection of the lower urinary tract for patients with locally advanced cervical cancer.

Methods
A retro- and prospective study for a period of 20 years (1993 – 2012) enrolled 46 patients with stage II B-IV A cervical cancer who underwent radical surgery with resection of the lower urinary tract: radical hysterectomy - 35, colpoparametrectomy - 3, radical hysterectomy with total colpectomy - 2, laterally extended parametrectomy - 5, laterally extended endopelvic resection – 1. Those procedures were combined with resecion of the distal ureter in 31 cases, bladder wall alone in 4, the distal ureter and hemitrigone in 11, both ureters and trigone - 3.

Results
The final stage to stage distribution after surgery was: IB-10, IIA-2, IIB-2, IIIB-14, IVA-17. Metastases to pelvic lymph nodes were present in 28 (60,8%) and paraaortic in 15 (32,6%) patients. Standard urinary tract reconstruction (in 42 cases) or with ileum interposition (in 4) achieved acceptable functional results in all patients. 4 early vesicovaginal and 1 ureterovaginal fistulae were repaired successfully 6 to 8 weeks after initial surgery. There was 1 early death due to thrombotic complications. All patients underwent radiotherapy to pelvic and paraaortic area according to the tumor spread. Overall survival for stages IIIB and IVA was 57% and 33% respectively.

Conclusions
The study seems to give credit towards an attitude for initial maximal surgical effort before radiotherapy for locally advanced cervical cancer.
Clinical Outcome of Patients with Microinvasive Adenocarcinoma of the Uterine Cervix

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Objectives
The objective of this analysis was to present the clinical outcome of patients with microinvasive adenocarcinoma (AC) of the uterine cervix treated at the Department of Obstetrics and Gynecology between 1999 and 2010.

Methods
We analysed 125 patients with microinvasive AC. The analysis involved the following parameters: women's age at operation, type of operation, number of positive lymph nodes and patient's survival. Additionally, a questionnaire about history and symptoms before diagnosis and about follow-up after operation was developed and analysed specifically for this study.

Results
The mean women's age at operation was 40.58 ± 9.58 years. In 70 women (56 %) the performed treatment was conisation, 34 women (27.2 %) had simple hysterectomy and 24 (19.2 %) had radical hysterectomy. In 14 (11.2 %) women the margins of the cone were not disease-free, in 9 of them we later performed radical hysterectomy. From 14 women who became pregnant after treatment 13 (16.9 %) gave birth. One of the 125 patients diagnosed with microinvasive AC died, the cause of death was rectal carcinoma.

Conclusions
We may conclude that conservative management of patients with microinvasive AC is safe when exact evaluation of tumor extension and surgical margins of the cone are considered, and results in very low risk of recurrence, lymph node disease, and death caused by cancer.
e-Posters: Cervical Cancer

ANTI-CANCER EFFECT OF BEE VENOM TOXIN AND MELITTIN IN UTERINE CERVICAL CANCER CELLS
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Objectives
We studied whether bee venom inhibits cancer cell growth through enhancement of death receptor expressions in the human cervical cancer cells, CaSki and C33A.

Methods
Apoptosis and activity of NF-kB in vitro were analyzed.

Results
Bee venom inhibited the growth of CaSki and C33A cervical cancer cells by the induction of apoptotic cell death in a dose dependent manner, but apoptosis was more induced in CaSki cells than in C33A cells. Expression of DR3 and DR4 was increased in both cells, but expression of them in CaSki was more increased than C33A. Expression of DR downstream pro-apoptotic proteins including caspase-3 and Bax was concomitantly increased, but NF-kB activity and the expression of Bcl-2 were inhibited by treatment with bee venom in CaSki and C33A cells. However the effects were more significant in CaSki cells. Combination treatment of expression of TWEAK and TRAIL (a ligand of DR3 and DR4) and bee venom synergistically inhibited the cervical cell growth with further down regulation of NF-kB expression. Moreover, deletion of DR3 and DR4 by small interfering RNA significantly reversed bee venom induced cell growth inhibitory effects as well as NF-kB inactivation.

Conclusions
Bee venom induces apoptotic cell death in cervical cancer cells through enhancement of DR3 and DR4 expression and inhibition of NF-kB pathway, however, the sensitivity of bee venom is different by the status of p53 in the cervical cancer cells. These results suggested that it may be applicable as an anti-cancer agent for cervical cancer, especially p53 wild type cancer.
ROLE OF COX-2 AS A PROGNOSTIC FACTOR IN CARCINOMA CERVIX

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Objectives
Cyclooxygenase-2 (Cox 2) expression has been extensively studied and has emerged as a prognostic and predictive factor in various malignancies such as rectum, breast, ovaries, cervix etc. Cancer cervix still being the most common malignancy amongst females in the developing countries needs a strong biomarker to identify patients with adverse outcome. We felt a need to test Cox-2 expression in the proven cases of carcinoma cervix as a prognostic factor in a prospective trial having large sample size as most of the published articles are retrospective in nature and had small number of patients.

Methods
Tissue from 323 histopathologically proven cases of carcinoma cervix were analyzed for Cox-2 expression. Tissue from the cervical growth was immediately cooled to -80 degree Celsius. Assessment of Cox-2 expression was done using Western Blot technique. Patients were then subjected to definitive treatment in the form of Radiotherapy with or without concurrent chemotherapy.

Results
There was no co-relation between Cox-2 expression levels and various known prognostic factors such as age, stage, histopathological differentiation etc (Table: 1). Also there was no correlation of Cox-2 expression with the clinical outcome of the patients (Table: 2).

Conclusions
In the present study we intended to evaluate the expression of COX-2 keeping track of the correlation between the clinicopathologic factors Patients survival and prognosis. We could not find any significant correlation between Cox 2 expression and any of the clinico-pathologic parameters.
e-Posters: Cervical Cancer

CASE REPORT: MYELOID SARCOMA OF THE UTERINE CERVIX WITH MIXED MYELOMONOCYTIC DIFFERENTIATION

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Objectives
Published case reports have contributed to the expansion of medical knowledge by providing information often missed or undetectable in trials. We present the management of an extremely rare myeloid sarcoma of the uterine cervix in a 57-year-old woman with a short history of postcoital bleeding.

Methods
Case report

Results
A 57-year-old woman was referred to our unit with a 2-week history of postcoital bleeding. Her medical background included a left oophorectomy for a benign ovarian cyst and tubal ligation. Colposcopy and cervical biopsy confirmed the presence of a myeloid sarcoma with mixed meylomonocytic differentiation rather than pure granulocytic or monocytic maturation. Imaging showed a cervical mass with left iliac lymph node involvement and urgent referral to Haematology/Oncology was arranged. Clinically the patient progressed to AML, but bone marrow analysis showed no involvement and normal karyotype. The patient was commenced on chemotherapy and later received pelvic radiotherapy and allogenic stem cell transplant.

Conclusions
Myeloid sarcomas are extramedullary masses of myeloblasts and their manifestation at the female urogenital tract is extremely rare with an estimated incidence of less than 2 per million in adults. They are usually found at the ovary with the uterus and cervix being the second most common organs involved. The majority of patients show evidence of AML, but the challenging patients are those without any history of AML where the sarcoma is an isolated mass and there are nonspecific symptoms. Despite the advances in chemotherapy the survival remains <20% for most cases.
THE SIGNIFICANCE OF MATRIX METALLOPROTEINASE-2 EXPRESSION IN THE CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objectives
Left untreated, every fifth high-grade cervical intraepithelial neoplasia transforms into the invading cervical carcinoma. Matrix metalloproteinase (MMPs) has a significant role in degrading the extracellular matrix in the invading cervical carcinoma. Consequently, cancer cells leave the primary tumor invading the surrounding tissue and creating metastases. Increased expression of matrix metalloproteinase 2 (MMP-2) was observed in several types of genital cancer, including cervical carcinoma. The focus of this paper was to compare MMP-2 expressions in low-and high grade cervical intraepithelial neoplasia.

Methods
58 samples of cervical tissues using immunohistochemistry for MMP-2 expression were evaluated in surgical patients of the Department of Gynecology and Obstetrics, University Hospital Center Split, with histopathology findings in cervical intraepithelial neoplasia. Coloured samples of cervical tissues were evaluated positive whereas colourless samples were negative.

Results
Histopathology analysis showed that 16 (28%) patients had mild cervical dysplasia (L-SIL) and other 42 (72%) patients had severe dysplasia (H-SIL). Positive MMP-2 expression was detected in 2 (13%) of L-SIL samples and in 31 (74%) of H-SIL samples, which differ significantly (p < 0.001).

Conclusions
The expression of MMP-2 was more increased in cervical tissues of patients with higher degree of cervical dysplasia proving its activity in the inner lining of the cervix with precancerous changes. Further researches would show whether MMP-2 could be used as biomarker of an increased cervical cancer risk.
LAPAROSCOPIC RADICAL TRACHELECTOMY FOR YOUNG WOMEN WITH EARLY CERVICAL CANCER

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Objectives
To analyze surgical, oncological, and reproductive outcomes after laparoscopic radical trachelectomy (LRT) for young women with early cervical cancer.

Methods
We conducted a retrospective review of patients undergoing fertility-sparing LRT and simple trachelectomy for early cervical cancer at Asan Medical Center (AMC, Seoul, Korea) between 2004 and 2013.

Results
Seventy six patients tried planned LRT, but eight patients needed immediate completion of laparoscopic radical hysterectomy due to unfavorable intraoperative findings such as parametrial invasion and/or lymph node metastasis. The median age was 31 years (range, 22-41 years). Histologic type of tumor was squamous cell carcinoma in 52 patients, adenocarcinoma in 15 patients, and adenosquamous carcinoma in one patient. The median number of nodes retrieved was 22 (range, 0-56); Twelve patients (19 %) with pathologic risk factors for recurrence received adjuvant chemotherapy. Ten patients had recurrent disease and two of them died of disease after a median follow-up time of 33 months. Five patients (6.94%) suffered from postoperative cervical stenosis and all of them underwent cervical re-canalization. Nineteen patients attempted to conceive, 10 of them succeeded in pregnancy and gave births to 8 healthy babies.

Conclusions
LRT was a reasonable treatment option for selected patients with early cervical cancer. The reproductive outcomes after this surgery were promising.
Perspectives of Metronomic Chemotherapy in the Radiological Treatment of Cervical Cancer

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Objectives
A prospective direction in the treatment of cervical cancer (CC) is the sharing of chemoradiotherapy. Aim is evaluation of radiation therapy (RT) for CC with FIGO stage IIA-IIIB in combination with cisplatin in metronomic regimens.

Methods
116 of CC patients received treatment according to the following schemes: study group (n=54) – RT in combined with metronomic chemotherapy with cisplatin (40mg/m²) throughout 5 weeks of an irradiation (1, 8, 15, 22, 29 days); control group (n=62) have received only RT. The average dose of RT in study group was made to total focal dose (TFD) (point A)-73.6Gy, TFD (point B)-57.8Gy. Average single dose of cisplatin was made 50mg, and total dose 257.4mg. The average dose of RT in control group was made to TFD (point A) - 74.3Gy, TFD (point B) - 66.2Gy.

Results
Dynamic source of tumor regression were noted in the study group with volume from 80.9±5.3cm³ to 4.7±2.3?m³, and in control group with volume from 63.1±5.1cm³ to 11.9±4.1?m³. According to the MRT in the study group tumors had regress with a volume of 88.4±4.3cm³ up to 6.3±3.3cm³, and in control group - with 72.2±7, 9cm³ to 13.1±4.3cm³. Complete effect was achieved in the study group in 81.8±5.2%, which exceeded the control result in 1.3 times (54.8±6.3%). By ultrasound tomography change in treatment dynamics in the study group was characterized by reduction of topometrical indicators of cervix and degrees of the initial volume of tumor in 93.7% (in control group – 70%).

Conclusions
Metronomic chemotherapy with cisplatin significantly improves the efficiency of CC treatment without direct toxic effects.
FEASIBILITY OF LAPAROSCOPIC NERVE SPARING RADICAL HYSTERECTOMY IN THE MANAGEMENT OF EARLY CERVICAL CANCER

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Objectives
Radical hysterectomy (RH) is the treatment of choice for patients with early cervical cancer. However, it is associated with significant morbidity especially related to bladder, anorectal and sexual function. A nerve sparing approach to RH which preserves the pelvic autonomic nerves has been thought to reduce the rate of postoperative complications.

Objective: To assess the feasibility of laparoscopic nerve sparing radical hysterectomy (LNSRH), as opposed to standard laparoscopic radical hysterectomy (LRH) in the treatment of cervical cancer.

Methods
A retrospective review of all patients who had a radical hysterectomy (LNSRH and LRH) with pelvic lymphadenectomy between May 2011 and October 2012 was undertaken. Data was collected from the hospital notes regarding the duration of surgery, lymph node count, length of the vaginal cuff, time to removal of catheter and postoperative complications.

Results
23 patients underwent RH during the review period. Five patients had LNSRH and 18 patients underwent LRH. LNSRH, when compared to LRH, was associated with longer mean operating times (190 min v 168 min) but resulted in higher lymph node counts (32 v 21) and a longer vaginal cuff (35mm v. 20mm). The catheter was removed after 7 days in both groups. Immediate postoperative voiding dysfunction was seen in 3 patients in the LNSRH group but all of them resolved within 3 months.

Conclusions
LNSRH was feasible without compromising the radicality of surgery. The incidence of immediate postoperative voiding problems appears to be similar to LRH. The review is currently being extended to include more patients in the LNSRH group.
CLEAR-CELL CERVICAL CANCER OF A 16-YEAR-OLD PATIENT – CASE STUDY

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Objectives
The study’s objective is to present the applied diagnostic and therapeutic methods for a 16-year-old with a clear-cell cervical cancer.

Methods
The analysis covered the declared symptoms, the implemented diagnostic and therapeutic process.

Results
A 16-year-old patient was admitted to the Lower Silesia Oncology Centre with diagnosed clear-cell cervical cancer. After imaging examination and repeated biopsy of the tumor in the exocervical surface, the patient was qualified for neoadjuvant chemotherapy. The conducted imaging examination showed the tumor was in regression. The treatment’s next stage included conization of cervix. As radicality of the procedure raised doubts – areas free of tumor invasion within the exocervical surface – 0,3 mm and within the cervical canal – 0,6 mm – there was radical hysterectomy performed. Having obtained the results of the histopathological tests the patient was qualified for adjuvant chemotherapy. During the chemotherapy the patient was diagnosed with kidneys failure making continuing of chemotherapy impossible in the planned scope. At present, 12 months after the treatment, the patient remains in remission.

Conclusions
Description of the case of a clear-cell cervical cancer is significant due to rarity of occurrence of this type of tumor, young age of the patient and lack of elaborated standards of procedure. It is important to develop a data base allowing for developing optimal procedures in so rare diseases.
LYMPHOEPITHELIOMA-LIKE CARCINOMA OF THE UTERINE CERVIX.
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Objectives
Lymphoepithelioma-like carcinoma (LELC) of the uterine cervix is a quite rare and unusual occurrence with very few previously reported cases in the literature. We aimed to describe the clinical and histopathological findings of LELC patients with a brief review of the literature.

Methods
We analyzed patients who treated for cervical carcinoma (CC) between 2005 and 2012 at our institution retrospectively. We identified 3 patients with LELC and described the clinicopathological characteristics.

Results
Of the 158 patients with CC, only 3 (1.9%) had LELC histology. On histological examination, all tumors showed a typical syncytial growth pattern of undifferentiated cells accompanied by intense lympho-plasmacytic infiltrate. Median age for patients with LELC was 45 (range, 42-48). Two of 3 had clinically stage IB1, and one had stage IA1 disease. All patients underwent radical hysterectomy with pelvic lymphadenectomy. Patient with IA1 disease operated by total laparoscopic approach. Median tumor size was 1.1 cm (range, 0.4-2). Two cases with IB1 disease had greater than 66% stromal invasion. None of cases had lympho-vascular, parametrial or lymph node involvement. Surgical margins were negative in all cases. No adjuvant treatments were given. Median follow-up time was 39 (24-48) months. None of cases recurred, and all are alive with no evidence of disease.

Conclusions
LELC of the uterine cervix is a quite rare entity with distinct morphological features. As a variant of squamous cell carcinoma, it shows better prognosis.
e-Posters: Cervical Cancer

PRECISE DISCRIMINATION OF CERVICAL CARCINOMA SUBTYPES IN COMBINATION WITH SOMATIC MUTATION PROFILING CONTRIBUTES TO PREDICTING DISEASE OUTCOME

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Objectives
Squamous cell carcinoma (SCC), adenocarcinoma (AC), and adenosquamous carcinoma (ASC) are the most common histopathological subtypes of cervical cancer. Differences in somatic mutation profiles between SCC, AC and ASC are suggested, but reports are inconsistent. We investigated the prevalence of somatic mutations in three well-defined cohorts of SCC, AC and ASC and determined the additional value of mutation profiling in predicting disease outcome in relation to other well-established prognostic parameters.

Methods
A total of 307 cervical tumors were categorized into SCC (n=166), AC (n=61) and ASC (n=80) and clinicopathological data were collected. Mutation analysis was performed by mass-spectrometry for 155 somatic hot-spot mutations in 12 genes.

Results
In 97/307 (32%) tumors 119 mutations were detected (33% in SCC, 36% in AC, and 25% in ASC), the most in the PIK3CA (21%) and KRAS-gene (6%). PIK3CA mutations occurred more frequently in SCC compared to AC (P=0.050) whereas KRAS mutations were most frequently found in AC compared to SCC (P<0.001) and ASC (P=0.002). Positive mutation status correlated with worse disease-free survival (HR 1.6, P=0.041). CTNNB1 and HRAS mutations were independent predictors for disease-recurrence (HR 5.0, P=0.008; HR 27.5, P=0.005) besides tumor size (P<0.001), parametria involvement (P=0.017), lymph node metastasis (P=0.002) and, surprisingly, the ASC subtype (HR 1.9, P=0.045).

Conclusions
Somatic mutations occurred in 32% of cervical tumors, showed a different distribution amongst histopathological subtypes, and correlated with disease-recurrence. Precise discrimination of cervical carcinoma subtypes in combination with mutation profiling is of additional value in predicting disease outcome, and may guide the development and selection of tumor-specific treatment approaches.
e-Posters: Cervical Cancer

ASSESSMENT OF INTER-FRACTIONAL VARIATION OF BLADDER FILLING IN MRI BASED INTRAUTERINE BRACHYTHERAPY FOR INVASIVE CERVICAL CANCERS

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Objectives
Guy's and St Thomas' Hospital (London, UK) treats locally advanced invasive cervical carcinoma with radical chemoradiotherapy [50.4Gy/28# EBRT to the whole pelvis with concurrent weekly cisplatin chemotherapy (40mg/m²)] followed by 21Gy/3# of intrauterine brachytherapy (BT).

MRI-based BT planning is performed with each fraction to reduce variation from planning to treatment. Variations in bladder volume cause target organ motion and affects coverage and toxicity.

The aim of the study is to assess inter-fractional variation of bladder filling during BT and assess the role of bladder scans (US) in determining accurate bladder volume.

Methods
All BT performed May 2010 - December 2011 were analysed retrospectively and January - August 2012 prospectively with additional US.

Treatment applicators and a urethral catheter were inserted under spinal anaesthetic for each fraction of BT. 50mls of normal saline was inserted into the bladder prior to MR and CT imaging. An average of 3 US readings were taken immediately prior to imaging and treatment. The catheter is unclamped after each imaging modality. The treatment plan was then individually optimised.

Results
99 fractions were analysed in total. The mean bladder volume of all fractions was 173.2mls (range 47.6 - 577.3). Inter-fractional variation of bladder volume within individuals ranged 10.9 - 494.2mls. Mean change in bladder volume between patients ranged 81.8 - 372.9mls.

24 fractions received bladder scans. A good correlation exists between bladder volumes measured on US and CT (R²=0.793).

Conclusions
There is huge inter-fractional variation in bladder filling in individuals and between patients. Bedside bladder scans can be used to aid consistency in bladder filling between planning and treatment.
e-Posters: Cervical Cancer

THE IMPACT OF BLADDER VOLUME ON BLADDER DOSE AND TARGET COVERAGE FOR MRI BASED INTRAUTERINE BRACHYTHERAPY FOR INVASIVE CERVICAL CANCER

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Objectives

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There are many publications assessing the effect and variation of bladder size on radical prostate external beam radiotherapy. However, there is little work to the same effect on brachytherapy for gynaecological cancers.

The aim of the study is to assess the effect of bladder volume on bladder dose (D2cc) and target (HR-CTV) coverage.

Methods

All brachytherapy performed between May 2010 and December 2011 were retrospectively audited. Treatments between January 2012 and August 2012 were analysed prospectively.

Each patient received 3 fractions of BT treatment over 8 days. MR and CT images were acquired after treatment applicators were inserted under spinal anaesthetic. A standard plan was placed and individually optimised for treatment. This procedure was repeated for each fraction. A bladder D2cc dose constraint of <6.50Gy was preferrable per fraction.

Results

99 fractions of treatments were analysed. Despite plan optimisation, bladder volumes >250mls continued to have suboptimal bladder dose (D2cc<6.50Gy 15.4% if >250mls cf. 61.6% if 50-250mls p=0.002). However, target coverage was not significantly compromised (V100>90% 76.9% cf. 76.7%) with larger bladder doses.

Conclusions

Bladder volumes >250mls lead to compromise of bladder dose. Higher bladder doses were accepted on several fractions to prevent compromise to target coverage due to clinician’s priority to cover the target knowing potential lower bladder doses were possible in subsequent fractions.
DIFFERENT BRACHYTHERAPY TOXICITY FOR RADIOTHERAPY CERVICAL CANCER.

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Objectives
In our Institute we are developing a guideline for clinical practice of low-dose-rate (LDR), middle-dose-rate (MDR) and high-dose rate (HDR) brachytherapy for locally advanced cervical cancer.

Methods
In the present investigation were studied the data about 645 patients with carcinoma of the uterine cervix. For treating all patient was used the combine radiotherapy. Brachytherapy with LDR was underwent 221 patients. Adapted three modes for fractionating the summary target dose (STD): the first mode – 20Gy, once a week, STD=80Gy (BEDe=86, BEDl=148); the second mode - STD=100Gy (BEDe=107, BEDl=186); the third mode - STD=120Gy (BEDe=129, BEDl=223). Also three modes for fractionating STD were studied with MDR brachytherapy (227 patients) and HDR brachytherapy (197 women): the first mode - 7Gy, once a week, STD=28Gy (BEDe=48, BEDl=106); the second mode - STD=35Gy (BEDe=60, BEDl=133); the third mode - STD=42Gy (BEDe=71, BEDl=160).

Results
Number of acute toxicity among patients treated with MDR brachytherapy substantially (p< 0.05) was 10% less in comparison with LDR and HDR, due to the reliable (p< 0.05) decrease of a quantity early urinary bladder toxicity (to 6% in comparison with HDR), and rectum toxicity (to 8% - with LDR). The total number of late toxicity among patients treated with HDR brachytherapy substantially (p< 0.05) was 5% more in comparison with MDR and 8% more in comparison with LDR, due to a reliable (p< 0.05) increase in the quantity of early urinary bladder toxicity (to 5% in comparison with LDR).

Conclusions
Quantity early and late toxicity depend from different dose rate brachytherapy for combine radiotherapy carcinoma of the uterine cervix.
e-Posters: Cervical Cancer

EXPRESSION OF HYPOXIA MARKERS HIF-1ALFA AND CAIX ON WHOLE-MOUNT HISTOPATHOLOGICAL SECTIONS OF PATIENTS WITH CERVICAL CANCER
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Objectives
The presence of hypoxic regions within tumours is associated with a worse prognosis. HIF-1α is the key cellular survival protein during hypoxia, and can be used as a marker for assessment of tumour hypoxia.

In cervical cancer, conflicting results have been published regarding a correlation between a strong HIF-1α expression and treatment outcome. We hypothesize that these differences may be explained by a heterogeneous expression of HIF-1α in the cervical tumour. In this scenario, HIF-1α expression profiles in the diagnostic biopsy may not represent the profile for the whole tumour area, resulting in a limited predictive value.

Methods
The immunohistochemical expression profiles of HIF-1α, and the downstream target CAIX were evaluated in whole-mount histopathological sections of 13 patients with cervical cancer. Furthermore, tumor areas were delineated on whole-mount histopathological sections, subdivided into areas with the same size of the diagnostic biopsy, and compared with the corresponding diagnostic biopsy.

Results
HIF-1α and CAIX expression profiles were highly heterogeneous within tumors and between patients. Expression profiles of these markers differed significantly between the diagnostic biopsies and one or more of the subdivided areas of the whole-mount tumor section.

Conclusions
In this whole-mount cervical cancer study, HIF-1α expression is highly heterogeneous within tumors. Expression profiles in the diagnostic biopsies are thus not representative for the whole tumor, and may explain the limited predictive value.
e-Posters: Cervical Cancer

FERTILITY PRESERVING SURGERY IN PATIENTS WITH EARLY STAGE CERVICAL CARCINOMA: LAPAROSCOPIC RADICAL TRACHELECTOMY

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Objectives
Review a surgery technique: radical trachelectomy

Methods
Reviewing a clinical case

Results
We report the case of a 27 year old patient, with a cervical cytology of HSIL and possible areas of microinvasion. A conization was done, and the result obtained was an invasive epidermoid carcinoma, 3mms of deep and 15mms of superficial extension. The diagnosis was a cervical cancer FIGO stage Ib1. We decided to perform a laparoscopic radical trachelectomy. The postoperative course was favorable. She was discharged after three days. The pathological anatomy result was: absence of malignancy. Pelvic lymphadenectomy: 0/19 nodes.

Conclusions
Radical trachelectomy consists of removing the cervix, 2cms of upper vagina, parametrium and paracolpos. Previously, bilateral pelvic lymphadenectomy with intraoperative biopsy should have been done. The procedure should be completed only if the results are negative. The criteria for surgery are:
- Age < 40 years, strong reproductive desire, proven diagnosis of invasive cervical cancer, stage Ia1 with unfavorable histology, Ia2 and Ib1, Tumor < 2 cm.
A 70% pregnancy rate is reported in the women who wanted to conceive following this surgery.
The causes of infertility are postulated: cervical stenosis (75%), anovulation (12.5%) and idiopathic (12.5%). Possible complications are second trimester loss (5%) and preterm delivery (20%). Oncological results are as good as radical hysterectomy; but with the difference that the fertility is preserved.
The factors influences of knowledge level in cervical cancer patients about Pap smear examination

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Objectives
To describe the level of knowledge of Pap smear examination and its influencing factors in cervical cancer patients.

Methods
Patients meeting the inclusion criteria were asked to fill questionnaire. Acquired data will then be processed and analyzed statistically.

Results
This study was performed to 45 cervical cancer patients. We found that the majority of subjects was in the 41-45 years age groups (36%), housewife (87%), graduated junior high school (51%), and lived in Manado city (53.3%). Thirty one patients (69%) had a lacking knowledge about Pap smear examination. Among 25 respondents (56%) who had received the information before, only 13 respondents (52%) had already had their Pap smear examination. This unwillingness to participate in the examination was caused by fear (75%), laziness (8%), no complaint (8%), and no support from the husband (8%). The information factor had the greatest influence on the level of knowledge about Pap smear examination.

Conclusions
The knowledge level of Pap smear is still low and the most influencing factor for this result is the lack of information (p <0.05).
TREATMENT RESULTS OF DIFFERENT POSTOPERATIVE ADJUVANT THERAPY FOR STAGE IB-IIA CERVICAL CARCINOMA WITH RISK FACTORS

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Objectives
To investigate the effects of postoperative adjuvant chemotherapy and chemoradiotherapy or radiotherapy for IB-IIA cervical cancer with risk factors.

Methods
There were 137 patients who had undergone radical hysterectomy and systematic pelvic lymphadenectomy for Stage IB-IIA cervical cancer. These patients had intermediate risk factors include bulky tumor, lymph vascular space invasion, deep stromal invasion; high risk factors include positive surgical margin, parametrial invasion, and lymph node involvement. 79 patients were treated with chemotherapy, 58 were treated with radiotherapy or/and chemoradiotherapy. The 5-year survival and prognosis factors were analyzed, the prognosis was compared in the different adjuvant therapy groups.

Results
Whether in patients with high-risk factors or intermediate-risk factors, the 5-year overall survival and 3-year disease-free survival had no difference between chemotherapy and radiochemotherapy and/or radiotherapy groups respectively. Cox regression multivariate analysis of survival indicated that clinical stage, pathology, different risk factor were independent prognostic indicator. Patients with early stage, squamous cell carcinoma, intermediate risk factors had better prognosis. Univariate and multivariate analysis indicate that different postoperative adjuvant therapy had no effects on the prognosis. The 5-year overall survival was 88.6% in patients treated with chemotherapy, and 89.7% in patients treated with radiotherapy or/and chemoradiotherapy.

Conclusions
Chemotherapy has equivalent therapeutic results with radiotherapy or/and chemoradiotherapy for patients with risk factors after radical surgery, chemotherapy may be as one choice of postoperative adjuvant therapy for stage IB-IIA cervical carcinoma with risk factors.
TREATMENT RESULTS OF ADJUVANT CHEMOTHERAPY FOR PATIENTS WITH INTERMEDIATE-RISK CERVICAL CANCER

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Objectives
To investigate the effectiveness of postoperative adjuvant therapy for intermediate-risk cervical cancer.

Methods
The medical records of 119 patients who had undergone radical surgery for Stage IB-IIB cervical cancer were reviewed retrospectively. These patients had intermediate-risk factors including bulky tumor, lymph vascular space invasion, and deep stromal invasion. Of the 119 patients, 16 patients were followed up with no further treatment; 73 patients were treated with chemotherapy, 30 were treated with radiotherapy or chemoradiotherapy. The significance of the clinical parameters and disease free survival of each group were analyzed. Univariate and Cox regression model was used to analyse prognostic factors.

Results
No statistically significant difference was found in the 3-year or 5-year overall survival rate among the observation and treatment groups (3-year OS 100% and 94.4%, respectively; 5-year OS 100% and 92.3%, respectively; p < 0.05). No statistically significant difference was found in the 3-year or 5-year disease-free survival rate among the CT and RT or CRT groups (3-year DFS 93.6% and 96.4%, respectively; 5-year DFS 80.7% and 96.4%, respectively; p < 0.05). Univariate and multivariate analysis of survival indicated that there was no independent prognostic indicator (P < 0.001).

Conclusions
Chemotherapy has the equivalent therapeutic effect as radiotherapy or chemoradiotherapy for patients with intermediate risks after radical surgery. Chemotherapy or observation can be an option for selected patient postoperatively. A prospective randomized trial is needed to compare CT combined with radical hysterectomy and pelvic lymphadenectomy to RT or CRT.
e-Posters: Cervical Cancer

Clinical values of treating cervical cancer by surgery plus superselective catheterization for arterial infusion chemotherapy

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Objective
To study the clinical significance of surgery plus superselective catheterization for arterial infusion chemotherapy in the treatment of cervical carcinoma.

Methods
84 patients of stage Ib2, IIA and IIB, which received operation after arterial infusion chemotherapy from April of 2002 to January of 2010 were put into an integrated treatment team (8 cases without surgery), while 82 patients who just received surgery in the same time were put into a control team.

Results
The toxicity including 49% grade 0 leucopenia and 77.6% grade 0 anemia. By using of arterial infusion chemotherapy before operations, the tumor volumes of 76 patients became smaller, and the effective rate is 90.47%. All the surgical removals were successful. There is no significant difference between the two teams in the operation time, bleeding volume and complications (P>0.05). The 5-year survival rate was over 86.67%.

Conclusion
Surgery plus superselective catheterization for arterial infusion chemotherapy is safe and effective for treating late cervical cancer. It can improve the patient’s life quality and it is feasible.
MICROMETASTASES IN NON-SENTINEL LYMPH NODES IN CERVICAL CANCER: A PRELIMINARY STUDY

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Objectives
Lymph node (LN) micrometastatic disease came into prominence since ultrastaging has been shown to improve quality of LN procedures among epithelial cancers. The aim of this study was to evaluate the feasibility and diagnostic utility of micrometastases detection in both sentinel (SLN) and non-sentinel LNs (nSLN) in cervical cancer (CC).

Methods
12 consecutive patients with UICC CC stage IA to IIA in two groups A (7) and B (5) with and without SLN procedure with methylene blue dye underwent radical hysterectomy and lymph nodes removal. All LNs were evaluated in hematoxillin-eosin (HE) staining and immunohistochemically (IHC) in ultrastaging with anti-cytokeratins AE1/AE3. The detailed analysis was performed regarding technical and histopathological aspects of the procedure.

Results
More LNs could be extracted and studied in group A than in group B (210 vs. 70, mean 30 vs. 23.5, p <0.0005). There were 13 SLNs extracted, identification rate was 71% (5/7 in group A). There was one micrometastatic LN found in both groups (16% cases), but the stage was changed (from pN0 with HE to pN1 with IHC) only in the case of labeled nodes (group A).

Conclusions
The presence or absence of metastases in SLNs should not be guided by the operator or oncologist, who should have information from all removed lymph nodes sent to ultrastaging. The important condition for correct SLN operation is to ensure that sentinel node(s) were removed. The implementation of the assessment of the N status to the FIGO classification should be considered.
e-Posters: Cervical Cancer

LAPAROSCOPIC RETROPERITONEAL PARAAORTIC LYMPHADENECTOMY; ANALYSIS OF FIRST 50 CASES.
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Objectives
To evaluate the experience, outcomes and complications in patients with advanced cervical cancer who assented to conduct laparoscopic retroperitoneal paraaortic lymphadenectomy.

Methods
In 50 patients with stage IIb to IIIb cervical cancer, laparoscopic lymphadenectomy were performed between December 2003 and February 2010. Average age of patients were 51.3 (42-73). Forty-one patients had squamous cell carcinomas, 7 patients had adenocarcinomas and 2 patients had adenosquamous carcinomas of the cervix.

Results
All save 4 surgical procedures were completed laparoscopically. Two cases peritoneal defect, one case lymph node fixed on vena cava and one case with renal artery injury were the reason laparotomy conversion. The average operative time was 121.6 minutes (95-210 min.). Number of total lymph nodes were 762, 77 of theirs attacked with tumors. Average numbers of lymph nodes subtracted were 15.24 (11-23). Thirteen cases had positive nodes (26%).

Conclusions
Laparoscopic retroperitoneal paraaortic lymphadenectomy can be successfully completed in patients with cervical cancer with acceptable operation complications, a less injury and recovery time.
FIRST CASE OF LAPAROSCOPIC RADICAL TRACHELECTOMY FOLLOWED BY CHEMOTHERAPY IN A PREGNANT PATIENT WITH INVASIVE CERVICAL CANCER AT 18.6 WEEK GESTATION

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Objectives
Laparoscopic radical trachelectomy (LRT) has been an option for young patients with stage IB1 cervical cancers. But it has never been reported in pregnant women with cervical cancer.

Methods
A 26-year old nulliparous woman at 18 weeks gestation was diagnosed with a FIGO stage IB1 cervical mucinous adenocarcinoma. Because the patient strongly desires to retain her pregnancy, after careful counseling she underwent a laparoscopic pelvic lymphadenectomy with LRT at 18.6 weeks gestation.

Results
No intraoperative complications occurred and blood loss was 400 cc. Pathology revealed lymph node vascular space involvement, and the clear endocervical margin was less than 0.5cm. No lymph nodes were positive. After meticulous counseling the patient underwent three cycles of chemotherapy with paclitaxel (135 mg/m²) and carboplatin (AUC=5). She successfully carried the pregnancy to 34.2 weeks gestation and delivered a healthy female infant weighing 1750 g by cesarean hysterectomy. Final pathology showed no residual tumor. She accepted the fourth and last cycle of chemotherapy. After two months of follow-up, both the mother and the infant were uneventful.

Conclusions
Both abdominal and vaginal radical trachelectomies have been reported for mid-term pregnant women with stage IB1 cervical cancer. This is the first try of laparoscopic approach during pregnancy. The less invasive surgery and more broadened view demonstrate the advantage of LRT. Adjuvant chemotherapy in selected patients with high-risk pathologic factors is also feasible and safe. For physicians with experienced laparoscopic technique, this is a new option for selected pregnant patients with stage IB1 cervical cancer.
CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH HIGH-RISK HISTOLOGICAL SUBTYPES OF CERVICAL CANCER IN ST PAUL’S HOSPITAL OF KOREA

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Objectives
We sought to determine whether patients with NSCC have a worse prognosis than those with SCC and evaluated the characteristics of the NSCC including HPV types and tumor markers.

Methods
We retrospectively reviewed charts of women with NSCC and SCC at St Paul’s Hospital from 2004 to 2010. Parametric continuous variables were compared using the t-test for independent samples. Disease-free survival was calculated by Kaplan-Meier methods using SPSS 13.0 for Windows (SPSS Inc, Chicago, Ill)

Results
Among the fifteen patients with NSCC, thirteen patients had follow-up form 3 to 95 month. There were no differences between NSCC (n=13) and SCC (n=73) groups in age, distribution of stage, treatment methods. Operation cases were 9/13(69.2%) in NSCC group vs 56/74(75.7%) in SCC group. In the stage Ib, mean of disease free survival were 84.6 vs 74.3 month in NSCC and SCC (no statistical significance). Elevated CEA levels were associated with advanced stage in NSCC group. Most frequent HPV types were HPV-18 (30.8%) and HPV-16 (15.4%) in NSCC group vs HPV-16(50.9%), HPV-18(9.4%), HPV-31 and HPV-39(3.8%), respectively.

Conclusions
Patients with NSCC cervical cancer with less than stage 2 do not have a worse prognosis than SCC group. But, several studies have demonstrated that Pap smears are less beneficial in preventing NSCC. Potential of HPV testing as a screening method for the NSCC could be considered.
e-Posters: Cervical Cancer

HPV PREVALENCE IN ASYMPTOMATIC TURKISH WOMEN: A PILOT STUDY
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Objectives
HPV infection is the causative factor of the cervical cancer. It has been detected more than 100 types of this precancerous virus but WHO has determined 13 of them as high risk for cervical cancer. Different HPV-DNA tests have been started to be considered as the primary screening tool for cervical cancer. Turkish cervical cancer screening program is going on based on cytology for women between 30-65 years of age in every 5 years for more than 2 decades, however it still hasn't reached the preferred coverage rates. Primary screening with HR-HPV tests and triaging women at risk can be a solution for Turkish cervical screening program.

Methods
448 asymptomatic women called for routine cervical screening. After informed consent taken, both cytology and 2 different HPV tests have been performed to their cervical samples.

Results
9 of 448 women detected as positive with both of the two different HR-HPV tests. The results are summarised in the table below.

<table>
<thead>
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<th>REAL TIME PCR</th>
<th>INVADER©TECHNOLOGY</th>
<th>positive</th>
<th>negative</th>
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<tr>
<td>total</td>
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<td>437</td>
<td>448</td>
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</tr>
</tbody>
</table>

Conclusions
Although it is relatively high in African and Middle-Southern Asia, HR-HPV infection prevalence of asymptomatic women has been reported between 15-40% from North America and Europian regions. HR-HPV infection prevalence of Turkish asymptomatic women has been enounced as lower than 5% within several studies. We have compared two different HPV tests in our pilot study and although HPV infection prevalence is 2% consistency of different tests was more than 70%.
e-Posters: Cervical Cancer

PRECANCEROUS LESIONS AND CERVICAL CANCER INCIDENCES ARE INCREASING WITH THE SAME TREND, IN TURKEY.
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Objectives
Cervical cancer is the second cancer of women among worldwide. Although it is a preventable disease mortality rates are still high due to delayed diagnosis proportion at advanced stages, especially in developing countries. Turkey is a huge, crowdy country with more than 75 million citizens. Cervical cancer incidence rate among Turkish women stayed behind world average for years and still has a low rate.

Methods
Turkish cancer registry is a well organised registry system, built up in 2002, comprising more than 25% of all population actively. We got data for invasive cervical cancer and preinvasive cervical lesions from 12 active cancer registry centres, nationwide.

Results

![Graph showing cervical cancer incidence rate and CIN III](image)

Cervical cancer incidence rate increased from 2,3 per 100,000 to 4,0 per 100,000 between 2003 and 2008. The ranking of cervical cancer among Turkish women hasn't changed within years which is the 9 or 10th most common cancer of women in Turkey. Preinvasive cervical cancer incidence rate increased to 0,8 per 100,000 women with a similar trend to invasive cervical cancer.

Conclusions
Total cervical cancer incidence rate, have shown a similar increase trend with preinvasive lesions' increase trend. The increase in cervical cancer incidence in Turkey is probably due to increase in detection of early disease. Although Turkish population based cervical screening program hasn't reached the preferred coverage level, the quality of health services and access to these services have been improved since the last decade, in Turkey.
e-Posters: Trophoblastic Diseases

KIDNEY METASTATIC CHORIOCARCINOMA IN AN AMENORRHEIC WOMAN FOLLOWING NORMAL VAGINAL DELIVERY
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Objectives
Kidney is a rare site for metastatic choriocarcinoma and predicts a poor prognosis for this disease. We report a case of kidney metastatic choriocarcinoma presenting with flank pain, gross hematuria and long term intermittent amenorrhea after a normal vaginal delivery.

Methods
A 43 year old, G10, rural woman presented with left flank pain, gross hematuria and had a rising titer of serum β-hCG, 85000mIU/ml. She had a history of three years intermittent amenorrhea and vaginal bleeding following normal vaginal delivery. Pathologic examination of endometrial curettage specimen revealed choriocarcinoma. Ultrasound revealed enlarged uterus involved by an irregular mass with heterogeneous echo pattern and extensive myometrial invasion. A mass with similar echo pattern was also evident in the left kidney. Computerized tomography confirmed the intrauterine mass and involvement of the left kidney.
PLACENTAL SITE TROPHOBLASTIC TUMOR: CASE REPORT AND LITERATURE REVIEW
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Objectives
Placental site trophoblastic tumor (PSTT) is a very rare form of gestational trophoblastic disease, rising from intermediate trophoblast cells. The authors aim to present a case of a PSTT and a literature review on this rare disease.

Methods
Case report and literature review on Pubmed using as keywords “placental site trophoblastic diseases” and “PSTT”.

Results
A 34-year-old Portuguese woman, gravida:1 para:1, presented with amenorrhea eight months after a term birth of a female newborn. Serum levels of $\beta$-hCG were 16 mUI/mL and pelvic ultrasound identified a hematometra. Endometrial sampling was collected and histological and immunohistochemical evaluations allowed the final diagnosis of a PSTT. Further imaging studies (thoracic X-ray and pelvic magnetic resonance) did not identify extra-uterine disease. A laparotomy with a total hysterectomy (with ovaries preservation) and bilateral pelvic lymphadenectomy (because enlarged lymph nodes were identified) were performed. The final histological evaluation is still in course.

Conclusions
First described in 1976, only in 1985 Young et al described the malignant behavior of this disease. As in our report, most cases occurred in young women and presented as a vaginal bleeding or amenorrhea, weeks to years after a pregnancy of a female conceptus. Because it is a neoplastic proliferation of intermediate trophoblastic cells, PSTT is characterized by low $\beta$-hCG levels. The final diagnosis is histological and immunohistochemical and FIGO stage is the main prognostic factor. PSTT is resistant to commonly used chemotherapy agents and surgery remains the cornerstone of therapy.
A RARE PATHOLOGIC ENTITY: EXAGGRATED PLASENTAL SITE. REPORT OF THREE CASES WITH DIFFERENT SYMPTOMS AND CLINIC OUTCOMES

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Objectives
Exaggrated Plasental site (EPS) is a benign but rare pathologic condition.

Methods
Here we presented three cases with diagnosis of EPS with two different clinical outcomes.

Results
Case: 25 year old woman (G2 P1) referred with suspicion of gestational trophoblastic neoplasia (GTN). She had vacuum aspiration (VA) due to missed abortus 2 weeks before. Pathology was reported as GTN. She had no complaints and hCG levels was negative. TVUSG did not reveal any abnormality. After central pathologic review, pathology was confirmed to be EPS. Similarly second patient (39 years old woman with history of three abortus) was performed VA due to missed abortion of 8 weeks. EPS diagnosis was incidental finding without any following symptoms. Third patient was 35 years old nulliparous woman admitted for profuse vaginal bleeding. She had experienced recent missed abortion. As she was hemodynamically unstable, explorative laparotomy was performed. There was no intraabdominal bleeding. Hysteroscopy was performed, bleeding from a nodule measuring 2 cm on fundal part was observed and this nodule was excised. Final pathology revealed EPS. She was discharged on postoperative second day and after 15 months, she delivered a healthy baby with c section without any complication.

Conclusions
Every specimen’s retrieved in surgery for abortion should be sent for pathologic examination. PSE is benign but rare condition with different clinical outcomes. In asymptomatic patients, central pathology review will help to confirm diagnose and routine follow up is recommended. However PSE nodule could lead to profuse bleeding and fertility sparing surgery with hysteroscopic resection is an option.
e-Posters: Trophoblastic Diseases

REPRODUCTIVE HEALTH OF WOMEN AFTER TAKING CHEMOTHERAPY FOR GESTATIONAL TROPHOBLASTIC DISEASE

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Objectives

To show that even after undergoing 1-5 courses of chemotherapy for Gestational Trophoblastic Disease (GTD) reproductive health of women is intact and they conceive successfully after it.

Methods

Retrospective cohort analysis using data from the Lugansk regional maternity Hospital database of years 1993-2013, which shows n=18 females had GTD and underwent 1-5 courses of chemotherapy.

Results

Frequency of GTD was rare. All 18 patients (pts) belong to age group of 17-39 years, covering wide range of reproductive age. Out of 18pts, 15 had Hydatidiform mole (HM) while other 3 had Choriocarcinoma (CC). In anamnesis, among CC pts, 1 had early pre-eclampsia at 24weeks and 1 had 4th week of late postpartum(PP) bleeding, while all HM pts had genital inflammatory diseases, 1pt of HM during follow-up had High hCG and 3 times curettage in 5months.

18 women became pregnant for 25times after chemotherapy. Chemotherapy was given under indication of either high level of hCG, luteal cyst >6cm or path-morphological results of curettage. CC 3pts had (2 spontaneous abortions (SA), 2 term cesarean section (CS), 1 preterm CS). HM 15pts had (3 artificial abortion, 2 SA, 7CS [5 term and 2preterm], 8 vaginal deliveries [7term and 1preterm]).

Conclusions

During our research we got 22.2% preterm deliveries and 55.6% CS which is higher than the normal cases, but still all the 18 women were able to have kids successfully after chemotherapy. So we can conclude that chemotherapy for GTD was successful in keeping the reproductive health of women intact.
e-Posters: Trophoblastic Diseases

TUBAL PLACENTAL SITE NODULE WITH CONCOMITANT NORMAL PREGNANCY: A CASE REPORT

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Objectives
Lesions of intermediate trophoblast include placental site nodule (PSN), exaggerated placental site, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (ETT). PSN is a recently described, benign, asymptomatic and rare lesion that seems to represent the remnant of a previous pregnancy that failed to involute. For this reason it could be found at any site at which implantation occurs; however, the overwhelming majority of cases have been observed in the endometrium, in the endocervix and rarely in the Fallopian tubes.

Methods
A 40-year-old woman gesta 2 para 1 has been admitted in our Obstetrician Division at 26,1 weeks of gestation for IUGR and alterations in Doppler velocimetry of the umbilical and uterine arteries. After 18 days, due to Doppler velocimetry alterations, remarkable reduction of the amniotic fluid index and of the short term variability index in cardiotocographic fetal monitoring, the patient underwent a cesarean section and a 649 g female baby was delivered. During the surgical intervention, the left fallopian tube appeared discontinuous cause the presence within it of a yellow cystic formation that was removed.

Results
The final histologic examination revealed a PSN Immunohistochemically the cells of the lesion stained intensively with antibodies to cytokeratin and focally with antibodies to hPL and hCG.

Conclusions
PSN is a benign lesion with a nonneoplastic behavior but due to its peculiar microscopic appearance it shouldn’t be confused with PSTT, ETT and invasive squamous cell carcinoma of the cervix.
e-Posters: Trophoblastic Diseases

PLACENTAL SITE TROPHOBLASTIC TUMOR ARISING FROM MOLAR PREGNANCY: A CASE REPORT

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Objectives
Placental site trophoblastic tumor (PSTT) is a rare form of gestational trophoblastic disease. It is a tumor of intermediate trophoblast, seen commonly in reproductive age group.

Methods
Cases: A 32 year old G3 P1 D&C1 female present with vaginal bleeding. An early ultrasound examination diagnosed a missed abortion of 6 week gestation and a coexisting molar pregnancy. Dilatation and curettage was made. Her HCG level dropped from after curettage but rose shortly thereafter with the onset of recurrent vaginal bleeding. Curettage pathology revealed PSTT. Despite treatment with chemotherapy persistently elevated HCG led to hysterectomy.

Results
PSTT, like other gestational tumor develops following normal pregnancies, spontaneous abortions, termination of pregnancy, ectopic pregnancies and molar pregnancy. (1) This report describes a cases of PSTT preceded by molar pregnancy and first chemotherapy was used. Although the HCG level decreased for a short period with chemotherapy, it soon increased so after treated with hysterectomy.

Conclusions
PSTT is well recognized, but uncommon form of gestational trophoblastic disease. It is difficult to diagnose clinically as well as histologically. PSTT are not as sensitive to chemotherapy as other form of malignant gestational trophoblastic disease. Therefore it is important to distinguish these tumors histologically (2) surgery assumes a critical role in the management of PSTT (3,4)
e-Posters: Trophoblastic Diseases

A CASE OF HUMAN CHORIONIC GONADOTROPIN-BETA SUBUNIT SECRETING TUMOR AND UNKNOWN PRIMER ORIGIN PRESENTING HAEMOPYSIS. A CASE-BASED REVIEW OF THE LITERATURE

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Objectives
Gestational trophoblastic disease occurs rarely in perimenopausal women. We report primer orijin unknomn of a case of choriocarcinoma metastatic to the lung.

Methods
44-year-old woman visited for complaining of cough and haemoptysis. CT tomography of Chest revealed 3.5 cm size solid in lobus inferior segmentum laterobasale of pulmo sinister. A fine-needle aspiration biopsy showed choriocarcinoma. After the diagnosis, hysterectomy, bilateral salpingo-oophorectomi was performed for identifying primer focus of metastatic in our clinic.

Results
Histolical examinations wasn’t found abnormality. Combination chemotherapy which was EMOCO and CTSP+ETOP regimen had been administered for a six months. It didn’t respond chemotherapy. Therefore, the patient underwent left thoracotomy with inferior lobectomy. Histolical examinations showed pleomorphic carcinoma and immunhistochemical finding was metastatic choriocarcinoma. The patient has since received systemic chemotherapy with etaposid and cisplatin. The patient presented with unifocal pulmonary metastases and is not responding well to standard or experimental treatment regimen.

Conclusions
The patient presented with unifocal pulmonary metastases and is not responding well to standard or experimental treatment regimen.
e-Posters: Trophoblastic Diseases

ULTRASONOGRAPHY AND HCG LEVEL IN THE DIAGNOSIS OF GESTATIONAL TROPHOBLASTIC DISEASE.

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Objectives
Gestational trophoblastic disease is a manifestation of an aberrant fertilization event that leads to a proliferative process and, potentially, to an invasive neoplasm. The purpose of this study was to investigate whether or not the combined use of sonography and serum hCG determinations would enhance the specificity of the sonographic findings, and permit an earlier diagnosis. The criteria used were the absence of fetal heart movement, or a gestational sac not seen, by ultrasound when the hCG level was above 82,350 mIU/mL.

Methods
130 patients in first trimester of pregnancy were taken in this study. All patients were referred for sonography and hCG determinations because of bleeding in the first trimester.

Results
130 patients were selected to be examined. Ultrasound diagnosis in 67 cases was correct for hydatiform mole, 63 cases the diagnosis were missed abortion, blighted ovum, incomplet abortion. The combination of the ultrasound and the level of hCG 82-350 mIU/ml diagnosed correct 110 cases from 130 with hydatiform mole, and 20 cases the diagnose were incomplet abortion, blighted ovum, missed abortion.

Conclusions
Routine ultrasound examination in the first trimester have a 51.6% specificity in the diagnosis of hydatiform mole, specificity, which increases if done serial measurement of hCG and goes up to 84.6%. The combined use of hCG and ultrasound may permit the identification of patients at risk for gestational trophoblastic disease in the first trimester of pregnancy. An early diagnosis is very importante because diagnostic delay is associated with greater maternal morbidity and an increased risk of post molar trophoblastic disease.
PRIMARY GESTATIONAL OVARIAN CHORIOCARCINOMA: A CASE REPORT

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Maryovarian choriocarcinoma is a rare neoplasm and has two subtypes, gestational and nongestational. Differentiating the two subtypes is clinically important due to the difference in treatment and prognosis. This aims to report a rare case of gestational ovarian choriocarcinoma. This is a case of a 37-year-old multigravid who consulted for a 2 weeks history of vaginal bleeding with a background of 12 weeks amenorrhea. Pelvic examination revealed a small uterus with a 6 x 6 centimeters left adnexal mass, which was later confirmed to be tubal pregnancy on ultrasound. On laparotomy, superior and to the left of the uterus was a complex mass that measured 10 x 10 x 8 centimeters with smooth and intact capsule, which on cut section showed necrotic and hemorrhagic placental-like tissues. The uterus, right adnexa and left fallopian tube were grossly normal. Serum BhCG was 268,733 mIU/mL. Histopathology showed presence of clusters of cytotrophoblasts separated by streaming masses of syncytiotrophoblasts resulting in a characteristic dimorphic plexiform pattern of choriocarcinoma and absence of chorionic villi. She was diagnosed with Primary Ovarian Choriocarcinoma FIGO Stage I: WHO High risk. She refused to receive multiagent chemotherapy and succumbed several months after surgery.
METASTATIC PLACENTAL SITE TROPHOBLASTIC TUMOR WITH MULTIPLE PULMONARY METASTASES

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²Medical Oncology, Hospital del Mar, Barcelona, Spain
³Pathology, Hospital del Mar, Barcelona, Spain

Objectives
Placental Site Trophoblastic tumor (PSTT) is a rare gestational trophoblastic neoplasm arising from placental intermediate cytotrophoblasts cells. PSTT usually appears confined to the uterus therefore surgery is the treatment. 30% of PSTT can present with metastases, requiring chemotherapy. We present a patient with multiple metastatic lesions to the lungs of PSTT that was successfully managed with multiagent chemotherapeutic regimen and surgery of the primary tumor.

Methods
Patient is a 37 years old with an abnormal uterine bleeding. Her urine pregnancy test was positive and serum level of b-Human Chorionic gonadotropin 36510 mUl/ml. Based on this, a gestational trophoblastic disease (GTD) was suspected.

Pathologic examination of the endometrium demonstrated atypical intermediate trophoblasts consistent with a PSTT. Radiological staging revealed multiple pulmonary nodules and an intrauterine mass with miometrial and parametrial infiltration. Patient was treated with EMA-EP chemotherapy. After the forth cycle of chemotherapy there was pulmonary complete response and uterine partial response. A laparoscopic TH/BSO was performed. Patient continued treatment with EMA-EP until 8 cycles. Patient is without evidence of disease 20 months after finish treatment.

Conclusions
We present a patient with multiple metastases to the lungs of PSTT that was successfully managed with multiagent chemotherapeutic regimen and surgery. The rarity of this event has made the establishment of specific treatment guidelines impossible and groups extrapolate management strategies from other common high-risk GTD tumors. While multiagent chemotherapy is the first-line therapy for PSST with pulmonary metastases, surgery of persistent primary and distant tumor it could be a reasonable option.
POSTMENAPAUSAL GESTATIONAL TROPHOBLASTIC DISEASE IN TURKEY: FROM 1932 TO PRESENT. A STUDY OF 15 CASES
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Objectives
Background: The incidence of gestational trophoblastic disease (GTD) in postmenopausal period is extremely rare. It is usually persistant and malignant in this period of life. Additionally, due to low incidence of the disease and limited treatment options, treatment strategies must be individualised. Aim: To evaluate clinical behaviour and follow-up results of GTD in postmenopausal period.

Methods
We found 15 case reports originated from Turkey in the literature and collected datas of clinical and demographic characteristics, treatment and follow-up regimens and reviewed in the light of recent developments.

Results
There were six cases (40 %) with molar pregnancy, seven cases (46.6 %) with choriocarcinoma and two cases with (13.4 %) invasive mole. The average age of the cases with complete mole was 53.3 (range, 47-58), five of them underwent surgery, metotrexate chemotherapy administrated for one case, one case showed persistance and treated successfully with single agent chemotherapy. The average age of the cases with choriocarcinoma was 52 (range, 46-58). Metastatic disease was found in three cases and cure was achieved with combined chemotherapy in two of them. One case was died because of febrile neutropenia and sepsis related to chemotherapy. Other case was with end stage disease. The ages of cases with invazive mole was 53 and 55. They had successful surgical treatment and further intervention was not necessary.
Conclusions
There were only 15 case reports of postmenopausal GTD from Turkey, which is extremely rare. Hysterectomy was most common treatment option. Long-term results of treatment was found to be successful.
e-Posters: Trophoblastic Diseases

PLACENTAL SITE TROPHOBLASTIC TUMOR (PSTT) A TREATMENT DILEMMA OF YOUNG ADULTS: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

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Objectives
Placental site trophoblastic tumor (PSTT) is the rarest type of gestational trophoblastic tumors. Unlike the other form of GTD's PSTT is chemoresistant and Stage I disease is usually managed with hysterectomy. PSTT in a woman of childbearing age, the patient's desire for future fertility is a critical issue and a hysterectomy may be devastating.

Methods
Two women 27 and 26 years old was admitted to our clinic with abnormal uterine bleeding. In their examination enlarged uterus with containing a multiloculated lesion in their USG. First patient was delivered a baby 4 years ago and had a D&C after a history of abortion 15 months ago. Second patient's first and last pregnancy was delivered by spontaneous vaginal delivery 11 months previously. Their endometrial sampling revealed PSTT. Immunohistochemical studies revealed CD146, HPL positive p63 and PLAP negative neoplastic cells.

Results
First patient choosed hysterectomy as a treatment of choice. She has been disease free for 2 years. Despite of strong desire of childbearing, second patient has also unwillingly choose hysterectomy in another oncology clinic.

Conclusions
About 200 cases of PSTT have been reported all over the world. The patient's strongly desired of preserving fertility they was counseled on hysterectomy as first linetreatment but also primary chemotherapy. Paucity of data on primary chemotherapy restrain patient's fertility desire. Publication of new experiences about fertility sparing in PSTT is essential for determination of an appointed regimen and prognostic factors to give more reliable information to patients with a desire of fertility.
e-Posters: Trophoblastic Diseases

PLACENTAL SITE TROPHOBLASTIC TUMOR: A CASE REPORT

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Objectives
Placental site trophoblastic tumor (PSTT) is a rare variant of gestational trophoblastic neoplasia (GTN).

Methods
A 31 years old G1P2 woman presented with vaginal bleeding and irregular cycle. The personal history revealed 2 extra-uterine pregnancies. The physical examination and the vaginal ultrasound were normal. The blood test revealed HCG at 29.6mU/ml and 39mU/ml after 48h. After one week HCG was 41mU/ml. The possibility of an extra-uterine pregnancy was posed and the patient received a dose of 60mg intramuscular methotrexate (MTX). On the 10th day HCG was 109mU/ml. The endometrial biopsy showed atypical cells of trophoblastic origin that could be interpreted in the context of a GTN. An operative hysteroscopy was realised where a mass of the uterine fundus was observed and biopsied. The results revealed the presence of a PSTT. An extension control was realised. The pelvic MRI showed a tumoral infiltration of the uterus whereas the pelvic and lombo-aortic nodes were negative. The cerebral MRI and thoracic and abdominal tomodensitometry were negative. A total hysterectomy with pelvic and lombo-aortic lymphadenectomy was performed. The results confirmed a PSTT measuring 3.5 cm invading the serosa and 5 lombo-aortic lymph nodes were invaded (FIGO IV). We decided to administrate a chemotherapy EP/EMA. HCG levels were reduced immediately after surgery.

Results
Approximately 150 cases have been reported in the literature. To date FIGO staging remains the best predictor of overall survival.

Conclusions
We report the case of a PSTT FIGO IV where lombo-aortic lymphadenectomy was positive. A complete surgical staging should be considered in these cases.
EPI THELIOID TROPHOBLASTIC TUMOR OF THE LUNG WITH ANTECEDENT HYDATIDIFORM MOLE

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Objectives
Epithelioid trophoblastic tumor (ETT) is a rare type of gestational trophoblastic disease, which was first proposed by Mazar and Kurman in 1994 as an unusual type of trophoblastic tumor. It originates from the chorionic-type intermediate trophoblast.

Methods
We present a case of ETT of the lung at 10 months after suction curettage due to complete hydatidiform mole. She was 49-year-old and had two normal deliveries at the ages of 30 and 33 years and one cesarean delivery at the age of 36 years.

Results
Her serum β-hCG level was 0.7 mIU/ml 9 months after curettage. But it was elevated to 48 mIU/ml 1 months after that time. Her chest CT scan revealed two small nodules (3mm in size), suggesting metastatic lesions. Because no tumor lesions were detected in the abdomen and pelvis, wedge resection of metastatic foci in the lung was performed. On microscopic examination and immunohistochemistry, epithelioid trophoblastic tumor (ETT) was confirmed. She was treated chemotherapy with EMA-CO regimen. The serum β-hCG level decreased to 0.39 mIU/ml 4 months after last chemotherapy. So far most cases with ETT have been reported to have previous gestational events and tumor lesions inside the uterus, in addition to those in recognized extrauterine sites.

Conclusions
The present case had a pregnancy history of hydatidiform mole, showing two pulmonary nodules without apparent intrauterine lesion. With the high mortality experienced within ETT cases, it is important that there is an improved understanding of the nature and progression of this disease.
PARTIAL HYDATIDIFORM MOLE ASSOCIATED WITH MASSIVE CONCEALED INTRAUTERINE HEMORRHAGE

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Objectives
Hydatidiform moles are noninvasive, localized tumor which related to result of abnormal fertilization that leads to proliferative process. These moles comprise 90 percent of GTD cases. Patient with hydatidiform mole has these clinical features: vaginal bleeding, enlarged uterus, pelvic pain, anemia, theca lutein cysts, hyperemesis gravidarum, hyperthyroidism. We present a case of partial hydatidiform mole associated with massive concealed intrauterine hemorrhage.

Methods
The patient was 17 years old, whose chief complaint was only lower abdominal pain. Her initial vital sign was stable, but initial hemoglobin was 7.0g/dL without vaginal bleeding or any other bleeding focus. Beta-hCG exceeded over 1,000,000mIU/mL. Huge uterine enlargement (16.73 x 9.93cm) was noted and endometrial cavity was filled with echogenic material, but no fetus was seen.

Results
We performed dilatation and curettage. Profuse blood pooled in endometrial cavity during insertion of forceps was gushed out. There were gape like vesicles in intrauterine cavity and its histology result was partial hydatidiform mole. We checked beta-hCG serially, its result was decreased. Infrequently, uterus of partial hydatidiform mole associated with excessive uterine size and ovarian enlargement. In this case, there was concealed intrauterine hemorrhage with huge uterine enlargement (16.73 x 9.93cm) and enlarged both ovarian cysts.

Conclusions
This case suggests that atypical partial hydatidiform mole can associate with massive concealed intrauterine hemorrhage.
e-Posters: Trophoblastic Diseases

NOVEL NLRP7 MUTATIONS IN FAMILIAL RECURRENT HYDATIDIFORM MOLES: ARE NLRP7 MUTATIONS AT THE SAME TIME A RISK FOR RECURRENT REPRODUCTIVE WASTAGE?
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Objectives
Familial recurrent hydatidiform mole is an exceedingly rare clinical condition in which affected women have predispositions to molar pregnancies characterized by diploid, biparental rather than androgenetic, origins. Previously reported NLRP7 and currently addressed KHDC3L (C6orf221) are the only known genes presently associated with this predicament. Genetic dispositions in two large Turkish families with recurring molar conceptuses with current insights are investigated.

Methods
Copy number variation analysis was performed followed by NLRP7 gene sequencing. Findings of monoallelic condition in second family let us further investigate the adjacent NLRP2 and recently disclosed KHDC3L genes in the second family. Sampled molar tissues were genotyped by microsatellite markers.

Results
In the first family, homozygous single nucleotide insertion that causes a frameshift leading to an early stop codon, c.2940_2941insC (p.Glu981ArgfsX13), was identified in the affected sisters. In the second family, heterozygous 60 kb deletion eliminating the substantial portions of NLRP2 and NLRP7 genes on one allele was found. Screening of NLRP2 and KHDC3L genes revealed no alteration assessed to be pathologic. Genotyping of six independent molar conceptions demonstrated the presence of different types of molar conceptions, five diploid biparental and one diandric triploid origin.
Conclusions
Two novel protein-truncating mutations in NLRP7 gene were found to be associated with familial recurrent hydatidiform moles. Mutations in NLRP7 gene causing recurrent biparental hydatidiform mole may also be associated with other form of recurrent reproductive wastage.
LUNG METASTASES AND GESTATIONAL TROPHOBLASTIC DISEASE.
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Objectives
The presence of lung metastases in Gestational Trophoblastic Neoplasia (GTN) is considered a low risk factor not influencing prognosis. Consequences of such metastases on the course of disease are unclear. The present study evaluated parameters affecting prognosis and course of disease in patients with GTN and solitary lung metastases.

Methods
Patients with GTN between 1990 and 2011 were collected from the database of the Dutch Working Party on Trophoblastic Disease and the Central Molar Registry. Chemotherapy resistance, number of chemotherapy courses, recurrence rates and survival were compared between patients with solitary lung metastases and patients without metastases.

Results
We identified 69 GTN patients with lung metastases and 361 without metastases. Lung metastases were associated with an antecedent term pregnancy (17.4\% vs. 6.4\%; \textit{P}=0.025) and the histopathologic diagnosis of choriocarcinoma (28\% vs. 7\%; \textit{p}<0.001). Number of mono-chemotherapy courses significantly differed between the groups (6.7 vs. 6.1 courses; \textit{P}=0.04) and MTX resistance occurred more often in the study group (51\% vs 29\%; \textit{p}=0.01). GTN recurred in 14\% of patients with lung metastases and only in 2.8\% of controls (\textit{P}<0.001) even after correcting for antecedent pregnancy and interval. In the study group 7.3\% of patients died compared to 0\% (\textit{P}<0.001).

Conclusions
Patients with lung metastases are at risk for a complicated course of disease. This is not completely explained by coincident risk factors such as antecedent term pregnancy. Further research is needed to evaluate whether the presence of lung metastases is an independent risk factor that needs to be given more weight in scoring systems.
ROLE OF HE4 AND FOUR MALIGNANCY RISK INDICES IN THE PREOPERATIVE EVALUATION OF ADNEXAL MASSES: A PROSPECTIVE STUDY.

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Objectives
To assess the clinical value of HE4 and four risk of malignant indices in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods
Serum specimens were collected from 61 patients admitted to our Clinic because of adnexal mass. Ultrasound examination was done for each patient. Four risk of malignancy indices RMI I-IV were calculated depending on serum level of CA125, menopausal status and ultrasonographic features. Formulas of Jacobs, Tinglustad and Yamamoto was used for calculation of RMI I-IV. The definitive diagnosis of the adnexal pathology was established by the pathological examination of the excised lesions. The normal level of and HE4 was considered less than less than 70 pmol/L. Chi-square test was used for the statistical analysis.

Results
Seven cases (11,48%) were diagnosed with malignant disease. 13 patients (21,31%) were after menopause. The sensitivity of HE4, RMI I, RMI II, RMI III and RMI IV was 100,00%. The specificity was 98,15%, 100,00%, 96,30%, 98,15% and 98,15% respectively. The positive predictive value was 87,50%, 100,00%, 77,78%, 87,50% and 87,50% respectively. The negative predictive value was 100,00% for all the diagnostic methods.

Conclusions
HE4 and four risk of malignancy indices have similar diagnostic value in the preoperative assessment of adnexal masses.
ROLE OF HE4 AND SIMPLE ULTRASOUND RULES PROPOSED BY IOTA GROUP IN PREOPERATIVE EVALUATION OF ADNEXAL MASSES: A PROSPECTIVE STUDY.

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Objectives
To assess the clinical value of HE4 and simple ultrasound rules suggested by International Ovarian Tumor Analysis (IOTA) group in the preoperative differentiation between malignant and non-malignant adnexal masses.

Methods
Serum specimens were collected from 61 patients admitted to our Clinic because of adnexal mass. Serum level of HE4 was measured using chemiluminescent method. Ultrasound examination was done. According to IOTA group adnexal mass was classified as malignant, benign or not diagnosed. The definitive diagnosis of the adnexal pathology was established by the pathological examination of the excised lesions. The normal level of and HE4 was considered less than less than 70 pmol/L. Chi-square test was used for the statistical analysis.

Results
Seven cases (11,48%) were diagnosed with malignant disease. The level of HE4 was significantly increased among patients with malignant tumors ($\chi^2(1)=44,13; p<0,001$). The sensitivity, specificity, positive and negative predictive values were 100,00%, 98,15%, 87,5% and 100,00% respectively. The sensitivity, specificity, positive and negative predictive values of the simple ultrasound rules by IOTA were 100,00%, 90,74%, 63,64% and 100,00% respectively. The chi-square test showed an important statistical difference considering the use of simple rules in diagnosing malignant masses ($\chi^2(2)=26,91;p<0,001$).

Conclusions
HE4 and simple ultrasound rules by IOTA have similar sensitivity and specificity in the preoperative assessment of adnexal masses.
e-Posters: Ovarian Cancer

PERITONEAL LOW GRADE SEROUS ADENOCARCINOMA PRESENTING AS A CAECAL MASS. A CASE REPORT AND LITERATURE REVIEW

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Objectives
We report an extremely rare instance of low grade serous carcinoma presenting with anaemia and caecal mass in a young woman.

Methods
The patient was a 38 year old female who presented with anaemia (Haemoglobin 8.5). A CT scan showed an intraabdominal mass within the caecum with no other known site of disease. A colonoscopic biopsy of the tumour revealed a low grade serous carcinoma. She underwent laparotomy with right hemicolectomy, total abdominal hysterectomy, bilateral salpingoophrectomy and omentectomy.

Results
The macroscopic examination of the colon showed an ulcerating 30mm caecal tumour with serosal induration. The uterus, cervix, both tubes and ovaries appeared normal. No omental deposits were noted grossly.

Microscopic examination showed an infiltrative papillary tumour with psammoma bodies, consistent with a low grade serous adenocarcinoma involving the caecum and infiltrating the full thickness of the bowel wall. Metastatic tumour was noted in two out of thirteen lymph nodes. The ovaries showed scanty microscopic foci of superficial low grade serous carcinoma. The omentum was free from tumour.

Conclusions
Low grade serous carcinoma is a recently described entity usually affecting the peritoneum and/or ovaries. Tumour localization exclusively to colon and metastasis to regional lymph nodes in the absence of concurrent significant ovarian or peritoneal disease, suggests that this tumour may simulate the behaviour of primary colonic carcinoma. The clinicians should be aware of this aberrant behaviour and therefore should include it in the differential diagnosis of a colonic mass presenting in young female.
IS THERE ANY PROGNOSTIC EFFECT OF THE DIFFERENT SPACE SPLENIC METASTASES IN SEROUS EPITHELIAL OVARYAN CANCER STAGE III-IV

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Objectives
Aim of study is to evaluate between the different site of metastases in spleen and overall survival and complications.

Methods
123 patients who underwent splenectomy as a part of the cytoreductive surgery were retrospectively analyzed. (2007-2013)

Clinico-pathological variables and survival analyses was performed by using SPSS v.16.

Results
Median age of patients was 59.33 Of these 123 patients 33(%27) had hilum, 11(%9) had capsular 79(%64) combined splenic involvement (table 1). The overall survival rate for whole group was 51,2 months. The most common complications was fever (23 patients) follow on this ; pleural effusion (17), ileus (12) trombocytosis (8).

Table 1 splenic involvement and overall median survival
Tumoral involvement in spleen number patients median survival (mts)
Hilum 33 54
Capsular 11 33
Hilum+capsula 49 51
Capsula+hilum+paranchima 14 42
Hilum+paranchima 13 69
Capsula+paranchima 3 33
Total 123 51,2

Conclusions
The different site of splenic involvements are not significant prognostic factors in this study but splenectomy is necessary for the complete cytoreduction, additionaly we need for the studies reach clear conclusion
ACTIVATION OF FALLOPIAN TUBE STROMA AND ITS CONNECTION TO OVARIAN CANCER

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Objectives

The role of stroma in the tumor development is being more and more recognized and accepted. Since epithelium and the subjacent stroma exert instructive influences over each other, especially during embryonic and fetal development, in the conditions of inflammation these influences change. The possible role of inflammation in tumor development lies in the fact that proinflammatory microenvironment can induce and promote tumor growth. The distal end of fallopian tube has recently emerged as a potential origin of serous carcinoma of pelvis and possibly of ovarian cancer. The proposed route for serous carcinoma involves the fallopian tube fimbria, the formation of a preneoplastic precursor lesion or ‘p53 signature’ of secretory epithelial cells, and further progression to tubal intraepithelial carcinoma and invasive serous carcinoma.

Methods

By analyzing stroma of fallopian tube of women undergoing hysterectomies for benign indications, BRCA + women, and women with ovarian cancer, we could expect inflammatory/procarcinogenic tubal microenvironment in precancerous and cancerous lesions.

Results

Inflammation activates stromal cells like: fibroblasts, endothelial cells, and immune cells (macrophages). These cells then secrete: growth factors, chemokines, cytokines, extracellular matrix modifiers, and angiogenic factors. The key molecular link between inflammation and tumor promotion and progression is activation of the NF-kB transcription factor which regulates the expression of many genes whose products support tumor progression, angiogenesis, and metastasis.

Conclusions

This study could shed the light on several cancer theories: fimbrial origin of ovarian serous carcinoma, stromal role in induction and promotion of tumor and inflammation as a possible trigger and/or promotor of oncogenesis.
e-Posters: Ovarian Cancer

OVARIAN CANCER MANAGEMENT PATHWAYS AND OUTCOMES WITHIN WOLVERHAMPTON NHS TRUST
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Objectives
Recent national audit data of 2 and 5 year survival in Ovarian cancer have suggested variation in outcomes over the UK, raising the possibility of differences in management. A local audit was carried out of patients treated between January 2004 until December 2008 to review outcomes and treatment pathways.

Methods
Patients were found from electronic coding records and data obtained from a combination of electronic records and patient notes.

Results
106 patients were identified. Mean age at diagnosis 62 years, 26% stage 1, 7% stage 2, 59% stage 3 and 8% stage 4. Mean interval from surgery to chemotherapy was 38 (5.4 weeks) days. Most common regimes were carboplatin and paclitaxel (49%), single agent carboplatin (39%), intraperitoneal carboplatin within trials (6%) and other regimes (6%). Overall survival (OS) at 2 years was 91%, 50%, 65% and 44% respectively. OS at 5 years was 20% and 11% for stage 3 and 4 respectively, with 16% and 11% remaining in follow (median 62 and 54 months). Of patients who were platinum resistant (relapse within 12 months of chemotherapy) median OS was 18 months, while in sensitive disease median OS was 37 months.

Conclusions
The majority of patients received standard first line chemotherapy regimes, although sub-optimally timed with delay following surgery. OS and PFS increase with stage and significantly in platinum resistant patients, but are comparable with published national figures and ICON 7 trial data.
e-Posters: Ovarian Cancer

IMPACT OF SECONDARY CYTOREDUCTIVE SURGERY FOR RECURRENT EPITHELIAL OVARIAN CANCER
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Objectives
To study the impact of secondary cytoreductive surgery in recurrent ovarian cancer on prolonging survival and to define which variables might modify surgical outcomes.

Methods
We reviewed the charts of 50 patients underwent secondary cytoreductive surgery at MD Anderson Cancer Center, Madrid, between January 2003 and June 2011. Study inclusion criteria required: optimal primary cytoreduction, platinum free interval ≥6 months, no evidence of ascitis. All patients were evaluated clinically, radiologically (including PET-CT), and biochemically with CA-125. Optimal cytoreduction was considered residual disease ≤1.0 cm. The Cox proportional regression model and logistic stepwise regression were used in statistical processing data.

Results
Fifty patients met the inclusion criteria. The mean age was 57 years (ranged from 27 to 82 years). According to FIGO classification at initial diagnosis there were 11 patients stage I-II (22 %) and 39 stage III-IV (78%). Optimal secondary cytoreduction was achieved in 46 of 50 patients (92%). Intraoperative surgical complications were not encountered. We had 1 (2%) early postoperative death and 9 postoperative complications (18%). All patients received adjuvant chemotherapy. Median progression-free survival after secondary cytoreduction was 18 months. The mean follow up was 34,6 months. Median Survival has not been reached yet. The median overall survival after first diagnosis was 93 months.

Conclusions
In our experience, secondary cytoreductive surgery in selected cases, significantly obtained a substantial progression free and overall survival in patients with recurrent epithelial ovarian cancer. Important survival benefit increases when microscopic residual disease is left, in our experience optimal surgical is achievable with an acceptable morbidity and mortality.
SPLENECTOMY AS PART OF CYTOREDUCTIVE SURGERY IN OVARIAN CANCER

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Objectives
To describe outcomes of patients who required splenectomy as part of optimal tumor cytoreductive surgery in ovarian cancer.

Methods
Retrospective analysis of 25 patients with advanced ovarian cancer, who underwent a splenectomy as part of cytoreductive surgery from June 2006 to June 2011 at MD Anderson Madrid.

Results
Median age was 58 years (range 30-79). Splenectomy was carried out in 13 (52%) at the time of primary debulking surgery, in 12 (48%) in the recurrent setting.

The majority of patients had stage IIIC (76%), serous histology (68%), and high grade histology (64%). PET-TAC revealed splenic metastases in 44%. The purpose of splenectomy was to accomplish an optimal cytoreduction in 88% of cases (parenchymal 44%, surface metastases in 20% and hilar metastases in 24%). 64% of patients also required bowel resection and 12% distal pancreatectomy. Complete cytoreduction (R=0) was achieved in 84% of patients.

Short-term complications included wound infections (8%), thromboembolic events (16%), ileus (4%) and abscess or seroma in splenic area (16%). Most of patients needed blood transfusion during surgery (84%). Five patients required reoperation (20%) not related to splenectomy complications. The perioperative mortality rate at splenectomy was 8% (2 patients).

Mean length of stay was 10.24 days (UCI 1.36 days). Median time for first chemotherapy was 47 (22 – 105) days. The PFS for this group of patients was 16.5 months.

Conclusions
Spleen infiltration by advanced ovarian cancer is not a rare finding. Splenectomy is a surgical maneuver, feasible and safe, indispensable to achieve in some circumstances a complete cytoreduction.
COMPREHENSIVE LAPAROSCOPIC SURGICAL STAGING OF OVARIAN DYSGERMINOMA IN A 10-YEAR-OLD GIRL: A CASE REPORT
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Objectives
To described a case of comprehensive laparoscopic surgical staging of an ovarian dysgerminoma in a 10-year-old girl.

Methods
A case of comprehensive laparoscopic surgical staging of an ovarian dysgerminoma in a 10-year-old girl is described.

Results
This patient was referred to the gynecology oncology unit status post left salpingo-oophorectomy through a midline incision when the histopathology showed pure dysgerminoma. We then performed laparoscopic staging including peritoneal washing; resection of the left infundibulopelvic ligament; systematic pelvic, common iliac, and infrarenal bilateral paraaortic lymphadenectomy; and omentectomy. The uterus and right adnexum were spared to preserve future fertility. All surgical specimens including total of 24 pelvic and para aortic lymph nodes and the peritoneal washing revealed no evidence of neoplastic lesions, so the final diagnosis was a pure ovarian dysgerminoma at la stage (FIGO classification).

Conclusions
Although the role of laparoscopy in gynecologic oncology and particularly in the management of early ovarian cancer remains controversial and under evaluation, it is interesting to describe a minimally invasive approach used in a 10-year-old child girl for restaging of an ovarian dysgerminoma.
e-Posters: Ovarian Cancer

OUTCOMES OF OVARIAN CANCER IN YOUNG WOMEN IN HOSPITAL TENGGU AMPUAN AFZAN, KUANTAN: 2006-2012

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Objectives
To determine the histology, type of surgery and outcomes of ovarian cancer in young women.

Methods
A 6 year retrospective observational study of ovarian cancer in the women aged below 40 years.

Results
There were 20 cases of ovarian cancer. 60% (n=12) were malignant germ cell ovarian tumours (GCT) and 40% (n=8) were epithelial ovarian tumours (EOT). Patients with EOT were older compared to GCT, with the mean age of 32.4 versus 21.5 year-old (p= 0.011). The percentages of women who had fertility sparing and radical surgery were 55% and 45% respectively. The women who had fertility sparing surgery were significantly younger compared to those who had radical surgery (mean age of 20.6 versus 32.3 years, p=0.004). 70% (n=14) of the women had stage 1 disease at diagnosis. There was no difference in the percentage of women with stage 1 disease or other stages at presentation between EOT and GCT (p=0.550). Optimal cytoreductive surgery was achievable in 90% of the cases and the rate was similar between EOT and GCT (p=0.068). The mean duration of follow-up and overall survival was 30.6 months. There was no difference in the mean overall survival (p=0.511) and survival between women who had fertility sparing and radical surgery (p=0.338) between EOT and GCT.

Conclusions
Fertility sparing surgery has been shown to have similar outcomes as compared to radical surgery, thus it should be part of the management options in young women with malignant ovarian tumours.
e-Posters: Ovarian Cancer

RETROSPECTIVE ANALYSIS OF PATIENTS WITH BORDERLINE OVARIAN TUMORS: A TEN YEARS SINGLE-CENTER EXPERIENCE OF 53 CASES.
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Objectives
To evaluate clinico-pathological features of 53 cases with borderline ovarian tumors and present our experience.

Methods
Fifty-three patients with borderline ovarian tumors operated in Zeynep Kamil Hospital between 2001–2011 are included. Demographic and clinical findings, surgical methods, wish for the preservation of fertility, recurrences and survivals were evaluated.

Results
Average age of patients were 45.4±15.5. Time at diagnosis of 56.6% of the patients were in postmenopausal, 43.4% of patients were in premenopausal period. 67.9% of the patients had serous, 26.4% musinous and 5.7% mix histologic type. Tumor markers were elevated in %62.3(n=33) of the patients before the surgery (≥35IU/ml). Total abdominal hysterectomy (TAH)+bilateral salpingo-oophorectomy (BSO) 1,9% (n=1), unilateral salpingoophorectomy (USO)+contralateral ovarian biopsy 13,2% (n=7) , USO+bilateral pelvic and paraaortic lymphadenectomy (BPPLND)+omentectomy 26,4% (n=14) and TAH+BSO+BPPLND+omentectomy 58,5% (n=21) were the preferred surgical treatments. 92,45%(49/53) of the patients were stage I. 39,6%(n=21) of the patients were treated with fertility sparing surgery but five of them were reoperated in 1 year. Totally 30,2% (n= 16) of the patients were treated with fertility sparing surgery and none of them were reoperated until January 2013. We have had five babies and one ectopic pregnancy after fertility sparing surgery. Furthermore we have not seen any recurrence during our follows-up.

Conclusions
Borderline ovarian tumors have perfect prognosis. Surgery represents the most important therapeutic arm. Conservative treatment of borderline ovarian tumors should be consider in patients with fertility desire and at reproductive age but patients should be warned for recurrences rates. Our experiences are coherent with literature.
CORRELATION OF VARIOUS DNA PLOIDY PARAMETERS AND THE STAGE OF DISEASE

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Objectives
The purpose is correlation DNA ploidy parameters (Degree of Aneuploidy - DA) with the stage of disease.

Methods
Our study was carried out on 105 patients. DNA ploidy was measured in histological sections of malignant epithelial ovarian tumors.

To identify the prognostic significance of various DNA ploidy were performed multi-dimensional statistical analyzes.

Results
According to the results of the multivariate model analysis, patients with a degree of aneuploidy corresponding DA-30<60% has almost 2.6 times higher risk of adverse outcomes compared with patients when DA<30%, in the case when they staged as I-IIc. Patients with the degree of aneuploidy corresponding DA>60% has almost 12 times higher risk of adverse outcome compared to patients whose degree of aneuploidy corresponds to DA<30%, provided that they staged as I-IIc.

According to the results patients with stage III with DA- 30<60% have a 7.41 times higher risk of poor prognosis (Hazard Ratio-7.41, CI-0.91-60.16) compared to patients with stage I-II with DA<30%.

Patients with stage IV with DA-30<60% have a 36 times higher risk of poor prognosis (Hazard Ratio-36.22, CI-4.37-300.02) compared with patients with early stage and degree of aneuploidy DA<30%.

Conclusions
Stage of the disease has a major prognostic importance in determination the outcome. The data of the analysis shows that the deterioration in the degree of aneuploidy increases the risk of poor prognosis in patients of the same group which staged as I-IIc. DNA ploidy affect the survival of patients in both early and late stages of the disease.
e-Posters: Ovarian Cancer

BODY MASS INDEX CHANGE DURING CHEMOTHERAPY AND PROGNOSIS IN ADVANCED OVARIAN CANCER
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Objectives
To investigate body mass index (BMI) changes during chemotherapy for advanced ovarian cancer patients and to the association with survivals.

Methods
The medical records of the seventy patients who were treated by ovarian cancer from 1996 to 2007 at Korea University Hospital were reviewed retrospectively. After diagnosis and cytoreductive operation, body weight and height of patients were measured before first cycle chemotherapy and also after finishing sixth chemotherapy. Both pre-chemotherapy and post-chemotherapy BMI which was corresponded with WHO Asia-Pacific Guidelines were analyzed. Overall survivals according to the BMI, BMI change and body weight change were estimated by Kaplan-Meier.

Results
Body weight and BMI were increased from 55.16kg to 56.83kg (p<0.05) and 23.26 to 23.95 (p<0.05). Pre-chemotherapy BMI was not correlated with survival (p=0.758). On post-chemotherapy BMI, overweight patients have improved survivals than ideal weight (p=0.043) and have a trend than overweight (p=0.097). There was an improved survival in no BMI change (-1< <+1) patients than decreased (<-1) or increased (<+1) BMI patients (p=0.047).

Conclusions
Body weight and BMI are increased during chemotherapy. Minimal BMI change has improved survival but post-chemotherapy overweight has a trend to improved survival.
e-Posters: Ovarian Cancer

RETROPERITONEAL LYMPH NODES BEHAVE AS CHEMOTHERAPY-SANCTUARY IN EPITHELIAL OVARIAN CANCER

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Objectives
Lymphadenectomy is key in early ovarian cancer. However, its role in advanced disease remains controversial, although recent data suggest this procedure could improved survival. An explanation would be that retroperitoneal lymph nodes behave as chemotherapy-sanctuary.

The aim of this study was to compare the rate and distribution of positive retroperitoneal lymph nodes in patients with advanced ovarian cancer undergoing upfront versus interval cytoreductive surgery.

Methods
We reviewed the charts of women with advanced epithelial ovarian cancer treated in our center from December 2011 to April 2013. Our philosophy is to perform systematic pelvic and periaortic lymphadenectomy when achieving optimal cytoreduction seems feasible. The number of node retrieved as well as the rate of positive nodes and their anatomic distribution were assessed and compared between the two surgical groups described above. Statistical comparisons were made using SPSS 19.0.

Results
The median number of nodes harvested in the upfront and interval groups was 28 and 25, respectively (p 0.176); 71.4% of patients undergoing initial surgery had positive nodes compared to 54.5% of those receiving interval cytoreduction. There was no statistical difference between the median number of positive nodes (4 and 3, respectively; p 0.375). Regarding the location of the metastatic nodes, all of them involved the periaortic area in the upfront group, while 83% did it in the interval cohort.

Conclusions
A high rate of metastatic retroperitoneal lymph nodes is found in advanced ovarian cancer despite the use of chemotherapy. The periaortic area appears to be the preferred involved region.
e-Posters: Ovarian Cancer

THE USE OF HUMAN EPIDIDYMIS PROTEIN 4 FOR DIFFERENTIATION BETWEEN BENIGN AND MALIGNANT OVARIAN NEOPLASM

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Objectives
To assess and compare the sensitivity, specificity, predictive values of HE4 and CA125 in the prediction and evaluation of ovarian masses (whether benign, endometriomas or malignant)

Methods
Prospective study conducted in Kasr Al Aini university hospitals included 30 patients presented with adnexal masses and were treated surgically. Patients were grouped into 3 groups: patients with benign ovarian masses, endometriomas and malignant ovarian masses. History, examination, laboratory work up including HE4 by ELISA technique and CA125 on Immulite 2000 were done for all patients, in addition to abdominal and vaginal ultrasounds, surgical treatment or staging.

Results
There was a statistical significant difference in the levels of CA125 between the malignant and non-malignant lesions. There a statistical significant difference between the HE4 levels among benign (37.57) and malignant lesions (103.16), p value: 0.010. When ROC Curve was constructed the Area Under the Curve (AUC) in benign versus malignant ovarian lesions showed a 100% sensitivity and a 96% specificity for CA125 at a cut-off value of 40. While it showed a 100% sensitivity and a 67% specificity for HE4 at a cut-off value of 42.7.

Conclusions
Measuring HE4 can be useful in combination with CA125 in patients with ovarian lesions (whether benign ovarian cysts, endometriomas or malignant ovarian diseases).
e-Posters: Ovarian Cancer

STAGE IIIC TRANSITIONAL CELL CARCINOMA AND SEROUS CARCINOMA OF THE OVARY HAVE SIMILAR OUTCOMES WHEN TREATED WITH PLATINUM BASED CHEMOTHERAPY

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Objectives

Transitional cell carcinoma (TCC) of the ovary is a rare subtype of epithelial ovarian cancer (EOC). The aim of this study was to compare the outcomes of similarly treated stage IIIC transitional cell and serous EOC patients.

Methods

Clinicopathological and outcome data of patients with FIGO stage IIIC TCC and serous carcinoma (SOC) who had undergone primary surgery followed by six cycles of intravenous platinum/taxane from 2001 to 2012 were retrieved from the database of Hacettepe University Hospital. The Kaplan-Meier method was used to estimate overall survival (OS) and progression free survival (PFS), and survival differences were analyzed by the log-rank test. Cox regression analysis was performed to assess the potential influence of other prognostic factors.

Results

We identified 14 (10.9%) TCC and 114 (89.1%) SOC. The median follow-up duration was 28 months (range, 3-101 months). Univariate analysis revealed that TCCs and SOCs have similar PFS and OS. Patients with residual disease less than 1 cm had longer OS than patients with residual disease greater than 1 cm (75.0 vs 45.0 months, p=0.012). Cox regression analysis of all potential prognostic factors showed that the only independent prognostic factor significantly associated with OS was residual disease less than 1 cm (HR:0.38; 95%CI, 0.19 to 0.77; p=0.007).
Conclusions
Surgically treated advanced stage TCCs did not have a significantly better prognosis after platinum/taxane based chemotherapy when compared with SOCs. Residual tumor volume after primary surgery was the only independent predictor of OS in patients with EOC.
THE SIGNIFICANCE OF NEUTROPHIL/LYMPHOCYTE AND PLATELET/LYMPHOCYTE RATIOS IN PREOPERATIVE PREDICTION OF AN OVARIAN MALIGNANCY

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Objectives
To determine the clinical significance of neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) in preoperative prediction of ovarian malignancies.

Methods
The study was performed in Zekai Tahir Burak Training and Research Hospital in Ankara, Turkey. A retrospective patient chart analysis was undertaken for cases that were operated for an ovarian mass between January 2006 and December 2011. Clinical, pathological and laboratory data including complete blood count parameters were extracted from a database. NLR, PLR and CA125 values were compared between cases with benign and malignant pathology results. Mann-Whitney U test and ROC curve analyses were used to determine significant markers. P<0.05 was considered statistically significant.

Results
A total of 569 cases (316 benign, 253 malignant) were identified within the study period. Most common benign and malignant ovarian pathologies were endometrioma (n:124, 39.2%) and serous cystadenocarcinoma (n:105, 41.5%), respectively. CA125, NLR and PLR values were significantly lower in cases with benign ovarian pathology (p<0.001). In ROC curve analysis, NLR with a cut-off at 2.4 had 65% sensitivity, 72% specificity, 65% positive predictive value and 72% negative predictive value (AUC=0.737). PLR with a cut-off at 173.7 had 48% sensitivity, 81% specificity, 67% positive predictive value and 66% negative predictive value (AUC=0.684).

Conclusions
NLR and PLR had high specificity in prediction of an ovarian malignancy, and might be integrated to combined tumor marker panels. Future studies with larger sample sizes are needed to evaluate effectiveness of these markers.
e-Posters: Ovarian Cancer

SECOND LINE CHEMOTHERAPY IN EPITHELIAL OVARIAN CANCER- ISSUES OF QUALITY OF LIFE AND COST-EFFECTIVE RATIO: EXPERIENCE FROM A CANCER INSTITUTE OF EASTERN INDIA

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Objectives
The treatment outcome the platinum potentially resistant recurrent epithelial ovarian cancer is often very poor. Palliation is aimed at better response with good quality of life (QoL) and cost effective ratio (CER). No work is done so far to observe them in Indian patients.

Methods
From 2006 January to 2009 January a total of 35 platinum resistant advanced epithelial ovarian cancer cases were selected for a prospective study. Among them 21 cases came from neoadjuvant setting and other 14 cases were from adjuvant treatment group.

Results
Both refractory (6 cases) and resistant cases (29 cases) were randomized to receive monotherapy of Inj gemcitabine (9 cases), Inj topotecan (9 cases), Inj Doxorubicin (8 cases), Inj Docetaxel (6 cases) or oral etoposide (3 cases). Response rate was highest in Doxorubicin (37%, 3 cases) followed by gemcitabine, topotecan and docetaxel (33.3%, 3 cases in each group). 1 case in Etoposide group was responder. There was no significant difference in PFS (4 to 7 months) or OS (10 to 17 months) in any of the groups. Quality of life was found to be better in doxorubicin and gemcitabine group.

Conclusions
Doxorubicin was found to have best efficacy with good QoL and ICER. Molecular profiling may be important to increase PFS and OS as is done in recent Chinese study.
e-Posters: Ovarian Cancer

PROLIFERATION (KI-67) AND ENDOCRINE REGULATION (PROGESTERONE RECEPTOR) CORRELATE WITH PROGNOSIS IN OVARIAN CANCER – INVASION (UPA AND PAI-1) DOES NOT

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Objectives
The identification of prognostic markers might have clinical implications in ovarian carcinoma (OC). Here, we study marker for proliferation (Ki-67), endocrine regulation (progesterone receptor (PR) and oestrogen receptor (ER)) and invasion (urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1)) in patients with OC.

Methods
All OC patients, who were treated at our institution between 1997 and 2004, are enrolled in this study. Immunohistochemical analyses are conducted to determine the expression of ER, PR and Ki-67. Enzyme-linked immunosorbent assays are conducted to determine uPA and PAI-1 antigen levels.

Results
108 patients enter this study. In univariate Cox-regression analysis Ki-67 shows a negative impact on disease free survival (DFS) and overall survival (OS) in OC (Hazard ratio (HR) for DFS: 2.166; 95%CI, 1.181 to 3.975; p=0.013; HR for OS: 2.819; 95%CI, 1.329 to 5.978; p=0.007). PR shows a positive impact on prognosis in OC (HR for DFS: 0.353; 95%CI, 0.153 to 0.815; p=0.015; HR for OS: 0.361; 95%CI, 0.144 to 0.906; p=0.030). ER, uPA and PAI-1 are not associated with survival. Postoperative tumor burden and completeness of chemotherapy are associated with prognosis in contrast to Ki-67 and PR in multivariate Cox-regression analysis. The correlation of PR and ER and the correlation of postoperative tumor burden and tumor stage are strong in an explanatory Spearman correlation analysis (rho=0.759 and rho=0.426, respectively).

Conclusions
Ki-67 and PR are associated with prognosis of OC. Expression of PR and ER correlates in OC. Further studies are warranted to confirm our results and to elucidate the underlying mechanisms.
TREATMENT IN ELDERLY PATIENTS WITH ADVANCED OR METASTATIC OVARIAN CANCER: ANALYSIS OF THE MEDICAL ONCOLOGY OF CONSTANTINE

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Background

One third of women who presented ovarian cancer are more than 65 years old. Standard therapy of ovarian cancer including radical surgery, which is radical cytoreduction and combination chemotherapy, has considerable morbidity, and the age was not evaluated in this case.

Methods

Patients with epithelial ovarian cancer FIGO-Stages III-IV were included in this study. Patients were more than 65 years old. All patients were analysed and compared to surgery which was done; especially cytoreduction and had platinum-based chemotherapy. To analyse treatment strategies, theses patients were compared to the younger population with the same criteria.

Results

From January 2011 to June 2012, 34 patients were diagnosed with epithelial ovarian cancer. Only 12 patients had more than 65 years old, with median age of 71 years old. Surgery was less radical in this category of patients (more than 65 years old). Fewer lymph node dissections were done, and 41.6 % of patients in the elderly (n=5) had residual disease after surgery compared to younger patients despite similar FIGO-Stage disease. Furthermore, elderly patients with epithelial ovarian cancer received more often mono-chemotherapy with Paclitaxel because of the toxicity of the platinum in the regimen. Consequently, overall survival was 8 months in the elderly versus 13 months in the younger

Conclusions

Ovarian cancer in the elderly patients is treated less radical and had unfavourable outcome compared to younger population. Age itself is not a prognostic factor for progression free survival in multivariate analysis but it depends on reluctance of surgeons themselves against this disease.
DIFFERENT PATTERNS OF DISEASE SPREAD BETWEEN TYPE I AND II ADVANCED STAGE EPITHELIAL OVARIAN CANCER


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Objectives

Two types of epithelial ovarian carcinoma (EOC) have been distinguished in the last years due to their different pathology, biology and clinical course. To the best of our knowledge there are no studies assessing tumor localization at primary surgery. The aim of this retrospective study was to compare the pattern of disease spread in advanced stage type I and II EOC at primary surgery.

Methods

A total of 175 surgically staged FIGO III-IV EOC patients, 84 with type I (group A) and 91 with type II (group B), have been compared for tumor localization at primary surgery, considering involvement of Douglas pouch, peritoneum, vesico-uterine plica, uterus, diaphragm, liver serosa, omentum, mesentery, ileum, colon, rectum, appendix, caecum, presence of carcinomatosis and pleural effusions. A Pearson c2 test was performed to detect statistically significant differences in cancer localization.

Results

Tumor involvement was significantly higher in group B for the following sites: peritoneum (70% vs 34%, p=0.000), Douglas pouch (70% vs 37%, p=0.000), Vesico-uterine plica (53% vs 21%, p=0.000), Diaphragm (40% vs 17%, p=0.001), liver serosa (12% vs 5%, p=0.05), omentum (80% vs 56%, p=0.000), Mesentery (41% vs 19%, p=0.01), carcinomatosis (51% vs 28%, p=0.002), as well as the presence of pleural effusions (21% vs 11% p=0.05). No statistically significant differences were found for sigma-rectum, ileum, colon, appendix, caecum, gastric localizations.

Conclusions

Our study provides evidence to the dualistic model of carcinogenesis, suggesting that type I and II EOC are different entities, following different patterns of spread.
UNKNOWN PRIMARY ORIGIN METASTATIC OVARIAN CANCER
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Objectives
Ovarian cancer is a medical challenge. It has the highest mortality rate compared to other gynecological malignant tumors. 20% of ovarian tumors are metastatic. The implantation of the metastatic tumor into the ovary happens through the hematogenous and lymphatic spreading and by direct tissue extension from contiguous pelvic neoplasm as well.

Methods
Postmenopausal patient aged 55 was admitted to our hospital due to abdominal pain and flatulence. The ultrasound revealed 2 masses in the parametrium (7.5 cm, 4 cm.) with ascites. MRI confirmed the presence of two knobby formations in the rectouterine excavation. Tumor markers showed CEA 28,6?, CA19 9 47, 47 ?, CA 153 84, 4, CA 125 912,09 ?. The patient underwent exploratory laparotomy. Peritoneum, bowels and diaphragms, were covered with neoplastic diffuse plaques. The right and left components along with the omentum were removed and sent for frozen section which revealed extended infiltration of metastatic cancer.

Results
Metastatic ovarian cancer is classified according to the origin of the primary tumor. The spread of endometrium cancer is more frequent, with its direct implantation in the surface of the ovaries. Breast cancer metastasizes in the ovaries and the Krukenberg tumor (stomach, rectum, biliary).

Conclusions
Patients with metastatic disease of the ovaries should receive personalized cytoreductive surgery of the tumor’s dimensions. Survival rate after surgery and chemotherapy of metastatic cancer of the ovaries originating from breast and the gastrointestinal system is poor and varies from 3-12 months.
A NEW SURGICAL OUTCOME SCORE (SOS) INCLUDING HE4, CA125 AND ASCITES VOLUME CAN PREDICT SURGICAL OUTCOME IN PRIMARY OVARIAN CANCER PATIENTS.

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Objectives
This study aimed at evaluating of new predictive model named SOS (Surgical Outcome Score), which utilizes HE4, CA125 and ascites volume to assess the risk of suboptimal primary tumor debulking in EOC patients.

Methods
In this retrospective multicentric study, 425 primary EOC patients were included. Preoperative HE4 and CA125 serum levels were measured using ELISA technique. Predictive values of HE4 and CA125 were analyzed using the receiver operator characteristic (ROC) with the corresponding AUC. Separate logistic regression algorithms for pre- and postmenopausal women were utilized to categorize patients into low and high-risk groups for residual disease, using CA125, HE4 values and SOS model.

Results
Maximal tumor reduction was achieved in 68.5% patients. Both HE4 and CA125 correlated with residual disease. In premenopausal patients an AUC of 0.757(95%CI 0.61-0.904) for HE4 and 0.751 (95%CI 0.641-0.861) for CA125 was reached. In postmenopausal patients an AUC of 0.650(95%CI: 0.59-0.711) for HE4 and 0.605(95%CI 0.543-0.668) for CA125 was reached. The new model including menopausal status, ascites volume, CA125 and HE4, performed better in predicting surgical outcome than any biomarker alone, or combination. SOS algorithm yield a sensitivity and specificity of 82.4% and 76.7%, in premenopausal patients and a sensitivity and specificity of 73.2% and 51.4%, respectively in postmenopausal patients. The SOS cut-off values of 19.5% and 30. % were used, reaching an AUC of 0.811(p<0.001, 95%CI 0.696-0.926) and 0.664(p<0.001, 95%CI 0.604-0.724) in the pre- and postmenopausal patients, respectively.

Conclusions
The combination of HE4, CA125 and ascites within the SOS score seems to improve the prediction of surgical outcome. Further validation studies are needed.
ANALYSIS AND TREATMENT OF PATIENTS SUFFERING FROM OVARIAN CANCER

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Objectives
Ovarian cancer is the fourth most frequent malignant disease. It is hard to diagnose and in two thirds of cases symptoms appear only in the later stages of the disease.

Aim
Fifty patients who have been diagnosed and treated for malignant ovarian cancer were closely monitored and analyzed within the period of 2 years in Gak Narodni Front in Belgrade and a comparison with the data from the literature has been made.

Methods
By means of retrospective analysis, fifty patients have been analyzed in 2009-10. Medical history, consulting body decisions, histopathological findings and treatment procedures have been used.

Results
Average age of patients was 56. The percentage of the confirmed malignity in the stage II is 6%, stage III 43%, which is very close to the results from the literature. However, 46% was diagnosed in stage I, which is significantly different from 7.7% from the literature. In the group analyzed 46% of patients were serous, 8% mucosal, 12% endometrial, 18% clear cell, and 16% unclassified. Operative procedures: 90%HTA, 6%adnexectomy and 4%biopsy. From the additional procedures were used: 50%omentectomy, 6%Hartman’s procedure, 6%pelvic peritoneotomy, 4%colectomy and splenectomy.

Conclusions
The fight against this disease could be substantially improved by means of screening and systematic check-ups that would use serum markers for early diagnosis of the malignity. Setting up teams, educating the staff, enhancing treatment procedures and implementing electronic database network would provide an adequate follow up of the operated and treated patients with a view to choosing the best approach to the treatment.
Concomitant Pathologic Conditions Other Than Gynecologic in Origin with Borderline Ovarian Tumors (BOT)

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Objectives
To disclose incidental extra-gynecologic pathologic conditions in patients with BOT.

Methods
Patients data reviewed retrospectively and pathologic diagnosis other than gynecologic in origin were evaluated.

Results
There were 813 BOT cases since 1999 in our clinic. During study period many ovarian, uterine, appendiceal and omental concomitant pathologies were diagnosed as well as extra-genital pathologies. As a summary: there were 4 cases that had bilateral serous BOT and extra-ovarian incidental pathology. First case had pathologically confirmed renal methanephric adenoma that was diagnosed during follow-up after staging surgery. Second case had synchronous lymphoepithelioma type gastric carcinoma that was diagnosed per-operatively during staging and also she had a pelvic cyst diagnosed as hydatic cyst in permanent pathology. Third case had diffuse noninvasive peritoneal serous BOT implants with retroperitoneal desmoplasia and sarcomatous mural nodules that had increased mitosis and necrosis accompanying adnexal tumor mass. Another case with unilateral mucinous BOT had suspicional peritoneal biopsy, which revealed accessory spleen. A case with bilateral mucinous BOT had incidental appendiceal mucinous cyst-adenoma and diffuse peritoneal, omental mucinous tumor implantation, which resulted Disseminated Peritoneal Adenomucinosis. Appendiceal insular type carcinoid tumor was another incidental pathology concomitant with unilateral serous BOT. Furthermore Meckel diverticula was another incidental condition associated with unilateral serous BOT.

Conclusions
BOTs are heterogeneous tumors diagnosed in younger age than invasive epithelial ovarian cancer and have better prognosis. There might be multiple genital and extra-genital organ pathologies accompanying BOT. Surgeon's ability to recognize suspicional areas during surgery allow to diagnose concomitant incidental pathologies.
FATES OF APPENDECTOMY AND OMENTECTOMY SPECIMENS FOLLOWING BORDERLINE OVARIAN TUMORS (BOT); SINGLE CENTER EXPERIENCE OF 183 CASES
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Objectives
To realize interesting aspects of appendectomy and omentectomy specimens following BOT staging surgery.

Methods
Pathological reports of appendectomy and omentectomy specimens following BOT staging procedure in our hospital since 1999 were evaluated retrospectively.

Results
There were 183 patients diagnosed as BOT since 1999. Mean age at diagnosis was 40.6 years (range: 17-78) old. During staging surgery totally 153 appendectomy and 163 omentectomy operations were performed.

Appendectomy specimens of 88 patients had normal histology. Most common types of appendix pathology were lymphoid hyperplasia (n:29, one with local peritonitis) followed by peri-appendicitis (n:21) and luminal obliteration (n:11). Only one patient had acute inflammation of the appendix. There was a patient with appendiceal mucinous cyst-adenoma and disseminated peritoneal adenomucinosis concomitant with bilateral mucinous BOT. Another patient who had unilateral serous BOT also had 1.5cm insular type appendiceal carcinoid tumor. Endosalpingiosis (n:1), presence of reactive lymph node (n:1) and enterobiasis infection (n:1) were the other less encountered appendiceal lesions.

Omentectomy specimens of 129 patients had normal histology as a mature adipose tissue. Chronic inflammatory reaction (n:10), reactive lymph node (n:8), subacute peritonitis (n:4), mesothelial proliferation (n:3) and inclusional gland implantation (n:2) were most commonly encountered lesions. Only 3 patients had noninvasive omental BOT implants. Metastasis from gastric carcinoma (n:1), mucinous tumor infiltration (n:1, due to disseminated peritoneal adenomucinosis), endosalpingiosis (n:1) and chronic granulomatous process accompanying bilateral mucinous BOT were the other less encountered omental lesions.

Conclusions
Appendectomy and omentectomy materials might exhibit different disease process synchronous to primary BOT.
e-Posters: Ovarian Cancer

BORDERLINE OVARIAN TUMORS (BOT); SINGLE CENTER EXPERIENCE OF 183 CASES
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Objectives
To present BOT cases who were diagnosed between 1999-2013 in our center.

Methods
Pathological results were evaluated retrospectively.

Results
There were 183 patients diagnosed as BOT. Mean age at diagnosis was 40,6 years (range:17-78) old. Complete surgical staging was performed only to 119 cases (65%). Fertility sparing surgery was performed to 64 cases (34,9%). Totally 119 hysterectomy, 176 peritoneal washing, 153 appendectomy, 163 omentectomy and 159 pelvic-paraaortic lymph node dissection were performed. There were 12 cases with positive peritoneal washings correlated with BOT; 9 cases with noninvasive tumor implants located on Douglas, tubal serosa, bladder, sigmoid, omentum, small intestine and ureter. Mean number of dissected lymph nodes was 56,98 (range:12-173). Of the 159 cases of lymph node dissections only 10 cases had lymph node abnormalities other than lymphoid hyperplasia. Of these 4 cases had benign glands, lined by tubal-type epithelium also called endosalpingiosis; 3 cases had benign inclusional glandular implants; 2 cases had presence of serous BOT and one case who had synchronous serous adenocarcinoma on the contralateral ovary had tumor-positive lymph nodes. Most common type of BOT was serous in histology (n:115) followed by mucinous (n:59), endometrioid (n:5), brenner (n:2) and clear (n:1). Only one patient had both serous and mucinous BOT on separate ovaries. Six cases had micro invasive BOT (5-serous,1-serous&mucinous) and only 2 cases had serous micro papillary histology.

Conclusions
BOT are seen at younger age and have good prognosis. Surgery with the proper staging is the cornerstone of treatment. Patients with early stage disease can undergo fertility sparing surgery.
CHIPOR (HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR OVARIAN CANCER RELAPSE): ONGOING RANDOMIZED PHASE III STUDY EVALUATING HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN THE TREATMENT OF OVARIAN CANCER RELAPSE


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Objectives
Patients treated for an Advanced epithelial ovarian cancer will experience frequently a peritoneal relapse within a period of 2 years. Hyperthermic Intra Peritoneal Chemotherapy (HIPEC) is a heavy option for the treatment of this peritoneal failure of conventional strategies. CHIPOR is an ongoing phase III trial aimed to assess the survival impact of HIPEC for the treatment of the first ovarian cancer relapse.

Methods
A randomised multi institutional phase III trial. Main eligibility criteria: previous treatment for epithelial ovarian cancer, age >18 years, WHO<2, intraperitoneal relapse (>6 months after the end of initial treatment), with no extra abdominal metastasis. Design of the trial: after secondline platinum based chemotherapy, in case of a feasible complete secondary surgery (CSS), patients are randomised, during CSS, between HIPEC (cisplatinum, 75mg/m2 in 2 l, 1 hour at 42°C, with either the open or closed technique) or no HIPEC. The main objective is overall survival. Hypothesis is a one year survival improvement in the HIPEC arm. Secondary objectives are disease free survival, treatment related mortality and morbidity, pain and quality of live, pharmacokinetics, cost.

Results
15 Centers are including patients since january 2012. 87 Patients are yet included for a total number of 444 patients needed. One center is recently open in Barcelona and centers are approached in Belgium, Germany and Poland.

Conclusions
The real impact of HIPEC on patients survival in the case of a first relapse of ovarian cancer must be assessed through randomised trials.
CONCOMITANT UTERINE PATHOLOGIES OF BORDERLINE OVARIAN TUMORS (BOT); SINGLE CENTER EXPERIENCE OF 183 CASES

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Objectives
To describe histopathological features of hysterectomy specimens accompanying BOT.

Methods
Pathological reports of hysterectomy specimens in BOT patients treated between 1999-2013 in our hospital were evaluated retrospectively.

Results
There were 183 patients diagnosed as BOT since 1999. Mean age at diagnosis was 40.6 years (range: 17-78) old. Sixty-four patients had fertility sparing surgery. Hysterectomy was performed in 119 patients. Fifty-one patients had normal appearing uterine specimen with proliferative or secretory endometrial lining. Most common types of uterine pathologies were chronic cervicitis (n: 58) followed by myoma uteri (n: 34) and adenomyosis (n: 22). Thirteen patients had concomitant endometrial polyp, 4 patients had low-grade and 2 patients had high-grade squamous intraepithelial lesions. Three patients (1 with bilateral serous BOT, 1 with bilateral histologically serous-papillary type BOT and 1 with bilateral mucinous BOT) had tubal, paratubal and/or uterine serosal non-invasive implants. Concomitant uterine pathologies of another 4 patients with serous BOT were; degenerated placental tissues (n: 1), bilateral adnexal endosalpingiosis (n: 1), paratubal serous carcinoma at the same site with the BOT (n: 1) and tubal malign mixed mullerian tumor (MMMT) involvement of clear-endometrioid-leiomyosarcoma histology due to accompanying contralateral ovarian MMMT (n: 1). Chronic granulomatous lesions in endometrium and on the cervix with bilateral tubal salpingitis follicularis due to Tuberculosis infection was another entity that accompany unilateral Brenner BOT-Benign Brenner combination. Salpingitis, serosal endometriotic implants, endometritis and simple hyperplasia without atypia were the other less encountered uterine lesions.

Conclusions
Subtle but important pathological conditions might accompany any kind of grossly visible primarily diagnosed gynecological disease as occurred in this BOT case series.
CONCOMITANT IPSILATERAL OVARIAN PATHOLOGIES OF BORDERLINE OVARIAN TUMORS (BOT); SINGLE CENTER EXPERIENCE OF 183 CASES SINCE 1999
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Objectives
To become aware of ipsilateral ovarian pathologies accompanying with BOT.

Methods
Pathological reports of 183 cases were evaluated retrospectively.

Results
There were 111 BOT on right side and 92 BOT on left side. Ninety patients had unilateral right sided and 70 patients had unilateral left sided BOT. Twenty-three patients had bilateral BOT. Of the 90 patients who had right unilateral BOT only 12 cases had concomitant ipsilateral ovarian pathology and of the 70 patients who had left only 5 cases had concomitant ipsilateral ovarian pathology. Concomitant right ovarian pathologies with serous BOT were: 2-endosalpingiosis, 1-cyst-adenofibroma, 1-endometrioma, 1-serous cyst-adenoma & endometrioma, 1-synchronous intra-ovarian & ovarian surface serious BOT. Ipsilateral right ovarian pathologies accompanying with mucinous BOT were: 1-endometrioma, 1-mucinous cyst-adenoma & mucinous adenocarcinoma. A patient with a combination of right ovarian serous-mucinous-endometrioid BOT had also both endometrioma and mature cystic teratoma on the same ovary. Two cases with endometrioid BOT on the right ovary had 1-endometrioid carcinoma and 1-endometrioid carcinoma & endometrioid adenofibroma together. A patient with right ovarian clear cell BOT had clear cell carcinoma & adenofibroma & endometrioma combination. Ipsilateral ovarian pathologies accompanying with left sided mucinous BOT were: 1-mucinous cyst-adenocarcinoma, 1-benign Brenner tumor. Concomitant pathologies of serous BOT were 2-endometrioma respectively. A case with Brenner BOT on the left ovary had also benign Brenner tumor on the same side.

Conclusions
There are various ipsilateral concomitant ovarian lesions in BOT. Presence of invasive disease in the permanent pathology report changes the primary diagnosis of BOT, which was diagnosed especially in frozen pathology.
ACCOMPANYING CONTRALATERAL OVARIAN PATHOLOGIES OF BORDERLINE OVARIAN TUMORS (BOT); SINGLE CENTER EXPERIENCE OF 183 CASES SINCE 1999

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Objectives
To present concomitant contralateral ovarian pathologies.

Methods
Pathological reports were evaluated retrospectively.

Results
Ovarian pathological evaluation of 183 cases was performed either by wedge biopsy, cystectomy or oophorectomy. There were 111 BOT on right side (72-serous [3 micro-invasive, 2 micro-papillary], 33-mucinous [10 endocervical, 7 intestinal, 1 serous-mucinous-endometrioid], 5-endometrioid, 1-clear cell histology) and 92 BOT on left side (63-serous [3 micro-invasive, 1 micro-papillary], 27-mucinous [8 intestinal, 4 endocervical, 1 endocervical micro-invasive], 2-Brenner histology) respectively. Twenty-three patients’ BOT lesions were bilateral (18-serous, 1-mucinous, 1-serous micro-invasive, 1-serous micro-papillary, 1-serous & serous micro-invasive and 1-mucinous & serous micro-invasive). Ninety patients had unilateral right, 70 patients had unilateral left sided BOT. Concomitant left ovarian pathologies of 72 right ovarian serous BOT were: 20-serous BOT, 7-serous cyst-adenoma, 5-endometrioma, 2-endometrioid carcinoma, 1-ovarian malign-mixed-mullerian tumor, 1-adenofibroma and 1-fibromatous nodule. Concomitant left ovarian pathologies of 33 right ovarian mucinous BOT were: 4-endometrioma, 4-mucinous cyst, 3-serous cyst-adenoma, 1-micro-invasive serous BOT, 1-mucinous BOT and 1-fibroma. Concomitant left ovarian pathologies of 5 right ovarian endometrioid BOT were: 1-endometrioma & endometrioid cancer and 1-adenofibroma. Concomitant right ovarian pathologies of 63 left ovarian serous BOT were: 18-serous BOT, 3-serous cyst-adenoma, 2-ovarian serous carcinoma, 1-micro-invasive serous BOT, 1-mucinous BOT, 1-serous micro-papillary BOT, 1-ovarian micro abscess and 1-endometrioma. Concomitant right ovarian pathologies of 27 left ovarian mucinous BOT were: 1-mucinous BOT, 1-mature cystic teratoma and 1-mucinous cyst. There were no concomitant ovarian pathology of 2 Brenner and 1 clear cell BOT on right or left ovary respectively.

Conclusions
Inspection of contralateral ovary is needed during staging surgery for BOT.
INCIDENTAL TUBAL ENDOMETRIOID CARCINOMA IN SPITE OF BIOPSY PROVEN ENDOMETRIAL ORIGIN

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Objectives
Fallopian tubes are derived from Mullerian epithelium with ovaries and uterus. Therefore malign transformations of these structures have similarities. Endometrioid adenocarcinomas of fallopian tubes usually present at an early stage and have better prognoses. We present a case in which endometrioid adenocarcinoma was incidentally diagnosed.

Methods
A postmenopausal 52 years old multiparous (G4P3A1) woman underwent TAH+BSO for postmenopausal bleeding. Preoperative Pap smear was normal and endometrial biopsy resulted glandular structure with atypical epithelial cells support endometrial malignancy. CA 125 level was 12.7 U/ml. Her family history was positive for ovarian cancer. Intraoperative findings were normal and frozen pathology was negative for uterine malignancy. Final pathology revealed proliferative phase endometrium and FIGO grade 3 endometrioid type primary tubal carcinoma with full-thickness tubal involvement and ovarian metastasis. Therefore complementary staging procedure was performed.

Results
Endometrioid adenocarcinomas are second most common tubal carcinomas and little is known about their biologic behavior due to small sample sizes. Presentation might be with vaginal bleeding, discharge, pelvic pain, mass or without any symptoms as in this case incidentally. Because of similarities, FIGO staging system for ovarian cancer is used to stage tubal carcinoma and routine debulking operations and postoperative chemotherapy are applied as in the ovarian cancer.

Conclusions
Right diagnosis of primary fallopian tube cancer needs attention by a pathologist to differentiate the tumor origin. Also detailed pathologic examination of the tubes following TAH+BSO operations in benign conditions is necessary to catch incidental tubal carcinoma.
e-Posters: Ovarian Cancer

MORBIDITY OF SURGERY AFTER NEO-ADJUVANT CHEMOTHERAPY INCLUDING BEVACIZUMAB FOR ADVANCED OVARIAN CANCER
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Objectives
Neo-adjuvant chemotherapy followed by interval debulking surgery is an alternative for the management of advanced ovarian cancer (AOC). Because of unresectable disease at initial evaluation, some patients received bevacizumab in addition to neo-adjuvant chemotherapy. The aim of this study is to evaluate the safety and the post-operative course of patients who received bevacizumab prior to debulking surgery for AOC.

Methods
In 2012, we identified all patients with AOC who received bevacizumab in the neo-adjuvant before dedulking surgery. We recorded patient characteristics, surgical course and postoperative complications.

Results
Five patients were identified. 80% were FIGO stage 4 at diagnosis. All patients underwent surgery after six courses of neo-adjuvant chemotherapy with carboplatin, paclitaxel and bevacizumab. The median number of bevacizumab injection was 3 (3 – 4) and the median time between the last injection of bevacizumab and surgery was 54 days (34 to 110). One patient underwent a grade 3 complication (lymphocyst with puncture under CT scan).

Conclusions
In this preliminary study, debulking surgery after neo-adjuvant chemotherapy associated with bevacizumab doesn’t seems to be related with an increase in the post-operative course subject to a reasonable interval between bevacizumab injection and surgery. Larger studies are warranted to assess surgical safety after antiangiogenetic treatment in the neo-adjuvant setting for advanced ovarian cancer.
e-Posters: Ovarian Cancer

GANNET53: AN UPCOMING CLINICAL TRIAL BASED ON A DRUG STRATEGY TARGETING STABILISED MUTANT P53 TO COMBAT PLATINUM-RESISTANT OVARIAN CANCER


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on behalf of the whole GANNET53 consortium

Objectives
The GANNET53 clinical trial aims to substantially improve survival in Pt-R ovarian cancer patients by applying a highly innovative concept that has grown from solid basic research findings made by members of the GANNET53 consortium. This clinical trial has recently been positively evaluated for funding by the European Union (Seventh Framework Programm) and will start in fall 2013. With the present abstract the GANNET53 consortium aims to provide information on this upcoming clinical trial.

Methods
This is a drug strategy targeting a central driver of tumour aggressiveness and metastatic ability, namely mutant p53, via an innovative new Hsp90 (heat shock protein 90) inhibition mechanism. The clinically most advanced second-generation Hsp90 inhibitor will be used, Ganetespib, and applied in a stratified treatment approach in Type II ovarian cancer patients. The first part (Phase I) of the GANNET53 trial will test the safety of Ganetespib in a new combination with Paclitaxel weekly in Pt-R Type II EOC patients. The second part (randomised two-arm open-label Phase II) will examine the efficacy of Ganetespib in combination with Paclitaxel weekly versus Paclitaxel weekly alone in EOC patients with Pt-R Type II tumours. We have established a highly efficient consortium featuring powerful clinical capacities, compelling knowledge in clinical trail performance, research excellence, and management competence to guarantee fast bench-to-bedside translation of a highly innovative basic research finding.

Results
none

Conclusions
none

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INVASIVE BORDERLINE OVARIAN TUMOR

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Objectives
Borderline ovarian tumors (BOT) are neoplasms with favorable prognosis representing 10-15% of epithelial ovarian tumors. BOT are more common in premenopausal women.

Aim
We present two clinical cases of ovarian borderline tumors with invasive progression.

Methods
Clinical case report.

Results
Case 1: A 54 year old woman diagnosed with bilateral serous borderline tumor. Peritoneal implants were found during surgery so it was classified as stage IIIC. Complete surgery was performed for ovarian cancer with pelvic and para-aortic lymphadenectomy and later chemotherapy (carboplatin and paclitaxel) was administered. The patient is in remission with an overall survival of 30 months.

Case 2: A 73 year old woman diagnosed with adnexal tumor with negative tumor markers. Left adnexectomy was performed and the anatomic pathology was borderline serous cystadenoma. The patient rejected a complete surgery. Controls were normal for a year until a pararectal recurrence nodule was detected. Total hysterectomy, right adnexectomy, lymphadenectomy, omentectomy and appendectomy was performed. Also resection of infiltrated rectosigmoid and parietocolic implants was done. The anatomic pathology result was IIIC serous borderline tumor. Posterior chemotherapy (carboplatin and paclitaxel) was administered. A second peritoneal recurrence was diagnosed and treated with palliative chemotherapy. After two months the patient died.

Conclusions
BOT are a heterogeneous group of tumors, considered almost benign, but encompassing a spectrum of aggressiveness, from cystadenomas with BOT foci of less than 10% to aggressive and lethal tumors as the one presented.

Although BOTs usually have a favorable prognosis, there are cases capable of producing metastatic peritoneal implants and progress as an invasive carcinoma.
e-Posters: Ovarian Cancer

BILATERAL OVARIAN INVOLVEMENT AND HISTOPATHOLOGIC ANALYSIS: 107 OVARIAN NEOPLASMS
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Objectives
To determine the incidence of bilateral involvement in different morphologic subtypes of ovarian tumors.

Methods
One hundred and seven ovarian tumors treated between 2005 and 2013 in a Training and Research hospital was retrospectively investigated for histopathological subtype and bilaterality.

Results
Twenty-three ovarian tumors (21.4 %) were found in 12-40 years age group. Bilaterality rate was 52.3 % in all ovarian carcinomas. Malignant serous tumors were bilateral in 66 % of cases. Twelve percent mucinous carcinomas, 10.7 % metastatic carcinomas and 8.9 % other ovarian tumors (endometrioid, dysgerminoma, malign mixt mullerian tumor) were bilateral. Thirteen borderline tumors were included and accounted for 12.1 % of all ovarian tumors. Only one case of the borderline tumors showed bilateral involvement.

Conclusions
Ovarian tumors are well known for bilateral involvement. Approximately fifty-six (52.3 %) of the tumors are bilateral. In the present study, the most common ovarian tumor with bilateral involvement was malignant serous tumor (66 % bilateral). This was followed by 12.5 % of malignant mucinous tumors. Bilaterality is exceptional in borderline tumors in our study.
e-Posters: Ovarian Cancer

MORPHOLOGICAL FEATURES IN THE CONTRALATERAL OVARY OF WOMEN WITH UNILATERAL OVARIAN CARCINOMA

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Objectives
The aim of this study was to investigate the lesions in the contralateral ovary with unilateral ovarian carcinomas.

Methods
We retrospectively reviewed the records of all patients with unilateral ovarian cancer treated at the Training and Research Hospital between 2005 and 2013. The morphological features in contralateral ovaries from 51 patients with unilateral ovarian carcinoma (including 12 borderline tumors) were searched. The histological features considered were the epithelial inclusion cysts, stromal-epithelial hyperplasia, surface papillations, endometriosis, and follicle cysts.

Results
The mean age of patients with unilateral ovarian cancer was 58.9 years. Unilateral ovarian carcinomas were 46.3 % in all ovarian carcinomas. Ovarian carcinoma was located in the right side in 25 patients and in the left side in 26 cases. The findings of borderline tumors were follicle cyst (n:8) and no pathologic changes (n:4). Of the 39 ovarian carcinomas, 14 were serous, 7 mucinous, 4 granulosa, 4 clear cell, 2 endometrioid, 2 endodermal sinus tumor, 1 dysgerminoma, 1 lipid cell type, and 4 mixt type. Epithelial inclusion cysts were often seen (79 %). Six patients had ovarian endometriosis (11.7 %). Twenty-four percent of contralateral ovaries had surface papillations. Stromal – epithelial hyperplasia were seen in 35 % of the contralateral ovaries. Twenty-eight percent of contralateral ovaries were found have no pathologic changes.

Conclusions
The epithelial alterations (inclusion cysts, surface papillations and stromal-epithelial hyperplasia) were commonly seen in the contralateral ovary of women with unilateral ovarian cancer. The most frequent lesions of contralateral ovaries in borderline tumors were follicle cysts.
e-Posters: Ovarian Cancer

PSEUDOMYXOMA PERITONEI: AN ANALYSIS OF FOUR CASES

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Objectives
Pseudomyxoma peritonei (PMP) is a poorly understood condition characterized by the accumulation of abundant mucinous material within the peritoneal cavity and associated with a mucinous tumor of the gastrointestinal tract or ovaries. PMP was first described by Rokitansky in 1842. We present four cases of pseudomyxoma peritonei arising from appendiceal and ovarian tumors.

Methods
Four patients with a diagnosis of pseudomyxoma peritonei treated in our hospital between 2004 and 2012 were included in this retrospective analysis.

Results
The histological examination of the specimens revealed intestinal-type mucinous borderline ovarian tumors and well-differentiated mucinous carcinomas in two cases, and mucinous appendiceal cystadenocarcinoma in two cases. Four patients underwent surgical debulking, hysterectomy, bilateral salpingo-oophorectomy, appendectomy, peritoneal resections, omentectomy and pelvic–paraaortic lymphadenectomy. After operation, all patients received adjuvant chemotherapy.

Conclusions
Pseudomyxoma peritonei is a rare condition with an incidence of less than 2 in 10,000 surgical procedures, and occurs most commonly in mucinous tumors of the ovary and appendix, especially of well-differentiated or borderline malignancy types. This clinical entity is characterized by diffuse collections of gelatinous material in the abdomen and pelvis and mucinous implants (so-called “jelly belly”) on the peritoneal surfaces. Improving immunohistochemical techniques help to identify the origin of the disease. Optimal surgical debulking, including peritoneal stripping procedures and appendectomy in combination with intra-/postoperative intraperitoneal chemotherapy, is regarded as the standard treatment.
RELATIONSHIP OF SERUM CA125 LEVEL AFTER PRIMARY THERAPY OF EPITHELIAL OVARIAN CANCER AND DISEASE RELAPSE

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Objectives
The aim of this study was to assess the relationship of serum CA125 level at the end of primary therapy (surgery and chemotherapy) to appearance of epithelial ovarian cancer (EOC) relapse. Lower CA125 levels generally are associated with fewer relapses and longer survival.

Methods
This retrospective study assessed 75 patients with EOC. Chi-squared test (χ² test) was used to examine the relation between variables. Kaplan-Meier survival curves were compared using the Wilcoxon (Breslow, Gehan) test.

Results
The median follow up time was 15 months (range 1-121). The majority of patients had advanced stage III or IV disease (n=52, 69.3%). The analysis revealed that the lowest incidence of tumor recurrence have the patients in which CA125 level after initial therapy returned to normal values and persisted within these values. In this group of patients the incidence of relapse was 23.08%. If the CA125 level did not fall completely within the normal range or starts to rise again, the tumor relapses occur in 58.33 % and 95.24% (χ² = 18.630, p < 0.0001). The carboplatin and paclitaxel chemotherapy had very low efficacy if applied after secondary rise of CA125 level, since the incidence of tumor relapses in these patients (90%) was not lower than in patients who did not received preventive chemotherapy (85%) (χ² = 0.1, p= 0.3943).

Conclusions
The serum CA125 level at the end of primary therapy is associated with EOC relapse. Targeting therapy for an individual patient with secondary rise of CA125 level might be more effective than selecting drug empirically.
e-Posters: Ovarian Cancer

OVARIAN CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 1998-2012 PERIOD
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Objectives
The present study about the frequency of ovarian cancer covers the 1998-2012 interval.

Methods
The data being collected from the Histopathology Exams (HPE) registers.

Results
Ovarian cancer was discovered in 118 cases, representing 6, 74% of all genital cancers (1752 cases). Among the patients, 113 cases (95, 76%) were primary ovarian cancers, while five patients (4, 12%) had ovarian metastases (one with gastric, colic or mammary origin, one originating in the small intestine and three with unknown origin). Of the 113 primary cancers, 101 were carcinomas (89,38%), three were yolk-sac tumors (2,66%), three were tumors of the granulosa (2,66%), two were a malignant immature teratoma (1,78%), one was a disgerminoma (0,88%), one was a malignant mature cystic teratoma with carcinoma components (0,88%), one was a Seroli-Leydig tumor (0,88%) and one was an adenofibroma with a carcinomatous component (0,88%). One patient had a combination of cervical and ovarian cancer. The mean age of the group was 51, 66±14, 22 years (age range 18 to 77 years).

Conclusions
Ovarian cancer still remains a serious public health issue, thus demanding a well organized screening programme.
e-Posters: Ovarian Cancer

BEVACIZUMAB AND PLATINUM-BASED CHEMOTHERAPY IN RELAPSED OVARIAN CANCER TREATMENT
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Objectives
Ovarian cancer morbidity is around 15 on 100 000 of women and it presents at advanced stages of III-IV in 70%, and treatment in much consists of surgical resection followed by platinum-based chemotherapy. Bevacizumab was approved for first-line treatment of advanced epithelial ovarian cancer, in combination with carboplatin and paclitaxel chemotherapy. We proposed bevacizumab for second and third line for advanced ovarian cancer treatment.

Methods
Nine patients with stage III platinum sensitive ovarian cancer earlier had received from 3 to 5 regimes of carboplatin with paclitaxel, gemcitabin, doxorubicin, cyclofosfan and topotecan. Now they receive a chemotherapy course with bevacizumab and carboplatin in combination with or without of paclitaxel. Seven patients receive bevacizumab 7.5 mg/kg with paclitaxel 175 mg/m² and carboplatin AUC 5-6 every 3 weeks. Two patients receive bevacizumab and carboplatin AUC 5-6 every 3 weeks. Bevacizumab was continued alone in the same dosage until progression of the disease was revealed. All patients received 6-8 cycles of therapy (total 74 cycles). Toxicity level was tolerable despite of bevacizumab administration.

Results
Disease free condition was observed in 3 patients within 7 – 9 month, partial effect in 5 patients noted from 3 to 8 month, and disease stabilization for 4 month is in 1 patient.

Conclusions
Bevacizumab combination with platinum-based and paclitaxel chemotherapy seems to improve survival and progression-free survival compared with conventional platinum-based plus paclitaxel chemotherapy among patients with relapsed ovarian cancer.
e-Posters: Ovarian Cancer

PRIMARY CARCINOID TUMOR ARISING IN A MUCINOUS CYSTADENOMA OF THE OVARY: A CASE REPORT.
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Objectives
Carcinoid tumors are characteristically low grade malignant neoplasms with neuroendocrine differentiation that arise in various body sites, most commonly the lung and gastrointestinal tract. Carcinoid tumors of the ovary are rare, primary carcinoid tumors being even rarer, forming 0.3% of all carcinoid tumors.

Methods
We present a rare case of a primary, non-functioning, insular carcinoid of the right ovary in a 23-year-old nulliparous, asymptomatic woman, originating from the inner surface of a mucinous cystadenoma. Preoperational findings of biochemical investigations (including Ca 125) were within normal limits.

Results
Laparoscopic right sided ovarian cystectomy was performed due to persistence of right-sided ovarian cyst on ultrasound examination. Microscopically islands of carcinoid tissue within thickened mucinous cystadenoma wall were reported. The tumor cells demonstrated strong expression of Chromogranin A and Synaptophysin on immunohistochemistry. On the basis of this, a diagnosis of primary ovarian carcinoid was set. Somatostatin-receptor scintigraphy (OctreoScan®) followed; the scan did not demonstrate any abnormalities. The patient underwent laparoscopic appendectomy, unilateral salpingo-oophorectomy, as well as right sided pelvic lymphadenectomy. The histopathologic report did not show any abnormalities.

Conclusions
Early surgical intervention, together with careful surveillance and follow-up, can achieve successful long-term outcomes in patients with this rare malignancy.
**Epidural Analgesia Improves Disease Recurrence Free Survival Following Optimal Primary Cytoreductive Surgery for Advanced Stage Ovarian Cancer**

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**Objectives**

To determine the effect of regional analgesia on cancer recurrence following optimal primary debulking surgery for advanced stage ovarian cancer.

**Methods**

A case-control study was performed with 225 patients with Stage 3 or 4 epithelial ovarian cancer who underwent optimal primary cytoreductive surgery via laparotomy between 2007 and 2011 at a single cancer center. Patients receiving general anesthesia combined with epidural analgesia were compared with patients who received general anesthesia alone. Univariate analysis was performed to compare the differences of covariates and outcomes of interest between the two groups. Survival curves were constructed using the Kaplan-Meier estimators for overall survival and disease recurrence free survival. Multivariate analyses of factors related to overall and recurrence free survivals were performed using Cox's proportional hazards model.

**Results**

Patients in both groups were similar with respect to demographic, clinical, and pathologic variables. The groups were virtually identical in choice of first line chemotherapy and the number of cycles received. While there was no difference in overall survival between the two groups, general anesthesia combined with epidural analgesia resulted in a lower overall rate of cancer recurrence (38% vs. 20%, p=.004), with a trend towards longer recurrence free survival (p=.0627). In multivariate analysis, epidural analgesia was independently associated with improved recurrence free survival (hazard ratio, 1.534; 95% confidence interval, 1.039-2.264, p=.0313).

**Conclusions**

General anesthesia plus epidural analgesia enhances disease recurrence free survival among women achieving optimal cytoreduction for advanced stage epithelial ovarian cancer.
e-Posters: Ovarian Cancer

RECIPIROCAL IMMUNOEDITING BETWEEN ALLOGENEIC NK CELLS AND HUMAN EPITHELIAL OVARIAN CANCER CELLS
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Objectives
Build the immunoediting model of NK cells and epithelial ovarian cancer. Investigate the expression of NKG2D and MICA, and then discover the effect and significance of immunoediting to NK and cancer cells. At the same time, to discuss the clinical significance of NKG2D-NKG2DL on anti-tumor immunity.

Methods
Isolate NK cells by CD56 antibody immunomagnetic beads.

Measure the expression of the MICA, which express on ovarian cell surface, at the gene and protein level by real-time RT-PCR and western blot.

Expression of the active receptor NKG2D of NK cells was analyzed by flow cytometry.

Results
Purity of CD3-CD16+CD56+ cells isolated from 10 healthy persons by magnetic bead selection is (91.07±2.18)%

Expression of MICA mRNA on the surface of SKOV3 cells and SKOV3/CDDP cells at different time of immunoediting. Our experiment shows: MICA mRNA increased in edited SKOV3 cells, and increased in SKOV3/CDDP after 24h of immunoediting.

Expression of MICA protein on the surface of SKOV3 cells and SKOV3/CDDP cells at different time of immunoediting. Our experiment shows: compare to MICA mRNA, MICA protein decreased in edited SKOV3 cells, and decreased in SKOV3/CDDP after 24h of immuno-editing.

After immunoediting, the expression of NKG2D is decreased whether on SKOV3 cells or on SKOV3/CDDP cells.

Conclusions
Our findings unveiled that the existence of reciprocal-immunoediting between Allo-NK cells and SKOV3 cells and SKOV3/CDDP cells, which basic is the NKG2D-NKG2DL signal pathways and specificity of ligand-receptor engagement. That is the decrease expression of MICA and NKG2D of edited cells. Furthermore confirmed that regulating this signal pathways could boost edited Allo-NK cells function and enhance sensitivity of edited SKOV3 cells or SKOV3/CDDP cells to Allo-NK cells cytotoxicity.
SINGLE PORT ACCESS ROBOT ASSISTED -LAPAROSCOPIC SMALL BOWEL RESECTION IN PATIENTS WITH ADVANCED OVARIAN CANCER: FARGHALY'S TECHNIQUE

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Objectives
Ovarian cancer is diagnosed at an advanced stage in about 75% of patients. It is commonly spread along the peritoneal surfaces in the abdomen, and often involves the serosa of the bowel by direct extension or serosal implantation. Small bowel resection often, can be necessary to reduce the tumour burden when treating metastatic or recurrent disease. Minimally invasive surgery for small bowel resection at time of the primary surgery for debulking is thought.

Methods
Pre-operative computed tomography (CT), positron emission Tomography (PET) and magnetic resonance imaging (MRI) are used. Bowel prep is performed. Single port access robot assisted laparoscopic surgery is used to perform ultraradical cytoreductive surgery. The goal is to achieve macroscopic cytoreduction CCR-0/1, indicating tumor residues of < 2.5 mm. Small bowel resection is performed with GIA 2.5/60 mm cartridge. The bowel mesentry is transected with the Harmonic scalpel. A 5 cm periumblical midline laparotomy is performed and the specimen is extracted. Two inflow, and 2 outflow perfusion catheters are placed.

Results
The best results are achieved in patients with limited disease who have completed ultra-radical cytoreductive pelvi-abdominal surgery with less than 2.5 mm residual tumor and small bowel resection for the affected small bowel.

Conclusions
Farghaly's technique of SPA Robot-assisted laparoscopic small bowel resection at the time of primary cytoreduction surgery for ovarian cancer with optimal cytoreduction to less than 2.5mm residual disease results in improved survival. This technique has the advantage of reducing pain, and decreasing morbidity, hospital stay duration and post-operative recovery time.
e-Posters: Ovarian Cancer

HOW TO PREDICT OPTIMAL CYTOREDUCTION IN ADVANCED OVARIAN CANCER: A CT SCAN MODEL
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Objectives
The identification of a reliable tool for predicting optimal cytoreduction is hopeful in the management of ovarian cancer. We developed a computed tomography (CT) scan model to predict likelihood of suboptimal debulking.

Methods
Thirty women with a preoperative CT scan of abdomen and pelvis and a histologic diagnosis of FIGO Stage III or IV epithelial ovarian carcinoma who underwent primary debulking surgery were identified from our medical records. Sensitivity, specificity, accuracy, negative and positive predictive values were calculated for the following parameters: superficial liver metastases > 2cm, intraparenchimal liver metastases of any size, suprarenal aortic lymphnodes > 1cm, infra-renal aortic lymphnodes > 1cm, bowel mesentery involvement, multiple peritoneal implants or peritoneal thickening, large ascites, omental involvement. Also two clinical features were analyzed: CA 125 levels and age. No residual tumour was considered the optimal surgical result. Radiographic and clinical features achieving a specificity > 75%, a positive and negative predictive values > 50% were assigned a point of 1. A Predictive Index Value (PIV) ranging from zero to six was calculated for each patient.

Results
At a PIV > 2, the overall accuracy of the CT model was 73.3%. Sensitivity and specificity to predict suboptimal cytoreduction were 58.3% and 83.3%. The rate of inappropriate unexploration was 16.7%, while the rate of unnecessary exploration was 25%.

Conclusions
Our CT scan model can be considered a valid tool to predict the success of surgery in advanced ovarian carcinoma. However it needs to be validated in a prospective study.
e-Posters: Ovarian Cancer

CA 125, HE 4 AND ROMA-INDEX IN PATIENTS WITH EPITHELIAL OVARIAN CANCER
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Objectives
The circulating tumor markers are used in the diagnosis of ovarian cancer and for the monitoring of the patients during treatment.

Methods
This study examines preoperative and postoperative serum levels of CA125, HE4 and ROMA in samples from 110 patients with epithelial ovarian cancer.

Results
Elevated serum levels of CA 125 are found more frequently in serous ovarian carcinoma and in advanced stage (II-IV) disease in comparison with mucinous ovarian cancer and stage I disease. Mean values of serum CA 125 are 320 mmol/l for serous and 195 mmol/l for mucinous ovarian cancer. Age-specific elevation of serum HE4 is determined, with average values of 40 pmol/l for women aged 50, and 80 pmol/l for women aged over 65. Higher serum values are associated with serous ovarian cancer. Normalized serum levels of HE4 and CA 125 are observed in patients after radical surgical treatment.

Conclusions
Our results confirm that CA125, HE4 and ROMA are informative biomarkers in advanced stage disease and in patients aged over 50. ROMA- index exhibits excellent diagnostic capability for detection of epithelial ovarian cancer in postmenopausal patients.
CURRENT TREATMENT PATTERNS FOR RECURRENT EPITHELIAL OVARIAN CANCER IN 5 EUROPEAN UNION (EU5: FRANCE, GERMANY, ITALY, SPAIN, UK) COUNTRIES

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Objectives
To understand current treatment pathways for patients with advanced ovarian cancer (OC).

Methods
Data were collected from eligible physicians in EU5 countries using an ethics committee approved, validated, double-blind (to participants and those who analysed the data), web-based survey conducted in local languages. The questionnaire was semi-structured consisting of open-ended responses, multiple-choice fixed responses and case studies on the treatment of first-line and recurrent OC. Eligible physicians were specialists in oncology or gynaecology with ≥2 years' clinical experience; they were excluded if they had not treated any patients with stage III/IV epithelial OC, or had treated <10 patients with recurrent disease, in the last 12 months. Subgroups of patients with recurrent disease were identified based on time since previous platinum treatment.

Results
Most patients (75%) were diagnosed with stage III/IV cancer (Figure 1). Platinum-based chemotherapy was first-line therapy in 87% of patients; patients receiving non-platinum therapy increased with each line of treatment, rising from 42% at first recurrence to 84% at third recurrence (Figure 2). In partially platinum-sensitive patients, platinum-based combination chemotherapy was the most common treatment after 1 relapse in most countries. Duration of each therapy decreased with
increasing numbers of recurrences.

Conclusions
Most patients with OC initially present with advanced disease. Physicians reported using both platinum and non-platinum–based regimens in all lines of therapy, with an increasing proportion of non-platinum–based therapy after first-line treatment.
TREATMENT OF PSEUDOMYXOMA PERITONEI BY INTRAOPERATIVE AND INTRAPERITONEAL CHEMOTHERAPY

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Objectives
Pseudomyxoma peritonei occurs mostly in conjunction with the type of intestinal mucinous borderline tumour and is characterized by building up a lot of mucus pour of cells. The most common tumor is the pseudomyxoma peritoneii with mucinous borderline tumours of the ovaries or with mucinous tumours of the appendix, normally without showing a rupture of the ovarian tumour pre- or intraoperatively. The diagnosis of pseudomyxoma peritonei is mainly difficult and guidelines for the treatment are unknown.

Methods
In the period from 1991 to 2008, 52 patients with pseudomyxoma peritonei were treated by tumour debulking and intraoperative and intraperitoneal chemotherapy with Mitoxantron (40 mg in 300 ml of NaCl over 72 hours). During the tumour debulking a CUSA system was used.

Results
The median follow-up was 8.2 years. There were the following histologies: mucinous cystadenoma of the ovary n = 29, mucinous cystadenoma of the appendix n = 10, mucinous cystadenocarcinoma n = 13. Recurrences were seen in 4 patients. These patients were treated for recurrences by the same way as mentioned above. All these patients were now without any recurrences. The other 48 patients are still alive without recurrences.

Conclusions
The instillation of mitoxantron intraperitoneally and intraoperatively is an effective and safe therapy without any side effects after maximal tumour debulking of pseudomyxoma peritonei.
ADVERSE EVENTS IN HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC)

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Objectives
Peritoneal metastasis often is a sign of advanced disease of carcinoma of the ovary and Fallopian tube, but also of primary peritoneal carcinomas. So far, the surgical concept was palliative. Meanwhile it could be shown that after cytoreductive surgery, the prognosis is significantly improved. If it is possible to achieve a complete tumor free situation, HIPEC should further improve the prognosis.

In 29 patients we were able to achieve an optimal cytoreduktiv situation, so we could perform HIPEC. We reported the adverse events after surgery.

Methods
Patients with peritoneal malignancy underwent a cytoreductive surgery. In those where we could accomplish an optimal tumor resection HIPEC could be performed. Peri- and postoperative course was observed after HIPEC. Adverse events were recorded after the Clavien-Dindo classification. We evaluated grade III and IV complications.

Results
We treated 29 patients with HIPEC at 41°C of cisplatin solution (50mg/m²), mean age was 59.8y, the Peritoneal Cancer Index was between 3 and 18. 15 anastomoses were performed. We counted 13 adverse events in 8 patients, none with insufficiency of the anastomoses.

Conclusions
Nowadays the aim of a gynecologic surgeon is to achieve the complete cytoreduction in the surgical treatment of peritoneal metastasis. Multiple surgical procedures might be necessary in order to have no visible tumor left. HIPEC seems to have another positive effect on the median survival of patients with peritoneal metastasis. Since we had no more adverse events because of HIPEC we believe, that HIPEC is another important component of the treatment of peritoneal malignancy.
RARE METASTATIC SITES OF OVARIAN CARCINOMA: TWO CASE REPORTS

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Objectives
Ovarian cancer usually remains confined to the peritoneal cavity at presentation and throughout its course. Distant metastases may occur at the time of diagnosis or arise during the evolution of the disease.

Methods
We report a case of two women with ovarian cancer in these atypical metastatic sites (breast and skin).

Results:

Case-1: 52-year-old woman, presented with ascites and bilateral axillary lymphadenopathy. CT scan demonstrated peritoneal carcinomatosis, bilateral ovarian masses, supraclavicular, axillary, ilio-pelvic and retroperitoneal lymphadenopathy. Peritoneal fluid cytopathology was positive for adenocarcinoma. Fine-needle aspiration biopsy of both axillary lymph nodes and RMN-guided right breast biopsy was done. Histological and immunohistochemical examination favored metastasis of primary ovarian cancer. Cytoreductive surgery with pre- and postoperative platinum-based chemotherapy resulted in complete clinical response. Seven months later, recurrence was documented and chemotherapy resumed.

Case-2: A 44-year-old woman with recurrent ovarian cancer developed abdominal coalescing papules in the pubic and lower abdominal area, approximately 5 years after the initial diagnosis (Fig. 1). Skin biopsy revealed cutaneous lymphangitic carcinomatosis from adenocarcinoma, consistent with primary ovarian neoplasia. She underwent chemotherapy and electrochemotherapy, but died from progressive disease 9 months after skin metastasis diagnosis.

Conclusions
Ovarian cancer rarely metastasize to the skin (1.9 to 5%) or breast (< 1%). These usually occur late in the course of the disease, and often indicate a poor prognosis. Imaging, histology, and immunohistochemistry are important diagnostic tools. Such events may become more common with expected increase in survival in advanced ovarian cancer.
e-Posters: Ovarian Cancer

WOMEN WITH OVARIAN CANCER DO WORSE IN MERSEYSIDE AND CHERISH THAN THE REST OF ENGLAND: A DIAGNOSTIC PROBLEM, TREATMENT PROBLEM, OR SPURIOUS FINDING?

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Objectives
The 'Overview of Ovarian Cancer in England' (Trent Cancer Registry and National Cancer Intelligence Network, 2012) showed Cheshire and Merseyside as a significant outlier in terms of lower 1 year and 5 year survival. Lying between 2 and 3 standard deviations from the average, further analysis confirmed the findings, suggesting there may also be data issues. In response to these findings, the objectives for this project are:

To further analyse ovarian cancer outcomes in Merseyside and Cheshire, including the impact of data issues

To further understand reasons for differences compared to the rest of England, including disease presentation, diagnostics and treatment issues

To learn and take action, with subsequent impact evaluation

Methods
A multi-disciplinary and organisational approach with the Strategic Clinical Network, primary, secondary care and tertiary care, public health, patients and carers, and Third Sector will be used. Service improvement and project management methodology will provide appropriate controls. Analysis of quantitative data and consideration of data collection and recording methods within healthcare settings will be carried out together with reviews of processes and barriers applicable to disease presentation, diagnostics and treatment.

Results
The amalgamation of knowledge using the outlined method will facilitate improvement in earlier detection and solutions to diagnostic and treatment issues.

Conclusions
Utilisation of outcomes data has informed an extensive multi-organisational approach to addressing survival outcomes of ovarian cancer in Merseyside and Cheshire. This replicable methodology will provide a vehicle for change in line with national priorities outlined in Improving Outcomes: A Strategy for Cancer (DoH, 2011) for ovarian and other cancers.
e-Posters: Ovarian Cancer

ROLE OF CLASSIC PROGNOSTIC FACTORS IN EPITHELIAL OVARIAN CANCER
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Objectives
According to literature, staging, grading, residual tumor after surgery, ascites and positive peritoneal cytology represent the most important prognostic factors in patients with ovarian cancer.

Methods
We evaluated the characteristics of 105 patients with serous epithelial ovarian tumors treated with primary surgery and chemotherapy with Carboplatin and Paclitaxel in our Clinic, from January 1998 to December 2008. After, we focused on 2 groups of patients (A and B) with extreme opposite characteristics in term of OS (A<36 and B>84 months). Groups A and B were composed by 47 (44,76%) and 24 (22,86%) women respectively.

Results
We confirm, according to literature, that stage (P<0,01), residual tumor (P<0,01), ascites (P<0,01), positive cytology (P=0,039), CA-125 before surgery (P=0,420), and DFI (P<0,01) are able to define prognosis. In A and B group, stage (P<0,01), residual tumor (P<0,01), ascites (P<0,01), positive cytology (P<0,01), relapse (P=0,039) and DFI (P=0,01) maintain statistical relevance. Surprisingly, in long-term survival group (B), there were tumors at stage III and IV (58%), poorly differentiated (G3) (79%), cases of macroscopic residual tumor after surgical (37%), ascites (41%) and positive cytology (54%). Similarly, in short-term survival patients (A), were found unexpected elements.

Conclusions
Results from our analysis demonstrate that classic prognostic factors play an acknowledged role in defining prognosis in women with ovarian cancer. Nevertheless, in patients with “extreme” survivals, they are not able alone to justify the outcome. There must be some peculiar microscopic elements, defined by biological and genetic features, able to determinate the grade of cancer malignancy and to explain these marked differences in survival rates.
IS IT COST EFFECTIVE TO USE A MOLECULAR PROFILE TO PICK CHEMOTHERAPY FOR RECURRENT OVARIAN CANCER?

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Background
Many companies are trying to develop molecular profiles (MP) to help predict the most effective chemotherapy for recurrent cancer. The question we sought to answer was whether using a test to predict the most effective chemotherapy in the setting of platinum resistance could be cost effective.

Methods
A decision model analysis was developed based on three commonly used regimens for platinum resistant ovarian cancer: cisplatin/gemcitabine, weekly topotecan, and monthly liposomal doxorubicin. Parameters studied included progression free survival (PFS), cost and complications. Baseline cost of MP was $3,500. Sensitivity analyses were performed.

Results
The incremental cost-effectiveness ratio (ICER) for using a MP versus not using an MP is $1,732 / quality-adjusted progression free life year (QAPFLY) gained. Robust findings were present varying the cost of MP from $0 to $5,000. This amount far below an accepted threshold of $50,000/QAPFLY.

Conclusions: In this model, a MP costing $3,500 is acceptable for the treatment of these patients with an increase in cost of $1,732 / QAPFLY.
OUTCOMES OF INTRA-OPERATIVE FROZEN SECTION PROVEN BORDERLINE OVARIAN TUMORS

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Objectives
We assessed the accuracy of frozen section diagnosis and the outcomes of misdiagnosis in borderline ovarian tumors (BOT) according to frozen section analysis.

Methods
All pathology reports with BOT in both frozen section and permanent paraffin blocks were analysed between 2000-2012 at Tepecik research & teaching hospital. Frozen section diagnosis and permanent paraffin blocks were compared. Patient and tumor characteristics analysed for diagnostic accuracy.

Results
Agreement between frozen section and permanent diagnosis of BOT was observed in 58 of 113 patients. Mean age of patients with frozen section results were, benign 39.4, borderline 38.1, malign 50.6 years. The agreement, sensitivity and positive predictive values of frozen section diagnosis of BOT were 50%, 70% and 67%. Among the 87 patients with frozen section proven BOT, 58 (67%) patients were correctly diagnosed by frozen section analysis. Under diagnosis and over diagnosis occurred in 14 of 87 (16%) and 16 of 87 (18%) respectively.

Conclusions
Although frozen section diagnosis agrees with permanent pathology of malignancy in 90-94% of cases, over-diagnosis and underdiagnosis are relatively frequent in frozen proven BOT. Surgical decision making for BOT based on frozen section diagnosis should be done carefully and the other clinical characteristics (age, radiologic findings, ca 125 level etc.) of the patient should be considered.
SOLUBLE CXCL16 IS AN INDEPENDENT PREDICTOR OF POOR SURVIVAL IN OVARIAN CANCER AND MAY REFLECT PRO-METASTATIC ADAM PROTEASE ACTIVITY

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Objectives
The chemokine CXCL16 is a transmembrane protein, which can be cleaved into a soluble form (sCXCL16) by ADAMs. CXCL16 and its receptor CXCR6 are reported to aid the anti-tumor immune response, but also have pro-metastatic properties. Their precise role seems to depend on tumor type. In the current study, we aimed to characterize the role of sCXCL16, CXCL16, and CXCR6 in ovarian cancer.

Methods
Immunohistochemistry was performed for CXCL16 and CXCR6 on tissue samples from 306 ovarian cancer patients. sCXCL16 levels were determined in 118 patients using ELISA. To assess ADAM effects on CXCL16 processing, cell line A2780 and primary ovarian cancer samples were treated with ADAM inhibitor TAPI-2. CXCL16 expression was evaluated by confocal microscopy and sCXCL16 was quantified in culture supernatants using ELISA. The effect of TAPI-2 on cell migration was assessed using scratch assays.

Results
sCXCL16 was an independent predictor of poor survival (Hazard Ratio 2.28, 95% confidence interval 1.29-4.02, p=0.005), whereas CXCL16 and CXCR6 did not correlate with survival. sCXCL16 was not associated with lymphocyte infiltration, nor with transmembrane CXCL16 expression. Therefore, high serum sCXCL16 may not be associated with CXCL16/CXCR6 signaling, but reflect its processing by ADAMs. Accordingly, in vitro ADAM inhibition decreased CXCL16 shedding and strongly reduced cell migration of A2780 and primary ovarian cancer cells.

Conclusions
High serum sCXCL16 is a prognostic marker for poor survival, possibly reflecting higher pro-metastatic ADAM activity. ADAM activity is difficult to quantify in vivo. Therefore, serum sCXCL16 levels may be a useful pseudomarker that identifies patients with more aggressive tumors.
Abstracts from 18th International Meeting of the European Society of Gynaecological Oncology (ESGO), 19-22 October 2013, Liverpool, UK
TREATMENT STRATEGY FOR RECURRENT CLEAR CELL CARCINOMAS OF THE OVARY
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Objectives
Clear cell carcinomas of the ovary (CCCO) are generally diagnosed at early stage and complete resection at primary surgery is feasible; however, management for recurrence is difficult due to its relatively poor response to conventional chemotherapy. The purpose of this study was to review treatment outcomes in patients with recurrent CCCO and to explore effective treatment strategies.

Methods
All patients with CCCO treated at our institute between 1998 and 2010 were identified and their medical records were reviewed. Study protocol was approved by institutional review board. Variables were analysed using Fisher's exact test.

Results
Of 110 CCCO patients, 97 (88%, 97/110) achieved remission after primary therapy, of whom, 25 cases (26%, 25/97) developed recurrence. Overall response rate (RR) to primary chemotherapy for recurrence with measurable disease was 22% (4/18). In cases with more than 12 months of treatment-free interval (TFI), RR was 50% (4/8), whereas in those with less than 12 months, RR was 0% (0/10). Remission after recurrence, defined as one-year progression-free survival, was achieved in 11 cases (44%, 11/25), of whom, 9 cases (82%, 9/11) had surgery for recurrence, while none (0/14) of those without remission had (P<0.001). Eight (73%) of 11 patients with remission had TFI more than 12 months while 4 (29%) of 14 patients without had (P=0.04); however, RR to chemotherapy was not significantly different between the groups.

Conclusions
Chemotherapy for CCCO has little impact on prognosis after recurrence. Another treatment involving surgery, when indicated with long TFI, should be considered for disease control.
e-Posters: Ovarian Cancer

CYTOREDUCTION AND HIPEC VS ONLY CYTOREDUCTION SURGERY AFTER NEOADJUVANT CHEMOTHERAPY FOR TREATMENT OF OVARIAN CANCER NAIVE PATIENTS: A PHASE III MULTI CENTER RANDOMIZED ONGOING TRIAL.
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Objectives
Several phase II studies have reported favourable outcomes with the use of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for treatment of advanced epithelial ovarian cancer (EOC). In order to reduce postoperative complications and to achieve optimal cytoreduction, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery has been applied with encouraging results. To date, with standard treatment, the overall survival and progression free survival rate is still too poor. HIPEC is a heavy treatment that needs to demonstrate its efficiency in a large randomized trial. CHORINE (Cytoreduction and Hipec in the treatment of Ovarian cancer) aims to assess disease free survival, overall survival and the toxicity induced by HIPEC.

Methods
CHORINE is a multi-centre phase III prospective randomized trial comparing CRS + HIPEC (CDDP + Paclitaxel) vs CRS alone, in stage IIIC unresectable epithelial tubal/ovarian cancer with partial or complete response after 3 cycles of neoadjuvant chemotherapy with Carboplatin and Paclitaxel, followed by a further 3 cycles of the same chemotherapy regimen. A total of 96 patients in both arms are needed to complete the study.

Results
6 Italian Centres have been enrolled since June 2012. Two Centres are in the process of being enrolled.
To date, our Centre, has enrolled 7 patients: four in the cytoreductive surgery and HIPEC arm and 3 in the cytoreductive surgery arm.

Conclusions
CHORINE is the first randomized study aimed at assessing the role of HIPEC in the treatment of ovarian cancer using a combination of cis-platin and paclitaxel.
e-Posters: Ovarian Cancer

PROGNOSTIC AFFECT OF P16 AND P53 EXPRESSIONS ON STAGE 1A EPITHELIAL OVARIAN CANCER
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Objectives
Epithelial ovarian cancer (EOC) is the most lethal gynecological cancer in developed and developing countries. Whereas at early stages prognosis is better and 5-year overall survival is higher than %90. It is shown that some proteins (eg. P53,p16) are prognostic especially at advanced stages.

Based on this information in this study comparison of p16 and p53 expression's prognostic importance with other conventional parameters in stage Ia 29 EOC cases is planned.

Methods
Between 2007-2012, 257 EOC patients had primary surgery in our clinic and stage 1a 29 patients evaluated in this study. Appropriate examples in paraffin blockes were treated with p16 and p53 immunohistochemical staining. Age, grade and histologic type are the conventional parameters and compared with the p53 and p16 results.

Results
Univariant ve multivariant analysis indicated that p16 and p53 expression increased with grade but, due to the limited number of cases, p16 and p53 expression and other conventional parameters haven't been determined as prognostic.

Conclusions
Most of the studies in literature include all stage patients and early stage is usually demonstrated as stage 1-2 of which there is a significant difference in prognosis. Early stage ovarian cancer has a good prognosis especially in stage 1a. Larger case series in uniform patient groups may contribute to the literature.
GASTRIC METASTASIS FROM AN OVARIAN CANCER; A RARE CONDITION
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Objectives
Metastasis to the stomach from nongastric tumors is a rare condition. Here, we report a case of ovarian serous cancer metastasis to stomach.

Methods
A 55-year-old woman with abdominal pain and fullness was undergone laparatomy with the suspicion of ovarian cancer. During laparatomy a 11-cm right and a 9-cm left ovarian masses were detected. Frozen section analysis showed bilateral ovarian malignant tumor. There were common implants on peritoneal surfaces. Pathologic examination revealed high-grade ovarian serous cystadenocarcinoma. The patient was staged as IIIc ovarian cancer (FIGO 2009). The patient was submitted for standard chemotherapy for ovarian carcinoma. In the second year following the chemotherapy, her nausea, vomiting, and diarrhea complaints were emerged. On ultrasonographic evaluation a 7-cm pelvic mass and ascites were detected. A second cytoreduction was performed and during operation along with common tumoral implants a 5-cm mass on posterior wall of stomach is detected.

Results
The implant on gastric wall was resected and submitted for pathology. Histologic evaluation of this sampling revealed gastric metastasis of serous carcinoma.

Conclusions
Metastatic gastric tumors are uncommon conditions and mostly take root from breast cancer, malignant melanoma, and lung cancer. Gastric involvement of ovarian cancer is exceedingly rare, and if present mainly limited to serosal surface. Instead, in our patient there was a transmural gastric wall involvement. In conclusion, patients diagnosed with ovarian cancer have to be thoroughly evaluated for gastric metastasis when they have related symptoms during follow-up.
SEROUS PSAMMOMATOUS CARCINOMA OF THE OVARY INITIALLY PRESENTING WITH CERVICAL AND VAGINAL METASTASIS: A CASE REPORT

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Objectives
To describe a rare case of serous psammomatous ovarian cancer (OC), in which the patient initially presented with a metastatic cervical mass with vaginal involvement.

Methods
A 51-year-old postmenopausal woman applied to our institution because of malodorous vaginal discharge and intermittent vaginal bleeding since 3 months. On pelvic examination, a 4.5x3 cm tumoral mass was discovered, prolapsing from the cervical canal and extending to the vagina. Serum CA-125 was 35.3 U/ml. Transvaginal and transabdominal ultrasound examinations were performed, and approximately 3 cm anechoic cysts were reported on both ovaries. PET-CT was performed, and pathologic 18-FDG accumulation was reported on uterus. No metastatic accumulations were reported.

Results
Exploratory laparotomy was performed. Uterus, and bilateral tubes were macroscopically normal. Bilateral masses measuring 3 and 4 cm was found on the right and left ovaries, respectively. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. A 3 cm vaginal tumoral mass was excised alongside with 1/3 proximal vagina. Frozen section examination was reported as a malignant tumor on both ovaries and the vaginal mass. Bilateral pelvic+paraaortic lymphadenectomy, omentectomy and appendectomy was performed. Final pathology was reported as a serous psammomatous carcinoma of the ovary with cervical and vaginal metastasis. Metastases were also reported on one of the 43 lymphnodes, and omentum. Medical oncology department was consulted for further adjuvant treatment.

Conclusions
Ovarian cancer rarely presents with a cervical or vaginal mass. Careful evaluation of the patient is essential to determine the exact origin of the tumor and to rule out distant metastases.
A CASE OF OVARIAN CLEAR CELL CANCER WITH BORDERLINE ADENOFIBROMA AND ENDOMETRIOSIS

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Objectives
Borderline clear cell adenofibromas of the ovary are rarely seen tumors. They behave as the precursor lesions for ovarian clear cell carcinoma like endometriotic lesions. These tumors occasionally may be encountered with endometriosis. In this paper, we present a case of an ovarian clear cell carcinoma with borderline clear cell adenofibroma and endometriosis.

Methods
A 55-year-old woman is referred to our hospital with the complaints of abdominal pain for 4 months. On ultrasonographic evaluation a 12 x 10 cm semisolid pelvic mass is detected. CA-125 level was 390 IU/ml. She underwent laparotomy and frozen-section revealed malignant ovarian epithelial tumor. Surgical staging was performed.

Results
In final pathological investigation clear cell carcinoma is detected together with borderline clear cell adenofibroma and paratubal endometriosis in paraffin-embedded samplings. There was no capsular invasion and abdominal lavage fluid examination was negative for tumor cells.

Conclusions
Clear cell cancers constitute 5-25 % of epithelial ovarian cancers and differ from other epithelial subtypes with different clinicopathologic features. Pathogenesis of ovarian clear cell carcinoma is unclear and endometriosis and adenofibromas are proposed as the precursors for clear cell cancers by different mechanisms according to the well-known dualistic model of Kurman and Shih. In some clear cell cases, togetherness of adenofibrom and endometriosis with cancer is possible as in current patient. Some authors proposed the noncystic endometriosis as the root for ovarian adenofibromas, hence, there may be one route for emergence of ovarian clear cell cancer.
AN OVARIAN SERTOLI-LEYDIG CELL TUMOR WITH BORDERLINE MUCINOUS ELEMENTS AND ENDOMETRIOSIS: A RARE OVARIAN SCENARIO

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Objectives
Sertoli-Leydig cell (SLC) tumors are rare and account for 0.1-0.5% of all primary ovarian neoplasms. They have no predilection to being together with endometriosis that gives rise to epithelial ovarian cancers like endometrioid and clear cell ones. In this paper, as a rare scenario, a SLC tumor is presented with benign and borderline mucinous epithelial components along with endometriosis.

Methods
On ultrasonography of a 52-year-old woman with abdominal pain for a couple of months, a 10-cm left adnexal mass was detected. There was no ascites. Ca-125 level was in normal range. She underwent an explorative laparotomy and frozen analysis was reported as borderline mucinous ovarian tumor.

Results
Surgical staging was performed and the evaluation of paraffin-embedded samplings revealed SLC tumor with borderline mucinous tumor and endometriosis.

Conclusions
SLC tumors are mostly diagnosed in young women and may produce androgens, resulting in hirsutism, hoarseness and clitoromegaly. They are malignant in 15-20% of cases. Rarily, SLC tumors comprise heterologous components like mucinous epithelium, skeletal muscle and liver cells. Despite the well-description of etiologic relation between endometriosis and some types of epithelial ovarian cancers, this is not valid for sex cord tumors. But in many studies similar histologic appearance of SLC and granulosa cell tumor and some unusual variants of ovarian endometrioid carcinoma arising from endometriosis are reported. This creates a diagnostic pitfall in differentiation of these distinct pathologies. Therefore, further data is required to comment on etiologic or incidental nature of aforementioned condition.
e-Posters: Ovarian Cancer

PRIMARY MALIGNANT MIXED MÜLLERIAN TUMOR OF THE OVARY: 15 YEARS OF EXPERIENCE IN A SINGLE ONCOLOGY CENTER
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Objectives
To evaluate the clinicopathological characteristics, treatment, and prognosis of primary malignant mixed müllerian tumor (MMMT) of the ovary.

Methods
A retrospective review of our cancer registry database was conducted to identify patients diagnosed with ovarian MMMT between 1996 and 2011. We collected clinicopathological data to evaluate factors important in progression-free survival (PFS) and overall survival (OS). Kaplan–Meier curves were generated and log-rank tests were used to evaluate survival differences.

Results
Seventeen patients were diagnosed with ovarian MMMT at a median age of 55 years. The median follow-up time was 34 (range, 12–78) months. All patients underwent complete surgical staging, debulking, and postoperative chemotherapy. Optimal debulking was achieved in 13 (76.5%) patients. The median survival time of all patients was 34 months. The 5-year OS rate was 29.4%. Eleven patients were treated with a paclitaxel plus carboplatin chemotherapeutic regimen, and six patients were treated with ifosfamide plus cisplatin. No significant difference in PFS or OS was observed between groups (P = 0.99 and P = 0.94, respectively) or between patients with homologous (n = 11) and heterologous (n = 6) tumors (P = 0.84 and P = 0.76, respectively). Disease stage and optimal debulking surgery were important factors in PFS, whereas disease stage was the only prognostic factor for OS in multivariate analysis.

Conclusions
Ovarian MMMT is a very rare and aggressive tumor. We recommend a platinum-based combination chemotherapeutic regimen following optimal debulking surgery for the treatment of ovarian MMMT.
e-Posters: Ovarian Cancer

PRIMARY FALLOPIAN TUBE CANCER: A SINGLE INSTITUTIONAL CASE SERIES
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Objectives
Primary fallopian tube carcinoma is one of the least common gynecological cancers and is difficult to diagnose preoperatively. The aim of this study is to present a retrospective clinical pathological study of 39 cases of tubal malignancies.

Methods
A retrospective review of our Gynecologic Oncology database was conducted to include any patients with a diagnosis of fallopian tube carcinoma between the years 1996 and 2013. Clinical information and pathological data were obtained by review of hospital records. Carcinomas were staged according to the FIGO criteria; assignment of stage was made on the operative data and the pathological findings.

Results
The median age of the 39 cases was 54 years (range, 32-67 years), whereas the median follow-up time was 84 months. None of the 39 cases were diagnosed preoperatively. Patients most frequently presented with abdominal pain (46.2%) and an abnormal vaginal bleeding (41%). The most common histological subtype was papillary serous adenocarcinoma in 56.4% of cases. Two patients (5.1%) were in carcinoma in situ, 15 patients (38.5%) in Stage I, 8 (20.5%) in Stage II, and 14 (35.9%) in Stage III. Thirty-one patients had received postoperative platinum-based adjuvant chemotherapy. During the follow-up period, 13 recurrence was observed. The rate of nodal involvement (P < 0.001) and lenfovascular invasion (P = 0.004) werewere significantly higher in recurrence disease.

Conclusions
Primary fallopian tube carcinoma is hardly ever diagnosed preoperatively or intraoperatively due to its rarity. The treatment was surgical followed by adjuvant chemotherapy. The rate of nodal involvement and lenfovascular invasion were significantly higher in recurrence disease.
COMPARISON OF ROMA (RISK OF OVARIAN MALIGNANCY ALGORITHM), RMI (RISK OF MALIGNANCY INDEX) AND OTI (OVARIAN TUMOR INDEX) IN PATIENTS WITH ADNEXAL MASS

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Objectives
To compare of ROMA, RMI, OTI indexes in patients with adnexal mass.

Methods
A total of 51 patients with adnexal mass were enrolled in the study. Surgery was performed in all patients suspicious for malignancy. Demographic and clinical characteristics of the patients were identified. Morphological scores calculated via gray-scale and Doppler ultrasonography. Pre-operatively blood samples were taken to assess CA 125 and HE4 levels. Scores of ROMA, RMI and OTI were calculated of all the cases. We compared each other to sensitivity, specificity, positive (PPV) and negative predictive values (NPV) to find out the most beneficial one to detect the malignancy.

Results
Forty-three of the adnexal mass were benign, 2 were borderline and 6 were malignant. The mean of age of patients with benign and malign mass were 44.27±14.9 and 55.25±17.16, respectively (p=0.029). ROMA scores of sensitivity, specificity, PPV and NPV for pre and postmenopausal patients were 50%, 100%; 96.5%, 92,8%; 50%, 85,7%; 96,5%, 100% respectively. RMI scores of sensitivity, specificity, PPV and NPV were 87,5%, 100%; 100%; 97,6%, respectively. OTI scores of sensitivity, specificity, PPV and NPV were 100%, 79%, 57.1%; 100%.

Conclusions
ROMA value is detected more sensitive and specificity in postmenopausal patient group rather than other tests in this study. OTI is also has a remarkable sensitivity though the specificity is not enough at all. ROMA index is better on detecting malignant masses at postmenopausal patients and benign masses on premenopausal patients.
e-Posters: Ovarian Cancer

PROGNOSTIC IMPORTANCE OF SURVIVIN, KI-67, AND TOPOISOMERASE II ALPHA IN OVARIAN CARCINOMA

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Objectives
Stage, tumor grade and histological subtype determine clinical behaviour in ovarian tumors. Some additional factors are related to tumor cell biology and are useful predictors for the identification of patients with poor prognosis. The aim of this study is to evaluate the prognostic significance of survivin, Ki-67 and Topoisomerase IIα (TOPO IIα) in epithelial ovarian cancer (EOC).

Methods
Seventy-three patients with EOC were included in this study. Survivin, Ki-67 and TOPO IIα expression were studied by immunohistochemistry on formalin-fixed, paraffin-embedded tissue sections. Nuclear staining for all antibodies were scored on a three-tiered system and more than 10% staining was accepted as expression. The relationship between expression of survivin, Ki-67, TOPO IIα and clinicopathological parameters including age, stage, grade, platinum resistance and survival were evaluated.

Results
Survivin, Ki-67 and TOPO IIα expression were found in 20%, 82% and in 86% of the tumors, respectively. Ki-67 and TOPO IIα expressions were found to be related with poor overall survival (p=0.005, 0.004, respectively) while survivin expression did not associated with overall survival. There was no association between TOPO IIα and Ki-67 expression and histological subtype, stage or grade. However we found important association between TOPO IIα expression and platinum resistance (p=0.044). Platinum resistance was found independent prognostic factor in EOC.

Conclusions
Ki-67 and TOPO IIα expressions were found to be related with poor overall survival and TOPO IIα expression was found associated with platinum resistance.

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Objectives
To determine the accuracy of frozen section diagnosis of ovarian masses and the clinical properties of the borderline ovarian tumors (BOTS).

Methods
The study was designed as a retrospective cohort study. A total of 40 patients with histologically (frozen or permanent) proven BOTs, between ----/2000 and 12/2000 were included in the study. The rate of accuracy with the frozen section in BOTs was analyzed.

Results
The average age of the patients in the study was 49.3 ± 18.7. Histological distribution of BOTs were as follows; 1 (3 %) brenner BOT, 1(3%) endometrioid BOT, 10 (30 %) mucinous BOTs, 23 (66 %) serous BOTs. The mean morphology index score of BOTs and malignant ovarian tumors were 5±2 and 7.5±2.3, respectively. The rate of correct diagnosis, under-diagnosis and over-diagnosis of BOTs with frozen section were 78%,17% and 5% respectively. The sensitivity and positive predictive values in diagnosis of BTOs with the frozen section were 93.3 % and 82.3%. Positive Likelihood Ratio is 0.93 (95% CI:0.85 to 1.03).

Conclusions
The frozen section diagnosis is an important and convenient tool in the clinical management of patients with ovarian tumors. As well as low sensitivity and PPV, overdiagnosis and underdiagnosis are frequent. Therefore a more careful approach is needed in order to reduce the false diagnosis and surgical morbidity.
e-Posters: Ovarian Cancer

OUTCOMES IN MUCINOUS OVARIAN CARCINOMAS: 10 YEARS OF EXPERIENCE IN A TERTIARY CENTRE

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Objectives
There is a growing appreciation that epithelial ovarian cancers do not behave as a single clinical entity. We investigated the extent to which presentation and outcomes differed between serous and mucinous subtypes, with a particular focus on early stage disease.

Methods
We searched for all ovarian carcinomas of primary ovarian origin diagnosed between the year 2001 and 2010, inclusive. For analysis of outcomes in late stage mucinous tumours, an age- and stage-matched cohort was randomly selected from amongst serous cases for comparative analysis.

Results
Over a 10 year period we identified 460 ovarian cancer cases, of which 320 (70%) were serous and 32 (7%) mucinous ovarian carcinomas. Of mucinous cases, 23 (72%) presented with Stage I disease, as compared to 20 serous cases (6%). Significant differences in cancer biomarkers were observed between cohorts. In the early stage mucinous group, one patient (4%) with disease recurrence was identified. This rapidly progressed to multi-organ metastasis, leading to death 12 months from diagnosis. Of two recurrences (5%) which occurred in the serous cohort, one patient died 22 months from diagnosis, while the other remained alive at 34 months. In patients with late stage mucinous disease, median overall survival was 7.75 months, as compared to 57 months in the age- and stage-matched serous cohort (p=0.028, Log-rank Test).

Conclusions
For early stage disease in both mucinous and serous ovarian cancer, disease recurrence was rare. Consistent with previous findings, patients with late stage mucinous carcinomas had a significantly poorer prognosis than patients with comparable serous disease.
KRUKENBERG TUMOR AS A FIRST DIAGNOSIS OF CANCER. AN INSTITUTIONAL REVIEW BETWEEN 2011-2013

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Objectives
The purpose is to analyze presentation, diagnosis, treatment and follow up for the patients with Krukenberg's tumor as the first clinical manifestation of cancer in a single institution.

Methods
Is a retrospective analysis medical data from 14 patients who were referred to the Regional Cancer Institute Iasi, Romania between 2011-2013.

Results
The patients ranged from 39 to 64 years-old. 8 of them were pre-menopausal. The most common clinical presentations were abdominal distention or pain. Ascites was present in 11 patients and 3 of the tumors were unilateral. All patients were diagnosed using ultrasonography, computed tomography. CA125 were elevated in several cases. Surgery was performed in all cases, the most common being debulking surgery. The histopathology features suggested gastric carcinoma (adenocarcinoma and clear cell carcinoma) in 11 patients, colorectal carcinoma (mucinous adenocarcinoma) in 3 patients and pancreatic carcinoma (adenocarcinoma) in 1 patients. The protocols of chemotherapy were: cisplatin-capecitabine (patients with gastric cancer), gemcitabine (patients with pancreatic cancer) and XELOX, XELIRI and XELIRI-bevacizumab (patients with colorectal cancer). The median overall survival was 20,1 months.

Conclusions
Krukenberg's tumor as the initial clinical manifestation of cancer have a poor prognosis. Timing for diagnosis is frequently late. Gastric adenocarcinoma is the most common source. Surgery can improve survival only in cases of local extended disease.
FREQUENCY AND PATTERNS OF OVARIAN TUMOURS

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Objectives

This study was conducted to investigate the frequency and type of ovarian tumors amongst patients who underwent surgery for ovarian cyst diagnosed on ultrasound and also to compare a change in pattern of type of tumors between 2002 and 2009.

Study Design

Comparative, Observational study

Setting & Duration

This study was carried out in the department of obstetrics and gynaecology Foundation University Medical College, Fauji Foundation hospital Rawalpindi that is a tertiary care hospital, from 1st June 2002 to 31st May 2003 (Study period 1, n=90) and from 1st November 2008 to 31st October 2009 (Study period 2, n=93). All the patients who had ovarian cysts larger than five centimetres in size diagnosed on ultrasonography and planned for surgery were included in the study. All the relevant details were entered in proformas. Histopathology of excision biopsies was analysed.

Results

The overall incidence of ovarian tumors was 7.1% and 5.4% with a rate of malignancy 18% and 5.4% in period 1 and 2 respectively which was statistically non significant (p>0.05). The most common malignant tumour was serous cyst adenocarcinoma during both study periods. The most common benign tumor was simple follicular cyst 25% during study period one and serous cyst adenoma 23% during period 2.

Conclusions

The frequency and patterns of ovarian tumors has remained unchanged between 2002 and 2009.
e-Posters: Ovarian Cancer

BEVACIZUMAB IN HEAVILY PRETREATED OVARIAN CANCER: WHICH PLACE IN DEVELOPING COUNTRY?
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Objectives
The addition of bevacizumab to standard chemotherapy prolongs progression free survival in the first line treatment of epithelial ovarian cancer. Heavily pretreated patients will often be ineligible for clinical trials, and will usually have experienced several side effects from previous chemotherapy. For these challenging heavily pretreated patients we assessed the safety and efficacy of bevacizumab combined with monochemotherapy.

Methods
We treated 6 patients, mostly with platinum resistant EOC, who had received a median of five prior cytotoxic regimens, with bevacizumab 15 mg/kg q21 days in combination with either gemcitabine (n = 4), or weekly paclitaxel (n = 2). Bevacizumab was administered until disease progression. Tumor response was assessed by CA125 and CT-scan.

Results
We have found that the combination of gemcitabine or paclitaxel weekly and bevacizumab is effective but not well tolerated. All patients had combined clinical and biological response. Major related toxicities was bowel perforations in two cases.

Conclusions
Our study has several limitations, including the small sample size and the heterogeneity of chemotherapy regimens. Despite these caveats, our case-series study suggests that the combination of bevacizumab and chemotherapy is active in heavily pretreated patients with advanced epithelial ovarian cancer, but not always well tolerated. A comparative trial with conventional chemotherapy is warranted.
RESULTS OF OVARIAN CANCER TREATMENT IN GYNECOLOGY AND ONCOLOGY CLINIC JAGIELLONIAN UNIVERSITY COLLEGIUM MEDICUM IN KRAKOW IN 1998-2006.
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Objectives
1. To determine the influence of resection and clinical stage of the cancer on the recurrence rate and the overall 5-year survival rate.

2. To study the relationship between age, histological type, tumor grade and the 5-year survival rate.

3. To determine the Ca-125 level before treatment and it’s association with the FIGO stage, tumor grade, histological type and the presence of ascites.

4. To investigate the Ca-125 level prior to and after treatment and the overall 5-year survival rate.

5. Assessing the influence of the tumor’s size after cytoreduction on the 5-year survival rate.

Methods
The material consisted of 126 patients, aged 17-87 years, diagnosed and treated at the Department of Gynecology and Oncology of the JUMC.

Results
A statistically significant correlation was found between the 5-year survival rate and the FIGO stage, tumor grade and the presence of ascites (p<0.05).

Conclusions
1. The most important prognostic factor for 5-year survival is radical primary surgery.

2. Significant prognostic factors that reduce the chances of recovering from ovarian cancer are: high FIGO stage, low tumor grade and the presence of ascites.

3. A correlation is found between a high level of the tumor marker Ca-125 before surgery and the 5-year survival percentage, this also correlates with the FIGO stage and tumor grade. However, the Ca-125 level only slightly depends on the presence of ascites and does not at all depend of the type of tumor histology.

4. Low Ca-125 concentrations correlate both with the possibility of successful radical surgery and with a lower FIGO stage.
ENGINEERED LIPOSOMES BEARING SYNERGISTIC COMBINATION OF DRUGS FOR TREATMENT OF OVARIAN CANCER

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Objectives
In this debut study, dual approach using synergistically active combination of paclitaxel-topotecan (Pac-Top; 20:1, w/w) is investigated with utilization of characteristic features of tumor micro-environment and additionally over expressed folate receptors (FR-α) to achieve targeting to tumor site.

Methods
Various liposomes namely: Liposomes, PEGylated liposomes and FR-targeted PEGylated liposomes with lipid compositions viz. DPPC: DMPG (85.5:9.5), DPPC: DMPG: mPEG2000-DSPE (85.5:9.5:5) and DPPC: DMPG: mPEG2000-DSPE: DSPE-PEG-folate (85.5:9.5:4.5:0.5), respectively were developed using thin film casting method. They were characterized for surface charge, size and size distribution, % drug entrapment, in vitro drug release. Cytotoxicity studies and florescence study were performed to confirm the targeting potential of developed system.

Results
Liposomes were nanometric in size around 200 nm. In vitro drug release study showed initial burst release followed by sustained release for more than 72 hrs at physiological milieu (37±0.5ºC, pH 7.4) while burst release (i.e. more than 90%) within 5 min at simulated tumor milieu (41±1ºC, pH 4). SRB cytotoxicity assay in OVCAR-3 cell line revealed Pac-Top free (20:1, w/w) to be more toxic (GI₅₀ 6.5 µg/ml) than positive control (Adriamycin, GI₅₀ 9.1 µg/ml) and FR-targeted PEGylated liposomes GI₅₀ (14.7 µg/ml). Moreover, florescence microscopy showed the highest cell uptake of FR-targeted PEGylated liposomes so called ‘Smart Liposomes’.

Conclusions
Developed FR-targeted PEGylated liposomes were efficacious and safe for dual delivery of paclitaxel and topotecan. The data presented here, has historical evidence, suggest that liposomal co-encapsulation of anticancer drug combination can profoundly yield therapeutic outcomes and reduce the side effects of the treatment.

Mechanistic scene: How do ‘Smart’ liposomes work?
SURGERY FOR ADVANCED OVARIAN CANCER

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Objectives
Surgery is the cornerstone of treatment of advanced ovarian cancer. Surgical removal of the tumour allows proper staging procedure, improve patient's general condition and tumour response for future chemotherapy. Surgery has shown similar results when performed primary or after platinum-based neoadjuvant chemotherapy in large randomized clinical trials with residual tumour volume being the most significant prognostic factor. It is not yet clear whether patient will benefit from systemic lymph node dissection or not. Current clinical practice support removal of lymph nodes only when tumour optimally debulked.

The aim of study was to evaluate results of primary debulking surgery in advanced ovarian cancer patients.

Methods
We analysed data from 65 consecutive patients, treated at Kazakh Research Institute of Oncology & Radiology from 2008 to 2011, who were considered for primary debulking surgery. All cases were FIGO stage IIIC and IV. Mean age was 56.9 years. 56 patients were stage IIIC (86.2%) and 9 patients (13.8%) had stage IV disease.

Results
Optimal debulking took place in 77.1% of cases, whereas 15.6% of cases were suboptimal and 7.3% - unoptimal. 35 patients (53.8%) together with optimal debulking also underwent systemic pelvic and paraaortic lymph node dissection. 82.9% (29/35) patients had positive lymph nodes. Lymphadenectomy shows unexpectedly high rate of lymph node metastasis.

Conclusions
Primary debulking surgery in patients with advanced ovarian cancer looks feasible with 77.1% success. High rate of lymph node involvement suggest necessity of systemic pelvic and paraaortic lymphadenectomy in all patients with ovarian cancer.
SUPRADIAPHRAGMATIC LYMPH NODE METASTASIS DETECTED IN FDG PET/CT AS A PREDICTOR OF OVERALL SURVIVAL IN ADVANCED STAGE OVARIAN CANCER

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Objectives
To investigate if supradiaphragmatic lymph node(SdLN) metastasis detected in FDG PE/CT has prognostic effect on overall survival

Methods
From June 2003 to December 2010, 105 women with epithelial ovarian cancer have the result of whole body FDG PET/CT prior to start of anticancer treatment. In 56 patients who underwent primary debulking surgery and were diagnosed as stage III/IV ovarian cancer, overall survival and prognostic variables were analyzed on 15 January 2013. SdLN include neck, parasternal, axillary and mediastinal lymph nodes.

Results
Median age was 52.02 years (range 33-80 years). Stage IIIb, IIIc and IV patient were 7, 38 and 11 respectively. 19 patients showed FDG uptake on supradiaphragmatic lymph node in PET/CT. Paradoxically, mean overall survival were 49.7 months and 77.1 months in SdLN(-) group and SdLN(+) group respectively. (p=0.057) SdLN uptake was associated with abdominal lymph node metastasis. In SdLN(+) group, there were more patients with lymph node only stage IIIc than in SdLN(-) group. Number of abdominal lymph node showing metastasis was higher in SdLN(+) group. (11.0 vs. 1.78, p<0.05)

Conclusions
SdLN uptake in FDG PET/CT in ovarian cancer was not associated with poor prognosis. The longer survival might be caused by LN only stage IIIc patients.
e-Posters: Ovarian Cancer

STUDY FOR 43 CASES OF OVARIAN PRIMARY CANCER WITH RESECTION OF THE INTESTINE

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Objectives

According to the ovarian cancer treatment guidelines in 2010 edition in Japan, "the surgery for ovarian cancer should be maximum debulking surgery with the aim of complete resection, due to the correlation the residual tumor after surgery with the prognosis. There may need the case such as resection of intestine and peritoneum for removal of tumor as possible." We have examined 43 cases of ovarian cancer surgery needed intestinal resection.

Methods

The subjects are stage III or less stage cases in complete reductive surgery including resection of tumor adhesion or disseminated tumor of intestinal tract, and stage IV cases in optimal surgery after chemotherapy (Neo Adjuvant Chemotherapy).

The analysis is in perioperative management, histological type, complications, and progression.

Results

Majority is epithelial ovarian cancer (serous adenocarcinoma: 44.2%, endometrioid adenocarcinoma: 20.9%, clear cell adenocarcinoma: 11.6%).

Advanced ovarian cancer (stage III: 53.5%, stage IV: 18.6%), colon resection (sigmoid colon resection: 37.2%, low anterior resection: 30.2%, other colon resection: 25.7%).

In 31 cases of advanced ovarian cancer (stage IIIc: 67.8%, stage IV: 25.8%), serous cancer: 58.1%, overall survival of stage IIIc: 32.0 months and stage IV: 27.0 months. In 9 NAC cases (stage IIIc: 3 cases, stage IV: 5 cases), overall survival is 37.0 months and the criteria of chemotherapy effect G2 is 50%.

Conclusions

The surgery for 43 cases ovarian cancer with intestinal removal was performed successfully without any complications such as anastomotic insufficiency in all cases.

Tumor removal as possible including intestinal resection is assumed to be important in the strategy of ovarian cancer treatment.
MUCINOUS BORDERLINE TUMOURS AND THE APPENDIX: A RETROSPECTIVE STUDY.

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Objectives

It is debated whether mucinous borderline ovarian tumours (mBOT) originate in the ovary or whether they represent metastases of tumours of the appendix. Several studies conclude that the origin is the appendix. Therefore an appendectomy is suggested in case of a mBOT. The aim of this study is to assess the incidence of mucinous neoplasms in the appendix in case of ovarian pathology.

Methods

We performed a search in the pathology files for all ovarian mBOT and mucinous tumours of the appendix between 1990 and 2011 in two teaching hospitals.

Results

In total, 127 patients were retrieved from the files: 98 patients with a primary mBOT and 29 patients with primary mucinous tumour of the appendix. In only 13 (13%) patients with a primary mBOT the appendix was removed. On pathological examination the appendices were all normal. In 61 (62%) patients the appendix was not removed, but described as normal during surgery. In 31 (31%) patients the appendix was not removed, nor described. The median (range) follow-up in our series was 5 (2-23) years. In 2 patients the tumour recurred in the vaginal vault. The appendix was not involved at the time of recurrence.

In 8 (28%) patients with primary mucinous tumour of the appendix ovarian metastases were diagnosed. In all cases the appendix was described during surgery as abnormal.

Conclusions

A thorough inspection of the appendix should be performed in case of a mBOT. An appendectomy should be performed only when the appendix is macroscopically abnormal.
e-Posters: Ovarian Cancer

CHANGE IN CA-125 LEVELS DURING PRIMARY THERAPY BETWEEN EARLY RELAPSED VERSUS LATE OR NON-RECURRENT STAGE III/IV SEROUS OVARIAN CARCINOMA IN KOREA; A SINGLE INSTITUTE RETROSPECTIVE STUDY

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Objectives
This study was conducted to compare change in CA-125 levels during primary therapy (PT: debulking surgery followed by platinum based chemotherapy) between shortly relapsed (STR: disease free survival, DFS<12mo) versus late or non-recurrent (LTS: DFS>60mo) stage III/IV serous ovarian cancer.

Methods
In a retrospective analysis, the CA-125 level in 99 patients with stage III/IV serous ovarian cancer who had achieved complete remission (CR) after PT was determined and evaluated the results statistically in Asan medical center in Korea, from 2000 to 2010.

Results
Among 196 patients with stage III/IV serous ovarian carcinoma who had achieved CR after PT from 2000 to 2010, 38 patients are assigned to LTS according to DFS, 72 patients to STR. 2 from LTS and 9 from STR were dropped from study due to lack of laboratory result.

Age (p=0.376), hematologic toxicity (p=0.117), No. of days for delayed chemotherapy (CT)(p=0.966), interval between surgery and the first course of CT(p=0.458) was statistically irrelevant.

Of 36 LTS, CA-125 level of 34 patients was normalized (<35IU/mL) at the end of the 2nd course of CT. On the contrary, of 63 STR, CA-125 level of only 37 patients was normalized after 2nd course of CT(p=0.000). Up to 97% of both group reach normal CA-125 level at the end of 5th course of CT. Preoperative CA-125 was irrelevant between two groups(p=0.610).

Conclusions
The CA-125 level of LTS tend to normalize after second course of induction CT. This result can be used as favorable prognostic factor to expect long-term DFS in advanced serous ovarian cancer. Further investigation is needed.
COMPARISON OF LAPAROSCOPY AND LAPAROTOMY FOR THE MANAGEMENT OF EARLY-STAGE OVARIAN CANCER: SURGICAL AND ONCOLOGIC OUTCOMES

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Objectives
To investigate the results of laparoscopic surgery for early-stage ovarian cancers compared with laparotomy, focused on surgical and oncological outcomes.

Methods
Data of the patients who underwent surgical management for early-stage ovarian cancer between 2006 and 2012 was retrospectively reviewed. All patients presented stage I or II disease and underwent comprehensive staging surgery including total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, omentectomy, and peritoneal cytology.

Results
Seventy-seven patients who underwent laparoscopic surgery (24 cases, 31.2%) or laparotomy (53 cases, 68.8%) were identified. No one was converted from laparoscopy to laparotomy. There were no significant differences in basic characteristics of age, past surgical history, and histology type between groups. Mean operative time tended to be shorter and the estimated blood loss was lower in laparoscopy than laparotomy group without significant differences (193 min vs. 224 min, p=0.127 and 698 ml vs. 973 ml, p=0.127). Mean hospital stay and number of pelvic and paraaortic lymph nodes collected were also similar between groups. There were no differences with regard to the intraoperative and postoperative complications. During a mean follow-up period of 31 months, tumor recurrence occurred in 4 patients and disease-free survival was 59 months in laparoscopy and 66 months in laparotomy (p=0.367).

Conclusions
Laparoscopic surgery seems to be adequate and feasible for early-stage ovarian cancer with comparable results in terms of surgical outcomes and oncological safety. Surgery by more experienced surgeons may provide better outcomes in laparoscopy, but additional studies with large scale population are needed to confirm this.
e-Posters: Ovarian Cancer

OVARIAN MALIGNANCY IN <25 YEARS AGED WOMEN: SINGLE CENTER EXPERIENCE

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Objectives
To present different classes of ovarian malignancies and their management in young aged women.

Methods
Totally 16 patients <25 years of age were diagnosed between 2006-2012 in our clinic. Patients’ data were reviewed retrospectively.

Results
Mean age of diagnosis was 19.8 years (range 14-24) and abdominal pain was the predominate symptom to seek medical attention. Most common type of histology was ovarian dysgerminoma (4 cases), immature teratoma (3 cases) and Krukenberg tumor originated from GIS (2 cases). Other patients had one of each of the following histology Sertoli-Leyding cell, Granulosa cell, Yolk Sac, ovarian choriocarcinoma, mixed germ cell tumor composed of embryonal carcinoma-Yolk Sac-immature teratoma, malign struma ovarii and Burkitt’s Lymphoma. Fertility sparing surgery was performed 8 patients who had early (7 cases stage IA, 1 case stage IC) disease, only 4 patients had cytoreductive surgery in spite of young age because of advanced (3 cases with stage IIIC, 1 case stage IV) disease, one case to whom cytoreductive surgery was applied diagnosed as Krukenberg tumor after permanent pathology. The other two cases one with Burkitt’s Lymphoma and the other with Krukenberg tumor were diagnosed with frozen section-confirmed with permanent pathology-and cytoreductive surgery was not performed. One case who had oofectomy and diagnosis of struma ovarii denied re-staging surgery.

Conclusions
Most common types of ovarian malignancies in young aged women are germ cell tumors and they have usually bening course. However malign conditions must be differentiated. Also fertility preservation is an important issue during surgical staging and patient follow-up in these women.
THE EFFECT OF FIRST-LINE BASED ON PLATIN AND TAXANE CHEMOTHERAPY ON DENDRITIC CELLS IN WOMEN SUFFERING FROM OVARIAN CANCER

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Objectives
Ovarian carcinoma (OC) is often diagnosed at an advanced stage and requires effective chemotherapy treatment. However, chemotherapy may be associated with significant side-effects, like nausea, vomiting, hair loss, cognitive dysfunction, fatigue and changes in sexual functioning and reductions in quality-of-life ratings. Little is known about possible influence of chemotherapy on dendritic cells (DC) percentage and function, although it is well documented that primary and secondary cell-mediated immune responses are suppressed during this treatment.

The aim of this study was to estimate myeloid (M) and lymphoid (L) DC in the peripheral blood (PB) of 45 women with OC, before and during 6 courses of chemotherapy. The control group comprised of blood donors in good health condition (n=24).

Methods
The MDC and LDC were estimated by flow cytometry with the use of monoclonal antibodies: anti-BDCA-1 FITC, anti-CD19 Cy-Chrome and anti-BDCA-2 FITC, anti-CD123 PE, before and during treatment. Resultswere presented as a percentage of MDC and LDC in mononuclear cells.

Results
The percentage of both MDC and LDC was significantly lower (0.09% and 0.04%) in the PB of patients with OC in comparison to control group (0.25% and 0.33%). The percentage of both MDC and LDC subpopulations during chemotherapy, administered at 21-day intervals, did not differ from that found before treatment. However, the MDC to LDC ratio was significantly lower in patients received 6 courses of treatment.

Conclusions
These data may suggest that chemotherapy treatment of OC patients have influence on predominance of LDC.
INTEGRATIVE GENOMIC AND TRANSCRIPTOMIC ANALYSIS TO IDENTIFY BIOMARKERS OF CHEMOTHERAPY RESISTANCE IN SEROUS EPITHELIAL OVARIAN CANCER

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Objectives
Resistance to platinum-based chemotherapy remains a major impediment in the treatment of serous epithelial ovarian cancer. The objective of this study was to use gene expression and copy number profiling to delineate major deregulated pathways and biomarker networks associated with the development of intrinsic chemotherapy resistance with exposure to standard first-line therapy for ovarian cancer.

Methods
The study cohort comprised 28 high grade serous ovarian cancer patients divided into two groups based on their varying sensitivity to first-line chemotherapy using progression free survival (PFS) as a surrogate of response. Twelve patient tumors demonstrating relative resistance to platinum based chemotherapy corresponding to shorter PFS (less than 6 months) were compared to 16 tumors from platinum-sensitive patients (PFS more than 18 months). Molecular profiling was performed using Affymetrix high-resolution microarray platforms to permit global comparisons of gene expression levels and copy number profiles between tumors from the resistant group with the sensitive group.

Results
Microarray data analysis using statistical methods revealed a set of 204 discriminating genes of which expression levels may be influencing differential chemotherapy response between the two groups. Pathway analysis showed IGF1 network to be significantly altered between the two groups in addition to PI3K, NFkB, distinguishing the two groups. Copy number analysis showed differences in the chromosomal regions, 4q31.22, 5q13.2, 9p24.3, 2p23.2, 16q21, 6q14.1, 7p22.3, 12p13 and Xq.

Conclusions
In the next phase of the study copy number analysis will be performed to integrate and gene expression profiling with gene expression to delineate the drivers of chemotherapy resistance in patients undergoing standard platinum-based treatment of ovarian cancer.
HE4 AND CA125 IN OVARIAN CANCER PATIENTS

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Objectives
The application of the measurements of Human Epididymis Protein 4 (HE4) and CA 125 concentration, for the assessment of the probability of the occurrence of ovarian epithelial cancer on the basis of ROMA factor.

Methods
The determinations of CA 125 and HE4 were carried out, before treatment, on 90 patients including 36 with ovarian cancer, 9 with ovarian tumor of borderline malignancy, 45 with benign ovarian masses and 26 healthy women. Concentrations of CA 125 and HE4 were determined using the ROCHE instruments system.

Results
Among patients with benign ovarian masses, 4% presented elevated HE4 levels, 47% increased CA 125 levels, and 11% – increased ROMA factor. Whereas in patients with ovarian tumor of borderline malignancy 11% presented elevated HE4, and 22% – increased CA 125 and 22% ROMA factors. In patients with early ovarian cancer (FIGO I, II) the concentration of HE4 was elevated in 55% of patients, whereas in patients with advanced stage of the disease (FIGO III, IV) in 75% of patients. It has been demonstrated that the concentrations of HE4 and CA 125 and ROMA factors were significantly higher in patients with ovarian cancer when compared with their values in patients with benign ovarian masses, as well as in patients with ovarian tumors of borderline malignancy (p<0.0001).

Conclusions
The determination of ROMA factor can be helpful in separation of patients with benign ovarian masses and ovarian tumor of borderline malignancy from those diagnosed with ovarian cancer and the sensitivity for the presence of ovarian cancer prediction improvement.
e-Posters: Ovarian Cancer

RETROPERITONEAL LYMPHANGIOLEIOMYOMATOSIS SUSPECTED TO BE AN OVARIAN CANCER: TWO CASE REPORTS
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Objectives
To describe two cases of lymphangioleiomyomatosis (LAM), a rare progressive disease mimicking ovarian cancer.

Methods
Retrospective case clinical study.

Results
43- and 41-yr-old women were admitted in August 18, 2009 and January 1, 2012 with abdominal pain, ascites and with elevated serum CA-125. Ultrasound examination showed multicystic mass on the pelvic side wall. Both patients underwent laparotomy with the findings of chylous ascites and enlarged lymph nodes in the iliac and obturator area. Frozen section from the lymph nodes revealed a proliferation of fascicular cells. The immunohistoanalysis was positive for human melanoma black-45 (HMB-45), alpha-smooth muscle actin, vimentine, desmine, S 100 protein, estrogen and progesteron receptors. Positivity for HMB-45 is the key for the diagnosis of LAM. The patients were primary treated with megestrole acetate. The therapy with sirolimus was started after 2 years of diagnosis in the first of the patients for the progression of chylous ascites. The pulmonary form of LAM was diagnosed in the second patient after 6 months and she is now treated with sirolimus.

Conclusions
LAM is a rare disease affecting women of childbearing age occurring in 2-5 cases/million. There has been great progress in the pathogenesis, and the biology. Progress in therapy has come slowly. The inhibitors of regulators of cell proliferation, such as sirolimus or everolimus, appear to be the most promising therapeutic agents.
INVASIVE PURE MUCINOUS OVARIAN TUMOR IN A 19 YEARS-OLD WOMAN

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Objectives
Invasive mucinous cystoadenocarcinoma of the ovary is a rare pathologic entity usually diagnosed after the fourth decade of life. We report a young patient who was operated for an aggressive invasive mucinous tumor of the ovary.

Methods
A 19-years-old woman was referred to our Unit with diagnosis of a 20x19 cm left ovarian mass. On ultrasound examination the lesion appeared multicystic with solid areas and thick septae. All tumor markers were within normal ranges and CT scan of the abdomen and pelvis was negative for distant disease. In June February 2013 the patient underwent left adnexectomy with omentectomy, appendectomy and multiple peritoneal biopsies.

Results
Pathologic examination revealed a pure invasive mucinous cystadenocarcinoma of intestinal type. Colonoscopy and gastroscopy were negative and the patient received four cycles of carboplatin. One year later the patient developed right ovarian mass and multiple lung nodules. She underwent right adnexectomy and lung metastasectomy. Pathologic examination confirm diagnosis of recurrent disease and the patient started second line chemotherapy with paclitaxel and carboplatin.

Conclusions
Invasive mucinous cystoadenocarcinoma of the ovary can affect very young women and in such cases its behaviour is very aggressive.
e-Posters: Ovarian Cancer

INCREASED SERUM BETA-HCG LEVELS FOR 5 YEARS BEFORE CLINICAL DIAGNOSIS OF OVARIAN DYSGERMINOMA

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Objectives
Ovarian dysgerminoma is a rare tumor, with a rapid growth and good prognosis. It can be associated with an increase of a number of serum tumor markers such as LDH, CA-125 and alpha-fetoprotein.

Methods
We report a patient who had diagnosis of ovarian dysgerminoma 5 years after primary diagnosis of low increase of serum beta hCG.

Results
A 37-years-old woman had spontaneous abortion in January 2008, but had persistently elevated levels of serum beta hCG ranging between 17 and 45 UI/ml (normal values less than 5 IU/ml). CT scan, laparoscopy with multiple peritoneal and ovarian biopsies, PET and endometrial biopsies were repeated three times but were always negative. In December 2012 a 7x7 cm right ovarian mass was noted and the patient had right adnexaectomy with omentectomy and multiple peritoneal biopsies. Pathologic examination revealed a pure dysgerminoma. Following surgery her serum beta-HCG levels returned within normal values. The patient had three cycles of chemotherapy with cisplatin, etoposide and bleomycin and she has no sign of recurrent disease.

Conclusions
Persistent elevation of beta hCG, even with very low levels, may precede the onset of ovarian germ-cell tumors. Accurate follow-up of these patients is mandatory in order to achieve diagnosis of malignant disease as soon as possible.
e-Posters: Ovarian Cancer

OVARIAN CANCER: WHERE DO PATIENTS RECUR?
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Objectives
To describe sites of recurrence after contemporary management of early and advanced ovarian cancer.

Methods
Retrospective study of patients operated on for epithelial ovarian cancer between 2005 and 2009. The localization of the first recurrence was recorded. Risk factors for site of recurrence were searched. OS and PFS were computed using the Kaplan Meier method.

Results
Median PFS was 21.6 months for early disease and 19.3 for advanced stages. For advanced disease, most of recurrences (75%) involved the peritoneum and 40% were limited to the peritoneum. Risk of peritoneal recurrence was correlated to initial PCI score and residual post-operative tumor. Nodal recurrences were observed in 38% of advanced cases, mostly associated with peritoneal relapse. Isolated distant metastases were rare (8%).

Conclusions
Advanced epithelial ovarian cancer mainly recur on the peritoneum. Initial disease spread and post-operative residual disease are associated with the recurrence risk.
MALIGNANT STRUMA OVARII COMBINED WITH BRENNER CELL TUMOR: A CASE REPORT

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Objectives
Ovarian tumor composed only of Brenner tumor and struma ovarii is very rare. It is generally accepted that Brenner tumors are derived directly from ovarian surface epithelium, which undergoes metaplasia to form the typical urothelial-like components, whereas some investigators assume that Brenner tumors arise from immature germ cells.

Methods
Our patient had unilateral, large, multiseptated adnexal mass of 17*13*11 cm size without thyroid dysfunction. Staging laparotomy including total abdominal hysterectomy and bilateral salpingo-oophorectomy, pelvic and para-aortic lymphnode dissection and omentectomy was performed.

Results
Histopathological examination confirmed the coexistence of struma ovarii regarded as a form of teratoma and Brenner tumor in the same ovary.

Conclusions
Struma ovarii is a rare type of ovarian teratoma, consisting mainly of thyroid tissue. The incidence of malignant struma ovarii is below 1%. While there is strong evidence that pure Brenner tumors originate mostly from the ovarian surface, at least Brenner tumors associated with teratomatous elements may have a germ cell origin.
e-Posters: Ovarian Cancer

FEASIBILITY AND SAFETY OF LAPAROSCOPIC SURGERY FOR HUGE OVARIAN CYSTS: A CASE SERIES AND META-ANALYSIS
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Objectives
To understand the current status of the use of laparoscopic surgery (LSS) and investigate its feasibility and safety for huge ovarian cysts, we conducted a case-series and meta-analysis of relevant studies published till 2012.

Methods
We identified 18 reports including 95 patients, and 16 observational studies including 2,024 for the case series and meta-analysis.

Results
Malignant potential on preoperative imaging study was the only predictor for borderline or malignancy ovarian tumors (BOTs or MOTs; adjusted OR, 17.78; 95% CI, 3.29-96.22). The number of complete staging operation (CSO) performed in BOTs and upstage in MOTs were not different between LSS and laparotomic surgery (RRs, 0.14 and 0.50; 95% CIs, 0.06-0.33 and 0.20-1.27). LSS showed intraperitoneal spillage more frequently in BOTs and MOTs, and less postoperative complications in MOTs (RRs, 1.87, 1.15 and 0.32; 95% CIs, 1.51-2.31, 0.68-1.94 and 0.19-0.55). Intraperitoneal spillage failed to affect recurrence-free survival (RFS) in MOTs, whereas it decreased RFS in BOTs (HRs, 1.42 and 8.36; 95% CIs, 0.47-4.31 and 2.37-29.48). Moreover, cystectomy reduced RFS in comparison with adenexectomy in patients with BOTs of whom less than about 50% underwent CSO (HR, 7.18; 95% CI, 3.02-17.05).

Conclusions
The information about malignant potential and early-stage disease on preoperative imaging studies is important before LSS for patients with huge ovarian cysts. Furthermore, LSS is feasible and safe in the patients because of proper CSO and less complications, and the impact of intraperitoneal spillage on recurrence is not significant or minimal if we leave the ovarian tissues at least during CSO considering fertility preservation in the patients.
Clinical significance of serum CA125 and its half-life analysis in diagnosis and prognosis of ovarian cancer

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Objectives
To investigate the clinical significance of serum CA125 levels and its half-life in the treatment and prognosis of advanced ovarian cancer.

Methods
A retrospective case note review was performed for 45 patients with benign ovarian tumor and 50 patients with advanced ovarian cancer between 2005 and 2009. Pre-operative and post-operative serum samples were analyzed for CA125 levels by ELISA, respectively. During follow-up, serum CA125 levels at each visit were also recorded.

Results
In pre-operative serum samples, the CA125 levels in advanced ovarian cancer patients were significantly higher than that of benign ovarian tumor patients (P<0.01). When the cut-off value of CA125 was equal to 65µ/ml, the sensitivity and specificity of the diagnosis of ovarian cancer can be above 90%.

The descent of CA125 levels was associated with the size of residual postoperative tumors. Compared with the size of residual postoperative tumors >2cm, the descending level of CA125 were significantly higher when the size of residual postoperative tumors<2cm. The CA125 half-life correlated with recurrence of patients (P<0.05). When the CA125 half-life above 20 days, the mean recurrence of patients was 36.4±9.72, whereas the mean recurrence of patients was 14.33±9.72 when the CA125 half-life below 20 days.

Conclusions
This suggested that detection of CA125 levels has critical role in the diagnosis of ovarian cancer. CA125 half-life has the potent clinical significance for evaluating the disease progress, efficacy of treatment and prognosis of ovarian cancer.
**e-Posters: Ovarian Cancer**

**EXPRESSION AND PROMOTER METHYLATION PROFILE OF TRAIL SIGNALING PATHWAY GENES IN EPITHELIAL OVARIAN CARCINOMA**

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**Objectives**
The epithelial ovarian cancer (EOC) represents the seventh most important cause of morbidity and mortality worldwide among the female genital tract diseases. Despite the advances in the treatment of this malignancy, there were no equivalent improvements in the survival rates of affected women. This study aims to analyze the expression and Methylation profiles of TRAIL receptors (TRAIL-R2 and TRAIL-R3), CASPASE-8 and BCL-2 genes.

**Methods**
Samples were in 11 patients with serous cystadenoma, 16 with stage III/IV EOCs and 18 normal ovarian collected at Clinical Hospital of Universidade Federal de Minas Gerais in Brazil. The RNA and genomic DNA were extracted by TRIzol® reagent. The genetic expression were evaluated by real-time quantitative polymerase chain reaction and the promoters methylation profiles were analyzed by methylation specific PCR.

**Results**
Higher expression levels of all four markers were observed in metastatic EOC. In contrast, serous cystoadenoma overexpressed all markers, except for BCL-2. The primary EOC underexpressed, TRAIL-R3 and BCL-2, and overexpressed CASPASE-8 genes which suggest a genetic signature in TRAIL signaling pathway in EOC. Further studies have to consider this cytokine as an antitumor agent in EOC. In the epigenetic analyses, significant differences in methylation of TRAIL-R3 and CASPASE-8 genes were found between histological groups.

**Conclusions**
This event did not correlated with epigenetic silencing of these genes, which suggests the involvement of other transcriptional control mechanisms. This study provides a better understanding of the molecular biology of EOC and suggests that consideration of the genetic background of patients will likely play a role in personalized medicine.
PATHOLOGIC ANALYSIS OF TISSUE DESTRUCTION USING NEUTRAL ARGON PLASMA
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Objectives
Many electrosurgical devices and lasers have been developed over the years to aid tissue dissection and destruction. Each device has specific applications with advantages and disadvantages. Lateral thermal spread (LTS) and collateral tissue destruction (TD) are the principal concerns when considering a new operative energy source.

Objective
This study reports the histopathological effects of TD following neutral argon plasma (PJ) use on fresh ex-vivo human malignant tissues including at different power settings, tissue interaction time examining depth of destruction and LTS.

Methods
Following consent, fresh tissue was harvested intra-operatively. Following tissue excision, 1cm³ sections of bowel, diaphragm and omental tissue was exposed to PJ at 4 power settings (20%,40%,60%,80%) and increasing time of exposure ranging from 1-5seconds. Power is expressed stepwise as a percentage (10-80%) on the PJ. Specimens were formalin-fixed and stained after PJ exposure. Histological examination of TD included assessment of cavity depth and extent of burn at the base of cavity (eschar) is used as a surrogate marker of LTS.

Results
TD increased with power setting and ranged from 0.8 mm at (20%) to 2.95 mm at 80%. However, depth of eschar remained fairly constant despite increasing the power (0.12-0.20mm). Duration of tissue exposure appeared to be more important than increasing power settings.

Conclusions
PJ is a safe device that may be used on various tissue surfaces. Extent of tissue vaporisation produced is dependent upon both power settings and duration of exposure. However, increasing these parameters did not seem to impact on lateral thermal spread making the PJ an attractive electrosurgical device.
ARE PRE-OPERATIVE CT SCANS A RELIABLE INDICATOR OF OPTIMAL SURGICAL CYTOREDUCTION FOR STAGE 3-4 EPITHELIAL OVARIAN CANCER?

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Objectives
Epithelial Ovarian Cancer (EOC) remains the most lethal of the gynaecological cancers with some 7,000 new cases reported annually in the UK. Surgery is offered either upfront prior to any chemotherapy or following 3-4 cycles as interval debulking surgery (IDS) provided there has been response to chemotherapy following review of the imaging at a multi-disciplinary team meeting (MDT). Several studies of EOC have demonstrated that the maximal diameter of residual disease is an important prognostic indicator. Optimal surgery is associated with both a more favourable response to chemotherapy and prolonged survival.

Aim
The aim of this study is to assess reliability of CT scans in predicting optimal surgical cytoreduction pre-operatively in 115 cases.

Methods
Retrospective identification of patients from gynaeoncology database. Pre-operative patient demographics, surgical findings and outcome collected from medical records. CT scans of patients retrospectively scored by 2 radiologists blinded to the surgical outcome and to each others findings on visual analogue scale (VAS) for each criteria.

Results
15 cases analysed till date. Scoring of each case compared with case notes for assessment of disease involvement noted per-operatively and inter-observer variability. In 7/15 cases involvement of rectosigmoid by disease necessitating bowel surgery not identified by both radiologists on VAS. In 11/15 involvement of chest disease accurately reported. Diaphragmatic and pelvic disease only reported in 6/15 cases.

Conclusions
Study is currently ongoing and we hope to present more data as this will help improve CT reporting as well as managing patient expectations from surgery.

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e-Posters: Ovarian Cancer

DIAPHRAGMATIC SURGERY DURING DEBULKING FOR EPITHELIAL OVARIAN CANCER USING ARGON PLASMA

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Objectives
Cytoreductive surgery for ovarian cancer often involves ultra-radical surgery in both the pelvis and upper abdomen. Surgery to the diaphragm depends on various patient related factors including depth of tumour infiltration.

PlasmaJet™ (PJ), a new device producing a jet of argon plasma by heating argon gas may be used to vaporise small tumour nodules.

Aim
Evaluate the feasibility and outcome of diaphragmatic surgery using PJ to convert optimal cytoreduction (<=1cm) to microscopic disease in open and laparoscopic surgery.

Methods
Prospective study in tertiary oncology centre. PJ device was used during both primary and interval debulking surgery. Patient demographics, intra and post-operative data collected. Size/location of pre-surgical disease, procedures performed, tissue and anatomical location subjected to PJ, power settings and time taken to ablate tumour deposits recorded.

Results
Diaphragmatic surgery using PJ was undertaken in 11 cases. 8/11 had Stage IIIc disease and remaining Stage IV and involved a combination of ablation and stripping. Disease less than 5mm was ablated and larger than 5mm stripped. Stripping was unilateral and bilateral in 1 and 7 cases respectively. The remaining 3 cases underwent ablation of the tumour nodules and was undertaken with ease with minimal adverse effects. Optimal cytoreduction was achieved in all cases. In 1/11 entry into the pleural cavity was noted. No chest tubes were placed and no pleural effusions were noted post-operatively.

Conclusions
Preliminary data on feasibility and safety are reported suggesting that PJ is an innovative surgical device with several features well suited for diaphragmatic surgery providing encouraging results with minimal morbidity.
KRUKENBERG TUMOR IN PREGNANCY WITH POOR OUTCOME: A CASE REPORT

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Ongoing female patients with gastric cancer, only 2% were diagnosed with Krukenberg tumor, more so less common in pregnant women. This aims to report a case of Krukenberg tumor in a pregnant woman with poor outcome. This is a case of a 27 year old G2P1 1001, 26 weeks pregnant complicated with malignant ovarian tumor. She presented initially with non-specific gastrointestinal symptoms, like vomiting and abdominal pain, abdominal enlargement, which was mistaken to be due to pregnancy. She later developed ascites and pleural effusion. Suspicion of adnexal mass was made and later confirmed to have ovarian tumor by ultrasound. Surgery was done, which revealed a dead fetus in utero and a 28 x 19 x 7 centimeters right solid ovarian mass impacted into the cul desac, which on cut section showed cream-gray solid mass with areas of necrosis and hemorrhage. Histopathology showed presence of signet ring cells (clear cytoplasm with nucleus pushed to the side), tubular patterns and stromal proliferation, the characteristic features of Krukenberg tumor. Gastroscopy was done two months postoperatively due to hematemesis and noted a gastric mass, which on biopsy also showed signet ring carcinoma. The patient received 1 cycle of Epirubicin, Cisplatin and Capecitabine. She succumbed four months after the surgery, secondary to complications of advanced stage carcinoma. Pregnancy can mask symptoms of early Krukenberg tumor thus, high index of suspicion is essential.
e-Posters: Ovarian Cancer

LONG-TERM PROGNOSIS AND RISK FACTORS FOR RECURRENCE AMONG PATIENTS WITH BORDERLINE EPITHELIAL OVARIAN TUMORS IN A TERTIARY HOSPITAL

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A Retrospective Cross-Sectional study investigated the long-term prognosis of borderline ovarian tumors and determined risk factors for recurrence. This study was conducted by chart review of all patients seen in the Cancer Institute. Ninety-nine patients treated between 2002-2011 were investigated for clinical stage, histopathologic subtype, surgical techniques, intraoperative findings, adjuvant therapy, presence and absence of recurrence and prognosis. Follow-up ranges from 8 months to 144 months (median = 17 months). Result: The average age was 42 years old. Eighty-six (87%) of patients had stage 1 disease. Histopathologic subtypes include mucinous (80%), serous (17%), endometrioid (1%) and mixed epithelial type (1%). Conservative surgery was used in 39% of cases and radical surgery in 61% and staging procedure in 60% and post-operative adjuvant therapy in 23% of patients. Recurrence was found in 13 patients, including six patients diagnosed with pseudomyxoma peritonei, and one of which died of the disease. The average disease-free interval was 46 months (6-148 months). The 5 and 10-year overall survival for stage 1 disease was 98% and 93% respectively. Age (>50), stage (II-IV), unstaged procedure, tumor rupture, presence of peritoneal implants, and residual tumors were significantly associated with tumor recurrence (p value < 0.05). However, surgical procedure (conservative vs. radical surgery) and histologic type were not significantly correlated with recurrence. Conclusion: Management of borderline ovarian tumor requires more conservative approach as compared to frankly malignant ovarian tumors. Presence of risks factors associated with tumor recurrence would guide as to whether chemotherapy is warranted in a particular patient.
e-Posters: Ovarian Cancer

A TERTIARY CENTRE EXPERIENCE WITH GRANULOSA CELL TUMOURS OVER 23 YEARS
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Objectives
We present our experience with GCTs at St George’s Hospital over the last 23-year period.

Methods
We searched the pathology database for GCT and searched medical records and electronic patient records.

Results
We identified 25 patients with GCT. Five cases were diagnosed in the 1991-2000 decade, 16 patients were diagnosed in 2000-2010 decade and four patients have been diagnosed from 2011-till date. The apparent increase in diagnosis may partly reflect the centralisation of services for ovarian cancer. Eighteen patients were 40 yrs old or more, 4 patients were 30-40 yrs old and three were less than 15 yrs old. The presenting symptom in nine patients was post-menopausal bleeding (PMB), in 3 it was menorrhagia, in 5 patients it was related with pressure symptoms of the mass and in one case it was precocious puberty. Final stage was 1A in 13 patients, 1C in 8 patients, stage 3 in 2 patients and 2 patients were incompletely staged. All 7 patients under the age of 40 had a fertility preserving operation out of which 6 patients were still alive, with the remaining patient lost to follow-up. Only 2 out of 25 cases were of the juvenile GCT type. The average follow up was 43 months. 11 patients were alive at 5 years from diagnosis, 2 patients succumbed to the disease.

Conclusions
The apparent increase in GCT treated within each decade probably reflects centralisation of cancer care.
e-Posters: Ovarian Cancer

RECURRENCES AT OVARIAN CANCER PATIENTS.
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Objectives
To determine the tumor localizations of recurrences of ovarian cancer patients.

Methods
A retrospective observational study. It included 75 patients with ovarian cancer (IC-IV stage), which in the period to 2006 to 2012 performed a secondary cytoreductive surgery for recurrent tumor. All the patients were completed a complete or optimal cytoreduction. At 9 patients was carried pelvic peritonectomy (I group), 66 - without pelvic peritonectomy (II group).

Results
Mean age of the patients was 52.9 ± 8.3 years. II group: metastases in pelvis after combined treatment were developed in 23 (35%) patients, in 21 patients (32%) were developed metastases in the abdomen and pelvis after combined treatment, in paraaortal lymph nodes – 8 (12%), in pelvic lymph nodes – 7 (11%), in inguinal lymph nodes – 2 (3%), in retroperitoneal and pelvic lymph nodes – 4 (6%), in the spleen - 1 patient. Thus, recurrence in the pelvis observed in 67% of cases in patients with ovarian cancer IC - IV stage without performing pelvic peritonectomy. In 23 % patients recurrences were in paraaortal, pelvic lymph nodes.I group: 67% - mesentery of intestinum, 22% - pelvic lymphnodes, 22% - spleen.

Conclusions
It’s appropriate to include pelvic peritonectomy in the scope of the primary cytoreduction at patients with ovarian cancer. It’s necessary to the following studying the question to include a prophylactic pelvic and paraaortic lymphadenectomy also in the scope of the primary cytoreduction.
NEOADJUVANT TREATMENT OF OVARIAN CANCER AND LAPAROSCOPIC SURGERY
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Objectives
Ovarian cancer is the second most common gynecologic cancer and when it is diagnosed 75% of patients have stages III or IV. Treatment is based on citoreduction surgery and platinum–taxane chemotherapy.

All patients with ovarian cancer must be properly staged with complete physical valuation, baseline imaging and Ca-125 measurement to determine if they can be complete or optimally cytoreduced.

Methods
In 2012 some of our patients were diagnosed with stage III c disease and diffuse carcinomatosis, ascitis and large ovarian mass. They received between four and six platinum based cycles. After that, in imaging control, the good treatment response let us the chance of resecting all residual disease with laparoscopy.

Results
The abdominal cavity appearance was good. Non important postoperative complications were seen. In definitive study we found malignancy only in ovaries and a small focus on epiplon. We gave another two cycles after surgery. One year after there were not dates of recurrence and Ca-125 measurement was normal.

Conclusions
Survival is not improved compared to standard surgery and adjuvant therapy. Neoadjuvant therapy in selected patients with advanced ovarian cancer can reduce perioperative morbidity and mortality and increase the likelihood of resection even with laparoscopy.
e-Posters: Ovarian Cancer

PROGNOSTIC RELEVANCE OF COELIAC LYMPH NODE INVOLVEMENT IN OVARIAN CANCER

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Objectives
Aim of the study was to report on oncologic outcome of disease spread to coeliac lymph nodes in advanced-stage ovarian cancer patients.

Methods
All patients who had coeliac lymph node (CLN) resection as part of cytoreductive surgery for epithelial ovarian, fallopian, or primary peritoneal cancer were identified. Patient demographic data with particular emphasis on operative records to detail extent and distribution of disease spread, lymphadenectomy procedures, pathological, and follow-up data were included.

Results
Median follow-up was 26.3 months. Median overall survival in the group with positive and in the group with negative CLNs was 26.9 months and 40.04 months, respectively. Median PFS in the group with metastatic and in the group with negative CLNs was 8.8 months and 20.24 months, respectively (p 0.053). Positive CLNs were associated with progression during or within 6 months after the completion of chemotherapy (p 0.0044). Tumor burden and extensive disease distribution was significantly associated with poor PFS, short-term progression, and OS. In multivariate analysis only CLNs status was independently associated with short-term progression.

Conclusions
In this series CLN involvement is a marker of disease severity, associates to a high-risk group of patients with presumed adverse tumor biology, increased risk of lymph node progression and worst oncologic outcome.
e-Posters: Ovarian Cancer

BORDERLINE OVARIAN TUMOURS- THE LIVERPOOL EXPERIENCE.
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Objectives
Borderline ovarian tumours are generally benign in behaviour, but may recur and/or progress to frank malignancy. The role of surveillance after initial management remains uncertain.

Methods
All patients diagnosed with a borderline ovarian tumour between 1st of January 1993 and 31st October 2012 within the catchment area of the Liverpool Gynaecological Cancer Specialist MDT were eligible. Patients were identified through a search of patient databases, and clinico-pathologic data obtained from the case notes.

Results
A total of 113 patients, with a median age of 54 were identified. 88% of patients were stage 1 at diagnosis, and 48% and 45% of patients had a diagnosis of mucinous and serous borderline ovarian tumour respectively. The majority (77%) of patients were treated radically (TAH, BSO, omental biopsy) with the remainder treated with a unilateral salpingo-oopherectomy. 7 patients had either recurrence (2) or progression to invasive malignancy (5), after a median of approximately 3 years (range 10 months to 5.5 years). 3 out of the 7 patients with recurrence had residual disease after original surgery. No other factors were associated with subsequent relapse.

Conclusions
While this was a relatively small cohort of patients, the findings reinforce previous studies that have shown that risk of recurrence is low. In the absence of residual disease or implants, follow up/surveillance is unlikely to be beneficial. Following this audit, a prospective database will be set up locally to facilitate a more comprehensive assessment of the natural history of this rare disease.
e-Posters: Ovarian Cancer

UNDERSTANDING FACTORS THAT DRIVE TREATMENT DECISIONS FOR RECURRENT EPITHELIAL OVARIAN CANCER IN 5 EUROPEAN UNION (EU5: FRANCE, GERMANY, ITALY, SPAIN, UK) COUNTRIES

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Objectives
To understand the patient- and disease-related factors and treatment aims that influence treatment decisions in recurrent epithelial ovarian cancer.

Methods
154 physicians from EU5 countries responded to an ethics committee approved, validated, double-blind (to those who were surveyed and analysed the data), and web-based survey. Physicians were eligible if they were specialists in oncology or gynaecology with ≥2 years' clinical experience and excluded if in the last 12 months they treated no patients with stage III/IV epithelial ovarian cancer or <10 patients with recurrent disease. The semi-structured questionnaire included open-ended responses, multiple-choice fixed responses and case studies on the treatment of first-line and recurrent ovarian cancer. Subgroups of patients with recurrent disease were identified based on platinum-free interval (PFI).

Results
Treatment aims for recurrent disease varied depending on PFI (Figure 1). The longer the PFI, the more treatment aims focused on cure and extending survival. With shorter PFI, the aims were more about balancing disease control with quality of life and extending the PFI. Factors strongly influencing treatment choice were PFI and presence of platinum allergy or intolerance. However, the presence of co-morbidities, the number of prior treatments and the age and performance status of patients also played a role in physician decision-making when selecting treatments.

Conclusions
For patients with recurrent ovarian cancer, treatment aim varies by the PFI. A range of clinical and non-clinical factors plays a role in choosing treatment for patients with recurrent ovarian cancer.
EXPRESSION OF STEROID HORMONE RECEPTORS AND GPR30 PROTEIN IN EPITHELIAL OVARIAN CANCER

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Objectives
This work was aimed to compare the expression of estrogen receptor α (ERα), androgen receptor (AR), and GPR30 protein in epithelial cells of normal ovaries and epithelial ovarian tumors (EOC).

Methods
A total of 55 samples of normal ovaries and 31 samples of EOC were obtained from patients of the National Cancer Institute of Mexico. The tissue was handled according to the international ethical standards established for tumor banks. The detection of receptors and the GPR30 protein was made by immunofluorescence technique.

Results
The proportion of positive samples for ERα in EOC were increased in comparison to the frequency observed in epithelial cells of the surface epithelium and cortical inclusion cysts of normal ovaries (EOC: 0.73 versus Control ovary: 0.27). A similar increase was observed in the expression of AR in EOC samples (EOC: 0.82 versus Control ovary 0.44). No significant change in the proportion of positive samples between both groups was registered for GPR30 protein (EOC: 0.44 versus Control ovary: 0.66).

Conclusions
Present results confirm previous studies which indicate that estrogens and androgens are involved in ovarian tumor progression. On the other hand, GPR30 seems to be independent of ovarian carcinogenesis. Financial support from PAPIIT, UNAM IN218213
e-Posters: Ovarian Cancer

MICROSATELLITE POLYMORPHISM IN HEME OXYGENASE 1 GENE IS ASSOCIATED WITH THE THERAPEUTIC OUTCOME IN PATIENTS WITH OVARIAN CANCER

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Objectives
Heme oxygenase 1 (HMOX1) is a key enzyme involved in the heme metabolism and is known to be also involved in regulation of oxidative status and inflammatory reactions. Expression level of HMOX1 depends on the genetic variations within the promoter region, including the length of short tandem repeats (STR) of GT dinucleotides. The short (S) and long variant (L) correlates with the higher and lower expression level, respectively.

The aim of the study was to determine the STR variant in HMOX1 gene and correlate it with clinical outcome of paclitaxel/platinum analogue treatment in ovarian cancer patients.

Methods
The study included 109 patients, median age 54 (28-71), after standard surgical approach and treated with paclitaxel/platinum analogue. DNA isolation was followed by PCR amplification of STR region with fluorochrome-labeled primers. The length of STR region was determined using 3130 Genetic Analyzer (Applied Biosystems). The GT repeats above 27 was classified as L variant. The HMOX1 STR variants were correlated with the progression free survival and the overall survival.

Results
The frequencies of STR variants SS, SL and LL were 16,03%, 49,36% and 34,62% respectively. The PFS of patients carrying the S variant was 13,8 vs. 21.7 months in LL patients (p=0,034). The 3-years OS of LL and SS/SL was 72,2% and 51,8% respectively (p=0,045).

Conclusions
The HMOX1 as the regulator of the oxidative stress may influence the sensitivity of tumor cells to the chemotherapy. The S variant with higher expression level of HMOX1 correlates with poorer clinical outcome.
VALUE OF IMMUNOHISTOCHEMICAL WT-1 DETECTION IN WIDESPREAD SEROUS CARCINOMAS

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Objectives
In cases with widespread serous carcinoma it is difficult to determine primary tumor origin, as histology is similar and tumor localized in both ovaries and uterus. Immunohistochemical detection of WT1 is suggested to be valuable in differentiating uterine from extrauterine serous carcinoma. In the current study, WT1 expression in widespread serous carcinoma is analyzed, and if concurrent EIC is suggestive for an endometrial origin.

Methods
Immunohistochemical WT-1 staining was performed for fifteen cases with extensive serous carcinoma in both ovaries and endometrium, 12 cases with serous ovarian carcinoma and concurrent EIC, 17 with solitary endometrial carcinoma, and 15 with solitary ovarian carcinoma. TP53 mutation analyses performed in cases with ovarian tumor and concurrent endometrial pathology.

Results
Solitary serous carcinomas of ovarian or endometrial origin could be differentiated by using a threshold level of reactivity for WT-1 in more than 50% of tumor cells. Expression in ovaries and uterus of widespread serous carcinomas were concordant, and above the threshold level in one-third of cases. Expression in serous ovarian carcinoma and concurrent EIC were above the threshold level in one-third of cases, below in one-third and discordant in another third. No incompatible TP53 mutation were identified within cases with discordant staining.

Conclusions
Expression of WT1 has utility in differentiating serous uterine from ovarian cancer. Widespread carcinomas are putatively endometrial in origin in two-third of cases and ovarian cancers with concurrent EIC are probably primary endometrial in one-third of cases. Delineating tumor origin in these carcinomas is fundamental to understand their pathogenesis.
e-Posters: Ovarian Cancer

**EGFR AND C-MET HIGH CO-EXPRESSION WAS A GOOD PROGNOSTIC FACTOR IN OVARIAN SEROUS ADENOCARCINOMAS.**  
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**Objectives**  
There are a cross-talk between c-Met and EGFR receptors on cell membranes. The aim of this study was to research the correlation between c-Met and EGFR and the clinical significance of each receptor in ovarian serous adenocarcinoma (SAC).

**Methods**  
The microarrays were made from 146 patients with SAC treated at National Defense Medical College between 1984 and 2007. Protein expressions were evaluated by immunohistochemistry.

**Results**  
High expressions of c-Met and EGFR were 60 (61%) and 63 (43%), respectively. Among them, 35 cases had high expressions of both receptors, and there were the correlation between c-Met and EGFR (p<0.01). Between group of cases with co-expression (Group A) and group of others (Group B), there were no significant differences about ages, performance status, stage residual tumors, and response rate. There were no statistical significances about progression-free survivals in both two groups, but group A was better overall survival compared with group B. Multivariate analysis showed that co-expression was identified as an independent good prognostic factor of OS (HR 0.51, p<0.046).

**Conclusions**  
In SAC, there are the correlation between c-Met and EGFR, and this relation was a better prognostic factor. This co-expression might be a key of biological behavior.
e-Posters: Ovarian Cancer

CD44S PROTEINS WERE ASSOCIATED WITH THE TUMORIGENESIS, AND LOW CD44S EXPRESSION WAS RELATED WITH POOR PROGNOSIS IN OVARIAN MUCINOUS ADENOCARCINOMAS.

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Objectives
CD44s are transmembrane proteins correlated with tumor growth and metastasis. The aim of our study is to investigate the roles of the CD44s in tumorigenesis and prognosis of mucinous adenocarcinomas (MAC).

Methods
Tissue blocks are made from 71 patients with benign mucinous tumors (BMT), 35 patients with borderline mucinous tumors (BLM), and 60 patients with MAC who received surgery at the National Defense Medical College between 1984 and 2008. Protein expressions were immunohistochemically evaluated.

Results
Compared with BMTs, more cases with BLMs had strong CD44s expression (p=0.04). Conversely, less cases with MACs had strong CD44s expression than those with BLMs (p=0.04). Among 60 cases with MACs, there no statistical differences with age, performance status, stage, residual tumors, and the chemotherapy and response rate of primary adjuvant chemotherapy between high and low CD44s expression. Progression-free survivals (PFS) and overall survivals (OS) of MACs with low CD44s expression were worse than those with high expression (PFS, p=0.04; OS, p=0.02, respectively). On multivariate analysis, low CD44s expression was the poor prognostic factors of PFS and OS (p<0.01, p<0.01, respectively).

Conclusions
CD44s were associated with the development and progression of MACs. Low CD44s expression in MACs was a poor prognostic factor. Therefore, the levels of CD44s expression might be the novel target of new treatment.
e-Posters: Ovarian Cancer

PHYSICAL ACTIVITY AND SLEEP DISTURBANCES FOR WOMEN WITH RECURRENT OVARIAN CANCER UNDERGOING CHEMOTHERAPY
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Objectives
Recurrent ovarian cancer patients experience various physical and psychological side-effects during treatment. Sleep disturbances are commonly reported by patients. Physical activity has been shown to improve numerous treatment side-effects.

Aims: Determine sleep disturbance patterns in recurrent ovarian cancer patients and establish if a relationship exists between physical activity and sleep.

Methods
Twenty-four women undergoing treatment (n=14), off treatment (n=5) and age-matched controls (n=5) were recruited with a mean (S.D.) age of 58(9) years, BMI=24.4(5.1) and patient Karnofsky Performance Status scores between 60-90. Actigraph GT3X+ accelerometers were worn on the wrist for seven days and initialized at 50Hz to record the sleep-wake cycle and physical activity levels. Self-report questionnaires were used to quantify physical activity (IPAQ) and sleep quality (PSQI). Sleep efficiency <85% and global PSQI >5 are considered sleep disturbances.

Results
A moderate negative correlation occurred between MET-hours/week and minutes to get to sleep (r=-0.32). Sleep disturbances were confirmed for women undergoing treatment with a mean global PSQI of 10(4). Sleep efficiency was reduced during treatment compared with age-matched controls (86(8.8)% vs. 95(7)%). Patients undergoing treatment experienced 10.2(5.6) sleep awakenings compared to 7(1.6) off treatment and 5(2.6) for controls. There was a weak correlation between global PSQI, MET-hours/week and sleep efficiency, but it did not reach significance. Seven participants required using a form of sleeping medication.

Conclusions
Sleep disturbances were evident in women undergoing chemotherapy treatment. There was a minor relationship between physical activity and improved sleep quality. Larger study cohorts are required to further investigate this issue.
OVARIAN PRIMARY CHOROIDAL METASTASIS TREATED WITH CHEMOTHERAPY AND PLASMAPHERESIS: A PURPOSE OF A CASE

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Objectives
Ovarian cancer is associated with paraneoplastic syndromes. Some syndromes are associated with substances produced by the tumor and others for the production of antibodies by the immune system which can lead to a proliferation bilateral uveal melanocytic diffuse (1).

Methods
To show a case diagnosed in our service and treatments given.

Results
Fifty years old woman diagnosed in April 2012 of Clear cell carcinoma of right ovary pT1a pN1, Stage IIIC. The patient lost bilateral vision, with bilateral cataract and lesion creamy brown pigment spots and areas of focal thickening. The final diagnosis was of melanocytic proliferation in relation to paraneoplastic syndrome. High levels of IgG were found. Punch biopsy of skin lesions showed a melanocytic nevus spindle cell/epithelioid.

She received 4 cycles of Paclitaxel and Carboplatin (PC) followed by plasmapheresis every 48h for 2 weeks and PC for two, with improved vision gradually, improvement of areas of focal thickening and IgG decreased. In April 2013 an increase of IgG, loss of vision and normal PET were viewed. Currently she is on treatment every two days with plasmapheresis with significant recovery of vision and low levels of IgG.

Conclusions
Treatment with chemotherapy and plasmapheresis is an effective treatment option.

1- Sarah L Miles, Richard Niles, Sean Pittoch, et.al. A factor found in the IgG fraction of serum of patient with paraneoplastic bilateral diffuse uveal melanocytic proliferation causes proliferation of cultures human melanocytes. Retina 0:1-8,2012
RESULTS OF OXALIPLATIN-BASED HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN RECURRENT OVARIAN GRANULOSA CELL TUMORS

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Objectives
The aim of this study was to assess the morbidity and efficacy of cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) for relapsed ovarian granulosa cell tumors (OGCT).

Methods
Between 2007 and 2009, patients with relapsed OGCT who had been treated with HIPEC after CRS in our institution were retrospectively registered.

Results
We identified 7 patients who had undergone CRS plus HIPEC. Macroscopically complete cytoreduction was achieved in all patients. The location of the recurrence was pelvic alone in 2 cases and involved the pelvic and abdomen in 5 cases. We used intraperitoneal perfusion of oxaliplatin (460 mg/m²) or oxaliplatin (360 mg/m²) plus irinotecan (360mg/m²) heated to 41-43°C for 30 minutes. No post-operative mortality and no grade IV had occurred. We had observed one lymphocyst (grade III) which had twice required percutaneous drainage. Extra-abdominal complications (all grade II) had occurred in 6 patients. Median follow-up after CRS plus HIPEC was 32 months (range, 25-56). Among the 7 patients, 2 are disease free, 3 had relapsed with peritoneal carcinomatosis and 2 had relapsed with liver metastases.

Conclusions
HIPEC (using oxaliplatin or oxaliplatin plus irinotecan) should not be recommended to treat relapsed OGCT.
e-Posters: Ovarian Cancer

PROGNOSTIC FACTORS AFTER CONSERVATIVE TREATMENT OF “STAGE I” SEROUS BORDERLINE OVARIAN TUMOR: RESULTS OF A LARGE SERIES OF 119 CASES.
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Objectives
The aim of this study was to evaluate the prognostic factors of recurrence after conservative treatment of a large series of “apparent” stage I serous borderline ovarian tumors (SBOT).

Methods
A review of 119 patients treated conservatively between 2000 and 2010 with data on the follow-up. All pathological slides were reviewed by the same expert pathologist. Prognostic factors of recurrences were studied.

Results
Conservative procedures were: unilateral cystectomy/UC (n=43; 36%); unilateral salpingo-oophorectomy/USO (n=50; 42%); bilateral cystectomy (n=11; 9%) and USO+CC (n=15; 13%). Stages distributions were: IA (n=80; 67%); IB (n=18; 15%) & IC (n=21; 18%). Respectively 21 (18%) & 13 (11%) had stromal microinvasion and/or micropapillary pattern. With a median follow-up of 45 months, 40 (33%) patients recurred. Two of these 40 recurrent patients had evolution in the form of invasive recurrence. None patient died from disease. Only 2 prognostic factors of recurrence were identified in multivariate analysis: the young age of the patients (< 30 years old) & the bilaterality of the tumours.

Conclusions
In this series (representing the largest series reported of conservative management of stage I SBOT), the risk of recurrence is not related to the histologic subtypes of the tumor (micropapillary, stromal microinvasion) nor to the surgical procedures used (type of conservative approach, the use of staging surgery, the use of laparoscopic approach). Young age (< 30 years old) and bilaterality of the tumors are risk factors of recurrence suggesting that improvement of the fertility management should be improved particularly in theses subgroup of patients.
IDENTIFICATION OF BIOMARKERS ASSOCIATED WITH OVARIAN CANCER AS DIAGNOSTIC AND THERAPEUTIC AGENTS: A COMBINED IN SILICO AND MOLECULAR APPROACH

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Objectives
The main objectives of my research project was to identify candidate biomarkers for ovarian cancer, and then to generate an expression profile of the candidate genes across an array of cancer cell lines. Then test for antigenic properties of the candidate proteins and develop a lateral flow device by combining it with nanotechnology.

Methods
A gene list of potential ovarian cancer biomarkers were generated by mining two cancer databases; Oncomine and Gene Expression Atlas. The final candidate genes were identified based on their location on the cell surface using Gene Ontology annotations. Seven candidate genes were identified as potential biomarkers. The expression profiles of the candidate genes will be investigated using an array of cancer cell lines; this would determine the specificity and sensitivity of the genes as potential diagnostic agents. The genes that show high specificity for only ovarian cancer will undergo further analysis using protein profiling. Protein profiling will determine if the protein has antigenic properties which will enable it to be used in combination with nanotechnology to develop a diagnostic tool.

Results
Seven candidate genes for ovarian cancer were identified.

Conclusions
The seven candidate genes are currently undergoing experimental validation to determine the specificity and sensitivity of the genes as potential biomarkers for ovarian cancer.
A RARE CASE OF OVARIAN CANCER DURING PREGNANCY COMPLICATED BY PULMONARY EMBOLUS AND MYOCARDIAL INFARCTION: MANAGEMENT DILEMMAS

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Objectives
In this case report we:
1) Highlight the rarity of the diagnosis of advanced epithelial ovarian cancer in pregnancy
2) Argue that primary debulking surgery (PDS) remains the mainstay of treatment in patients with advanced ovarian cancer as compared to neoadjuvant chemotherapy.
3) Demonstrate that it is possible to perform extensive primary debulking surgery for advanced ovarian cancer even in critically ill patients as this provides the best possible outcome.

Methods
We describe our management of a young previously healthy woman who was diagnosed with advanced stage ovarian cancer (FIGO IIIc) at caesarian section. Post-operatively she developed a pulmonary embolus and a myocardial infarction. Both management options, neoadjuvant chemotherapy and PDS, are argued through review of the current literature and expert opinion.

Results
In this case, we favoured primary debulking surgery. Despite the patient’s critical status she underwent surgery 6 weeks after her diagnosis. This was only achieved through extensive anaesthetic involvement. She recovered well postoperatively with no major complications.

Conclusions
Maximal primary cytoreductive surgery remains the standard of care for women with advanced ovarian cancer. Patients with advanced stage ovarian cancer should be treated in specialized centres to maximise the chances of residual-free tumour debulking during primary surgery. This case report highlights the rarity of epithelial ovarian cancer in pregnant women and the possibility to perform primary debulking surgery even in critically ill patients with extended anaesthesiological monitoring and effort.
e-Posters: Ovarian Cancer

**SEROUS INTRAEPITHELIAL CARCINOMA (STIC) AND P53 SIGNATURES IN WOMEN WHO HAVE HAD RISK REDUCING BILATERAL SALPINGOOOPHORECTOMY: OUR EXPERIENCE**

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**Objectives**
Risk-reducing bilateral salpingo-oophorectomy (RRSO) results in a reduction of ovarian cancer by 95% in BRCA1 and BRCA2 gene mutation carriers. In these women a continuum of tubal epithelial change from a putative precursor lesion (P53 signature) through serous tubal intraepithelial carcinoma (STIC) to early invasive tubal cancer has been described. The clinical implications of these findings are still unknown.

**Methods**
This is a prospective study including women who underwent RRSO from Apr 2008- Feb 2013 at The Royal Marsden NHS Foundation Trust. A total of 149 women are included. 133 (89%) of them underwent genetic testing; 63 (42%) had BRCA1, 50 (34%) BRCA2, and one woman BRCA1 and 2 gene mutation. 17 women (11%) had a negative test result. Fallopian tubes and ovaries were sampled in their entirety according to our RRSO protocol.

**Results**
The median age was 46 years (range 30-71). Three women (2%) were identified with high grade serous ovarian cancer (2.6%); 2 with stage 1a, one woman had stage 3a. All three had a BRCA1 or 2 gene mutation. P53 signatures were found 22% of BRCA1/2 women, with STIC in 6%. In all, except one patient with ovarian cancer, peritoneal cytology was negative. Pre-operative Ca125 level was not associated with P53 signatures or STIC.

**Conclusions**
We identified three cases of ovarian cancer. Our P53 signatures and STIC data correspond with the literature. No abnormal peritoneal cytology was found in these women. The management of STIC remains a clinical dilemma, especially in case of negative cytology.
PLASMAJET® ABLATION AND RESECTION OF CARCINOMATOSIS IN OVARIAN CANCER TO ACHIEVE COMPLETE CYTOREDUCTION: INITIAL EXPERIENCE

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Objectives
Complete cytoreductive surgery (CRS) in advanced ovarian cancer improves overall survival. This is often difficult to achieve in women with small volume carcinomatosis especially that involving small bowel serosa and mesentery. We present our experience with Plasmajet® (PJ), a device which generates argon plasma that can ablate and resects disease with minimal collateral tissue damage.

Methods
From 1 March 2012 to 1 March 2013 we used PJ in 15 women with widespread small volume ovarian cancer. All of them underwent a laparotomy with the aim to achieve CRS. Eleven women had debulking for primary high grade serous ovarian cancer, two women had recurrent low grade ovarian cancer and two women had recurrent granulosa cell tumour. The cytoreductive outcome, surgical procedures undertaken, avoidance of bowel resection and peri- and postoperative complications were identified.

Results
CRS was achieved in 12 women (80%), and in 4 of them bowel resection was avoided when using PJ when otherwise this would have been necessary. The remaining 3 women had residual disease < 0.5 cm.

Peri-operative complications involved blood loss of more than 1 litre in 3 women. Postoperative complications included vomiting (n=1), prolonged ileus (n=1), admission local hospital with haematoma pelvis (n=1) and lower lobe atelectasis (n=1). None of these complications were considered to be related to the use of PJ but mainly due to extensive and prolonged surgery.

Conclusions
Our impressions are that PJ is a safe and effective new energy device. It permits CRS in women with widespread carcinomatosis that could not otherwise be achieved or only by extensive bowel resection.
e-Posters: Ovarian Cancer

ULTRASOUND GUIDED TRU-CUT BIOPSY AS A MINIMALLY INVASIVE PROCEDURE IN THE MANAGEMENT OF ADNEXAL MASSES
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Objectives
We hypothesized that ultrasound guided tru-cut biopsy is reliable and effective method in the differential diagnosis of adnexal masses and to begin testing this hypothesis, we have evaluated the patients who underwent tru-cut biopsy in our gynecological oncology department.

Methods
We reviewed the medical records of 55 patients whom underwent ultrasonography guided tru-cut biopsy in our gynecologic oncology department. Patients who have suspected ovarian malignancy but not suitable for optimal debulking surgery, who may have higher rate of morbidity and mortality because of poor performance status or suspected non gynecological tumor and peritenal tuberculosis were the indications of ultrasonography guided biopsy.

Results
The indications for ultrasonography guided tru-cut biopsy were candidates for suboptimal cytoreduction (n=32, 58%), poor performance status (n=11, 20%), suspected non-gynecological tumor (n=12, 22%). Biopsy materials were to found be sufficient by the pathologist in 53 of 55 cases (96%). Histopathologic evaluation revealed primary ovarian tumor in 36 (65.4%) patients. Tuberculosis was found to be second comon disease (n=8, 14.6%) among patients who underwent tru-cut biopsy procedure. In two patients histology revealed metastatic colorectal cancer.

Conclusions
Ultrasonography guided tru-cut biopsy can be preferred as a minimally invasive procedure in the management of adnexal mass and may be performed especially in advanced ovarian cancer patients with high comorbidity who may benefit from neoadjuvant chemotherapy and suspected non-gynecologic tumors including pelvic tuberculosis.
ADVANCED OVARIAN MALIGNANCY IN A 32 YEAR OLD.

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Objectives
To present the case of a 32 year old Multipara with advanced Ovarian Cancer

Methods
Case report of Mrs K, a 32 year old multipara who presented to the gynaecology clinic with abdominal swelling of four months duration.

Results
Case report and pictures at Laparotomy.

Conclusions
Ovarian Cancer can occur in all age groups and affect all parities. Efforts must be intensified to produce and provide guidelines for screening and prevention.
e-Posters: Ovarian Cancer

GEMCITABINE AS A SALVAGE CHEMOTHERAPY FOR RECURRENT PATIENTS WITH OVARIAN CANCER.
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Objectives
We aimed to determine the efficacy and the toxicity of single agent gemcitabine in Japanese patients with recurrent ovarian cancer.

Methods
From 1st October 2010 to 31st September 2012, 15 patients were treated with gemcitabine alone for platinum-resistant recurrent ovarian cancer. Gemcitabine (1000 mg/m2) was given on days 1, 8, and 15 of every 28 days.

Results
All 15 patients had previously received combination chemotherapy of paclitaxel and carboplatin and their disease had become platinum-resistant. The median number of previous regimens was 3 (range 2-7). The median number of administration cycle was 4 (range 2-16). Grade3/4 hematological toxicity included neutropenia (40%), anemia (20%), and febrile neutropenia (6.7%). No grade3/4 non-hematological toxicity was observed. Although no complete response or partial response was observed, there were 7 cases of stable disease. The disease control rate was 46.7%. The median progression-free survival was 4.5 months. The median overall survival was 9 months.

Conclusions
The efficacy and toxicity of gemcitabine in Japanese recurrent patients with ovarian cancer was similar to those in Western countries as previously reported. We can consider gemcitabine as an acceptable agent for recurrent patients with ovarian cancer in Japan.
e-Posters: Ovarian Cancer

CT AND ABDOMINAL LAPAROTOMY CORRELATION IN OVARIAN CANCER
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Objectives
Assess the value of the CT scan for identification of tumor size, lymph node and peritoneal metastases in patients undergoing subsequent radical surgery for ovarian cancer in our centre.

Methods
A retrospective study analyzed ovarian cancer patients with the CT scan diagnosis and subsequently underwent surgery (n = 26), between: January 2009 - December 2011.

Type of tumor, size (maximum diameter), bilateralism, and nodal and peritoneal metastasis in the CT test and correlation with pathology, also will study the two-year survival was analyzed variables.

The mean age of the patients was 51.6 years (40-76 y).

The histological type was: papillary serous cystadenocarcinoma (63.6%), mucinous (18.3%), clear cell (13.6%), endometrioid type (2.25%) and the undifferentiated (2.25%).

Results
The CT and sizes surgical specimen correlation was of 44.4% (differences if <1cm.). CT overestimated 50% of cases and underestimated other 50%.

Bilaterality was in 37.5% of patients.

The detection of lymphadenopathy by CT has a false positive rate (FP) of 17.6% and false negative (FN) 5.9%.

Peritoneal metastases were positive in 58.3% of the TAC and 68% of pathology: concordance of 75%. FN and FP rates were: 16.6% and 8.3%.

In 77% of patients were performed debulking surgery, 23% of the cases were unresectable primary surgery.

Median survival at 2 years in patients with resectable tumors was 75% while in unresectable was 0%. In patients undergoing prior chemotherapy was 25%.

Conclusions
The CT has a poor agreement in the determination of tumor size and other aspects of OC study. CT scan are limited value for surgical decision.
e-Posters: Ovarian Cancer

EXPRESSION OF VEGF GENE IN OVCAR-3 CELLS AFTER EXPOSED TO EPIGALLOCATECHIN-3-GALLATE AND PACLITAXEL COMBINATION

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Objectives
The aim of this study is to evaluate the therapeutic effect of Epigallocatechin-3-gallate (EGCG) and Paclitaxel combination on ovarian cancer cell line, which might be a new candidate as an anticancer therapeutic agent.

Methods
In the present study, the effects of EGCG and carboplatin combination on cell proliferation were investigated in the OVCAR-3 ovarian cancer cell line. OVCAR-3 cells were exposed to different concentrations of EGCG (350, 450 and 550 mM) and Paclitaxel (1.25, 2.5 and 5 nM) combinations for 24+24 h. Cellular growth was assessed using a cell viability assay (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoium bromide (MTT)). rt-PCR was used to determine VEGF mRNA expression.

Results
We observed a significant decrease in the cellular growth of OVCAR-3 cells exposed to paclitaxel after EGCG treatment for 24 hours. A significant decrease in VEGF expression in OVCAR-3 cells exposed to combination of EGCG and paclitaxel was observed.

Conclusions
We found that EGCG and paclitaxel combination inhibits cellular growth and proliferation in a dose-dependent manner in ovarian cancer cells (OVCAR-3). Additionally this combination maybe useful for blocking metastasis by decreasing VEGF mRNA level. Our results indicate that EGCG and paclitaxel combination might be a promising candidate for potential anticancer therapeutic use. Additional studies are in progress to evaluate the effects of EGCG and paclitaxel combination in several gynecological cancer cells.
SEROUS INTRAEPITHELIAL CARCINOMA OF ENDOMETRIUM AND TUBA UTERINA. WHICH ONE IS THE ORIGIN: A CASE REPORT

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Objectives
Endometrial cancer is most common malignant tumor of female genital tract in developed countries. Serous carcinomas comprise up to %15 of endometrial cancers. In most cases multifocal serous carcinomas are presumed to originate from single sites except endometrial serous carcinomas where multiple sites of origin have been documented by genetic studies.

Methods
59 years old female patient was refered to oncology clinic with the pre-diagnosis of peritoneal carcinamatosis. Ultrasonography revealed extensive peritoneal solid structures. Ca-125 level was slightly elevated (65 IU/ml). She was performed a staging surgery. During intraoperative examination bilateral ovarian and omental tumor involvement were determined.

Results
After staging surgery, pathological examination of the specimen revealed serous intraepithelial carcinoma of endometrium and right tuba uterine with omental and left ovarian tumor metastasis. Pathologist determines the site of origin as STIC.

Conclusions
Classifying serous tumors as originating from the upper genital tract where multiple foci is present is still a dilemma for the pathologists. Without genetic data it is impossible to determine whether such tumors originate in the endometrium or the fimbria. By SEE-FIM protocol extensive examining of fimbria in such serous intraepithelial tumors can reveal STIC more than expected. Determination of STIC in multiple foci tumor can change the treatment protocol and also the overall survival. Although, role of serous tubal intraepithelial carcinoma (STIC) in the pathogenesis of uterine serous carcinoma is controversial, presence of STIC should be verified and documented for defining the protocol in such cases.
e-Posters: Ovarian Cancer

CLINICAL DIFFERENCES BETWEEN EPITHELIAL OVARIAN CARCINOMA AND ENDOMETRIOSIS ASSOCIATED OVARIAN CARCINOMA
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Objectives
Endometriosis is a common gynecologic disorder characterized by ectopic growth of endometrial glands and stroma. Major risk factor in prognosis of endometriosis is the progression of the endometriotic tissue to malignant tumor. Some kinds of epithelial ovarian tumor have high incidence in correlation with endometriosis as clear cell and endometrioid type.

Methods
The medical histories of patients with epithelial over carcinoma diagnosis in a tertiary health care center were retrospectively reviewed. Median ages, histological types, FIGO stage of cancer at the time of diagnosis were evaluated. Total 384 of patients were determined with epithelial ovarian cancer, 23 of patients have endometriosis associated malignancies according to pathological examination.

Results
Comparison between endometriosis associated and non-endometriosis associated ovarian cancer revealed that cancer in the endometriotic tissue has a high incidence of clear cell and endometrioid type. Only 3 of 23 patients with endometriosis associated malignancies have serous epithelial tumor. 13 of 23 patients have clear cell 7 of 23 patients have endometrioid type pathology. Median age of endometriosis associated patients was significantly lower.

Conclusions
Endometriosis associated ovarian cancer differ from non-endometriosis associated ovarian cancer in clinical and biologic characteristics. Therefore, endometriosis diagnosis itself and related neoplasms need special attention in clinical practice.
e-Posters: Ovarian Cancer

DISSEMINATED PERITONEAL ADENOMUCINOSIS MIMICKING OVARIAN CARCINOMA
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Objectives
Mucinous cystadenoma (appendiceal mucocele) is a rare neoplasm of the vermiform appendix found %0, 3 of appendiceal specimens. It is characterized by villous adenomatous changes of the appendiceal epithelium with marked distension of appendiceal lumen with mucin. Clinical significance lies with the possibility of rupture of the appendix and spillage of mucin into peritoneal cavity resulting in pseudomyxoma peritonei.

Methods
65 years old female (Gravida 11 Parity 7 Abortus 4) presented with abdominal pain that had worsens for 10 days. Ultrasonographic examination revealed a thick-walled 54x55 mm adnexial mass with internal echoes and particulated fluid in the right para-ovarian region and in the Douglas pouch.

Patient was prepared for exploratory laparotomy. Intra-operative findings included mucinous ascites, right ovary with multiple cystic mucoid implants and dilated appendix. Frozen section revealed mucinous tumor in the right ovary. Distinction of malignant or benign cannot be verified.

Results
TAH+ BSO+ Appendectomy+ Omentectomy+ BPPLND was performed. Final pathological findings revealed disseminated peritoneal adenomucinosis with low grade mucinous neoplasia of appendix.

Conclusions
Appendiceal mucoceles are clinically silent tumors and majority of them are discovered incidentally. Rupture of the cystic structure results acute abdominal pain resembles acute appendicitis. Especially when acute septic intraperitoneal condition is absent, imaging studies leads to suspicion of other lesions as ovarian tumors.

Mucinous neoplasia of the appendix should be kep in mind in patients who have pseudomyxoma peritonei. Preoperative imagings especially with gadolinium- enhanced MR images are most accurate for depicting cellular peritoneal tumors in pseudomyxoma peritonei. Tumoral resection may be the definitive treatment in the low grade neoplasias.
NOT ALL MULTIPLE INTRAABDOMINAL LESIONS ARE MALIGNANT: A DISSEMINATED PERITONEAL LEIOMYOMATOSIS CASE

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Objectives
Disseminated Intraperitoneal leiomyomatosis is a rare condition characterized by multiple solid nodules in peritoneal surfaces and omentum. It is hard to differentiate DPL from malignancy either screening techniques or even by macroscopic examination. Exact diagnosis is usually confirmed with microscopic evaluation.

Methods
56 years old postmenopausal women was admitted to our clinic with abdominal pain. Pelvic ultrasonography showed enlarged uterus with multiple myomas and large, lobulated solid mass in left adnexial region. Serum Ca-125 level was slightly elevated (52 IU/ml). Laparatomy was performed with a pre-diagnosis of ovarian cancer. At laparatomy uterus with multiple myomas were noted. Solid multiple nodules were detected in left adnexial region including peritoneal surfaces and adjacent omentum. Frozen section revealed benign solid mass.

Results
In her final pathological examination disseminated Intraperitoneal leiomyomatosis with multiple endometriotic foci was diagnosed.

Conclusions
LPD is a rare form of benign smooth muscle proliferation of which less than 140 cases have been reported. Because of their estrogen susceptibility they are common in reproductive age and symptomatic especially during pregnancy. Use of Oral contraceptives, Hormone Replacement Therapy and endometriosis are noted as known risk factors. Only in 6 of LPD cases malignant transformation were described in the literature. LPD should be considered in the differential diagnosis of ovarian carcinoma. Because it’s macroscopic appearance resembles peritoneal carcinomatosis. Frozen section is seemed to be the best way in differential diagnosis with the awareness of this entity.
e-Posters: Ovarian Cancer

BENIGN MULTICYSTIC PERITONEAL MESOTELIOMA MIMICKING OVARIAN CANCER
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Objectives
Benign multicystic mesothelioma (BCM) is a rarely encountered tumor arising from the peritoneal mesothelium. Since the first description of benign cystic mesothelioma in 1979, approximately 130 cases have been reported. Despite its benign nature, it has a high recurrence rate and rare malignant transformation. Its symptoms are uncharacteristic. Histologic examination is essential for its diagnosis and surgery is the only effective treatment.

Methods
A 25-year-old woman with abdominal pain was evaluated. On physical examination a right adnexal mass and tenderness were detected. On ultrasonographic evaluation, a 10 x 8 cm septated complex adnexal mass was detected. High levels of Ca-125 (201 IU/ml) and Ca 19-9 (603 IU/ml) were found. She underwent a laparotomy.

Results
Ovaries were found as normal in operation and the frozen evaluation of excised mass was reported as benign. The final pathologic result was BCM.

Conclusions
BCM occurs mainly in women in reproductive age. Its pathogenesis is unclear and a controversy exists regarding its neoplastic and reactive nature. It has a strong predilection for the surface of the pelvic viscera. When found in the peritoneal cavity, it is usually attached to serosal surfaces of the intestine. Differential diagnosis includes a number of lesions that present as cystic abdominal or pelvic masses. It is very difficult to establish preoperative diagnosis of peritoneal mesothelioma. Most patients are diagnosed incidentally during examination or laparotomies for other reasons. In current case, following laparotomic excision diagnosis was established by evaluation of paraffin-embedded sampling of pelvic mass.
SIGNIFICANCE OF 18(F) FDG-PET/CT IMAGING IN THE MANAGEMENT OF OVARIAN CANCER.
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Objectives
To evaluate the clinical role and accuracy of 18(F) FDG-PET/CT imaging in patients with ovarian cancer.

Methods
This is a prospective study of 10 women with ovarian carcinoma, 36-55 years old, who had whole-body PET/CT at department of nuclear medicine and PET/CT, All India Institute of Medical Sciences, New Delhi, India from 15th October 2010 to 14th April, 2011. Ct guided biopsy was also taken ,which was positive for recurrent/residual disease in all patients.We analysed the patients outcomes from medical records and compared them to the interpretation of the PET/CT scans. A dose of 10mCi (370Mbq) FDG (F) IV was injected to all patients and CT scan followed by PET scan was performed and results were interpreted.

Results
All patients had advanced stage ovarian cancer and the study was requested for re-staging. A total of 10 patients was examined.3 patients had one scan, 3 patients had two scans and four patients had more then three scans. All the patients were examined for CA-125.18(F) FDG- PET/CT had a sensitivity and accuracy of 100% for detection of ovarian cancer and recurrence and distant metastasis of the disease.The SUV max of the detected lesions ranged from 10 to 37. The CA-125 tumor marker ranged from 12.6 to 318 kU/ml in patients with positive scans.

Conclusions
This study confirms the good results of F-FDG PET/CT for identification of residual/recurrent ovarian cancer, as well as for distant metastases localization. PET/CT should be done to evaluate patients with high-risk ovarian cancer or rising values of tumor markers (CA-125).
ROLE OF ULTRASOUND IN THE DETECTION OF RECURRENT OVARIAN CANCER.
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Objectives
Appropriate follow-up of patients treated for ovarian cancer is contentious with little evidence to justify many of the regimens in use.

The Royal Derby Hospital have adopted a regime of ultrasound (US) based surveillance which has continued since publication of the OVO-5 study which showed that CA125 levels, although sensitive for recurrence, did not improve patient outcome. Women with invasive ovarian disease were assessed regularly by clinical examination and US. We wished to determine if this approach was successful and worthy of further investigation/validation.

Methods
56 random sets of notes from our ovarian cancer database were examined to find patients with no residual disease remaining after primary surgery who subsequently developed recurrent disease within 5 years. 'Optimal cytoreduction' alone was not included. All patients had to be followed-up according to the unit protocol.

Results
Six cases were identified. Initial staging ranged from 1a–3c and CA125 ranged from 26–2050u/ml (mean 448.5u/ml). All patients were initially treated with neo-adjuvant or adjuvant chemotherapy. 35 US scans were performed in total. US detected two-thirds of the recurrences. Clinical examination or CT detected the remainder. The mean CA125 at recurrence was 520.2iu/ml (range 108-1021iu/ml). A confirmatory biopsy was performed in 33%. Further management involved surgery (16.7%), chemotherapy then surgery (16.7%) and chemotherapy alone (66.6%).

Conclusions
US detected disease recurrence before clinical examination in two-thirds of cases. All recurrences would have been detected by CA125. Whether US-detected recurrence improves outcome needs further investigation.
HIPEC WITH CISPLATIN AND PACLITAXEL IN ADVANCED EPITHELIAL OVARIAN CANCER: RESULTS OF A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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Objectives

Feasibility and safety of cytoreductive surgery (CRS) associated to hypertermic intraperitoneal chemotherapy (HIPEC) performed with cisplatin and paclitaxel in patients with peritoneal carcinomatosis for epithelial ovarian cancer (EOC).

Methods

We enrolled in this open, prospective, phase II study patients with advance EOC. Diffusion was evaluated with Peritoneal Cancer Index (PCI) and completeness of cytoreduction (CC) by the size of the residual peritoneal implants: no residual (CC0); nodules less than 2.5 mm (CC1); between 2.5 mm and 2.5 cm (CC2); greater than 2.5 cm (CC3). HIPEC was performed open or closed using cisplatin (100 mg/m²) and paclitaxel (175 mg/m²) for 60-90 minutes. Peritoneal and outflow thermal plateau was 41.5°C. Complications were classified according to the Common Terminology Criteria for Adverse Events (CTCAE scale).

Results

We enrolled 48 patients. Mean age was 54 years (33-72). CC0 was achieved in 39 (81.3%) patients, CC1 in 9 (18.8%). Mean operation time was 8.8 hours (7-12). Mean stay in Intensive Care Unit was 5.6 days (range 1-34) and mean hospitalization was 24.3 days (1-77), without intraoperative death. Three patient (6.2%) died within 30 days for septicemia. Complications are listed in the table. Six patients (12.5%) needed relaparotomy for intestinal complications. Twentynine patients (60.4%) recurred with a mean time of 8.9 months (2.2-25.5). Median DFS and OS were 6.3 and 11.3 months.

<table>
<thead>
<tr>
<th>CTCAE scale</th>
<th>Complication</th>
<th>N pts.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>wound dehiscence</td>
<td>3</td>
<td>6.3</td>
</tr>
<tr>
<td></td>
<td>gastrointestinal fistula</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>leukocytopenia</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>thrombocytopenia</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>wound infection</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>deep vein thrombosis</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>anaemia</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>acute renal failure</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Grade 4</td>
<td></td>
<td>4</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>bowel obstruction</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>leukocytopenia</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>thrombocytopenia</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>septic shock due to perforation</td>
<td>1</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Conclusions
CRS plus HIPEC with cisplatin and paclitaxel was feasible and safe in patient with advanced EOC. High paclitaxel concentration and prolonged hyperthermia did not increase morbidity.
e-Posters: Ovarian Cancer

OVARIAN EPENDYMOMA – EXTREMELY RARE OVARIAN TUMOR, CASE REPORT

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²Center of solid organ transplantation, University Hospital Merkur, Zagreb, Croatia
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Objectives

The ovarian ependymomas belong to the group of neuroectodermal tumors. These monophasic teratoma are composed exclusively or almost exclusively of neuroectodermal tissue and they are extremely rare worldwide. Data to 2007. Disclosed approximately 60 cases primary ovarian tumors of this type. We present the case of a 37-year old woman (from abroad) who was admitted to our institution with recurrence of intraabdominal tumor after several surgery procedures and incorrectly interpreted pathohistologic findings (extra muros).

Methods

Our ultrasound examination revealed; liver metastasis 120x90x75 mm and intraabdominal formation 95x80x80 mm with solid and cystic components, that cranial continue in several smaller cysts. We also performed the audit with histological samples from previous operation. Histopathology revealed: neuroectodermal ovarian tumor with predomination of ependymoma.

Results


Conclusions

The final pathology confirmed reccurent of primary ovarian ependymoma. The review of the literature shows that patients with stages I and II were treated surgically, whereas those with stage III or IV received additional chemotherapy or radiation. How the tumor is exteremely rare and there is no standardized algorithm for adjuvant chemotherapy, we recommend polychemotherapy: BEP protocol during 3-4 cycles. In the case of recurrence it is possible to continue with oral Etoposide (VP-16) 50 mg / 21 days with 8 days pause (gradual dose reduction).
**MOLECULAR CYTOGENETICS OF PRIMARY DIAGNOSED ADVANCED OVARIAN CANCER**

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²Chemotherapy, Regional Oncological Center, Krasnodar, Russia
³Pathological, Regional Oncological Center, Krasnodar, Russia

**Objectives**

Ovarian cancer morbidity is around 15 on 100 000 of women and presents at advanced stages of III-IV in 70%. Despite improvements in chemotherapy, short progress free period, high mortality level and the 5-year survival less than 35%, forced oncologists to find new targets applicable to ovary cancer. Multiple chemotherapy cycles caused immunodeficiency, anaplastic blood conditions, psychological distress, significantly deteriorate of life quality.

**Methods**

Formalin-fixed paraffin-embedded tissue specimens were retrieved from the initial surgical resection for 30 stage III platinum sensitive ovarian cancer patients who had received from 3 to 7 regimes of chemotherapy combined with Paclitaxel, Gemcitabin or Doxorubicin. Molecular cytogenetics was performed for the detection of somatic chromosomal alterations of the BRCA1, BRCA2, HER2, ER, PR, and Proliferative Index Ki-67.

**Results**

Nine patients were with low grade, and 21 with papillary ovarian cancer. In 1 patient BRCA1 and in 1 patient BRCA2 genes mutations were positive. In 27 patients ER and in 23 PR tumor receptors were positive. In 17 patients HER2 was positive and in 13 negative. In 20 patients high proliferative index Ki-67 (55-80%) was found. All ER positive patients receiving Tomoxifen 20 mg daily and after 3 month control reassessment was done by CT and CA-125. Eleven patients from 27 ER positive, had progress of the disease, and 16 patients had no signs of progression.

**Conclusions**

The personalized genomic information can help a treatment planning by identifying novel potentially targetable genomic alterations that can be used by clinicians to choose rational directed therapies for patients with chemo-resistant ovarian tumors.
Objectives
Capacity of nadir CA-125 levels to predict the prognosis of epithelial ovarian cancer (EOC) remains controversial. This study aimed to explore whether the CA-125 comparing to HE-4 serum levels could predict the progression in patients with EOC.

Methods
The results of 89 patients from the Krasnodar Regional Oncological Center of Russia between 2009 and 2012 who have shown complete clinical response to primary therapy and have rising CA-125 and HE-4 levels were retrospectively analyzed. The Student-Fisher test was used to assess the associations between the clinicopathological characteristics, CA-125 and HE-4 levels and PFS duration.

Results
Mean value of HE-4 and CA-125 before therapy was 267.4 pmol/l and 480.7 U/ml, and have dropped down to 37.6 pmol/l and 18.4 U/ml after treatment (P=0.001). Within 8 to 31 month (mean 23 month) 49 patients (55.1%) had progressed. Mean level of HE-4 and CA-125 had elevated up to 207.6 pmol/l and 270.6 U/ml accordingly. After secondary therapy in 24 (48.9%) patients markers dropped down to 40.4 pmol/l and 28.9 U/ml (P=0.002). In 16 (32.6%) of patients clinical assessment revealed no progression, and HE-4 and CA-125 was 148.7 pmol/l and 26.9 U/ml, however after reassessment, disease progression was observed. Nine patients had no response to therapy.

Conclusions
The nadir HE-4 and its elevation is more sensitive predictor of the progression than CA-125 in 32.6% of cases in EOC patients. Further prospective studies are required to optimize the diagnostic methods for earlier treatment administration in patients with higher HE-4 level when CA-125 level still remains normal.
SINGLE AGENT PACLITAXEL IN RELAPSED OVARIAN AND PRIMARY PERITONEAL CANCER – A UK TERTIARY CENTRE EXPERIENCE

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Objectives
To assess efficacy and tolerability of single-agent paclitaxel administered weekly at 80mg/m² (WP) or 3-weekly at 175mg/m² (3-WP).

Methods
A retrospective case note review was performed of patients with relapsed ovarian or primary peritoneal cancer treated with single-agent paclitaxel over a 5 year period.

Results
Between January 2008 and December 2012, 53 patients received WP and 15 received 3-WP (median ages 65 vs 68; median previous lines of chemotherapy 2 (both groups); median number of paclitaxel doses given, 7 vs 3).

Responses for WP and 3-WP using radiological criteria were: partial response 26% vs 10%; stable disease 49% vs 40%, progressive disease 23% vs 50%. Biochemical CA125 responses were 47% vs 49%. Median progression-free survival was 4 months vs 2 months. Median overall survival was 6 months for both regimens. Response was best in patients who were platinum sensitive (WP radiological response rate 80%).

For all CTC grades, peripheral neuropathy, myalgia and nausea/vomiting occurred more with 3-WP than WP (27% vs 5%; 7% vs 2%; 13% vs 8%). Infection, infusion reaction, diarrhoea and mucositis occurred more with WP than with 3-WP (13% vs 0%; 4% vs 0%; 10% vs 0%; 2% vs 0%).

Grade 3-4 toxicity occurred only with WP: anaemia=25%, neutropenia=9%, hypomagnesaemia=10%, hyponatraemia=10%, ALT rise=4%

Conclusions
WP and 3-WP regimens show similar response rates and overall survival, with better results in platinum sensitive disease. Further work is needed to establish the role of WP in unselected patients.
THE POTENTIAL FOR STATINS IN THE TREATMENT OF OVARIAN CANCER

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Objectives
Statins are widely used to treat hypercholesterolaemia, but are also being investigated in both preclinical and clinical studies as therapeutics in a number of cancer types.

Methods
We evaluated the effects of six lipophilic statins (rosuvastatin, simvastatin, simvastatin acid, atorvastatin, lovastatin and fluvastatin) and one hydrophilic statin (pravastatin) on cell growth and survival in seven ovarian cancer cell lines.

Results
All statins except pravastatin caused cell death in monolayer and spheroid cultures. Statins were effective in cells relatively resistant to carboplatin. Cell death was only evident after 48 hours continual exposure to simvastatin, an observation that should be considered in clinical trials because many statins have a relatively short half-life. Simvastatin activated caspases in three cell lines tested, suggesting apoptosis was one mechanism of statin-induced death. Simvastatin also altered the levels of LC3-II, p62 and Rab7, regulators of the autophagy pathway, and this may also contribute to the anti-cancer activity of statins. The addition of mevalonate or geranylgeraniol but not farnesol reversed the effects of simvastatin on cell proliferation, apoptosis and autophagy indicating that the primary mechanism of action of statins was through depletion of geranylgeranylation. Simvastatin was additive or mildly antagonistic when combined with either carboplatin or paclitaxel in all the cell lines, particularly if cells were exposed to simvastatin prior to carboplatin.

Conclusions
These observations suggest that clinical trials of statin in ovarian cancer deserve serious consideration and may preferably evaluate statins as monotherapy rather than in combination with chemotherapy.
RADIATION EXPOSURE OF OVARIAN CANCER PATIENTS: CONTRIBUTION OF CT EXAMINATIONS ACCORDING TO DIFFERENT ACQUISITION PROTOCOLS

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Objectives
To assess radiation dose given to ovarian cancer patients by CT examinations acquired with different protocols and possibility of reducing doses.

Methods
CT examinations, performed on ovarian cancer patients between Apr 2008 and Feb 2011, were retrospectively evaluated to select studies extended to thorax, abdomen and pelvis, which represented our study cohort. CT dose index (CTDI vol) and dose length product (DLP) for each exam and phase acquired were extracted from the protocol page summary sheet. The effective dose (E), as indicator of the radiation received by patients, was calculated from the DLP of each series and for the entire CT exam according to updated dose per unit DLP (E/DLP) conversion factors.

CTDIvol, DLP, E and extension of acquisitions were described by mean, standard deviation, maximum and minimum value. The parameters distribution was tested for normality by the Kolmogorov-Smirnov test. The mean total effective doses of two different protocols to be used to scan thorax, abdomen and pelvis (TAP), including either multiple phases (Protocol A) or only the portal venous phase (Protocol B), were calculated.

Results
Study cohort included 157 CT examinations. Mean age of patients scanned was 57±12 years (age range 34-80). The mean total effective doses of Protocol A and Protocol B were 27.2 mSv and 13.0 mSv, respectively.

Conclusions
Radiation dose given by CT to ovarian cancer patients increases according to high number of phases acquired. Reduction of dose may be achieved by selecting appropriate parameters and by minimizing multiple phases scanning.
USE OF DESENSITIZATION PROTOCOL FOR CARBOPLATIN AFTER HYPERSENSITIVE REACTION

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Objectives
Ovarian cancer has a low cure rate. 60-70% of patients experience recurrent disease and need subsequent treatment. 75% of the recurrences occur >6 months after termination of adjuvant chemotherapy, and patients are retreated with carboplatin based regimens. In these patients carboplatin offers good chance of response and remains the most active drug. Hypersensitive reactions (HR) to carboplatin have been described in up to 40% of patients receiving more than 6 course. If untreated, on next course HR may represent a life threatening condition. Desensitization protocols have been described, enabling continuation of carboplatin for protracted periods.

Methods
Summarize our institution experience with desensitization protocol. Data was collected retrospectively from patient’s files. Pts with HR to carboplatin were treated with desensitization protocol - consisting of oral premedication drugs (Prednisone, Ranitidine, and Loratidine) for 3 days prior to carboplatin, Intravenous Dexamethasone, Ranitidine, Promethasineon prior to treatment and escalating dose of carboplatin on each of next courses.

Results
16 patients (15 gynecological malignancies, 1 breast cancer) were treated. Median number of doses before HR was 9 (range 1-24). 15 pts tolerated the treatment well and continued to receive carboplatin for a median of 4.5 (range 1-23) doses. Treatment with carboplatin was stopped in 11 patients: 6 achieved complete response, 5 progressed on carboplatin. 4 patients are receiving ongoing treatment. Only 1 patient stopped because of recurrent allergic reaction.

Conclusions
Desensitization protocol for carboplatin may be used safely, allowing further treatment in responding patients after HR has occured.
EVALUATION OF NOVEL NEGATIVE MODULATORS OF EPITHELIAL CADHERIN EXPRESSION IN OVARIAN CANCER

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2Biomedicine and Translational Oncology, Research Unit in Biomedicine and Translational Oncology, Barcelona, Spain

Objectives
Ovarian cancer is the 4th leading cause of death in women. However, there are no molecular markers for its detection/monitoring. Epithelial cadherin (Ecad) is a key protein in cell-cell adhesion and its diminished expression is accompanied by cadherin switch (Ecad to neural and/or placental cadherins: Ncad, Pcad) and other Epithelial Mesenchymal Transition (EMT) events, such as expression of transcriptional repressors (Twist, Snail) and mesenchymal markers (vimentin). More recently, a decrease of Ecad has been linked to Dysadherin (Dys) expression, a glycoprotein overexpressed in various tumors and related to tumor metastasis. In ovarian cancer, lower levels of Ecad expression have been associated with metastatic spread. Although EMT has been reported in this cancer, current available data is not conclusive. Moreover, Dys expression has yet not been reported.

Aim
To evaluate expression of Ecad, EMT markers and Dys in four ovarian cancer cell lines: TOV-112D (primary tumor), SKOV-3, OAW-42 and OV-90 (ascites).

Methods
mRNA: standard/real-time PCR, protein: Western immunoblotting/immunocytochemistry.

Results
An inverse correlation was observed when expression levels (mRNA, protein) of Ecad were compared with those of Twist, Ncad, Pcad, Vimentin, and Dys. Contrasting, Snail expression was similar in all cell lines.

Conclusions
The analysis of EMT markers led to the identification of cell lines with epithelioid (OV-90), mesenchymal (TOV-112D) or mixed (SKOV-3, OAW-42) molecular profiles. This is the first report that describes the expression of Dysadherin (mRNA and protein) in ovarian cancer.
e-Posters: Ovarian Cancer

LITERATURE REVIEW OF THREE-WEEKLY VERSUS WEEKLY PACLITAXEL USE IN OVARIAN CANCER

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2Global Value Access and Policy, Amgen, Thousand Oaks, USA
3GmbH, Amgen, Munich, Germany
4PRMA, PRMA Ltd, London, United Kingdom

Objectives
3-weekly paclitaxel administration is the standard therapy for ovarian cancer (OC), but recent evidence in breast cancer (BC) and non-small cell lung carcinoma (NSCLC) has suggested improved efficacy and reduced toxicity with once-weekly dosing.

Methods
A literature review of published clinical trials between 2000 and 2012 comparing 3-weekly vs. weekly paclitaxel administration using terms ‘ovarian cancer, cancer, paclitaxel weekly, dose-dense paclitaxel’ in ovarian cancer was conducted. Three comparative trials in OC (Table 1) were identified.

Results
Using once-weekly paclitaxel, efficacy was similar or improved in all identified comparative trials. Safety was also similar or improved, except for increased anemia in a study by Katsumata et al.

Table 1: Efficacy and safety in 3-weekly vs. weekly paclitaxel trials in OC

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall survival (OS)</th>
<th>Progression-free survival (months)</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shen et al, 2005</td>
<td>Similar between arms 85.3 vs. 78.7 months (P &gt; 0.05)</td>
<td>Similar between arms 15.7 vs. 13.6 (P &gt; 0.05)</td>
<td>Myelosuppression: 46% vs 28%</td>
</tr>
<tr>
<td>Katsumata et al, 2009</td>
<td>77.7% vs. 83.6% (P = 0.03)</td>
<td>17.2 vs. 28.0 (P = 0.0015)</td>
<td>Anaemia: 44% vs 69%</td>
</tr>
<tr>
<td>Rosenberg et al, 2002</td>
<td>Similar between arms 14.7 vs. 13.6 months (P = 0.98)</td>
<td>Similar between arms 6.1 vs. 8.1 (P = 0.85)</td>
<td>Neutropenia: 45% vs 18%</td>
</tr>
</tbody>
</table>

Conclusions
These results suggest that once-weekly paclitaxel dosing may offer a positive risk-benefit profile over the three weekly regimens. It may be an appropriate treatment options for patients with recurrent OC.
e-Posters: Ovarian Cancer

TRABECTEDIN AS SINGLE-AGENT IN HEAVILY PRETREATED PATIENTS WITH RELAPSED OVARIAN CANCER (ROC): RESULTS FROM A RETROSPECTIVE STUDY

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Objectives
Trabectedin (Yondelis®) has shown efficacy in ROC, both as a single agent and in combination with PLD. In this multicenter, retrospective study we evaluated the efficacy and safety of trabectedin monotherapy in heavily pre-treated patients with ROC.

Methods
Patients with measurable ROC and at least 2 prior treatments were eligible. Patients received trabectedin (1.3 mg/m², n=56; 1.1 mg/m², n=42) given as a 3-hour infusion every 3 weeks. Evaluations of the ORR (primary endpoint) as per RECIST, TTP, OS and safety profile were performed.

Results
Ninthy-eight patients (median age at recurrence diagnosis: 53 years, range: 29-79) with PS (n=44), partially PS (n=23) or platinum-resistant disease (n=31) were included. Median number of previous chemotherapy regimens was 4 (range: 2-6). The ORR was 28.6% (5 complete/23 partial responses); 32 patients (32.6%) experienced stable disease (2 patients ≥6 months), and 38 (38.8%) progressed. The ORR was higher in PS (38.6%) compared to partially PS (26.1%) and platinum-resistant patients (16.1%) (p=0.071). No difference in the ORR was found according to number of prior treatments or trabectedin dose. After a median follow-up of 8 months, median TTP and OS were 5 and 13 months, respectively. The most common grade 3/4 toxicities were transient and non-cumulative neutropenia (17.5% of patients), AST (7.1%) and ALT (13.3%) increases. Four anthracycline-pretreated patients had cardiac toxicity, of whom one died due to acute arrhythmia.

Conclusions
Trabectedin monotherapy represents a valid approach in the treatment of patients with heavily pre-treated ROC with meaningful clinical benefit and acceptable and manageable safety profile.
E-Posters: Ovarian Cancer

OVARIAN SMALL CELL CARCINOMA OF HYPERCALCEMIC TYPE: A CASE REPORT OF METASTATIC DISEASE

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6Radiologische Klinik, Klinikum Dortmund, Dortmund, Germany

Objectives
Ovarian small cell carcinoma is a rare, aggressive malignancy that occurs at an average age of 24 years. In about two thirds of the cases, the tumor is accompanied by paraneoplastic hypercalcemia. There is no standard treatment because of the rarity of the malignancy. The prognosis is very poor, with an overall 5-year survival rate of about 10%.

Methods
We report on a 34-year-old woman with abdominal pain suspicious of ovarian torsion. The laboratory tests showed elevated white blood count (15.30x10³/ul), CRP (7.9mg/dl), LDH (368U/l) and CA12-5 (394U/ml). The explorative laparotomy revealed a right-sided 14 cm adnexal mass. After adnexectomy, the frozen-section analysis suggested an ovarian dysgerminoma. The CT-Scan of the chest and abdomen showed enlarged retroperitoneal lymph nodes and a liver lesion, suspicious of liver metastasis. After histopathological and immunohistochemical work-up the diagnosis of small cell ovarian carcinoma of hypercalcemic type was made. After consultation with the MAKEI study coordination center, we planned a treatment with Carboplatin 120mg/m² days1-5, Ifosfamide 1500mg/m² days 1-5 and Doxorubicin 45mg/m² day 1 (CarboPIA). Considering the patient's Meniere's disease only 80% of the dose was administered.

Results
After two cycles, the staging investigations showed complete remission of the liver metastasis and of the retroperitoneal lymph masses. A hematopoietic stem cell apheresis was performed. We completed a total of six CarboPIA cycles. The application of one consolidation cycle of high-dose Carboplatin-Etoposide followed by autologous hematopoietic stem cell transplantation is planned.

Conclusions
Our observation confirms that ovarian small cell carcinoma is a chemosensitive tumor, even at a metastatic stage.
e-Posters: Ovarian Cancer

BORDERLINE OVARIAN TUMOURS: DIAGNOSIS AND TREATMENT IN A REGIONAL CENTRE

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Objectives

To review the cases of borderline ovarian tumours (BOTs) in our centre, to evaluate the available preoperative information; intraoperative biopsy inform and the final diagnosis.

Methods

Retrospective study of patients surgically attended in our regional centre with diagnosis of BOT, from 1994 to 2012. We include either intraoperative as postoperative diagnosis of BOT.

Results

From the 36 patients with BOT diagnosis in any moment of their treatment, 31 had a definitive diagnosis of BOT (14 serous, 13 mucinous, 2 intestinal type and 2 mix); 4 ovarian carcinoma and 1 ovarian pseudomixoma.

In 21/36 cases an intraoperative biopsy was performed. 14 matched up with the definitive BOT diagnosis. 3 informed as benign resulted into BOT, 2 informed as carcinoma into BOT and 1 informed as BOT had carcinoma as definitive diagnosis.

FIGO stage at diagnosis were: 29 cases were at I and 2 at III (both with progression-free survival at 4 years)

Women age mean at diagnosis was 43,03 (11-75). 51’6% of patients were ≤ 40 years old. From this group, 10 were candidate for fertility-sparing surgery.
Referring to the diagnosis (in 6 cases preoperative dates were not available):

<table>
<thead>
<tr>
<th>1st Symptom</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Valid percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>10</td>
<td>32.3</td>
<td>40.0</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>4</td>
<td>12.9</td>
<td>16.0</td>
</tr>
<tr>
<td>Casual discovery</td>
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Conclusions
Abdominal symptomatology in women with ultrasound cyst detection must aware us. Since preoperative information (symptoms, serum makers and image) has not enough specify for malignancy differentiation; intraoperative biopsy is the most reliable tool to avoid iatrogenic surgery.
e-Posters: Ovarian Cancer

TVCD FLOW INDEX – RI AS A PREDICTOR OF PLATINIUM RESISTANCE IN EPITHELIAL OVARIAN CANCER

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Objectives
To evaluate the prognostic significance of flow index RI in predicting drug resistance in epithelial ovarian cancer (EOC).

Methods
We analyzed data from 68 relapsed cases, primarily diagnosed as having stage III EOC (44 serous, 4 mucinous, 10 endometrioid, 10 undifferentiated. Pulsed Doppler spectral analysis was used immediately before cytoreductive surgery followed by adjuvant platinum and paclitaxel based chemotherapy. To evaluate tumor vascularity RI from the tumor was measured. Blood flow of primary malignant tumor according to the number of platinium-sensitive (PS) and platinium-resistant (PR) relapses was finally analyzed.

Results
Among 68 women the mean age was 59.9, ranged 42-73 years. 12 of them had IIIa, 4 had IIIb and 52 had IIIc primary EOC. There were 4 G1, 12 G2 and 52 G3 cases. Optimal cytoreductive surgery underwent 36 (52.9%) patients. In PS and PR cases mean RI was 0.33 (+/- 0.02) and 0.53 (+/- 0.53) respectively – p<0.0001. Similarly in cases of optimal and suboptimal surgical cytoreduction in PS and PR cases RI was significantly different 0.35 vs.0.42 (p<0.005) and 0.31vs.0.64 (p<0.0001) respectively.

Conclusions
Platinum sensitive tumors reveal significantly lower flow impedance as compared to platinum resistant cases both in optimal and suboptimal cytoreductive patients. Hence this blood flow index can predict drug resistance in relapsed EOC and could became the future prognostic factor of response.
PROGNOSTIC FACTORS FOR THE EFFICACY OF CATUMAXOMAB IN PATIENTS WITH MALIGNANT ASCITES (MA) DUE TO OVARIAN CANCER (OC): META-ANALYSIS FROM TWO PHASE III STUDIES

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2 Klinik für Viszeral- Gefäß- und Transplantationschirurgie, Kliniken der Stadt Köln gGmbH, Köln-Merheim, Germany
3 Universitäres Krebszentrum Leipzig (UCCL), Universitätsklinikum Leipzig, Leipzig, Germany
4 Department of Surgery, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom
5 Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, Universitätsklinikum Carl Gustav Carus Dresden, Dresden, Germany
6 Medical Affairs, Fresenius Biotech GmbH, München, Germany
7 Klinik für Gynäkologie gynäkologische Endokrinologie und Onkologie, Universitätsklinikum Standort Marburg, Marburg, Germany

Objectives
In two phase III studies (IP-REM-AC-01, IP-REM-AC-03), catumaxomab has demonstrated efficacy for treatment of MA in patients with OC.

Methods
To identify prognostic factors for the efficacy of catumaxomab a meta-analysis was performed including all randomized OC patients of both studies: 194 patients treated with catumaxomab plus paracentesis and 44 control patients (paracentesis only). Efficacy parameters were puncture-free survival (PuFS), time to first puncture (TTPu) and overall survival (OS). The impact of potential prognostic factors on efficacy parameters was analysed in the following subgroups: Karnofsky Index (KI): ≥70%, ≥80%, ≥90%, distant metastases: yes/no, total protein: low/normal, interval between 1st and 2nd chemotherapy (CTX): ≤6 months, >6 months, 6-12 months, >12 months, number of prior CTX: 1, 3, >3. Furthermore, the impact of CTX after catumaxomab was evaluated.

Results
Catumaxomab demonstrated significant ascites control (PuFS, TTPu) in all prognostic subgroups. OS was significantly longer compared to control in catumaxomab patients without distant metastases (133 vs. 81 days, p<0.0001), 6-12 months interval between 1st and 2nd CTX (147 vs. 55.5 days, p=0.0054), and in patients with 3 prior CTX (163 vs. 39 days, p=0.0136). Catumaxomab patients with normal protein had significantly longer OS compared to catumaxomab patients with low protein (124 vs. 99 days, p=0.017). OS was significantly longer in catumaxomab patients with post-CTX compared to those without post-CTX (261 vs. 75 days, p<0.0001).

Conclusions
The results may be helpful for selection of patients that benefit most from catumaxomab. Integration of catumaxomab into a treatment strategy in OC is currently investigated (ENGOT ov8).
A CASE WITH CONCURRENT HIGH-GRADE SEROUS CARCINOMA AND BORDERLINE MALIGNANT TUMOR DEMONSTRATING DIFFERENTIAL CHEMO-SENSITIVITY.

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²Department of pathology, Jikei Daisan Hospital, Tokyo, Japan

Objectives
Recently, new paradigm on ovarian tumorgenesis has been proposed based on molecular genetic analysis, and the epithelial tumors are classified into two categories designated type I and type II tumors. Type I tumors tend to be low-grade neoplasms, while type II tumors are high-grade neoplasms. We report here an extremely rare case with concurrent high-grade serous carcinoma and borderline malignant tumor, demonstrating distinctive differential chemo-sensitivity.

Methods
Case; a 68-year Japanese woman was suspected as advanced ovarian carcinoma. MRI showed cystic tumor containing solid component of the right adnexal region with massive ascites and peritoneal dissemination. Serum CA125 was elevated to 138 u/ml, however no remote metastases were detected. Laparotomy revealed peritoneal carcinomatosis spread out to omentum and subphrenic area. We removed omentum containing big tumor nodules which histologically demonstrated the high-grade serous adenocarcinoma coexisting with serous borderline tumor. After 6 cycles of postoperative chemotherapy with docetaxel and carboplatin, she received second surgery, where the known residual bilateral adnexal and subphrenic disseminated tumors were resected. Pathological examination of the tumor revealed the serous borderline tumor with invasive implant and no evidence of residual high-grade serous carcinoma. Immunohistochemical analysis showed deeply positive staining for P53 and Ki67 in high-grade serous carcinoma, whereas weekly staining for Ki67 in borderline tumor.

Results
This is clearly indicating the fact that chemo-sensitive high-grade serous carcinoma was eradicated consummately while the borderline malignant cells survived chemotherapy.

Conclusions
This could be a role-model case showing the coexistence of type I and type II ovarian cancer with differential chemo-sensitivity.
e-Posters: Ovarian Cancer

THE PROGNOSTIC SIGNIFICANCE OF PREOPERATIVE LEUKOCYTOSIS IN EPITHELIAL OVARIAN CARCINOMA
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2Obstetrics and Gynecology, Ansan Hospital Korea University College of Medicine, Seoul, Korea
3Obstetrics and Gynecology, Anam Hospital Korea University College of Medicine, Seoul, Korea

Objectives
Hematologic paraneoplastic manifestations, such as anemia, thrombocytosis, and leukocytosis, are frequently observed in various malignancies. The negative prognostic associations between preoperative leukocytosis and some gynecologic malignancies are well established, except for epithelial ovarian carcinoma (EOC). The aim of this study is to evaluate the prognostic impact of preoperative leukocytosis on patients with EOC.

Methods
The medical records of 155 patients who underwent primary debulking surgery and adjuvant platinum-based chemotherapy for EOC between January 1993 and October 2011 were reviewed. Patients were divided into two groups based on the presence or absence of preoperative leukocytosis (WBC > 10,000/uL). We performed univariate analysis by comparing the Kaplan-Meier curves of each group using the log-rank test. Cox proportional hazards regression model was used to identify significant independent prognostic factors for recurrence-free and overall survival.

Results
Of 155 patients, 23 (14.8%) with leukocytosis and 132 (85.2%) without leukocytosis were identified. Patients with leukocytosis showed significantly shorter recurrence-free survival (P<0.001), and overall survival (P<0.0001) than patients without leukocytosis. The leukocytosis group also showed significantly increased mortality rate than non-leukocytosis group (P<0.0001). Multivariate analysis revealed that preoperative leukocytosis and advanced stage were significant prognostic factors in recurrence-free survival (HR, 95% CI; 2.15, 1.55-4.41, 95% CI; 3.12, 1.44-6.75, respectively). In addition, preoperative leukocytosis was independently associated with decreased overall survival (HR, 95% CI; 7.66, 2.78-21.16).

Conclusions
Preoperative leukocytosis in patients with EOC is an independent prognostic factor for recurrence-free and overall survival.
ANALYSIS OF PROGNOSTIC FACTORS IN BORDERLINE OVARIAN TUMOURS WITH LONG FOLLOW-UP

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²Pathology, Cancer Center and Insitute of Oncology, Warsaw, Poland
³Biostatistic, Cancer Center and Insitute of Oncology, Warsaw, Poland

Objectives
Retrospective analysis of 316 patients with borderline ovarian tumours treated in the Maria Sklodowska Curie Memorial Cancer Center in Warsaw from 01.01.1982 to 30.12.2010 with long term follow-up.

Methods
Survival curves calculated by the Kaplan-Meier method have been applied to assess the treatment efficacy. For comparison, the survival curves logrank test was used. Differences were tested at a significance level of 0.05. Univariate analysis of prognostic factors was performed.

Results
Except the FIGO stage which was confirmed to be the prognostic factor, the presence of extraovarian implants (p=0.022) and the presence of free fluid (p=0.023) were statistically significant factors of disease free survival. The histopathologic pattern (p=0.523), the tumor capsule rupture (p=0.541) and the microinvasion (p=0.463) were not statistically significant factors.

Conclusions
The significant factors influencing disease free survival in patients with borderline ovarian tumours with long follow-up were: FIGO stage, the presence of extraovarian implants and the presence of free fluid in peritoneum.
ENORMOUS TUMOR OF THE MESOSALPINX IN YOUNG PATIENT. CASE PRESENTATION.

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¹2ND Department of obstetrics and gynecology university of athens, Aretaieion hospital, Athens, Greece
²Department of pathology university of athens, Aretaieion hospital, Athens, Greece
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⁴2nd Department of obstetrics and gynecology university of athens, Aretaieion hospital, Athens, Greece

Objectives
To present a rare case of an enormous tumor of the mesosalpinx.

Methods
We report a case of a 20 year old patient (para 0, gravida 0), with no family history, presented in our Department with symptoms of abdominal pain over a month. The U/S examination revealed a cystic mass diameter 25x20 cm located in the left ovary. All the tumor markers were negative. The patient underwent an abdominal laparotomy. Inside the peritoneal cavity a cystic formation diameter 20 cm in the left mesosalpinx was perceived. She underwent an excision of the cystic mass and the left salpinx as well. The frozen section revealed a serous cystadenoma diameter 25 cm located in the left mesosalpinx. The final histological examination confirmed the frozen section.

Results
Steroid cell tumors are often associated with endocrine manifestations and generally do not stain for alpha-fetoprotein. These unilateral and always benign tumors mimic serous or endometroid neoplasms and Sertoli cell tumors. Unlike the latter tumors, they typically occur in the broad ligament or mesosalpinx, but when larger in size they were misinterpreted as ovarian tumors. They arise from mesonephric (wolffian) remnants. Grossly, the tumors appear solid and gray, tan or yellow. They range from 2 to 20 cm in diameter.

Conclusions
Tumors located in the region of mesosalpinx are rare and arise from mesonephric remnants. Most unlikely are to be found in young patients, such in our case. Early diagnosis is always the key for an appropriate and successful treatment.
ANTI-CANCER EFFECT OF SNAKE VENOM TOXIN IN OVARIAN CANCER CELLS

C.W. Lee1, J.T. Hong2, M.J. Song1
1obstetrics and gynecology, college of medicine the catholic university of korea, seoul, Korea
2pharmacy, college of pharmacy chungbuk national university, cheongju, Korea

Objectives
In this study, we investigated the apoptotic effect of snake venom toxin in human ovarian cancer PA-1 and SK-OV3 cells.

Methods
Apoptosis and activity of NF-kB in vitro were analyzed.

Results
Snake venom toxin dose dependently (0~10 μg/mL) inhibited ovarian cancer cell growth with IC50 values 4.5 μg/mL in PA-1 cells, and 6.5 μg/mL in SKOV3 cells. Our results also showed that apoptotic cell death increased by snake venom toxin in a dose dependent manner (0~10 μg/mL). Consistent with increased cell death, snake venom toxin increased the expression of pro-apoptotic protein Bax and caspase-3, but down-regulated anti-apoptotic protein Bcl-2. Untreated ovarian cancer cells showed a high DNA binding activity of nuclear factor B (NF-kB), but it was inhibited by snake venom toxin accompanied by inhibition of p50 and p65 translocation into the nucleus as well as phosphorylation of inhibitory kB. Snake venom toxin also inhibited DNA binding activity of the signal transducer and activator of transcription 3 (STAT3). Moreover, the combination treatment of NF-kB (salicylic acid, 1 or 5 μM) and STAT3 (stattic, 1 μM) with snake venom toxin (1 μg/mL) further enhanced cell growth inhibitory effects of snake venom toxin.

Conclusions
These results showed that snake venom toxin from Vipera lebetina turanica caused apoptotic cell death of ovarian cancer cells through the inhibition of NF-kB and STAT3 signal, and suggested that snake venom toxin may be applicable as an anticancer agent for ovarian cancer.
IS IT POSSIBLE TO PREDICT THE LONG SURVIVOR AFTER RECURRENCE OF OVARIAN CANCER?


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Objectives
Epithelial ovarian carcinoma often achieves good response to first-line treatment. However, most of advanced cases develop recurrence within 2 years after primary therapy, and many patients die of the disease during this period. However, some patients attain surprisingly longer survive after recurrence. The patients who achieved survive after recurrence more than 5 years (Long survivors, LS) and the patients who died within 5 years (Short survivors, SS) were retrospectively reviewed.

Methods
We identified the 86 patients who were treated for recurrent disease after primary therapy at National Defense Medical College Hospital between 1995 and 2006. Clinico-pathological differences between LS and SS were retrospectively analyzed.

Results
LS (n=18) and SS (n=68) were included in this study. Statistically, clinical features of LS are as follows; there were no residual tumors at primary surgery (p<0.01), platinum-free interval were more than 6 months (p=0.03), and the serum CA-125 at time of relapse were under 64 (median score) (p<0.01). On multivariate analysis, three factors were identified as prognostic factors: no residual tumors at primary surgery (p=0.02), lower performance states at recurrence (p=0.02), and receiving secondary debulking surgery (p=0.04).

Conclusions
Three factors were identified for becoming LS after recurrence of ovarian cancer. Although clinical significance of these factors is needed to be evaluated by further analysis, we have to find recurrence when the patients have these factors, and adequate treatment should be achieved.
e-Posters: Ovarian Cancer

OUTCOME PROGRESS IN PATIENTS WITH ADVANCED OVARIAN CANCER TREATED BY NEO-ADJUVANT PLATINUM/TAXANE-BASED CHEMOTHERAPY AND LATE INTERVAL DEBULKING SURGERY

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²Pathology, Institut Bergonié, Bordeaux, France
³Biostatistics, Institut Bergonié, Bordeaux, France
⁴Radiotherapy, Institut Bergonié, Bordeaux, France
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Objectives
Steady survival progress is observed after standard treatment by surgery and chemotherapy in patients with advanced ovarian cancer (AOC), but little is known about progress after alternative neo-adjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS). We aim to assess if NAC + IDS offers comparable outcomes.

Methods
Retrospective data-base analysis in patients with AOC stages IIIC and IV treated by NAC + late IDS (after 6 cycles) comparing overall survivals (OS) between the platinum and platinum/taxane periods. Independent prognostic factors for surgical morbidity and OS are determined in the platinum/taxane group.

Results
118 patients with stages IIIC-IV AOC (median age: 64 years, stage IV: 31%) received platinum/taxane NAC + IDS with 68% complete resections. Major morbidity was 18%. OS was 42 months across all patients (95%CI: 35.3-49.1), and 80 months in stage IIIC. This is higher by 15 months than after platinum-based treatments. Higher morbidity was associated with bowel resection (HR: 51; CI: 1.9-13.9). Longer OS was associated with ASA class I, stage IIIC, no bowel surgery, and no residual disease.

Conclusions
Conclusions: The neo-adjuvant approach with late IDS offers OS rates and outcome progress similar to that reported by standard treatment. The goal of IDS surgery is complete resection, while sparing surrounding organs.
e-Posters: Ovarian Cancer

POSITIVE SYMPTOMS AND PHYSICAL EXAMINATION DID NOT AFFECT THE SURVIVAL IN RECURRENT OVARIAN CANCER PATIENTS

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Objectives
Some recurrent ovarian cancer patients developed the symptoms and found abnormal physical examination. To identify that either symptoms or abnormal physical examination could be affect the survival outcome of these patients, we conducted this study.

Methods
The ovarian cancer patients who achieved complete or partial response and developed tumor progression at the follow up time between January 2004 and December 2010 were reviewed. The basic data, the symptoms, the physical examination finding, CA 125 level and the imaging results at the tumor progression time were recorded.

Results
144 ovarian cancer patients met the inclusion criteria with the mean age of 51 years. Complete response was achieved by 89 patients (61.8%). The median progression free survival and overall survival were 15.5 months and 37.5 months, respectively. Abnormal symptoms presented in 49.3% of the studied patients and 59.7% of the studied patients developed physical examination abnormalities. In addition, CA 125 was rising in 89.6% of the studied patients while 74.3% of the studied patients were identified tumor progression by CT-scan. With Cox regression model analysis, only the short treatment time interval and the high level of CA 125 were significant independent prognostic factors for the survival outcomes while either the symptoms or positive physical examination did not reached the statistically significant factors.

Conclusions
Symptoms and positive physical examination of the recurrent ovarian cancer patients did not affect the survival outcome.
EXOSOMES IN PLASMA OF PATIENTS WITH OVARIAN CARCINOMA – A POTENTIAL BIOMARKER OF TUMOR PROGRESSION AND RESPONSE TO THERAPY

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³Pathology, University of Pittsburgh, Pittsburgh, USA

Objectives
In patients with ovarian cancer (OvCa) exosomes released by tumor cells are present in the plasma and could be involved in tumor progression. This study examines the association between exosomes presence/protein content in plasma of OvCa patients and disease outcome, response to standard therapy and/or tumor resistance to therapies in patients studied at diagnosis and also serially during and after therapy.

Methods
Exosomes were purified from the plasma of patients with OvCa (n=12) or benign tumors (n= 15) and (n=10) healthy controls (NC) using ultracentrifugation. Exosomes were visualized by scanning electron microscopy and their protein content was measured. Their partial molecular content was determined using Western blots.

Results
The OvCa patients’ plasma contained higher levels of exosomes (p<0,05) compared to those in the plasma of benign tumor patients or NC. Exosomes from plasma of subjects with OvCa carried TGF-beta and MAGE3/6 that distinguished patients with cancer from those with benign tumors and NC. High protein levels of exosomes were seen in newly diagnosed as well as less and more advanced patients. The exosome levels variably changed in chemotherapy treated OvCa patients and correlations between the exosomes quantity and clinical data suggested that exosomes protein levels are prognostically important in OvCa patients.

Conclusions
Analysis of plasma exosomes levels offers a novel approach to diagnosis and monitoring response to therapies in OvCa patients.
COMBINATION CHEMOTHERAPY WITH TEMSIROLIMUS AND TRABECTEDIN IN PATIENTS WITH RECURRENT AND REFRACTORY CLEAR CELL CARCINOMA OF THE OVARY.

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⁶Department of Basic Pathology, National Defense Medical College, Tokorozawa, Japan

Objectives
Clear cell carcinoma (CCC) of the ovary showed exceedingly chemo-resistant phenotype, especially in the case with recurrent or refractory to previous therapy. We evaluated the effect of combination therapy with temsirolimus and trabectedin for patients with recurrent/refractory CCC.

Methods
Patients with recurrent/refractory CCC of the ovary were treated with weekly regimen using two drugs: 10mg/m² of temsirolimus and 0.15mg/m² of trabectedin (3 weeks, one week rest) with written informed consents. Treatment was continued until development of progressive disease (PD) or unmanageable adverse effects. Responses were evaluated by RECIST criteria, and adverse effects were analyzed by NCI-CTCAE v4.0.

Results
A total of 12 patients treated with the regimen, and there were no cases that discontinued the therapy due to toxicities. Median age was 60 years (range: 42-69), and median number of previous chemotherapy was 3 (range: 1-5). One patient (8%) had a complete response (CR), and another (8%) achieved a partial response (PR), and 4 patients (33%) had stable disease (SD) beyond three months, resulting in clinical benefit rate (CBR; CR+PR+SD>3month) of 50%. Median response duration in CBR case was 3.5 months (range: 3-12+). There were no cases that developed toxicities more than grade2.

Conclusions
The present preliminary study demonstrated combination therapy with temsirolimus and trabectedin was effective in patients with recurrent/refractory CCC of the ovary. These results warrant further study in such clinical settings.
PROGNOSTIC PREDICTORS AND SPREAD PATTERNS IN ADULT OVARIAN GRANULOSA CELL TUMORS: MULTICENTER LONG TERM FOLLOW-UP STUDY OF 108 PATIENTS
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2Obstetrics and Gynecology, Ankara University School of Medicine Ankara Turkey
3Obstetrics and Gynecology, Ege University School of Medicine Izmir Turkey

Objectives
To identify prognostic predictors and spread-patterns in adult ovarian-granulosa-cell-tumors (OGCTs).

Methods
Retrospective available data of 108 patients with OGCTs managed at three-centers between 1/1/91–31/12/10 were abstracted and analyzed.

Results
Stage distributions at diagnosis for stage I, II and III were 84.3%, 5.4% and 9.3%, respectively. Optimal cytoreduction with no-macroscopically visible disease was achieved in 99/108 (91.6%) patients. The median disease-free interval to first-recurrence was 61 months. The overall 5- and 10-year survival rates were 93.3% and 90.9%, respectively. Disease recurred in 18 (16.6%) patients and eight (7.4%) patients died due to disease. First-recurrence sites included pelvic periton (n=10), liver/liver-capule (n=5), rectosigmoid colon (n=4), retroperitoneal lymph nodes (n=3), omentum (n=3), small bowel mesenterium (n=2) and vaginal cuff (n=2). Multiple-site recurrence was observed in 9/18 (50%) patients. Secondary cytoreduction requiring extensive surgery was performed in 14 patients with an optimality rate of 71.4%. Remaining four patients received only chemotherapy. Definitive retroperitoneal lymph-node metastasis at initial and recurrent-setting was 5.1% (3/58) and 21.4% (3/14), respectively. Both stage and residue-tumor were significantly associated with recurrence in univariate and multivariate cox-analysis.

Conclusions
Stage and residue-tumor are the predictors of recurrence. Nodal, pelvic-peritoneal and hepatic involvement, and also multiple-site spread-pattern requiring extensive surgery appear to be more at recurrent setting of OGCTs.
**e-Posters: Ovarian Cancer**

**A RARE OCCURRENCE PRIMARY OVARIAN SIGNET RING CELL CARCINOMA PRESENTED AT PREGNANCY**

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Signet ring cell carcinoma of the ovary almost always appears as metastasis of gastrointestinal tumors. Primary signet ring cell carcinoma of the ovary is extremely rare and occurrence in pregnancy is even more infrequent. We present a 29 years old women with 32 weeks of gestation underwent caesarean section due to a growing left adnexal mass that has reached 20 cm at the time of operation. With caesarean section left oophorectomy and abdominal exploration were also performed and several biopsies taken from omentum and contralateral ovary despite the lack of any suspicious lesions. Pathology examination revealed a signet ring cell carcinoma of the ovary. Further investigations about a gastrointestinal malignancy failed to demonstrate any. Thereby this indicates a primary occurrence of signet ring cell carcinoma of the ovary that developed in the course of pregnancy. After 2 months she admitted with abdominal discomfort. Imaging modalities revealed extensive ascites and right adnexal solid mass. Patient has consulted to medical oncology and 6 cycles of carboplatin/paclitaxel treatment was planned. Ascites and the size of right adnexal mass were observed to be regressed in the course of chemotherapy. Following the 5th cycle of chemotherapy, patient has admitted abdominal pain and underwent a laparotomy due to acute abdomen. Laparotomy revealed an approximately 30 centimetered solid right adnexal mass and tubo-ovarian torsion. Total abdominal hysterectomy, right adnexectomy, total omentectomy, appendectomy with bilateral pelvic and paraaortic lymph node excision performed and second line chemotherapy was planned.
THE IMPORTANCE OF MESENTERIC LYMPH NODES IN PATIENTS WITH EPITHELIAL OVARIAN CANCER WHO UNDERWENT BOWEL RESECTION

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Objectives
Maximal cytoreduction is the cornerstone of surgical treatment for epithelial ovarian cancer. To achieve zero residual sometimes it is needed to resect bowel and also some other organs involved with metastatic tumor. The number of mesenteric lymph nodes reflects the radicality of bowel resection especially for rectosigmoid tumors which define true mesometrial resection.

Methods
The patients treated for epithelial ovarian cancer including bowel resection were included for this analysis with respect to bowel lymph node status.

Results
Overall 45 patients were subject of this study. Forty patients were treated at primary surgery and five patients at secondary surgery. Twenty-one patients underwent rectosigmoid resection, 14 had total colectomy, 7 had hemicolectomy, 1 had transverse colectomy, and the remaining 2 had hemicolectomy plus rectosigmoid resection. The median resected bowel lymph node number was 8 (range, 1-61), and the distribution of these patients according to categorizes 1-3, 4-10, and >10 were 17 %, 35%, and 48%, respectively. The colon lymph node metastasis rate for 1-3 group was 25%, for the group of patients with 4-10 was 56%, and this rate for more than 10 lymph nodes was 62%. The metastatic involvement was highest for muscularis and mucosal invasions with a rate of 80%.

Conclusions
The radicality of bowel resection is very important since the rate of metastatic mesenteric lymph node number increases parallel to resected lymph node number. It is more important for patients with muscularis or mucosal invasions with a highest rate of metastatic involvement.
THE FEASIBILITY AND LONG-TERM SURVIVAL EFFECT OF TOTAL ABDOMINAL COLECTOMY IN THE SETTING OF PRIMARY DEBULKING SURGERY

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Objectives
Total abdominal colectomy (TAC) is controversial area of interest with only published two series reporting the results of 32 patients. This is the largest second series with morbidity and long-term survival effect of this aggressive procedure at primary cytoreductive surgery.

Methods
The patients who underwent TAC for epithelial ovarian cancer were included. The data was obtained from prospectively recorded special gynecologic oncologic forms.

Results
Overall eighteen patients were subject of this study and optimal cytoreduction was achieved for all patients. Ileorectal or –anal anastomoses were performed with diverting ileostomies except for two patients. Anastomoses were end to end for 14 patients, side to end for 3, and ileal J pouch for the remaining one patient. Only one patient had anastomotic leak which was treated successively with conservative management. Several additional surgeries were performed besides TAC to achieve debulking. There was only one surgical mortality within postoperative 30 days who was died of sudden MI at postoperative 15th day without any other problem. The median survival for all group was 32 months, and six patients were alive more than 36 months.

Conclusions
TAC is a feasible procedure at experienced centers having morbidity no more than patients with bowel resection, and also it may have satisfactory survival rate. There are only a few patients reported in the published series and it is needed more knowledge to suggest this aggressive procedure routinely. But both the current series and the others have promising results for further larger studies.
THE ROLE OF PREOPERATIVE SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR AND MIGRATION INHIBITOR FACTOR IN THE DIFFERENTIATION OF BENIGN AND MALIGNANT ADNEXIAL MASSES

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Objectives
The aim is to identify the role of preoperative serum vascular endothelial growth factor (VEGF) and migration inhibitor factor (MIF) in the differentiation of benign and malignant adnexial masses and the relationship between the prognostic factors and VEGF and MIF in the ovarian cancer patients.

Methods
21 patients with malignant and 20 patients with benign adnexial masses who administered to Ege University Obstetrics & Gynecology Department between November 2010 and March 2012 are included. Serum samples are obtained preoperatively and saved at -80°C. Patients are divided into two groups according to their pathology as benign or malignant. The age of patients, CA125 levels, grade, stage, presence of assist and the degree of cytoreduction performed are noted. The preoperative serum VEGF and MIF levels are calculated with the help of RayBio® Human VEGF ELISA Kit ve RayBio® Human MIF ELISA Kit. Thermo Scientific® Multiscan FC spectrometer is used.

Results
There is no significant difference between two groups for serum VEGF, MIF (p>0.05), CA125 levels are significantly higher in malignant group (p<0.05). There is no significant difference between two groups for tumor grade, stage, presence of assist and the degree of cytoreduction performed (p>0.05).

Conclusions
The use of VEGF and MIF which are angiogenic markers neither in the differentiation of malignant and benign adnexial masses nor as the prognostic factors are not suitable. Because there are opposite results in the literature, larger studies are needed to elucidate this topic.
NEW MODELS OF ULTRASOUND PARAMETERS IN PREOPERATIVE TRIAGE OF ADNEXAL TUMORS

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Objectives
The aim of this study was to determine the predictors of tumor nature from standard ultrasonographic data, and based on them, form models that could be used in preoperative triage of adnexal tumors.

Methods
Study involved all women that were operated due to adnexal tumors throughout a period of 36 months in the Clinic for Gynecology and Obstetrics, Clinical Center of Serbia. On admission expert ultrasound scan was performed for every woman. We registered if the tumor was multilocular, bilateral, had solid parts, septa, mixed consistency and papillae, was accompanied by ascites, and measured tumors diameter (<5cm, 5-10cm, >10cm), Doppler RI and PI. Achieved data were compared with postoperatively obtained histopathological findings of tumors (malignant, benign). Method of multiple binary logistic regression was applied in order to create the models of associations.

Results
Study included 609 women. Statistically significant model was achieved using Enter method (χ²=887.224; p=0.000 classification success=75.0%; R² Nagelkerke=0.816): MALIGNANCY = 0.290 + 0.724xDIAMETER + 0.877xSOLID PARTS + 2.118xPAPILLAE + 2.272xASCITES – 8.707xRI.

Conclusions
The best predictors of malignancy are the larger diameter of tumors, more solid parts and papillae, presence of ascites and lower RI. For more reliable triage of adnexal masses and better understanding of ultrasound findings we propose introduction of this model in routine clinical practice.
GRANULOSA TUMORS OF THE OVARY – OUR EXPERIENCE

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Objectives
This study wants to evaluate cases with granulosa ovarian tumor treated by surgery in our clinic.

Methods
Between January 2003 and December 2011, 289 women with ovarian cancer, invasive and with low malignancy were treated in the 1st Clinic of Obstetrics and Gynecology from Iasi. Only 12 were with granulosa cell tumors. Clinical and pathologic information were obtained from medical records.

Results
The mean age of these patients was 50.75±4 years. Almost all women were at menopause - 10 patients. 9 of them presented abnormal vaginal bleeding and other 3 pain in the abdomen, but all cases had at the pathological exam endometrial hyperplasia. CA 125 was normal before surgery for all women. Dimension of the tumor was between 6cm and 23cm. The tumor was always unilateral, more often on the left side – 9 cases. For 11 patients we decided total abdominal hysterectomy with bilateral salpingo-ooforectomy and only for one young woman unilateral salpingo-ooforectomy. All tumors were found in stage I. 5 of them presented ascites and 1 hemoperitoneum. Only 1 patient received chemotherapy – carboplatin, 3 months after surgery, because CA125 was elevated. Recurrence occurred for 2 cases, one after 2 years in pelvis and one after 10 years with lung metastases.

Conclusions
A Granulosa Cell Tumor is one of the rarest forms of ovarian cancer – 1.97% in our study. It is more common in post-menopause women. Surgery is the mainstay of initial management for histological diagnosis, and appropriate staging. Prolonged surveillance is mandatory because tumors tend to recur years after the initial diagnosis.
AUDIT OF COMPLETENESS OF STAGING OF FIGO STAGE 1 OVARIAN CANCER AT CHELTENHAM GENERAL HOSPITAL (CGH)

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Background
The management of stage I ovarian cancer where disease is limited to one or both ovaries is summarised within the NICE guideline CG122 and the associated Quality Standard 18. These state that women with suspected stage I disease should have optimal surgical staging including retroperitoneal lymph node sampling¹. Up to 22% of patients with apparent stage 1 disease may have micro metastases in the lymph nodes, which would upstage the disease from I to III, and have an impact on chemotherapy offered.

Methods
A search of the South West Cancer Registry database identified all possible or definite stage I ovarian cancers having a procedure at CGH between January 2010 and December 2011. Definite stage I diagnoses were identified and details of their operations obtained from electronic systems and case notes. A similar search identified patients with a stage I diagnosis between April 2012 and March 2013, and dataset was obtained for these patients in order to compare practice.

Results
12 cases identified in 2010-11. 8% had only PA node sampling, 8% had only pelvic node sampling and 8% had both PA and pelvic nodes.

9 cases identified in 2012-2013. 89% had PA nodes and 67% had pelvic nodes.

Conclusions
Since the introduction of the NICE guideline and Quality Standard in 2011/2012, the percentage of patients with stage I ovarian cancer having optimal surgical staging has improved, however, it is still falling short of 100%. One key area where improvement could be made is in the sampling of pelvic nodes.

References
WOLFFIAN ADNEXIAL TUMORS: REPORT OF TWO CASES
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Objectives
Wolffian adnexial tumor (WAT) is a rare tumor arising from remnants of the mesonephric duct. These tumors usually considered as benign, although in some cases metastasis or recurrences have been reported.

Methods
We analyzed patients who treated for gynecological cancer between 2005 and 2012 at our institution retrospectively. We identified 2 patients with WAT and described the clinicopathological characteristics.

Results
49 and 51 year old two postmenapausal women underwent laparatomy with a diagnosis of pelvic mass. Case1: Intraoperative frozen section diagnosis of the tumor was Carcinoid. Total abdominal hysterectomy (TAH), bilateral salpingoophorectomy (BSO), pelvic and paraaortic lymphadenectomy (PPALND) and omental biopsy was performed. Final pathology revealed WAT with capsule invasion, 4/10 Mitosis, calssified and bony material inside tumor. Immunohistochemical staining was positive for kalretinin, vimentin, inhibin and SMA. Lymph nodes and cytology were negative for tumor spillage. Follow-up has been carried out for 5 years after 6 cycles of Paclitaxel and Carboplatin, and the patient remains free of signs of relapse. Case2: Intraoperative frozen section was not diagnostic for this patient. Because of the malignant appearence TAH, BSO, PPALND and omental biopsy was performed. Final pathology revealed WAT with wide necrosis and no mitosis. Immunohistochemical staining was positive for kalretinin, vimentin and CK-7. Lymph nodes and cytology were negative for tumor spillage. Follow-up has been carried out for 6 years after 6 cycles of Paclitaxel and Carboplatin, and the patient remains free of signs of relapse.

Conclusions
Due to scarce literature support to determine the treatment of this rare tumor, we need more data beyond we had.
A RARE ASSOCIATION OF NEUROFIBROMATOZIS-1 AND OVARIAN CANCER

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Objectives
Neurofibromatosis 1 (NF1) is a tumor predisposition genetic syndrome with autosomal dominant inheritance. NF1 results from a loss of function in the NF1 gene resulting in decreased levels of neurofibromin. Neurofibromin is a negative regulator of intracellular signaling pathways involved in the proliferation of cell. Thus loss of function in the NF1 gene, may predispose NF1 patients to certain malignancies. Somatic mutations in NF1 may lead ovarian carcinoma.

Methods
A case report

Results
A 39 year old women with neurofibromatosis type 1, underwent laparotomy with diagnosis of bilateral ovarian mass. Preoperative Ca125 level was 906 U/ml. Intraoperative frozen-section analysis revealed at least borderline serous neoplasia. Total abdominal hysterectomy, Bilateral salpingooopherectomy, pelvic and paraaortic lymphadenectomy, omentectomy and appendectomy were performed. Final pathologic examination detected bilateral low grade serous carcinoma with appendiceal, omental, paraaortic lymph node metastasis and malignant cells on peritoneal washings. Adjuvant chemotherapy was offered with 6 cycles of Paclitaxel and Carboplatin. The patient is still free of relapse.

Conclusions
The association between neurofibromatosis and gynecologic malignancies is rarely reported in the literature. Early age at onset of malignancy with NF1 suggests genetic predisposition to these cancer. One study reported a family with two linked mutations at the NF1 and BRCA1 loci and NF1 associated multiple coelomatic cancers including ovarian cancer affecting individuals of this family. Both BRCA1 and NF1 genes are located on the long arm of chromosome 17. Now with the scarcity of data it is difficult to ascertain which of these are random occurrences or may represent true associations with NF1.
e-Posters: Ovarian Cancer

ADNEXAL MASS IN PATIENTS WITH GASTROINTESTINAL MALIGNANCY
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Objectives
Adnexal masses are importantly from the ovarian origin whether benign or malignant or metastatic. Adnexal mass with gastrointestinal malignancy creates a dilemma for gynecologists.

Methods
74 patients with primary gastrointestinal system malignancy who had undergone surgery for an adnexal mass between January 2000 and January 2011 were retrospectively studied.

Results
Of the 74 cases, the most seen primary origin was colorectal cancer with 49 patients (66.21%), and followed by gastric cancer with 20 patients (27.02%). The mean age of the patients was 49.1. Fourty eight (64.8%) women were postmenopausal. The most common presenting symptom was pelvic pain with 43 women (58.1%). Fourty four of these patients (59.45%) have been metastasized from the gastrointestinal system. The other thirty had an adnexal mass originated from the ovary and 23 of them (31.1%) were benign whereas the other 7 women were (9.45%) with primary ovarian malignancy. 32 of metastatic lesions were adenocarcinoma whereas 12 were in krukenberg pathology. Complexity of the adnexal mass was found to be significant for malignancy (p<0.001). Most metastasized tumors involved bilateral ovaries (p<0.001). Adnexal mass >5cm size was an important factor for the risk of malignancy additionally a greater part of metastasized tumors were >5cm. Increased levels of CA 125 was a risk factor for malignancy so did CEA with a p value 0.047.

Conclusions
Simultaneous serum CA 125 and CEA levels with sonographic characteristics should be considered during the evaluation of adnexal masses in patients with gastrointestinal malignancy.
LYMPH NODE METASTASIS IN PATIENTS WITH EPITHELIAL OVARIAN CANCER MACROSCOPICALLY CONFINED TO THE OVARY: REVIEW OF A SINGLE-INSTITUTION EXPERIENCE

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Objectives
To evaluate the patterns of lymphatic spread in epithelial ovarian cancer macroscopically confined to the ovary and risk factors for lymph node metastasis.

Methods
All patients with clinical stage IA/B epithelial ovarian cancer who underwent staging laparotomy were identified retrospectively. Lymph node positivity and surgical-pathologic findings were recorded and risk factors that may have been associated with upstaging of the cancer were assessed.

Results
Two hundred and thirty-six (n: 236) consecutive patients were operated for primary epithelial ovarian carcinoma. Forty-one of these patients (17.3%) who underwent comprehensive staging laparotomy with systematic pelvic and paraaortic lymphadenectomy had tumors confined to one or both ovaries (stage IA/B). Of these 41 patients, 9 patients (21.9%) were found to have microscopic metastasis after post-operative pathological evaluations and their disease was consequently upstaged. After reviewing of the pathological specimens, the final staging of the patients were 32 IA/B (78%), 3 IC (7.3%), 3 IIA (7.3%), 1 IIA (2.4%), and 2 IIIC (4.9%). Two patients (4.9%) had lymph node involvement. Both of these patients had lymph node metastases in the ipsilateral pelvic lymph nodes, their ovarian capsules were intact and the tumors were grade 3. None of the patients had para-aortic or contralateral pelvic lymphatic involvement. While presence of ascites was not associated with an increased risk of lymph node involvement (p: 0.47), positive peritoneal cytology (p: 0.018) and grade 3 disease (p: 0.013) were significant predictors of lymph node involvement.

Conclusions
In clinical stage IA/B ovarian cancer patients, comprehensive staging surgery added diagnostic value beyond careful inspection of all benign appearing tissues.
e-Posters: Ovarian Cancer

DESIGN AND VALIDATION OF A PHYSICIAN-BASED SURVEY TO DETERMINE CURRENT PATTERNS OF TREATMENT FOR RECURRENT EPITHELIAL OVARIAN CANCER

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Objectives
To develop a robust, validated, web-based survey for physicians about treatment patterns for recurrent epithelial ovarian cancer (OC).

Methods
The survey was conducted double-blinded (to participants and those who analysed the data) in 9 countries (Australia, Brazil, Canada, France, Germany, Italy, Spain, UK, US) via a semi-structured web questionnaire of open-ended responses, multiple-choice fixed responses and case studies on the treatment of first-line and recurrent OC. Four physicians contributed to the questionnaire design to ensure content validity. Eligible physicians were specialists in oncology or gynaecology with ≥2 years’ clinical experience. Physicians were excluded if in the last 12 months they had not treated patients with stage III/IV epithelial OC or had treated <10 patients with recurrent disease. The questionnaire was translated to local languages and validated in a pilot phase completed by 2 respondents per country (19 physicians total). Following completion of the pilot survey, minor amendments were made based on pooled results to ensure construct validity. The main survey aimed to collect data from 30 physicians from each country (60 US) and was approved by the University of Technology, Sydney, and Human Research Ethics Committee.

Results
311 physicians from 9 participating countries completed the main survey (Table). Physicians were primarily medical oncologists in university or community hospitals. Completion rate (311/355; 88%) was high for a web-based survey.

<table>
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<th>Recruitment, n</th>
<th>Australia</th>
<th>Brazil</th>
<th>Canada</th>
<th>France</th>
<th>Germany</th>
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<td>560</td>
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</tbody>
</table>

Conclusions
This validated survey allows collection of detailed clinical practice information that will improve understanding of current treatment patterns for OC.
**Diagnosis of Delayed Subacute Cerebellar Degeneration in a Patient with Ovarian Cancer**

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**Objectives**
Here, our aim is to represent a subacute cerebellar degeneration case emerged in a patient after the diagnosis of ovarian cancer.

**Methods**
We reviewed the medical records of the patients.

**Results**
Paraneoplastic syndromes can be defined as remote effects of cancer that are caused by mechanisms other than metastases, metabolic and nutritional deficits, infections, coagulopathy or side effects of cancer therapy. Here, we describe a patient with peripheral neuropathy and cerebellar dysfunction with known synchronous ovarian and endometrial cancer.

A 61-year-old woman was underwent exploratory laparotomy for a pelvic mass. In the final histology synchronous high grade ovarian serous carcinoma and endometrial serous carcinoma were reported. Following the third cycle of chemotherapy she was suffered from numbness and tingling on her toes. After fourth cycle these complaints spread to her hands after fifth one she needed assistance during walking. On the approaching days of last chemotherapy cycle her complaints of weakness, nausea, tightness in chest and unable to stand up from sitting position emerged. Anti-yo (purkinje cell antibody-1) level was found as ‘3 positive’ using western blot. Cranial MRI scan was uncharacteristic.

**Conclusions**
It is unusual to detect paraneoplastic neurologic manifestations after the diagnosis of an underlying malignancy. The current patient received the diagnosis of paraneoplastic neurologic syndrome five months after the primary surgery for pelvic malignancy. Due to their high specificity, the best way to diagnose a neurologic disorder as paraneoplastic is to identify one of the well-characterized anti-onconeural antibodies in the patient’s serum.
e-Posters: Ovarian Cancer

OVARIAN BURKITT’S LYMPHOMA IN AN ADOLESCENT: A CASE REPORT.
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Objectives
Our aim is to declare a rare pathology, a primary ovarian Burkitt's lymphoma seen in an adolescent.

Methods
We reviewed the medical records of the patient.

Results
Majority of ovarian Burkitt’s lymphomas is the result of spread from other organs. Primary ovarian Burkitt's lymphoma is a rarely encountered tumor and can not be easily distinguished from other ovarian malignancies clinically or with imaging methods. Herein, we represent a case of ovarian Burkitt’s lymphoma in an adolescent girl.

An adolescent girl with the complaints of abnormal vaginal bleeding for two months was admitted to our clinic. In physical examination and pelvic ultrasonography, bilateral ovarian masses and ascites were found. The right mass was 7 cm and the left one was 6 cm in size. An explorative laparotomy was performed. During laparotomy, frozen-section evaluation of ovarian wedge biopsy revealed malignant round cell tumor resembling non-hodgkin lymphoma. Final pathologic and immunohistochemical evaluation revealed ovarian Burkitt’s lymphoma. With the consultation of department of pediatric haematology, chemotherapy was planned.

Conclusions
Primary ovarian Burkitt’s lymphoma is an uncommon entity. Despite its rarity, ovarian Burkitt’s lymphoma is one of the masquerading conditions of other ovarian malignancies especially of epithelial ones. Although it mimicks ovarian cancer in appearance, its primary treatment is chemotherapy. In order to avoid unnecessary surgery one must utilize frozen-section during operation of an ovarian mass especially in adolescent patients.
NRF2 MEDIATES CISPLATIN CHEMORESISTANCE THROUGH ACTIVATION OF AUTOPHAGY IN OVARIAN CARCINOMA

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Objectives
Cisplatin chemoresistance remains a severe challenge for ovarian carcinoma treatment. NF-E2-related factor 2 (Nrf2), a nuclear transcription factor has an important role in chemotherapy resistance. However, the underlying mechanism between Nrf2 and cisplatin chemoresistance is unclear.

Methods
We derived human ovarian carcinoma cell line, A2780, and its cisplatin-resistant variant, A2780cp. Cell viability was determined by WST-8 assay. Western blot was used to detect the expression of Nrf2, microtubule-associated protein 1 light chain 3 (LC3) and p62. The ultrastructural analysis of autophagosme was performed by transmission electron microscopy (TEM).

Results
Nrf2 was overexpressed in A2780cp compared with that in A2780. Knocking down of Nrf2 by RNA interference resensitized A2780cp to cisplatin. Interestingly, we found that autophagy protein marker LC3-II and autophagy substrate p62 were also downregulated accompanied with decreased Nrf2. Further, we demonstrated that in both cell lines cisplatin could induce the formation of autophagosome and upregulate the expression of autophagy protein marker LC3-II, analysis of which showing that the level of autophagy in A2780cp cells was significantly higher than that in A2780. Co-treatment of cisplatin with autophagy inhibitor 3-Methyladenine (3-MA) could increase A2780cp to cisplatin-induced cell death, suggesting that inhibition of autophagy rendered resistant cells more sensitive to cisplatin. Taken together, Nrf2 signaling may regulate cisplatin resistance through the activation of autophagy response.

Conclusions
Nrf2-activated autophagy may function as a novel mechanism causing cisplatin chemoresistance. Prospective studies are necessary to elucidate the detailed mechanism of how Nrf2 regulates autophagy in chemoresistant patients.
e-Posters: Ovarian Cancer

STRICT CRITERIA FOR SELECTION OF WOMEN WITH ADNEXAL MASS TO LAPAROSCOPY
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Objectives
Compare the indication of laparoscopy for diagnosis and treatment of adnexal masses based on strict rules defined by risk scores and tumor diameter with the indication based on surgeon’s experience

Methods
Prospective study with 174 women who underwent surgery due to the presence of adnexal tumors (116 laparotomies and 58 laparoscopies). Surgeries completed by laparoscopy with benign diagnosis were considered successful. Laparoscopies that needed conversion to laparotomy, had a malignant diagnosis or cyst rupture were considered failure. Two groups were defined for laparoscopy indication: 1- absence of ACOG (American College of Obstetrics and Gynecology) guideline for referral of high risk adnexal masses (ACOG negative) associated with 3 different tumor sizes (10, 12 and 14cm); and 2- IRM (Index of Risk of Malignancy) with cutoffs at 100, 200, 300, associated with the same 3 tumor sizes; were compared with the indication based on surgeon’s experience to verify if the selection based on strict rules would improve the rate of successful laparoscopy

Results
ACOG negative and tumors of ≤10cm restricted the indication of laparoscopy to 49 women with 38 (78%) successful cases. The IRM with cutoff at 300 points and tumors ≤10cm result the same (78% success). Although there was an increase in the success rate of laparoscopy with both types of standardized selection compared with the results of the surgeon’s experience, those data were not statistically significant

Conclusions
The selection criteria at study performed similarly as the experience of a gynecology oncologist and could be used to select women to laparoscopy by general gynecologists
Objectives
Cyclooxygenase-2 (COX-2) expression has been reported to be elevated in many neoplasms. The new hypothesis of ovarian cancer pathogenesis divides tumors into two groups: type I and type II. Both COX-2 enhanced expression and type II ovarian cancer are related to the worse prognosis. It can be hypothesized that COX-2 overexpression is associated with the mechanisms of development of type II tumors. The aim of this research was to verify if COX-2 expression is related to the new pattern of tumorigenesis.

Methods
Ovarian cancer tissues were obtained from 65 patients in FIGO III stage. COX-2 protein expression was evaluated by immunohistochemistry. The assessment of COX-2 expression was done by a semi-quantitative scale. For statistical analysis U Mann-Whitney test, the log-rank test and Kaplan-Meier curves were applied.

Results
COX-2 expression was revealed in 91% of tissue samples. The distribution of type I and type II ovarian cancer tissues was 25% and 75%, respectively. Both overall survival (OS) (p=0.0369) and progression free survival (PFS) (p=0.0218) were diminished in patients with increased COX-2 expression. Type I tumors were not related to improved prognosis; OS (p=0.7146), PFS (p=0.4116). There was no difference between COX-2 expression in type I and type II ovarian cancer (p=0.6720).

Conclusions
COX-2 overexpression is related to an unfavorable prognosis in ovarian cancer. The tumor progression model dividing ovarian cancer into type I and type II does not reflect the overall survival and progression free survival. There is no relationship between COX-2 expression and hypothesized pattern of tumorigenesis.
e-Posters: Ovarian Cancer

THE INFLUENCE OF FIBRONECTIN ON THE FORMATION OF MULTI-CELLULAR SPHEROIDS OF OVARIAN CANCER

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Objectives

It was reported that the multi-cellular spheroids in ascites in ovarian cancer were closely related to invasion, migration and progression of the neoplasm. A study indicated that ovarian cancer ascites contains more FN than the peritoneal flushing fluid of patient with benign ovarian tumor. To investigate whether Fibronectin participates in the formation of multi-cellular spheroid of ovarian cancer and which integrin receptor involves in this progress.

Methods

In vitro the model of multi-cellular spheroid of SKOV3 was constructed by liquid overlay technique and the influence of Fibronectin on the formation of the spheroid was observed. Finally, the gene expressions of potential integrin receptors were examined from mRNA and protein level by reverse transcription real time PCR and western-blot.

Results

1) Fibronectin stimulates the formation of multi-cellular spheroid of ovarian cancer bigger than 250μm; 2) Fibronectin suppresses the expression of subtype of integrin receptor ITGA5 from mRNA and protein level.

Conclusions

1) Fibronectin can enhance the formation of multi-cellular spheroid of ovarian cancer; 2) Subtype of integrin receptor ITGA5 probably involves in the formation of multi-cellular spheroids.
ROBOTIC SURGERY DOES NOT INCREASE THE RISK OF TROCAR SITE METASTASIS IN PELVIC CANCERS
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Objectives
To assess the risk of occurrence of trocar site metastasis after robotic surgery for pelvic cancer

Methods
Retrospective study from January 2007 to February 2013. Patients with gynecologic cancer who underwent robot-assisted surgical treatment were included. We collected preoperative data, including characteristics of patients and FIGO stage, intraoperative data (surgery performed, number of ports), and postoperative data (occurrence of metastasis, occurrence of port site metastasis).

Results
115 patients were included in the study: 61 with endometrial cancer, 50 with cervical cancer and 4 with ovarian cancer. The surgical procedures performed were: hysterectomy with bilateral salpingo-oophorectomy, radical hysterectomy, pelvic lymphadenectomy, para-aortic lymphadenectomy and omentectomy. All surgical procedures have necessitated the introduction of 4 ports, 3 for the robot and 1 for the assistant. With a mean of 504.8 days (452.2 days for cervical cancer, 550.1 days for endometrial cancer, and 472.5 for ovarian cancer), we observed 8 recurrences but no port-site metastasis.

Conclusions
There is no increase of recurrence on trocar site with robotic surgery for pelvic cancers.
e-Posters: Translational Research

POTENTIAL FUNCTIONAL IMPLICATIONS OF NSSR1 IN ENDOMETRIAL CARCINOGENESIS
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Objectives
NSSR1 is a member of the serine / arginin rich protein family and acts as a repressor of alternative splicing processes. Initially NSSR1 expression was detected in neural tissues. Later, NSSR1 expression was found in tissues of reproductive systems, e.g. epithelial endometrium suggesting a potential functional role in regulation of gene expression in these organs. NSSR1 is one potential novel target gene that might play crucial roles in endometrial carcinogenesis and metastasis. Functional in vitro analyses were designed to investigate potential alterations in expression profiles of NSSR1.

Methods
Experimental setup mimicked hypoxic conditions, extracellular acidosis or hyperthermia vs. regular conditions (control) in vitro. mRNA expression levels were analyzed by qPCR, followed by statistical analyses. Protein expression levels were determined by Western blot and immunocytochemistry. Protein expression levels were determined by Western blot and immunocytochemistry.

Results
Functional analysis revealed variable effects of hypoxia, acidosis and hyperthermia on the mRNA and protein expression of NSSR1 in regard to different cell lines. Acidic conditions induced a significant up-regulation of NSSR1 mRNA expression in all endometrial cell lines, under hypoxia and hyperthermia differing response reactions were observed in the cell lines tested. In contrast; NSSR1 protein translocated from the nucleus to the cytoplasm after acidosis and hypoxia, and variant responses were observed after hyperthermia.

Conclusions
Hypoxia, extracellular acidosis and heat shock response are known as tumor microenviromental epiphenomena or exogenous stresses. We have demonstrated their effect in vitro, and based on our results we reached a better understanding of molecular NSSR1 gene regulation under these conditions.
e-Posters: Translational Research

POTENTIAL FUNCTIONAL ROLE OF EZH2 IN ENDOMETRIAL CARCINOGENESIS
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Objectives
Functional in vitro analyses were designed to investigate potential alterations in expression profiles of EZH2 in endometrial cancers in vitro. In detail, typical microenvironmental epiphenomena of solid tumors (hypoxia, extracellular acidosis) as well as therapeutical approaches (hyperthermia) were mimicked in cell culture models. The polycomb group protein EZH2 acts as a transcriptional repressor and controls cellular memory and methylation processes. So far, the factor was found highly expressed in malignant vs. physiological tissues in several tumor entities.

Methods
Endometrial cancer cell lines were cultured to more than 80% confluence. Experimental setup mimicked hypoxic conditions, extracellular acidosis or hyperthermia vs. regular conditions (control). mRNA expression levels of EZH2 were analyzed by quantitative RT-real-time PCR, followed by statistical analyses. Protein expression levels were determined by Western blot and immunocytochemistry.

Results
Acidic conditions as well as hyperthermia were identified as strong inductors of increased EZH2 expression levels in all cell lines tested. In contrast, hypoxia uniformly caused a down-regulation of EZH2 expression. EZH2 protein localization switched from complete nuclear expression under regular culture conditions to nearly complete deficiency of nuclear protein under hypoxia, acidosis and hyperthermia.

Conclusions
The obtained results clearly indicate the regulatory effects of acidosis, hypoxia and hyperthermal treatment on both, the mRNA and protein expression levels of EZH2. Thus, this factor might be of important relevance for tumor progression and metastasis with inferential therapeutic implications.
NOVEL ALTERNATIVELY SPLICED ISOFORM OF SYNUCLEIN GAMMA

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Objectives
Since Synuclein γ (SNCG) is found highly expressed in advanced breast cancer it was initially described as breast-cancer specific gene (BCSG1). SNCG can stimulate ligand-dependent transcriptional activity of estrogen receptor alpha. Thus, SNCG might be an auspicious prognostic marker and therapeutic target for the treatment of estrogen-dependent cancers. We analyzed expression of SNCG mRNA isoforms in regard to typical tumor epiphenomena in vitro in endometrial cancer.

Methods
Endometrial cancer cell lines with varying receptor status and one SNCG-positive breast cancer cell line T47D were cultured under hypoxic, acidic or control conditions. RNA and protein isolation was followed by PCR, Western blot and immunohistochemistry.

Results
In comparison to T47D, endometrial cancer cells displayed a general significantly reduced expression of SNCG isoform 1 - 4. In contrast, a novel, shortened mRNA variant of isoform 2 was identified. Hypoxia and acidosis triggered a marked up-regulation of the novel isoform 2 short, while the expression of constitutive isoform 2 did not significantly change under altered conditions. Protein analysis revealed a hypoxia- and acidosis- dependent increase in SNCG protein expression.

Conclusions
We hypothesize, that the novel SNCG isoform 2 short bears a specific oncogenic potential in endometrial cancer cells, since it could be detected in elevated levels under hypoxic and acidic conditions, as typical epiphenomena of solid tumors. Furthermore we postulate that this novel isoform is capable to code for a biologically active protein isoform. Since up to date no isoform-specific antibody is available for explicit SNCG isoform characterization, a definite verification is subject to current further analysis.
INFLUENCE OF HYPERTHERMIA ON ESTROGEN-DEPENDENT FACTORS IN BREAST CANCER IN VITRO

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Objectives
Hyperthermia is frequently applied in anti-cancer treatment procedures, usually in addition to classical adjuvant treatment. So far, the accessory positive effects of the combined therapy are poorly understood in regard to its molecular background and deserve detailed study. The RNA helicases p68 (DEAD-Box5, DDX5) and p72 (DEAD-Box17, DDX17) act as transcriptional co-activators of various tumor-relevant genes, e.g. estrogen receptor alpha (ERα). DDX17- and DDX5-expression correlates with respectively decreased and increased Her2/neu expression in breast cancer. Both factors regulate ERα activity in carcinoma of the breast. Estrogen sulfotransferase 1 (SULT1E1) catalyzes the conjugation of a sulfate group to the estrogen molecule, whereby strongly limiting the linking of estrogen to ERα, hence most probably inhibiting its activity. In this study, we analyzed the potential regulatory influence of hyperthermia on breast cancer-relevant factors ERα, DDX5, DDX17 and SULT1E1.

Methods
Several ERα-positive breast cancer cell lines (MCF-7, T47D, ZR-75-1, BT474) received hyperthermal treatment. Parallel culture of cell lines under regular culture conditions served as control. Gene expression of ERα, DD5, DDX17, and SULT1E1 was analyzed by RT-PCR, Western blot and immunocytochemistry.

Results
Hyperthermia triggers a decrease in ERα, DDX5 and DDX17 expression on mRNA and protein level. In contrast, SULT1E1 expression is upregulated by hyperthermia.

Conclusions
The analysis reveals significant regulatory effects of hyperthermia on the breast cancer-related factors in vitro. Our findings demonstrate positive effects of hyperthermal treatment by modulation of important tumor-biological factors on the molecular level, thereby supporting classical anti-cancer strategies. Hyperthermia-dependent signaling pathways and its concomitant phenomena are subject of further studies.
CHEMOTHERAPEUTIC EFFECT ON THE CANCER CELL IN BIOMECHANICAL ENVIRONMENT

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Objectives
Chemotherapy is always the first choice for patients with cancer. Cisplatin and paclitaxel modulate the signaling pathways involved in apoptosis by DNA damage. DNA damage was increased in a time dependent manners by comet assay. Combination drug effect of cisplatin and paclitaxel was confirmed by scanning electron microscopy (SEM). This study suggests the cancer cell with chemotherapy is altered in biomechanical environment.

Methods
Six cancer cell lines and two primary cells, were used in this study. Cervical (HeLa, KB), Ovarian (SNU-8, -119, NIH:OVCAR-3, SK-OV-3, Ishikawa) cancer cell lines, primary cervical and ovarian cancer cells were investigated to define chemotherapeutic effect in cancer microenvironment

Results
Cytotoxicity of cisplatin(50uM) and paclitaxel(50uM) combination drugs is expressed as IC50 values. Combination drugs caused 50% reduction of absorbance at 540 nm relative to untreated cells, confirmed by the MTT assay. Cervical cancer cells and ovarian cancer cells decreased time dependently. Length of the comet tail per length of the comet head, which was defined as DNA damage, was measured in at least 80 cells per sample. Cervical cancer cells (primary cell, HeLa and KB) became bigger with blebs. Ovarian cancer cells (primary cell, SNU-8, -119, SK-OV-3, Ishikawa) have appeared with shrinkage of cytomembrane which forming apoptotic bodies after the combination treatment.

Conclusions
The biologic mechanisms are supported by experimental data. This research hope to shift the paradigm of cancer management from cytotoxic therapies to more individualized ones that are targeted against specific pathological features of each cancer and move from an organ-specific approach towards a more target-specific strategy.
SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs) ANALYSIS OF BRAC AND ERCC1 AS PREDICTOR OF RECURRENCE AFTER CHEMORADIATION FOR CERVICAL CANCER PATIENTS.

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Objectives
A number of patients with locally advanced cervical cancer will recur despite presenting initial response to chemoradiation. SNPs of DNA repair genes have been found to be predictors to efficacy of chemotherapy and radiotherapy.

Methods
We evaluated the presence of SNPs in ERCC1, BRAC 1 and 2 genes. We analysed paraffin-embedded biopsies from patients who had relapsed after receiving treatment with chemoradiation for SNPs of the mentioned genes. The status of the alleles wild type (wt) or at least 1 SNP was compared with time to progression (TTP) and toxicity.

Results
90 patients who experience recurrence of their cervical cancer were included in the analysis. Of those, we only could obtain evaluable tumour from 43 patients. Median age: 52.5 yrs (31-81). Histology: 32 squamous cell, 8 adenocarcinoma, 3 adenosquamous. We did not find any difference between mutated and no mutated SNP in ERCC1. One SNP in BRAC1 (rs12516) was found to be significantly associated with better TTR for the mutant variant compared to the wild-type (124 m. vs. 14 m.). Furthermore, all six patients who presented with severe (grade 3-4) toxicity had this wild-type SNP (rs12516) in BRAC1 gene. Instead, two mutated SNPs in BRAC2 were associated with higher risk for recurrence comparing the...
Conclusions:
We have identified SNPs in BRAC1 and BRAC2 which seem to correlate clinical outcome in patients with cervical cancer. Further prospective analysis need to be done to clarify their prognostic value.
e-Posters: Translational Research

SERUM LEVEL OF L1CAM AND ALCAM IN WOMEN WITH OVARIAN OR ENDOMETRIAL CANCER – PILOT STUDY.
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Objectives
Adhesive molecules, including L1CAM and ALCAM, are cell surface glycoproteins responsible for cell-to-cell and cell-to-matrix adhesion. It has been proved that they may play an important role in oncogenesis. The aim of the study was to assess the serum level of L1CAM and ALCAM in women with endometrial or ovarian cancers compared to healthy controls and verify their potential value as cancer markers for further research.

Methods
Specimens of human serum from 37 patients (13 with ovarian cancer and 24 with endometrial cancer) were taken to assess the concentration of L1CAM and ALCAM. The expression of the molecules was also measured in 42 healthy controls. The serum concentration of the two molecules was measured with a standard ELISA test (Uscn E90002Hu and Uscn E90959Hu).

Results
There was no significant difference in the ALCAM expression between the ovarian or endometrial cancer groups and healthy patients. In patients with endometrial cancer the average L1CAM expression was higher than in healthy controls, but the difference was not statistically significant (p>0.05). There was no difference in L1CAM expression between the ovarian cancer and the control group.

Conclusions
This is a pilot study to determine the role of L1CAM and ALCAM in ovarian and endometrial cancers. ALCAM doesn’t seem to be an interesting target for further research in gynecological cancers. There may be a place for L1CAM expression analysis in endometrial cancer, although its expression did not significantly differ between patients and controls. This result and all the presented data should be verified by a further research in larger groups of patients.
Abstract

RISK FACTORS FOR GYNECOLOGIC CANCERS ON HEALTHY WOMEN AGE 30-65
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Objectives
Was to determine the risk factors of gynecological cancer in a healthy women population.

Methods
The study comprised 30 women aged 30-65, lives in Baglica Village, between 1-30th March 2012. Data was collected by home visits.

Results
Risk factors for gynecologic cancer was following: %13.3 of working women earn minimum charge. %59.4 of women have 3 or more child. Women married under age 18 was 60%. 30% of women smoking.

16.7% of women have bleeding during/after sexual intercourse. %46.7 of women have dyspareunia. 30% of women with more than one partner for life. One women (%3.3) state had a history of sexually transmitted infections.

One women has infertility history and one women in postmenopausal period (33.3%). 6.7% of women have family history of breast cancer, 10% have colon cancer and 10% endometrium cancer. 33.3% of women are among 45-55 age and one women in postmenopausal period. 1 women (%3.3) had HRT for their menopausal period.

23.3% of women at risk for not exercising. 16.7% of women have diabetes. 30% of women was obese, 10% morbid obese. 50% of women mainly feeding with animal fat.

Conclusions
Women don’t know well about the risk factors for women's gynecological cancers identified. They stated about the reasons don’t to participate in screening that lack of information about about the screen programmes, not having the symptom, neglect, embarrassment respectively. The awareness materials and programmes was performed during the study.
THE EFFECT OF PRE-PROCEDURAL STATE-TRAIT ANXIETY ON PAIN PERCEPTION AND DISCOMFORT IN TURKISH WOMEN UNDERGOING COLPOSCOPY

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Objectives
To determine if pre-procedural anxiety has a significant effect on pain and discomfort in Turkish women undergoing colposcopy for evaluation of abnormal cervical cytology.

Methods
The study was performed at the gynecologic oncology department of Zekai Tahir Burak Women's Health Education and Research Hospital in Ankara, Turkey. After taking pre-procedural informed consent, a 14-item questionnaire and Spiegel's State-Trait Anxiety Inventory (STAI) form was asked to be filled by women who were admitted to our outpatient unit for colposcopy between January 1st-April 1st 2013. STAI scores were calculated for each participant. Immediately after the procedure, visual analog scale (VAS) scores for procedure related pain and discomfort were obtained. Associations between STAI and VAS scores were investigated. P values less than 0.05 were considered statistically significant.

Results
A total of 222 women underwent colposcopy for a cervical cytological abnormality within the study period. Mean patient age was 38.2±9.6. Majority of the patients (59%) had fear before the procedure. Median state and trait anxiety scores were 47 and 46, respectively. Median VAS score for pain and discomfort were 4 for both variables. State anxiety had a weak but significant correlation with procedure related discomfort (p=0.02), but not with pain. Trait anxiety did not have any significant association with VAS scores.

Conclusions
Although pre-procedural state and trait anxiety scores were relatively high, this did not translate into increased pain. However, state anxiety had significant effect on procedure related discomfort. Future studies should focus on methods to reduce anxiety for women undergoing colposcopy.
DIAGNOSTIC VALUE OF DIAGNOSTIC HYSTEROSONPY FOR GYNAECOLOGIC SCREENING IN LYNCH SYNDROME: OFFICE VS GENERAL ANAESTHESIA.

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Objectives
To compare accuracy and performance of diagnostic hysteroscopy with or without General Anaesthesia (GA) for the detection of endometrial abnormalities, atypical hyperplasia, and endometrial cancer in Lynch Syndrome (LS).

Methods
Prospective study in patients with LS (1998-2012) who underwent a flexible diagnostic hysteroscopy with endometrial biopsy. Yearly follow-up included office hysteroscopy (Group 1) or hysteroscopy under GA combined with screening colonoscopy (Group 2). Endometrial biopsy was considered as the gold standard. Hysteroscopic and histologic findings were compared to assess diagnostic performance of hysteroscopy.

Results
94 patients with 253 hysteroscopies were included (Group 1: n=208 and Group 2: n=45). Failure of hysteroscopy occurred in 9 (4.3%) and 3 cases (6.7%) (p=0.45) respectively. Hysteroscopy showed abnormal mucosa respectively in 57 (27.4%) and 7 (15.6%) patients (p=0.10), and a suspicious lesion in 1 case for Group 1. One complex atypical hyperplasia and one endometrial cancer were diagnosed by endometrial biopsy in patients who had suspicion of polyps by hysteroscopy. Sensitivity and negative predictive value of hysteroscopy for the detection of endometrial abnormalities, were respectively 75% (IC95% [0.48-0.93]) and 96% (IC95% [0.90-0.99]) in Group 1 and 60% (IC95% [0.15-0.95]) and 92.6% (IC95% [0.76-0.99]) in Group 2 with no significant difference. For the detection of atypical hyperplasia and endometrial cancer, sensitivity and negative predictive value were respectively 0 % (IC95% [0-0.84]) and 98.8% (IC95% [0.95-1]) in Group 1 and non evaluable and 100 % (IC95% [0.89-1]) in Group 2.

Conclusions
Accuracy and diagnostic performance of diagnostic hysteroscopy are similar with or without GA.
CORRELATION BETWEEN CERVICAL CITOLOGY, COLPOSCOPIC BIOPSY AND CERVICAL CONIZATION IN THE TREATMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA - OUR EXPERIENCE.

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Objectives
To correlate cytological diagnosis with colposcopy, biopsy findings and histopathological analysis from conization.

Methods
97 women who underwent conization by the loop electrosurgical excision procedure (LEEP) for CIN and microinvasive carcinoma from January 2012 to December 2012 were evaluated. For statistical analysis, we used the kappa agreement coefficient.

Results
Among 83 patients submitted to biopsy the cytological diagnosis was ASC-US (26%), LSIL (34%), HSIL (22%), AGUS (1,2%) and adenocarcinoma (2,4%). Biopsy had no correspondence to cytology on about 59% to ASC-US and 42% to LSIL. All of HSIL corresponded to a high grade lesion.
In cases who underwent colposcopically directed biopsy before the conization, the cone presented the same grade of lesion in 41 and a higher grade in 26 cases and in four of them was a microinvasive carcinoma. Among the 33 women who underwent the cone biopsy with a previous biopsy suggestive of cervicitis or CIN 1, 30% had CIN 2 or 3 in the cone. Among the 14 women without previous biopsy, 43% had CIN 2 or 3.

Conclusions
Colposcopy association with cytopathological screening, on those selected patients, significantly raises the diagnostic accuracy of cervical cancer precursor lesions. On other hand, the results of this study emphasize the importance of proceeding with a diagnostic or therapeutic conization in order to avoid undertreatment specially when there is little experience on colposcopy.
A STRATEGIC ASSESSMENT OF CERVICAL CANCER PREVENTION AND TREATMENT SERVICES IN THE DISTRICTS OF ALBANIA

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Objectives
In an effort to assess the need and potential for improving the quality of cervical cancer prevention and treatment services Albania, a strategic assessment was conducted in the Tirana and Durres.

Methods
Data were collected by an assessment of the quality of cervical cancer services was carried out by a multidisciplinary team of stakeholders. The assessment included a review of the available literature, observations of services, visits of hospital and the conduct of qualitative research (in-depth interviews and focus group discussions) to assess the perspectives of women, providers, policy makers and community members.

Results
There were gaps in provider knowledge and practices, potentially attributable to limited provider training and professional development opportunities. In the absence of a prevention programs on cervical cancer, screening of asymptomatic women was opportunists. Cytology-based cancer screening tests were often used to help diagnose women with symptoms of reproductive tract infections. Access to appropriate treatment of precancerous lesions was limited. Cancer treatment facilities were equipped but only in Tirana, inaccessible for women in need. Finally, policy makers, community members and clients were mostly aware about cervical cancer and its preventable nature, and expressed a strong interest in having services available to women in their communities.

Conclusions
To address gaps in services and unmet needs, state policies and integrated interventions have the potential to improve the quality of services for prevention of cervical cancer in Albania. The existing health network provides Albania an excellent foundation for the implementation of screening programs and utilizing this network would encourage participation in the screening programs.
COORDINATION OF PREVENTION SERVICES OF THE REPRODUCTIVE TRACT CANCERS WITH MATERNAL HEALTH PROGRAMS THAT PROVIDE HEALTH SERVICES TO WOMEN

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Objectives
To introduce cancer prevention in Albania

Methods
Data were collected by a detailed survey performed in Albania.

Results
Albania’s good performance for Maternal Health indicators demonstrates there is sufficient nationwide capacity to deliver these services while the knowledge and skills required to deliver MH services have substantial overlap with those required for cervical screening.

Albania will need to develop a Cytopathology capacity for the diagnosis of other diseases and it will not be possible to compare the cost-effectiveness of hrHPV testing to the Pap test until there are reliable Albanian data on Pap-test provision. The development of conventional Pap-test capacity appears that Albania should start with while ensuring the process will facilitate a transition to hrHPV testing, LBC (Liquid-Based Cytology).

Also, hrHPV testing reagents and equipment must be purchased outside Albania while the reagents and equipment needed for the conventional Pap test either are or could be made in Albania. Therefore, implementing hrHPV testing would contribute to Albania’s current account deficit (12.2% of GDP in 2011) and reduce scope for investment in public services. This is not an option for a national organised cervical screening program.

Conclusions
This existing network therefore provides Albania with an excellent foundation for the implementation of these screening programs. Therefore, utilizing this network would help to encourage participation in the screening programs. Further, the international community has prioritised cancer prevention and is capable of offering a substantial amount of support for the implementation of these breast and cervical screening programs that will yield benefits for many other areas of the health system.
Objectives
Invasive cervical cancer is the commonest gynecological cancer in
Kazakhstan, ranking the 5th among cancers in female population and ranking
10th by its mortality. The standardized incidence cervical cancer has been
estimated at 8.8 per 100,000 of population annually with 4.0 mortality rates in
2011. Organised cervical cancer screening program in Kazakhstan is cytology-
based and offered free of charge for all women aged 30 to 60 years every five
years. Screening program has been approved by Ministry of Health in 2008.
Aim of study was to evaluate current screening program and to suggest future
cervical cancer prevention strategies in Kazakhstan.

Methods
In four regions of Kazakhstan 3726 women from 18 to 65 years, representing
general female population underwent screening with conventional pap smears
and human papillomavirus (HPV) co-testing. All women with history of pre-
invasive disease or cervical cancer and HPV infection were excluded.

Results
The median age was 40.0 years. 2408 HPV tests and 2429 smears out of 3726
were considered eligible after primary data analyses. We found 59.4%
negative smears and 28.3% HPV positivity with 25.1% of them being high risk
HPV infection. We have also found high incidence of ASCUS reports – 22.5%,
with relatively low number of LSILs – 5.0% and HSILs – 1.3%.

Conclusions
Adding HPV tests to screening could be beneficial in increasing quality of
screening and decreasing large number of unnecessary additional tests.
Extending budget for HPV test will save money for unnecessary follow up
expenses for women with ASCUS and LSIL cytology results.
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POPULATION-BASED EVALUATION OF TYPE-SPECIFIC HPV PREVALENCE AMONG THAI WOMEN IN BANGKHAYAENG, PATHUMTHANI PROVINCE, THAILAND
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Objectives
To determine the HPV prevalence and genotype distribution for providing the effective cervical cancer screening among Thai females in Bangkhayaeng area.

Methods
1,086 Bangkhayaeng permanent or current resident Thai women, aged 20-70 years (mean age, 44.0 years; range 20-70 years), were recruited at Bangkhayaeng sub-district hospital, Pathumthani province, Thailand during February 4 – March 26, 2013. HPV genotyping (Linear array, Roche, USA) and liquid-based cytology (Surepath, Becton and Beckinson, USA) were utilized as the screening tools. 249 females were excluded.

Results
Of 837 women, the overall HPV prevalence was 13.0 %, with 5.7 % high risk (HR) type, 8.2 % low risk (LR) type, and 1.1 % probable HR type. The most frequent HR-HPV types included HPV52 (1.4%), HPV16 (1.2%), HPV51 (1.2%), HPV68 (0.6%), HPV58 (0.5%). HPV18 was 0.2 %. Common LR-HPV types were HPV72 (2.2%), HPV62 (1.6%), HPV CP6108 (1.1%), HPV84 (0.8%), HPV54 (0.7%) and HPV71 (0.7%). HPV 6, 11 was 0.1, 0 %. HPV infection was decreased with age. The more severity of abnormal cytology represented the higher HPV positivity.

Conclusions
The HPV infection rate in Thai women was 13.0% with variable genotypic subtypes. Lower HR-HPV was noted when compared to western countries. However, HR52 was surprisingly and distinctively found in our cohort as highest HPV type, unlike other regions worldwide.
OPINION SURVEY AND RECOMMENDATIONS ABOUT ADULTS WOMEN HPV VACCINATION, WITH OR WITHOUT INFECTION BY THE HPV AND CERVICAL INJURY.

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Objectives
Create a recommendations guide about adult’s women vaccination against cervical cancer, with or without infection by human papilloma virus (HPV) and cervical injury, to support health professional and improve HPV vaccinations in Spain.

Methods
A survey in 2010 Spain 2010, among cervical pathology gynecologist result from show the necessity of improve knowledge about indications of HPV vaccine in women more 14 years old, independent of HPV state or abnormal cytology, skilled on cervical pathology and public health elaborate the guide based on medical evidence, publish in “Progresos en Obstetricia y Ginecología”, September 2012.

Results
The recommendation guide was endorsed by SEGO (Obstetrics Gynecology Spanish Society), AEV (Vaccinology Spanish Society) AECCP Spanish Association of Cervical Pathology Colposcopy), and two principal Societies of Family Doctors. High acceptance among health providers in Spain.

Synthesis
Most women sexually active, take advantage of vaccination: New infection significant risk and persistent infection increase with age, vacunal efficacy very high (>90%). Safety is proved Women without previous or present infection, obtain maximum vaccination benefit.
Women with present infection for any of vaccine HPV type obtain high protection due to other HPV vacunal types. Vaccine is not therapeutics. HPV 16-18 co-infection in adult women is very uncommon <1%.
Women with previous VPH infection and viral clearance can be protected for reinfection and reactivation.
Vaccination in women under treatment of cervical lesion reduce risk of seconds lesion.
The vaccine administration does not interferes the result of necessary cervical treatment.

Conclusions
Recommendations guides about adults women vaccination against cervical cancer Will support health professional and improve HPV vaccinations.
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OPPORTUNISTIC SALPINGECTOMY: IMPACT OF A REGIONAL PROGRAM FOR OVARIAN CANCER PREVENTION

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Objectives
In September 2010, we implemented a Provincial ovarian cancer prevention campaign that included recommending bilateral salpingectomy (BS) at the time of other gynecologic surgery in all women who had completed childbearing. We assessed procedures performed and associated complications.

Methods
Hospital discharge data on demographics, procedure, complications and readmissions were requested for 2008-2011. Age-adjusted odds ratios (aOR) were determined for BS at time of hysterectomy or sterilization.

Results
From 2008-2011, hysterectomy with BS increased from 45 to 79% and BS for sterilization increased from 0.5 to 33% with the greatest change observed between 2009-2010. Mean age of women undergoing hysterectomy with BS was 43.5 yrs (95% CI 43.3-43.8) and 41.9 yrs (95% CI 41.7-42.1) for BS sterilization. Mean length of hospital stay (LOS) did not differ significantly between those undergoing hysterectomy with or without BS (2.80 versus 2.53 p-value=0.602). There were no significant differences in the aOR of receiving a blood transfusion or being readmitted to hospital for women who underwent hysterectomy with BS compared to hysterectomy alone (aOR=0.82 (95%CI 0.64-1.05), aOR=0.86 (95%CI 0.71-1.04)), respectively) nor BS sterilization (aOR=1.01 (95%CI 0.48-2.10), aOR=0.82 (95%CI 0.56-1.20)). Regional differences across BC are apparent with “missed” opportunities of hysterectomy without BS (or BSO) ranging 2.5 fold (22% to 55.6%) and BS sterilization encompassing 0-22.5% of a districts surgical sterilization procedures.

Conclusions
Marked increased uptake of salpingectomy for all indications suggests the recommendations have been incorporated into practice with no measurable negative sequelae observed. There is room for further procedural increase. It will be many years before the impact of this campaign can be appreciated, in terms of number and histologic distribution of new ovarian cancer cases.
EXPRESSİON OF P53, P63 AND KI-67 IN PATİENTS WITH CIN
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Objectives
Cervical intraepithelial neoplasia (CIN) is a process of a dysplastic cervical squamous epithelium with potential of malignization to cervical cancers. The aim of our study was to identify and compare expression of the three potential biomarkers – p53, p63 and Ki-67 in patients with various degrees of cervical intraepithelial neoplasia, as well as to compare whether these three markers are useful in prediction of cervical intraepithelial neoplasia progression.

Methods
31 patients admitted to Latvian Oncology Center were enrolled in the study. The patients had different degrees of abnormal cervix cytology. The control group consisted with 5 patients without any clinical and cytological suspicion for dysplasia. Each patient underwent a colposcopically directed biopsy or electroexcision of the cervix. The tissue was stained with haematoxylin-eosin and immunohistochemically to reveal p53, p63 and Ki-67 positive cells.

Results
Obtained results showed that 8 patients had CIN I, 10 patients had CIN II and 8 patients had CIN III. The results of our study showed a significant increased expression of p53, p63 and Ki-67 in squamous epithelium in the cases with CIN3 compared to CIN2 and CIN1 patients (p <0.001). p63 followed by Ki-67 demonstrated significant correlation with cancer progression compared to p53.

Conclusions
In conclusion, quantitative detection of 53, p63 and Ki-67 expression allows more accurate assessment of CIN degree and subsequent prediction of the disease progression.
BILATERAL SALPINGECTOMY AS A PROPHYLAXIS OF MALIGNANCY IN PATIENTS OPERATED FOR BENIGN GYNECOLOGICAL CONDITIONS. PRIMARY SEROUS INTRAEPITHELIAL CARCINOMA OF THE FALLOPIAN TUBES - CASE REPORT

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Objectives
Recent data imply that serous ovarian cancer originates from the epithelium of the fimbriated ends of the fallopian tubes or from the peritoneal epithelium which further spreads to the ovaries. It leads us to the reconsideration of the extent of the surgical procedures performed for benign gynecological conditions.

Methods
Forty six years old female (Para-2, Aborta-0) was hospitalized with recurrent abnormal uterine bleedings leading to secondary anemia. Sonography showed enlarged uterus with multiple uterine myomas. Preoperative endometrial biopsy revealed normal proliferative endometrium. Since patient did not wish another pregnancy and did not respond to standard hormonal therapy we decided to perform subtotal hysterectomy combined with bilateral salpingectomy.

Results
Postoperative pathological examination confirmed the presence of proliferative endometrium, myomas and bilateral oviduct major grade dysplasia with the intraepithelial carcinoma. Therefore, we recommended laparoscopy with bilateral ovariectomy and staging in accordance with FIGO guidelines. CA 125 level was in normal range (9.8 U/mL). There were no suspicious masses or ascites in the abdominal cavity, apart from extensive adhesions in former operation site. Final pathology report was negative for malignancy.

Conclusions
Prophylactic bilateral salpingectomy performed during gynecological procedures in menopausal women or women with completed reproduction could be of value in reducing risk of adnexal malignancy.
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OPPORTUNISTIC SCREENING FOR CERVICAL CANCER IN DEVELOPING COUNTY – CLINICAL CENTER ZEMUN EXPERIENCE

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Objectives
Organized presymptomatic detection of cancer - screening is not yet implemented in Serbia. The aim of the study was to determine the incidence of positive findings in opportunistic screening.

Methods
Opportunistic screening that included all women who willingly and on their own initiative come to the gynecologist was performed. Study has been conducted in 13,675 women, divided into six age groups, in period from 01.01.1998. till 31.12.2012., using cytodiagnostic analysis (Pap smear) and colposcopy with Schiller's probe. Collected data were analyzed statistically.

Results
Of the total number of samples, 9.2% were Pap positive. The most frequent positive finding was PA III (89%), while the most frequent colposcopic findings were AW epithelium (23%). Regarding the age distribution of patients with positive findings, the highest incidence was in the group of 40-49 years (43%). Histopathological confirmation of the diagnosis was variable in different years of study, ranging from 58-96%.

Conclusions
In countries without organized screening for cervical cancer opportunistic screening is suitable solution. Importance of education and training of gynecologists-oncologist and cytologist is high.
PARENTAL ACCEPTANCE OF HUMAN PAPILLOMAVIRUS VACCINATION FOR ADOLESCENT GIRLS IN LAGOS, NIGERIA

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Objectives
Human papillomavirus (HPV) vaccination is recommended for adolescent girls and would offer a long term solution to cervical cancer especially in developing countries. However, parental perception and acceptance is a critical success factor. This study examined the degree of parental acceptance of HPV vaccination for adolescent secondary school girls in Lagos, Nigeria

Methods
A descriptive cross-sectional survey of adolescent girls’ parents was undertaken in 2 urban and 2 rural secondary schools in Lagos. Univariate and multivariate analysis were done using logistic regression to determine correlates of parental acceptance of HPV vaccine.

Results
Of the 318 respondents, 45.9% had poor knowledge of cervical cancer and HPV infection while 29.6% had good knowledge. Majority (54.7%) also had poor knowledge of HPV vaccine while 26.7% had good knowledge. Most (72%) would vaccinate their daughters if vaccines were free, while only 35.5% would, if not free. Poor knowledge of cervical cancer and HPV infection significantly reduced the likelihood of vaccination even if free (adjusted OR = 0.48; 95% CI = 0.24-0.94; p = 0.0325), while good knowledge of HPV vaccines (adjusted OR = 6.11; 95% CI = 1.37 -27.34; p = 0.018) and tertiary education in the mother (adjusted OR = 29.17; 95% CI = 3.98 – 214.08; p = 0.0009) increased the likelihood, if not free.

Conclusions
HPV vaccination was acceptable to most parents if offered free. Poor knowledge of cervical cancer, HPV infection and vaccine may hinder acceptability. Improving parental knowledge of vaccines is required.
**Objectives**
Bettocchi hysteroscopy \(^1,2\) is a good example of evolution of operating methods leading towards an innovative and minimally invasive surgery. This system uses hysteroscope with an outer diameter of 2 and 2.9mm, as a result of which the patient undergoing the procedure does not require a general anaesthesia.

Hysteroscopic technique \(^1,2\) allows evaluation of pathological lesions in the endometrium and determination of their severity. The examination may be combined with a simultaneous therapeutic surgery such as removal of intrauterine adhesions or endometrial polyps.

**Methods**
During a transvaginal ultrasound, a 43-year-old patient had a 7x10mm lesion found in the uterine cavity which may have been an endometrial polyp. As a continuation of the diagnostic and therapeutic procedure, the patient was offered Bettocchi hysteroscopy and consented to it.

**Results:**

Pic. 1. Picture shows endometrial polyp removal using Bettocchi hysteroscope

During the hysteroscopy and examination of the uterine cavity, an endometrial polyp of 12x15mm was found and removed. Hystopathological examination of the sampled material confirmed the initial diagnosis.

**Conclusions**
Bettocchi hysteroscopy is a highly effective, minimally invasive and safe method for a patient with indications for hysteroscopic diagnostics.

**References**
THE IMPORTANCE OF COLPOSCOPY FOR PERSISTENT INFLAMMATORY CYTOLOGY IN A PRIVATE CLINIC IN BRAZIL

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Objectives
The aims of this study were: compare cytology and histology results of women with persistent inflammatory cytology results into a private gynecology clinic in Brazil.

Methods
During a period of 1 year 89 women in a middle size city in Brazil had a colposcopy exam and biopsy performed in women with at least 3 previous exams with inflammatory cytology result. The inclusion criteria to the study were: patients more than 18 years; history of less than 3 years of sexual activity. The exclusion criteria were: history of treatment for cervix lesions, any immunosuppressive condition, or pregnancy. The exam was performed in a private clinic.

Results
The mean baseline age was 33.57 years. The final biopsy results were: 8 cases of CIN1 (9%); 1 case of CIN2 (1%); 2 cases of CIN3 (2%); 1 case of invasive squamous carcinoma (1%) e 1 case of in situ adenocarcinoma (1%). Negative or cervicitis represented 76 cases (75%).

Conclusions
The colposcopy exam can be used in private clinics to improve the specificity of cervical neoplasia diagnostic in Brazil, as a developing country, where public health policy is insufficient.
PREVALENCE OF GENITAL WARTS IN THE UNITED ARAB EMIRATES AND THE KINGDOM OF SAUDI ARABIA

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Objectives
The aim of this study was to estimate the prevalence of genital warts (GW) in physician practices in three emirates in the United Arab Emirates (UAE) and in the Kingdom of Saudi Arabia (KSA).

Methods
Physicians in 6 private and 6 public institutions located in Dubai, Sharjah, and Al Ain (13 gynaecologists (OBGYN), 15 primary care physicians (PCP), 3 dermatologists (DERM) and 2 urologists (URO)) prospectively recorded daily logs of patients (N=4,212) for a 2-week period to estimate prevalence of GW between October 2011 and March 2012. In KSA, 56 physicians from 9 public institutions (20 PCP, 18 OBGYN, 9 DERM, and 9 URO) located in Riyadh and Jeddah also completed daily logs of patients (N=5,728) for a two week period between December 2011 to May 2012. Prevalence was obtained for each physician and calculated into a single estimate across all physician types.

Results
Overall prevalence of GW in our study population in UAE was 0.0126 (95% CI: 0.0075-0.0178) and 0.0102 (95% CI: 0.0067-0.0137) in KSA for patients age 18-60 years. In UAE, the unweighted prevalence estimate in PCP practices was 0.01 (95% CI: 0.0051-0.0149), 0.019 (95% CI: 0.0126-0.0254) in OBGYN practices, In KSA, the unweighted prevalence estimate in PCP practices was 0.0062 (95% CI: 0.0034-0.0091), 0.0235 (95% CI: 0.0163-0.0307) in OBGYN practices, In females, prevalence was 0.0086 (95% CI: 0.0039-0.0134) in UAE and 0.0121 (95% CI: 0.0077-0.0164) in KSA.

Conclusions
In our study sample population GW is prevalent in physician practices in UAE and KSA.
ACCEPTANCE OF HUMAN PAPILLOMAVIRUS VACCINE BY ADOLESCENT GIRLS AND THEIR PARENTS IN TURKEY
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Objectives
The aim of this study was to identify the opinions of Turkish adolescent girls and their parents about HPV vaccination and the consistency.

Methods
This descriptive study covered 301 girls and their parents. Questionnaires were developed by the researchers based on findings within the literature and applied for data collection.

Results
The mean age was 19.4 for girls, 44.2 for mothers and 47.9 for fathers. It was found that 43.5 percent of girls and 31.9 percent of mothers wish to be vaccinated against HPV. Also, 45.5 percent of mothers and 44.9 percent of fathers wish for their daughters to be vaccinated against HPV. A moderate consistency was found between mothers and fathers; a low consistency was found between fathers and girls, and between mothers and girls.

Conclusions
The study indicates that an appropriate background has been partially provided about the acceptability of the vaccine between parents and their daughters in Turkey. However, the vast majority of adolescent girls and parents are indecisive or reluctant about HPV vaccination. This study also showed that the decisions of adolescents about vaccination may be affected by the opinions of the parents.
INCIDENCE OF OTHER MALIGNANT NEOPLASMS IN PATIENTS WITH GYNAECOLOGICAL CANCERS

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Objectives
The multiple neoplasms and their trends have not been identified yet in the Czech females with gynaecological cancers (GC).

Methods
The cancers of cervix (CC), corpus uteri (CU) and ovary (CO) based in the Czech Cancer Registry in 1976-2010, associated with other neoplasms were analysed by age-time-space distribution and clinical stages.

Results
A total 20,101 multiple GC included 4,694 CC, 9,692 CU and 5,715 CO. As the primary diagnosis were registered 3,283 CC, 6,153 CU and 2,436 CO, as the subsequent diagnosis 1,411 CC, 3,539 CU and 3,279 CO. The average interval between primary GC and other neoplasms was 9.2 years of CC, 8.5 years of CU, 6 years of CO. The most frequent synchronous cancers after primary GC were 40.1% of other gynaecological and 19.3% digestive organs, 12.9% breast, 7.5% urinary tract. In early stages of primary GC were reported 69% CC, 76.9% CU and 50.7% CO, in advantage stages 13.4% CC, 5.1% CU and 30.3% CO; in early stages of subsequent GC were 49% CC, 64% CU and 30.5% CO, in advantage stages 23.7% CC, 10.1% CU and 43.3% CO. The number of primary GC was highest in the age group of 50-59 years, of subsequent GC of 70-79 years. Up to 2012 survived 31.3% primary and 29% subsequent CC, respective 33.1% primary and 40.7% subsequent CU, 29.3% primary and 20.2% subsequent CO.

Conclusions
Most of the subsequent cancers, especially those in advanced stages, must be prevented by the therapeutic guidelines and standards for long-term medical care and preventive interventions not only in gynaecology.
Utility of HPV Genotyping in the Management of Cervical Low-Grade Squamous Intraepithelial Lesion (LSIL)

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Objectives
To test the utility of HPV genotyping in the management of LSIL.

Methods
We conducted a retrospective study analysing liquid-based cytologies specimens (Hologic) in the years 2006 and 2007 at the Hospital del Mar area of reference in Barcelona (Spain). We used the Cobas 4800 HPV test (Roche Molecular) to genotype, which allow us to classify them as HPV16, HPV18, other high-risk HPV positive (hrHPV) or HPV negative (negHPV).

Results
We studied 57 patients with a median age of 28±11.4 years. 19.3% were HPV16, 5.3% HPV18, 64.9% hrHPV and 28.1% negHPV. There were 9 patients (15.9%) with coinfections: 7 positive for HPV16 and hrHPV, 1 positive for HPV18 and hrHPV and 1 positive for HPV16, HPV18 and hrHPV. We didn't analyse HPV18 data nor the coinfections except HPV16 plus hrHPV because of the low number of patients positive for them. 45.5% of HPV16 patients, 16.2% of hrHPV and none of the negHPV progress to CIN2+. These results for both HPV16 and negHPV were statistically positive. The relative risk (RR) for progression for HPV16 was 5.9 and for hrHPV 1.6 (both significatives). When studied the subgroups HPV16 vs HPV16 plus hrHPV we found no differences, no additional risk was carried by coinfection. Mean time to progression and regression were 351 and 338 days respectively. Time to CIN2+ was similar for HPV16 cases (310 days) and hrHPV (330 days).

Conclusions
HPV16 positive LSIL needs more strict control that others, and negHPV LSIL could be maybe managed as a chronic disease.
SCREENING OF FAMILIES WITH HEREDITARY SUSCEPTIBILITY TO CANCER OF FEMALE REPRODUCTIVE ORGANS.

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Objectives
1) identify families with accumulation of malignant neoplasms of female reproductive organs (endometrial cancer, ovarian cancer, breast cancer and multiple primary malignant neoplasms (MPMN)); 2) detection of early stages of malignant neoplasms in families with high risk of cancer; 3) creation of Family Cancer Registry (FCR) of families with hereditary susceptibility to cancer of female reproductive organs.

Methods
1) Formation of risk groups based on pedigree analysis, clinical, genetico-molecular tests; 2) DNA testing for mutations of MLH1, MSH2, MSH6, and BRCA1 in individuals.

Results
Frequency among first-degree relatives with malignant neoplasms constituted 28.2 ± 2.53%. Endometrial cancer was detected in 18 (4.9 ± 1.14%) individuals, ovarian cancer - 12 (3.4 ± 0.96%), breast cancer in 14 relatives (4.4% ± 1.78), MPMN (the first tumor in the uterus) - 12 and (the first tumors in the ovaries) - 14 relatives. DNA testing in 25 families with high risk detected mutations in genes MLH1, MSH2, MSH6, and BRCA1 in 10 (40%) cases.

Conclusions
The FCR was created for families with high risk of cancer and provides the ability to detect early stages of malignant and benign tumors in families with hereditary susceptibility to cancer of female reproductive organs, by using data of mutations in genes MLH1, MSH2, MSH6, and BRCA1 for identification of genetic risk.
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GYNECOLOGICAL CANCER TRENDS SINCE 2002 IN TURKEY
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Objectives
Top three women cancers are mainly consisting from breast, cervix and colon-rectum cancers worldwide. Regarding to gynecological cancers besides the cervical cancer ovarian and uterine corpus cancers are only taking place at 7th or 8th line of women cancers. Our aim with this study is to throw into sharp relief of Turkish epidemiological data regarding gynecological cancers.

Methods
Data stream to be provided from Turkish cancer registry system, which is consisting of 12 active cancer registry centres nationwide comprising more than 25% of the population.

Results
Most common cancers among women are breast, thyroid, colo-rectum, uterus-corpus, lung, stomach, ovary, Lymphoma, Brain and cervical cancer in Turkey. The table below is showing that all gynecological cancers have figured an increase trend in the last decade. Although uterus cancers, excluding endometrial cancers, which is pointing the sarcoma cases have remained steady.

Conclusions
The figure of women cancers in Turkey is similar to the world epidemiological data, besides the cervix. Howsoever Turkish cancer rates are still laging behind of Europian numbers. Most of the reproductivity and hormone related cancers have shown a slight rise in Turkey from 2002 to 2008. This can be due to either the improvement of registry system or the increment of diagnostic health care services in Turkey rather than a real increase of cancer cases.
APPLICATION OF 2011 IFCPC COLPOSCOPIC TERMINOLOGY OF CERVIX IN CLINIC
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Objectives
To evaluate the colposcopic accuracy and reproducibility to the International Federation for Cervical Pathology and Colposcopy (IFCPC) 2011 terminology

Methods
Cases derived from abnormal cytology interpretation. 2 blinded colposcopists involved in this study. Use the Colposcopic terminology to evaluate, classify, grade and document the findings. All abnormal colposcopic findings were taken biopsy at the right abnormal sites under the colposcope, if could not see SCJ, ECC should be considered

Results
The IFCPC terminology was easily reproduced between two observers. The sensitivity and specificity in distinguishing abnormal colposcopic findings from normal findings is 85.2%, 83.4% respectively. Between Grade 1 (minor) and grade 2 (major) lesions, the sensitivity and specificity is 70.1% and 95.3% respectively. Most of grade 2 lesions locate inside the transformation zone. When grade 2 lesion was found outside the transformation zone, we should aware of VAIN presentation. The colposcopic abnormalities within the transformation zone and large lesions were more closely related to grade 2 lesions. The two new signs, the “inner border sign” and “ridge sign” could be found in Grade 2 lesion, and” ridge sign” is more common than “inner border sign”.

Conclusions
the new IFCPC terminology is an effective tool to evaluate cervical lesion. General assessment is very useful for clinical evaluation. For abnormal findings, general principles to describe the lesion localization and the relationship to the transformation zone are very important to make clinical management.
PATIENT OUTCOMES FOR WOMEN POST LAPAROSCOPIC HYSTERECTOMY FOR EARLY ENDOMETRIAL CANCER

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Objectives
To explore the patient outcomes for women who have undergone laparoscopic hysterectomy for early endometrial cancer.

Methods
Systemic review of RCT’s including women who have undergone laparoscopic hysterectomy for early endometrial cancer was undertaken. Specific search strategy to identify RCT’s was developed and data extraction was performed with the aid of specially adapted tool. Meta-analysis of findings was performed using RevMan from Cochrane Collaboration and COSORT statement standards were applied for quality appraisal.

Results
Meta-analysis found statistical significance in favouring the laparoscopy group when measuring surgical complications (p<0.00001) and length of hospital stay (p<0.0001). Laparotomy group was favoured in the length of operative time (p<0.00001). No difference was found in overall survival and recurrence rates.

Conclusions
Meta-analysis was not able to determine superiority of one treatment arm over the other but it supports the findings in literature that laparoscopic hysterectomy is safe and effective treatment for women with early endometrial cancer without compromising their oncological outcomes. Further research is recommended in assessing the education needs and mode of delivery for these women as reduced length of hospital stay has also led to reduced one to one time with the nurse caring for them.
EXPERCTATION AND PERCEPTION OF NURSING SERVICE QUALITY OF CLIENTS AT GYNECOLOGIC OUTPATIENT DEPARTMENT IN UNIVERSITY HOSPITAL

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Objectives
Purposes of this research were to study (1) level of quality nursing service, (2) comparison of quality nursing service expectation and perception among women with gynecological problem in outpatients' department, and (3) comparison of quality nursing service expectation and perception between women with and without gynecologic oncology problem in outpatients' department in university hospital.

Methods
This study was descriptive and cross-sectional research. Participants included 315 women who visited at university hospital during July 2012 - April 2013. The instruments were (1) the personal health and illness data, (2) the quality nursing service expectation and perception questionnaires. Alpha cronbach's coefficient for quality nursing service expectation and perception questionnaires were .98 and .97 respectively. Data were analyzed by descriptive, paired t-test, and independent t-test in case of normal distribution.

Results
Results found that the level of quality nursing service expectation was highest but the level of perception was high. There were significant different between overall quality nursing service expectation and perception at .001 level. In addition, there were significant different between quality nursing service expectation and perception all 5 parts at .001 level. There were nearly all 5 parts of quality nursing service expectation had significant different between women with and without gynecologic oncology problem, meanwhile, there were some parts of quality nursing service perception had significant different between women with and without genecological problem.

Conclusions
Findings from the study can be used as evidence-based data to provide and improve quality nursing service and satisfaction in gynecological outpatients' department university hospital.
e-Posters: Nursing

ASSESSMENT OF ANXIETY AND INFORMATION NEED IN WOMEN WITH GYNECOLOGICAL PROBLEM BEFORE OPERATION
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Objectives
This study was aimed to (1) assess level of anxiety and information need (2) factors related to anxiety and information need and (3) comparison anxiety and information need between women with tumor and gynecological oncology problem before operation.

Methods
Data were collected in 132 women with gynecological problem before operation admitted in university hospital. Two instruments were (1) the personal, disease and treatment data and (2) the Amsterdam preoperative anxiety and information scale (APAIS) Thai version. The APAIS was used to assess the anxiety and information need. Instrument was test in 30 patients with Cronbach’s alpha reliability .86.

Results
Results found that level of anxiety and information need in women with gynecological problem before operation was in moderate level. Age had negative significant correlation with surgery-related anxiety at .05 level, however, it had no significantly correlation between age and anesthesia-related anxiety, information desire component and combined anxiety component. Age group, co-morbidity, operative experience, occupation were had different anxiety component with significant at .05 level but types of tumor had no different anxiety component at .05 level.

Conclusions
Results of this study can provide information data about anxiety components. Health care profession can use these data to reduce anxiety in each group of women with gynecological problem before operation effectively.
THE ROLE OF HE4 AND CA125 IN THE DIAGNOSIS OF UTERINE MALIGNANCIES: A PROSPECTIVE STUDY.

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Objectives
The aim of the study was to assess the clinical value of serum level of HE4 and CA125 in the differentiation between malignant and nonmalignant uterine pathologies.

Methods
Serum specimens were collected from 79 patients admitted to the Clinic because of suspicion of uterine pathology. Serum specimens were collected within 72 hours before surgical operation. The definitive diagnosis of the uterine pathology was established by the pathological examination of the excised lesions. The normal level of CA 125 was considered less than 35 IU/ml. The clinical value of HE4 was analyzed using three levels: less than 70, 100 and 150 pmol/L. Mann-Whitney test was used for the statistical analysis.

Results
21 cases had malignant disease (26,58%). HE4 was significantly increased in patients with malignant diseases considering 70, 100, and 150 pmol/L cutoff. The sensitivity of HE4 in diagnosing uterine malignant disease was 61,90%, 42,86% and 19,05% for 70, 100 and 150 pmol/L cutoff respectively. The specificity was 91,38%, 94,83% and 98,82% respectively. The negative predictive value was 86,89%, 82,09% and 77,03% respectively. The sensitivity of CA125 was 28,57% and the specificity was 91,38%. The negative predictive value was 77,94%. CA125 was not significantly increased in patients with malignant diseases.

Conclusions
HE4 is more sensitive and specific for diagnosing uterine malignancies than CA125. HE4 can be used as a marker for uterine malignancies.
IS DIENOGEST EFFECTIVE IN POSTOPERATIVE MANAGEMENT OF ENDOMETRIOSIS COMPARED TO GNRH A?

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Objectives
Few randomised controlled trials were published but no systematic review was conducted on dienogest. The aim is to investigate whether is it effective or not in treatment of endometriosis.

Methods
All randomised controlled trials comparing dienogest vs GnRHa in women with endometriosis were recruited and data were extracted. Data were plotted in Revman software and fixed effect model was used to estimate the effect of the intervention.

Results
There was no significant difference between interventions on the absolute reduction in pain on the visual analogue scale (MD -1.60, 95%CI -9.17 to 5.97; p 0.68) or the proportion of women who reported pain improvement (OR 1.26, 95%CI 0.27 to 5.80; p 0.77). Two trials reported a significantly higher difference in BMD (305 women) following Dienogest compared with GnRHa (MD 2.74, 95%CI 0.14 to 5.35; p 0.04), but there was marked heterogeneity among the trial results (I² 83%). In one trial (248 women), the mean urine calcium level was not significant difference between groups (MD 26.10, 95%CI -39.89 to 92.09; p 0.44). Regarding the safety profiles, two trials (503 women) reported significantly less headaches (OR 0.62, 95%CI 0.40 to 0.95; p 0.03; I² 0%), and one trial (248 women) reported significantly less sleep disorders (OR 0.20, 95%CI 0.04 to 0.93; p 0.04), with Dienogest. There was no significant difference in other reported safety outcomes.

Conclusions
Dienogest can be used with relative safety for managing pain with endometriosis.
CARBOPLATIN AND PACLITAXEL IN THE ADJUVANT TREATMENT OF ENDOMETRIAL CANCER – A RETROSPECTIVE STUDY

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Objectives
Adjuvant treatment after surgical staging for endometrial cancer (EC) remains controversial. Adjuvant radiotherapy (RT) has been shown to reduce locoregional recurrence, without overall survival (OS) benefit. Adjuvant chemotherapy can be considered in high-risk histologies or stage I and advanced stage. The aim was to assess the clinical effectiveness (disease free survival-DFS, OS) and toxicity of adjuvant carboplatin-paclitaxel (CP) in patients with endometrial cancer.

Methods
Retrospective analysis of patients with EC treated with adjuvant CP on a q3w schedule and RT between 2005-2011 at IPOP. Acute toxicity was evaluated. DFS and OS were estimated using Kaplan-Meier curve.

Results
92 patients were reviewed. Median age was 64 years (range 49-80) and all had ECOG 0-1. FIGO stage was: I 40,2%, II 18,5 %, III 39,1% and IVA 2,2%. The histology subtypes were: serous (26,1%), endometrioid (19,6%), carcinosarcomas (18,5%), clear cell (16,3%) and mixed type (19,5%). Mainly grade 3. All patients were submitted to surgical staging followed by CP(3 cycles)-RT-CP(3 cycles) (93,5%), CP(6 cycles)-RT (5,4%) or CP (6 cycles)(1,1%).

The main toxicities G2/G3 were neutropenia (7,6%), peripheral sensory neuropathy (4,3%) and thrombocytopenia (4,3%). With a median follow up of 31 months (5-95), 22 patients had recurrence (59,1% at distant) and 20 died of disease. Median DFS was 15 months. Estimated 5-year OS was 67%.

Conclusions
Adjuvant sandwich regimen is feasible and well tolerated, with good locoregional control. However distant metastasis continued to occur in advanced stages. More randomized prospective studies are needed to understand the real impact of this treatment, mainly the sandwich protocol.
SURGICAL STAGING OF EARLY STAGE ENDOMETRIAL CANCER: COMPARISON BETWEEN LAPAROTOMY AND LAPAROSCOPY
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Objectives
The aim of the present study was to compare the feasibility of surgical staging of early stage endometrial cancer between laparoscopy and conventional laparotomy.

Methods
Retrospective data were collected and analysed for morbidity, amount of intraoperative bleeding, complication rate, total resected and laterality specific number of lymph nodes, number of positive lymph nodes, and operation time of the laparoscopic approach to early-stage endometrial cancer compared to the traditional laparotomic approach.

Results
Seventy nine stage I endometrium cancer subjects were found to be eligible for the trial purposes and 21(26.6%) treated by laparoscopy (LS) and 58 (73.4%) treated by laparotomy (LT). In LT group there was no difference in the number of lymph nodes between the right and left sides (10±5.8 and 8.7±4.8 respectively, p=0.19) but in LS group the number of lymph nodes resected from the right side were higher then the left side (9.8±5 and 7±3.5 respectively, p=0.039). The amount of intraoperative bleeding and the need for blood transfusion were significantly higher in LT group. Seventy nine patients had a median follow-up of 30 months. The two groups were similar for disease-free survival and overall survival.

Conclusions
There was no significant difference between the two methods in terms of number of total resected lymph nodes. In early stage endometrial carcinoma, laparoscopy has provided adequate staging and similar survival rates with laparotomy.
e-Posters: Endometrial Cancer

PREDICTORS OF LYMPH NODE METASTASES IN ENDOMETRIAL CARCINOMA
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Objectives
The goal of this study was to investigate and to evaluate the risk factors of lymph node metastases in endometrial cancer.

Methods
Retrospective single institution analysis of patients surgically staged for endometrial cancer at Ankara Oncology Hospital from 1996 to 2010. The role of prognostic factors such as age, histological type, and grade, depth of myometrial invasion, cervical involvement, peritoneal cytology, and tumor size in prediction of lymph node metastases was evaluated. Fisher's exact test and logistic regression analysis were used to assess the effect of the various factors on lymph node metastases.

Results
288 patients were operated for endometrial cancer and lymph node dissection was performed to 279 (96.8%) of them. Lymph node metastases was significantly more common in the presence of higher grades of tumor, deep myometrial invasion, cervical involvement, >2 cm tumor size and positive peritoneal cytology. The logistic regression analysis was revealed that myometrial invasion remained the only independent risk factor for lymph node metastases.

Conclusions
The incidence of lymph node metastases is influenced independently by deep myometrial invasion.
FACTORS INFLUENCING CHOICE OF LAPAROSCOPIC VERSUS LAPAROTOMIC HYSTERECTOMY FOR UTERINE CANCER TREATMENT

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Objectives
To determine factors that influences the selection of laparoscopic versus laparotomic approach for hysterectomy in treating uterine cancer.

Methods
A retrospective analysis of women who underwent laparoscopic hysterectomy (group I, n=83) or laparotomic hysterectomy (group II, n = 31) due to uterine cancer during one year period was carried out at University Hospital in Kaunas, Lithuania. Correlation between patients’ age, body mass index (BMI), comorbidities, stage of cancer, size of uterus, histological type, surgeon and surgery type were evaluated. Logistic regression was used to identify independent predictors of hysterectomy approach.

Results
Compared with women who underwent laparotomic hysterectomy, those who had laparoscopic hysterectomy were younger (61 ± 11.4 versus 68 ± 11.9 years, p < 0.05) and more often had endometrioid adenocarcinoma (98.8% and 87.1%, p < 0.05). There was a significant correlation between the different gynecologists and surgery type (p < 0.05). BMI, comorbidities, stage of cancer, size of uterus were not associated with hysterectomy approach in univariate analysis. Logistic regression analysis revealed that non-endometrioidal histology (OR 0.04, 95% CI 0.01-0.5) and one of surgeons (OR 0.07, 95% CI 0.01-0.5) was associated with a significantly decreased odds of laparoscopic hysterectomy.

Conclusions
The choice of laparoscopic or laparotomic hysterectomy for uterine cancer depends on the histological type of cancer and the surgeon performing the procedure.
e-Posters: Endometrial Cancer

IS SERUM SPERM-ASSOCIATED ANTIGEN-9 A SIGNIFICANT MARKER FOR DETECTION AND PROGNOSIS OF ENDOMETRIAL CANCER?

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Objectives
To investigate the significance of serum sperm-associated antigen 9 (SPAG9) in detection of endometrial cancer (EC) and its association with prognostic clinicopathological parameters.

Methods
This prospective study was performed at a tertiary referral center in Ankara, Turkey, after gaining approval from the institutional review board. Preoperative serum samples were collected from patients surgically treated for endometrial cancer between January-December 2012. Healthy women with no gynecological diseases or malignancies were used as controls. Serum SPAG9 levels were measured with enzyme-linked immunosorbent assay (ELISA) method. Association of serum SPAG9 levels with clinicopathological data was investigated with SPSS 20.0 software. P values less than 0.05 were considered statistically significant.

Results
A total of 63 women with EC and 27 controls were included in the study. Mean age in EC group was 58.7±1.1. Mean preoperative serum SPAG9 levels were significantly lower in women with EC when compared with controls (15.5±1.2 vs. 20.6.0±1.5 ng/ml, p<0.001). In patients diagnosed with EC, mean SPAG9 levels were similar between prognostic factor groups.

Conclusions
In this study, SPAG9 was not found to be a significant diagnostic and prognostic marker in patients with EC. Future studies are needed to reach a final conclusion.
GLYCOSILATED HEMOGLOBIN AND INSULIN LEVELS IN NON-DIABETIC CASES OF ENDOMETRIAL CANCER: A PILOT STUDY
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Objectives
To investigate insulin and glycosilated hemoglobin (HbA1c) levels in non-diabetic endometrial cancer (EC) cases, and to seek associations between CA125 level, disease stage and histological type.

Methods
This study was performed after gaining approval from the institutional review board at the gynecological oncology department of Zekai Tahir Burak Women’s Health hospital in Ankara, Turkey. Sixty consecutive non-diabetic patients who were treated for EC between April 2012-April 2013 at our institution were included in the study. Insulin and HbAa1c levels were measured for each participant. Clinicopathological data were obtained from patient charts and pathology reports. Associations were investigated between insulin- HbA1c levels and clinicopathological data. P values less than 0.05 were considered statistically significant.

Results
Mean patient age was 56.5 +/- 9.05 (range, 40-81). Mean body mass index was 31.1 +/- 4.1. Mean insulin and HbA1c levels were 12.7 +/- 5.9 and 5.9 +/- 0.5, respectively. Insulin and HbA1c levels did not have a significant association with patient age, BMI, histological type, disease stage and CA125 level.

Conclusions
Our study failed to demonstrate a significant association between insulin-HbA1c and important clinicopathological parameters. Further studies are needed to reach a final conclusion.
OBJECTIVES
Endometrial cancer is diagnosed in about 4% of women less than 40 years of age, which may desire fertility sparing options. However we reported a case of failed conservative treatment.

METHODS
A 26-year-old obese woman presented at our evaluation with occasional hysteroscopic diagnosis of atypical endometrial hyperplasia, during a gynecological assessment for colorectal cancer. The patient was treated with progestin 30 mg/d. The first follow-up, 3 months after therapy, showed a partial response (i.e. regression of atypical hyperplasia to typical), on hysteroscopic biopsies. However at the second control, 6 months after therapy, we found a clinical report suggestive for endometrial cancer on posterior uterine wall, confirmed at histologic evaluation that reported well differentiated endometrioid carcinoma. After a counseling with the patient, a conservative treatment was planned: we performed a partial hysteroscopic resection of endometrial lesions, followed by megestrol acetate 160 mg/d.

RESULTS
Three months later, we observed a progression of disease: the carcinoma was moderately differentiated at hysteroscopic specimens and on transvaginal USG and MRI, myometrial invasion was evaluated in the < ½ myometrial invasions. So, after a new counseling, we planned a hysterectomy.

CONCLUSIONS
Fertility-sparing treatment with hysteroscopic resection of endometrial atypical lesions preserving the basal endometrial layer, followed by medical treatment can be considered a good therapeutic option in young patients with well-differentiated early-stage endometrioid endometrial adenocarcinoma. However, women must be fully informed about the necessity of a close follow-up and the possibility of treatment failure, especially if coexist risk factors (obesity and inherited genetic predisposition).
e-Posters: Endometrial Cancer

LAPAROSCOPY VERSUS ROBOTICS IN THE SURGICAL MANAGEMENT OF ENDOMETRIAL CANCER: COMPARISON OF HISTOLOGICAL FINDINGS AND ONCOLOGICAL OUTCOMES
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Objectives
To assess the contribution of robotic surgery compared to laparoscopy in histological results and oncological outcomes in the surgical management of endometrial cancer.

Methods
Retrospective study from 2002 to 2011. Patients with endometrial cancer who underwent laparoscopic or robot-assisted surgical treatment were included. We collected preoperative data, including characteristics of patients (age, BMI, medical and surgical history) and tumors (circumstance of discovery, preoperative biopsy results), intraoperative data (route of surgery, surgical act), postoperative definitive histological results (histological type and grade, depth of myometrial invasion, cervical invasion, results of pelvic and paraaortic lymphadenectomy) and oncological outcomes (adjuvant treatments, overall survival, free disease survival). All these data were compared between both groups.

Results
146 patients were included in the study: 106 patients in the laparoscopy group and 40 in the robot-assisted surgery group. The two groups were comparable in terms of demographic and preoperative data, operative data and final histological FIGO staging. The number of pelvic lymph nodes removed was significantly higher in the robot group. There was no significant difference between the two groups about overall survival and free disease survival.

Conclusions
With similar results in terms of overall survival and disease-free survival, robot-assisted surgery can take a larger number of pelvic lymph nodes.
SYNCHRONOUS PRIMARY OVARIAN AND ENDOMETRIAL CARCINOMAS: A CASE REPORT AND A CLINICO-PATHOLOGICAL REVIEW

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Objectives
Synchronous primary cancers of the endometrium and of the ovary coexist in approximately 10% of all women with ovarian cancer and in 5% of all women with endometrial cancer. It is important for the clinician to distinguish the presence of two independent primary tumors from a metastatic cancer to an adjacent organ. This distinction is important in terms of therapeutic management and prognosis.

Methods
We report a case of coexisting primary endometrioid carcinomas of the uterine corpus and of the ovary. The epidemiological, clinical and histopathological features are discussed, as well as the prognosis.

Results
Presentation of case
We report a case of coexisting primary endometrioid carcinomas of the uterine corpus and of the ovary in a 37 year-old patient. A total abdominal hysterectomy with a bilateral salpingo-oophorectomy, an omentectomy and a pelvic lymph node curage were performed. Given that there was no evidence of spread of both the endometrial and the ovarian tumors, the histopathological examination concluded to a synchronous grade 2 endometrioid adenocarcinoma of the right ovary and of the endometrium, classified FIGO staging pT1 for both the ovary and the endometrium. The patient underwent adjuvant chemotherapy. The outcome was favourable after two years of follow-up.

Conclusions
The review of literature showed that these tumors are associated with a favourable prognosis, particularly those of the endometrioid type.
HISTORICAL EVOLUTION OF THE SURGICAL APPROACH TO ENDOMETRIAL CANCER IN A DEPARTMENT OF GYNAECOLOGIC ONCOLOGY: IS CHANGE POSSIBLE?
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Objectives
To compare the safety and associated morbidity of a laparoscopic approach to endometrial cancer versus laparotomy and to describe the historical evolution of the surgical approach to endometrial carcinoma in the Department of Gynecologic-Oncology of a tertiary-health centre.

Methods
A prospective study was conducted between January 2005 - December 2010, including 348 patients diagnosed with clinical stage I endometrial cancer, 160 of them treated with laparotomy and 188 with laparoscopy. Both groups were compared for epidemiological and clinical characteristics, surgery outcomes, pathology, hospital stay and intraoperative and postoperative complications.

Results
No differences were found in terms of median age, previous laparotomy and median BMI. Median operating time was longer for the laparoscopy group, although the difference was not significant (134.8 ± 58.5 vs. 126.6 ± 43.6; p = 0.1). Estimated blood loss was significantly lower in the laparoscopy group (100 ± 16.2 vs. 300 ± 26.6; p < 0.0001). No differences were observed in terms of intraoperative complications (3.2% vs. 6.8%; p = 0.1); however, postoperative adverse events were significantly less frequent among patients in the laparoscopy group (21.4% vs. 13.3%; p = 0.03). Hospital stay was significantly longer for patients in the laparotomy group (6 ± 7.8 vs. 3 ± 2.1 days). No significant differences were found in the rates of readmission, reoperation and treatment-related death.

Conclusions
Laparoscopy is a safe and effective surgical approach to the management of endometrial cancer that can be applied by trained professionals in any health-centre. Drastic change in the surgical management of endometrial cancer, with significant reduction of associated morbidity seems possible.
ENDOMETRIAL CANCER PRESENTING AS BILATERAL FLANK PAIN: A CASE REPORT AND REVIEW OF THE LITERATURE

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Objectives
Endometrial cancer is the most common gynecologic malignancy and the fourth most common cancer in women. It has a high cure rate as 92 percent of women are detected in stage I and II of the disease and most present with vaginal bleeding as the chief complaint. A case report and review of the literature are presented.

Methods
A 76 years old, post-menopausal, caucasian woman gravida 10, para 7 was admitted under the care of the general surgeons presenting with a few days history of bilateral flank pain. She had no bowel or urinary symptoms. Her medical history was significant for obesity, hypertension, diabetes and previous breast cancer. A CT scan was requested and revealed a huge uterus.

Physical examination revealed a huge uterus. She was then referred to the gynaecologists who carried out a pipelle endometrial biopsy and a transvaginal ultrasound scan which showed a large fluid filled cavity suggesting a large pyometra that was drained.

Results
Endometrial currettings were also obtained and an endometrioid adenocarcinoma was diagnosed. Exploratory laparotomy with total abdominal hysterectomy with bilateral salpingoopherectomy was done.

Conclusions
Uterine fluid is common in postmenopausal women and is frequently associated with cervical stenosis, such cases must prompt early assessment to rule out underlying malignancy.
METFORMIN MAY REDUCE THE INCIDENCE OF ENDOMETRIAL CANCER RECURRENCE IN OBESE WOMEN
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Objectives
Obesity is the major risk factor for developing endometrial cancer. It is felt that high estrogens and insulin in the obese woman promotes cancer development. Metformin, a medicine for non-insulin dependent diabetes, has been associated with lower incidence and longer survival in a number of different cancers. This study reviews our experience with obese (BMI>30) women with endometrial cancer and compares outcomes of those on metformin with those who are not.

Methods
This is a retrospective review of all women with endometrial cancer from 2006-2011 with a BMI>30. Data was extracted for pathological risk factors and rate of recurrence. Metformin use at the time of diagnosis was also determined.

Results
257 women were identified with endometrial cancer who were obese. The mean age of patients was 58 yrs. Median BMI was 40 kg/m². 173 underwent complete surgical staging. Metformin users had a higher mean BMI (44.6 vs 41.6 p=0.05). There was no difference between Metformin users and non-users with regard to tumor grade, depth of invasion, stage, lymph node status, or use of adjuvant therapy. There was a higher recurrence rate for non-users (17%) versus those on Metformin (6.5%) p=0.05. Disease recurrence or pathologic risk factors did not stratify on the basis of daily Metformin dose.

Conclusions
Metformin use in obese women who with endometrial cancer did not impact the presence of pathologic risk factors for recurrence. However, the overall recurrence rate was significantly lower in those women on Metformin, suggesting a beneficial role in this population.
CLINICOPATHOLOGICAL FEATURES OF ENDOMETRIAL CARCINOMA IN YOUNG AND OLD WOMEN

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Objectives
The objective of this study was to examine clinicopathological features of endometrial adenocarcinomas in patients older than 65 years, compared to younger women.

Methods
We performed a retrospective cohort study of patients who were diagnosed with endometrial carcinoma between October/2008 and December/2012 and surgically staged. The age of patients ranged from 39 to 96 years (65.3±9.8y), median 65 years. Patients older than 65 years were compared to younger according to body mass index, surgical technique, surgical stage, histological type, histological grade, level of myometrial infiltration, size of tumor, lymphovascular space involvement (LVSI), and lymph node involvement.

Results
One hundred thirteen women (45.9%) were older than 65 years and 133 (54.1%) has 65 years or less. There was a trend to more surgeries by laparotomy rather than laparoscopy (p=0.08). Older patients presented a higher frequency of non-endometrioid histology (24.1% vs 9.7%, p=0.004) and high grade carcinomas (35.1% vs 17.7%, p=0.003). Body mass index, LVSI, deep of miometrial invasion, tumor size, node status, and FIGO stage were not different in two groups.

Conclusions
Older patients present more aggressive endometrial carcinomas (non endometrioid and high grade), despite the same stage characteristics.
INFLUENCE OF BODY MASS INDEX ON CLINICOPATHOLOGICAL PRESENTATION OF ENDOMETRIAL CARCINOMAS

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Objectives
To examine the influence of obesity on the clinicopathologic features of endometrial cancer.

Methods
We performed a retrospective cohort study of 246 patients who were diagnosed with endometrial carcinoma between October/2008 and December/2012 treated by surgical staging. Patients were divided into three categories as <25, 25-29.9 and ≥30 according to body mass index (BMI). We compared age of patients, surgery technique, histological type, tumor grade, lymphovascular invasion, myometrial invasion, node status, and FIGO stage between the three groups using ANOVA (age) and chi-square statistical test (categorical variables).

Results
BMI were <25 in 76 (30.9%), 25 to 29.9 in 114 (46.3%), and ≥ 30 in 56 (22.8%) patients. Laparotomy surgery was preferred for BMI >30 patients. There were no differences in pathological characteristics between the BMI groups.

Conclusions
Clinicopathological presentation of surgically treated endometrial cancer is not affected by the BMI.
e-Posters: Endometrial Cancer

A CRITICAL DECISION MAKING: DIAGNOSIS OF ENDOMETRIAL ADENOCARCINOMA DURING INFERTILITY FOLLOW-UP

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Objectives
To present bothersome endometrial adenocarcinoma presence in ≤40 years of age infertile women.

Methods
Totally 29 women were diagnosed as endometrial adenocarcinoma at ≤40 years of age in our center. Exclusively 7 of them were primary infertile and diagnosed during infertility workup. Medical records of these women reviewed retrospectively.

Results
Women were diagnosed incidentally by endometrial sampling because of abnormal endometrial visualization during diagnostic hysteroscopy. Mean value of age and duration of infertility at the time of diagnosis were 33.1 years (range 28-40) and 7.2 years (range 2-18) respectively. Mean value of endometrial thickness and CA 125 levels were 11.25mm (range 7-19) and 37.17 U/ml (range 9.8-85.1) respectively. Endometrial sampling results revealed endometrial adenocarcinoma diagnosis in all except one patient who had complex atypical hyperplasia. Of 6 patients 5 had FIGO grade I and 1 patient had FIGO grade II tumor differentiation. Only 71.4% of patients (5 cases) had history of Polycystic Ovarian Disease as a risk factor. Two of the 7 cases had elected surgical staging instead of infertility workup and both of them were diagnosed as stage IA disease at surgery. The others were treated with high dose oral Megestrol acetate and progesterone containing intrauterine device. Endometrial biopsy evaluations were done at three months intervals and there were no progression. Only one patient had pregnancy with live birth.

Conclusions
Young women with infertility and PCOD are at increased risk for endometrial adenocarcinoma. It is important to sample endometrium in the presence of endometrial abnormalities in case of infertility to differentiate probable malignancy.
ENDOMETRIAL ADENOCARCINOMA IN YOUNG WOMEN: SINGLE CENTER EXPERIENCE
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Objectives
To evaluate clinicopathological characteristics of endometrial adenocarcinoma patients at 40 years old and younger.

Methods
Medical records of 577 endometrial adenocarcinoma patients who received staging surgery in our center were reviewed. 29 of 577 endometrial adenocarcinoma patients were 40 years of age or younger. However 25 patients’ records were reached.

Results
Minimum age at diagnosis was 28 years old (mean 35,5). Mean thickness of endometrium on ultrasonography was 16,1mm (range: 7-57mm). 84% of patients had a primary symptom of menometrorrhagia, 8% pelvic pain, 8% pain and hypermenorhea together. There were 11 nulligravid patients whom 7 of them were infertile and 13 nulliparous patients whom 2 of them had recurrent pregnancy loss. Only one patient (4%) had abnormal glandular cells on PAP smear evaluation. Up to 24% (6 cases) of patients’ pathology diagnosis were complex atypical hyperplasia with well differentiated adenocarcinoma could not be excluded. Five patients who desire future fertility had no surgery and they are under high dose oral and progesterone containing IUD treatment with negative endometrial biopsy. Two infertile patients were surgically staged according to patient desire. Two patients (8%) who had had biopsy proven endometrial malignancy had negative result in staging surgery. Most of the patients’ disease (endometrioid morphology) were limited to uterus with 12% (3 case) stage 1B and 4% (1 case with serous&clear cell morphology) stage 3C2 disease with para-aortic lymph node involvement.

Conclusions
Women with abnormal uterine bleeding regardless of age must be carefully evaluated for endometrial carcinoma.
RESISTANCE AGAINST CANCER, TOOK THE BABY HOME
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Objectives
To present a case with endometrial cancer who insists on child bearing.

Methods
Thirty-three years old woman with the diagnosis of primary infertility for 5 years was admitted to our hospital with abnormal uterine bleeding. Upon admission transvaginal ultrasound revealed irregular endometrial line with polycystic-ovarian architecture. A possible endometrial polyp was thought and operative hysteroscopy was planned. There were two vegetative polyps on inspection and polypectomy was performed. Pathological diagnosis was endometrioid adenocarcinoma grade I with atypical complex hyperplasia background. Staging surgery was recommended but patient denied surgery and wanted to have infertility work-up. According to patient desire 160-mg/day 3-month progesterone prescribed. Control P&C was performed after 3 months and decidualized endometrium was revealed. Patient had IVF treatment and had a pregnancy that resulted with abortion at 8 weeks gestation. Two weeks after abortion office hysteroscopy-endometrial sampling revealed endometrial polyp recurrence. Unfortunately patient resisted against follow-up and readmitted 2 years later for infertility evaluation. On admission P&C was performed and atypical complex hyperplasia was diagnosed. Progesterone treatment was administered. Control biopsy revealed complex hyperplasia without atypia and progesterone treatment was continued. After biopsy proven negative results patient had a second course of IVF treatment that resulted uncomplicated pregnancy and term birth.

Results
Staging surgery was advised 3 times to this patient but she resisted against suggestions. After labor again she denied staging surgery and now she is on medical follow-up.

Conclusions
Young women with the diagnosis of clinical early stage endometrial cancer should have enough medical attention to have a chance for reproduction.
MALIGN MESENCHYMAL TUMORS OF UTERUS IN YOUNG AGED WOMEN

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Objectives
To present malign mesenchymal tumors in ≤40 years of aged women.

Methods
Medical records of 65 uterine mesenchymal tumor patients who received staging surgery in our center were reviewed. 10 of 65 patients were 40 years of age or younger. Medical records of these women evaluated retrospectively.

Results
Minimum age at diagnosis was 29 years old (range 29-40; mean 35). Seven women had menorrhagia and 3 women had pelvic pain as a causative reason to seek medical attention. There were no nulligravid-nulliparous women with range of gravidy 2-5 and range of parity 2-4. Six women had at least one myomectomy operation before the definitive diagnosis. Mean tumor mass was 9 cm (range 4-17cm). There were 3 low grade endometrial stromal sarcoma patients whose tumors were limited to uterus (stage 1). Seven women had leiomyosarcoma; 3 with myxoid and 1 with epitheloid differentiation. Only one patient had stage 3C disease with positive pelvic lymph nodes in leiomyosarcoma group.

Conclusions
Uterine mesenchymal tumors have poor prognosis with a five-year survival rate 25-30%. Most common types of uterine sarcoma are Malign Mixed Mullerian Tumors, leiomyosarcoma and endometrial stromal sarcoma. Revised FIGO 2009 staging system is used to clarify patients. Disease stage is the most important prognostic factor. Tumor size, degree of coagulative tumor necrosis and mitotic index are the other factors that effect the prognosis. Young women especially who have large and recurrent pelvic mass must be evaluated against possible mesenchymal tumors.
METRONOMIC CPT-11 CHEMOTHERAPY COMBINED WITH ULTRASOUND IRRADIATION FOR A HUMAN UTERINE SARCOMA XENOGRAFT
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Objectives
Metronomic chemotherapy is the frequent administration of low doses of chemotherapeutic agents targeting tumor associated endothelial cells. Recent studies have showed that low-intensity ultrasound (US) irradiation enhances the effect of chemotherapeutic agents. This study was the first to examine the efficacy of metronomic CPT-11 combined with low-intensity US in a human uterine sarcoma xenograft.

Methods
FU-MMT-3, a human uterine sarcoma cell line that shows an elevated expression of VEGF, was used in this study. The FU-MMT-3 xenografts in nude mice were treated with conventional or metronomic CPT-11 in early regimen, and combination of metronomic CPT-11 and US in late regimen. The outcome was assessed by contrast-enhanced color Doppler US, while the number of circulating endothelial progenitor cells (CEPs) was determined by flow cytometry, in addition to the prolongation of survival.

Results
Low dose SN38, an active metabolite of CPT-11, and low intensity US significantly inhibited the tube formation of HUVEC cells and the VEGF expression of tumor cells. Metronomic CPT-11 in early regimen significantly reduced CEPs and tumor growth in comparison to control and conventional dose treated mice. The combination treatment in late regimen significantly inhibited the mobilization of CEPs, and intratumoral vascularity in comparison to control. This treatment also showed significant reduction in tumor volume, resulting in a significant prolongation of survival, in comparison to each treatment alone.

Conclusions
These results suggest that the effect of metronomic chemotherapy for uterine sarcoma was accelerated by US irradiation in vivo and this combination might therefore be a potentially effective for new cancer therapy.
e-Posters: Endometrial Cancer

ANDROID FAT IN CORRELATION WITH LIPOCALIN – RISK FACTOR FOR ENDOMETRIAL CANCER

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Objectives
Obesity induces metabolic disfunctions characterized by an increased plasmatic level of insulin and cytokines, but also an increased level of lipocalin, directly connected to endometrial cancer. The study aims to evaluate the presence of a correlation between android adiposity assessed by dual-energy X-ray absorptiometry (DXA) and plasmatic level of lipocalin in patients diagnosed with endometrial cancer.

Methods
The study is a case-control analysis including 2 groups of patients: group I – 44 patients diagnosed with endometrial cancer, group II – 44 patients without gynecological pathology or inflammatory disorders. The diagnosis of endometrial cancer was made following histopathological examination that evaluated the tissue, material obtained following endometrial biopsy. After clinical examination and anthropometric measurements, these patients underwent DXA examination, in view of determining the android fat. At patients included in this study, we also determined plasmatic levels for lipocalin. The Student t test was used for the comparison of the means and the Mann-Whitney test for rank comparison in two independent samples.

Results
At patients diagnosed with endometrial cancer, the android fat area evaluated by DXA and plasmatic level of lipocalin is significantly larger compared to the control group. A correlation was also found between android fat evaluated by DXA and plasmatic level of lipocalin.

Conclusions
An android fat evaluated by DXA larger than 45.65% is a risk factor for endometrial cancer. The measurement of android fat by DXA in correlation with plasmatic level of lipocalin can be a screening method for endometrial cancer in obese patients.
e-Posters: Endometrial Cancer

UTERINE CANCER IN THE “DR. SALVATOR VUIA” CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 1998-2012 PERIOD

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Objectives
The purpose of this study is to examine the frequency of uterine cancer in our hospital during the 1998-2012 interval.

Methods
The data being collected from the Histopathology Exams (HPE) registers.

Results
Uterine cancer was discovered in 556 cases, representing 31.73% of all genital cancers (1752 cases). One patient had a combination of cervical and uterine cancer, and another had a combination of cervical and ovarian cancer. Most cases (531 or 95.50%) were represented by carcinomas, twenty patients (3.60%) had sarcomas and there were also four cases of carcinosarcoma (0.72%) and one case of carcinoma-carinosarcoma combination (0.18%). Endometrioid carcinoma appeared in 87.33% of all carcinoma cases. Sixteen cases of sarcoma were endometrial stromal sarcomas and four were leiomyosarcomas. Eight cases of carcinoma were combined with endometrial hyperplasia (1.44%) and one with CIN II (0.18%). The mean ages of the patients were 61.92±9.55 years for all cases of uterine cancer (age range 32 to 88 years). A number of 207 patients belonged to the 51-60 year age group, representing 37.23% of all uterine cancer cases.

Conclusions
Uterine cancer, although less aggressive, still remains a serious public health issue in Romania as many cases are discovered too late.
Micro RNA-106b modulates epithelial-mesenchymal transition by targeting TWIST1 in invasive endometrial cancer cell lines

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Aim
Type II endometrial carcinoma is an aggressive subtype of endometrial cancer (EC). TWIST1, a helix-loop-helix transcription regulator, is known to induce epithelial-mesenchymal transition (EMT) and promote tumor metastasis. MicroRNAs (miRNAs) also serve as important regulators of EMT and metastasis by regulating EMT-related genes. In this study, we sought to explore the role of TWIST1 in inducing EMT in representative type II EC cell lines, and to determine the miRNAs involved in regulating TWIST1 gene expression.

Methods and Results
Functional analysis suggested that TWIST1 contributes to the EMT phenotypes of EC cells, as evidenced by the acquisition of fibroblast-like properties, enhanced invasiveness, and induction of an EN-switch (downregulation of epithelial marker E-cadherin and upregulation of mesenchymal marker N-cadherin). Conversely, silencing of TWIST1 by siRNA inhibited cell invasion and the mesenchymal phenotype, which was accompanied by a reversion of the EN-switch. We also observed a novel post-transcriptional regulatory mechanism of TWIST1 expression mediated by miR-106b via its direct interaction with TWIST1 mRNAs at the 3’-untranslated region.

Conclusions
Our data suggest that TWIST1 is a critical inducer of EMT in invasive EC cells and that miR-106b could suppress EC cell invasion by downregulating TWIST1 expression.
LOW SERUM ADIPONECTIN AND VASPIN LEVELS AS NOVEL RISK FACTORS FOR POSTMENOPAUSAL ENDOMETRIAL CANCER

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Objectives
Insulin resistance is a well-documented risk factor for the development of endometrial cancer. Adipokines, such as adiponectin and the more novel vaspin, are insulin sensitizing proteins that are secreted from adipose tissue. A clear association between serum levels of adipokines and endometrial cancer has yet to be established.

Methods
Consenting post-menopausal women with histologically or cytologically confirmed endometrial cancer and volunteers who were evaluated between April 2012 and January 2013 were included in this cross-sectional controlled study. The two groups were compared in terms of insulin resistance and serum levels of adiponectin and vaspin, measured by enzyme-linked immunosorbent assay.

Results
A total of 60 patients with confirmed endometrial cancer, and 70 controls were enrolled. Median HOMA-IR value was significantly higher in the study group compared to controls (2.93 vs. 1.27, p< 0.0001), whereas mean QUICKI value was significantly lower (0.33 ± 0.02 vs. 0.37 ± 0.37, p<0.0001). Median values for both adiponectin and vaspin were significantly lower in patients with endometrial cancer compared to the control group (4.09 vs. 17.13 µg/mL, p<0.0001 and 0.21 vs. 0.39 ng/mL, p<0.0001, respectively). Low adiponectin and vaspin levels were found to be significantly associated with an increased risk for endometrial cancer after adjustment for confounding factors, such as age, body mass index, insulin resistance.

Conclusions
Our results show that lower levels of circulating adiponectin and vaspin levels are associated with increased risk of developing endometrial cancer.
CORRECTION OF IATROGENIC INJURY OF THE OBTURATOR NERVE BY THE USE OF SURAL NERVE GRAFTS

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Objectives
Evaluation of microsurgical technique that uses the interposition of sural nerve graft for correction of iatrogenic lesion of the obturator nerve.

Methods
We present a case of a 52 years-old woman who underwent to endoscopic treatment for a moderate-differentiated endometrial adenocarcinoma. An iatrogenic total transaction of the obturator nerve occurred during the right iliac lymphadenectomy. Patient was promptly assisted by neurosurgeon, who proceeded a microsurgical repair of the nerve injury through the interposition of sural nerve grafts (pictures 1B to 3B).

Results
After an intensive physiotherapy, patient demonstrated complete recovery of the adduction of the right leg. Electroneuromiography performed 6 months after showed unequivocal signs of reinnervation of the adductor longus muscle.
Conclusions
The correction of the obturator nerve injury using the technique of sural nerve graft interposition maybe be considered as an efficient and save alternative when primary anastomosis is not possible.
EVIDENCE OF SUCCESS IN TERM OF SURVIVAL USING PROGESTIN THERAPY IN THE TREATMENT OF LOW-GRADE ENDOMETRIAL Stromal SARCOMA (LGESS): A CASE REPORT

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**Objectives**

LGESS are uncommon uterine mesenchymal tumours characterised by a good prognosis despite a high tendency to recur after long disease-free interval. LGESS often express oestrogen (ER) and progesterone (PR) receptors; using progestin therapy is possible to bind progesterone receptors causing down-regulation of gene transcription, which leads to reduction of endometrial gland and stromal proliferation.

**Methods**

In 2000 a 55-year-old woman was diagnosed with low grade endometrial stromal sarcoma (PR receptors positive) and underwent total hysterectomy and anmassectomy surgery. After treatment, clinical and instrumental examination showed absence of disease and the patient was followed-up for 77 months. In 2007 pelvic examination revealed presence of a solid lesion involving left vaginal vault; a total body CT scan showed pulmonary, bladder and pelvic recurrent lesions. On July 2007 the patient started the treatment with 80 mg daily of Acetate Megestrol. The therapy appeared to be effective and on January 2009 CT scan evidenced a complete absence of disease. Because of few collateral effects and a good compliance with therapy, we decided to continue the treatment.

**Results**

After 74 months, and a survival of more than 13 years from the first diagnosis, the patient is still on treatment and has got a good quality of life, with the exception of weight gain, even with an adequate diet.

**Conclusions**

For the proven efficacy showed in term of survival and quality of life, we confirm, according to the literature, that the progestin therapy should be routinely adopted even in the treatment of recurrent low-grade EES.
TREATMENT OF HIGH INTERMEDIATE RISK ENDOMETRIAL CANCER
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Objectives
Trials have analyzed the survival differences among treatment strategies for women with high intermediate risk stage I endometrial cancer (HIR). In this study, we sought to evaluate the cost effectiveness of treatments for HIR.

Methods
A decision model was developed from Gynecologic Oncology Group protocol 99, ASTEC and PORTEC. Regimen 1 is total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAHBSO) with radiation therapy (XRT) (TAHBSO XRT). Regimen 2 is TAHBSO lymph node dissection (LND) with XRT (TAHBSO LND XRT). Regimen 3 is TAHBSO LND. Cost effectiveness analysis (CEA) was performed using data from Medicare and published studies incorporating costs, complications, recurrence rates, and overall survival. Incremental cost-to-effectiveness ratios (ICER) were determined for any non-dominated treatment options. Sensitivity analyses were performed.

Results
The average cost per patient for TAHBSO LND XRT was $23,026; TAHBSO XRT was $25,596; and TAHBSO LND was $8,122. TAHBSO XRT had increased cost and decreased effectiveness compared to TAHBSO LND. The ICER between TAHBSO LND XRT and TAHBSO LND was $459,716 /per percentage of 5 year survival. Although TAHBSO XRT was dominated in analysis, a one-way sensitivity analysis was performed, demonstrating that if 5 year survival was increased to 90%, this treatment would be cost effective with an ICER of $45,658/ per percentage of 5 year survival. Even if the TAHBSO XRT were free, it would not be cost effective according to sensitivity analysis.

Conclusions
Performing TAHBSO LND without radiation for HIR is the most cost effective treatment; therefore, TAHBSO XRT should not be recommended as treatment.
SYNCHRONOUS SEROUS CARCINOMA OF THE ENDOMETRIMO AND FALLOPIAN TUBE

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Objectives
1-10% of endometrial carcinomas are serous carcinomas. Serous carcinoma usually develops on the basis of atrophic endometrium or endometrial polyps. Primary carcinomas of the fallopian tube are very rare. Which are mostly adenocarcinomas of serous origin and are generally poorly differentiated.

Methods
A 62 year-old postmenopausal woman referred to the gynecology clinic with postmenopausal vaginal bleeding. D&C was performed to the patient. Totally abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymphadenectomy was performed with the diagnosis of endometrial adenocarcinoma.

Results
At macroscopy, 3x1x1 cm polyloid tumoral lesion was seen in uterine cavity which had dominantly papillary structure. Nucleus to cytoplasm ratio was high with a large number of atypical mitosis and extensive necrosis. The tumor was defined as "serous carcinoma". 1/2 superficial myometrial invasion and tumor trombuses in lymphovascular area were seen. Immumohistochemical features were P53 90%, Ki 67% 20 positive, ER and PR negative.
Both ovaries and fallopian tubes appeared macroscopically normal. In random sampling of right fallopian tube, there were atypical cells with pleomorphism of tumoral tissue and large hyperchromatic nuclei. The tissue formed papillary structures protruding into the lumen. Tumor invasion was detected in lamina propria but not in muscular tissue. Severe atypia were observed in tubal epitellium. "Tubal serous carcinoma" was diagnosed with these findings.

Conclusions
The primary tubal serous carcinomas are rare and for their diagnosis, ovarian and endometrial serous carcinoma metastasis should be excluded. For diagnosis, determinination of focus of carcinoma and tumor-adjacent intraepithelial dysplasia is important. We present our case because of its rarity.
CASE REPORT: EXISTENCE OF LOW GRADE ENDOMETRIAL ADENOCARCINOMA AND UNDIFFERENTIATED CARCINOMA (DEDIFFERENTIATED CARCINOMA)

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Objectives

Undifferentiated carcinoma has been defined as loss of structural and functional differentiation of tumor by WHO. Dedifferentiated carcinoma is the existence of undifferentiated carcinoma with low grade endometrial adenocarcinoma.

Methods

Grade 1 endometrial adenocarcinoma has been diagnosed in a postmenopausal patient of 63 years of age. Materials from TAH+BSO, pelvic lymphnodes and omentectomy evaluated. Ulcerative vegetative tumoral mass of 9.5x5.5x4 cm has been observed in macroscopy filling the endometrial cavity. Tumor showed diffuse necrosis areas that have Grade 2 endometrial adenocarcinoma areas and also undifferentiated carcinoma areas which were diffuse-solid, non-patterned and without glandular structures and are compromised by spherical nucleated highly mitotic cells. 40% of tumor was made of undifferentiated carcinoma areas and tumor was invading the cervix. There were no tumoral metastasis in pelvic lymphnodes, bilateral ovaries and omentum. Immunohistochemistry staining showed properties of EMA+, vimentine+, Ki-67%40+, P53%70+, progesteron%10+, estrogene-, NSE-, chromagnine-, P16+, LCA-, pancitokeratine- and cerbB2-.

Results

The case is reported as the existence of grade 2 endometrial adenocarcinoma and undifferentiated carcinoma (dedifferentiated carcinoma). Relaps was observed after 2 months in postoperative controls which presented with vaginal bleeding. Biopsy was positive in vaginal cuff.

Conclusions

Dedifferentiated carcinoma should be considered in differential diagnosis of early relapsing endometrial adenocarcinoma due to its bad prognosis and its aggressive clinical progress. It is crucial to use this definition in diagnosis for both prognosis and appropriate therapy.
MECKEL’S DIVERTICULECTOMY DURING GYNECOLOGIC CANCER SURGERY: THREE CASES
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Objectives
Meckel’s diverticulum is the most common congenital anomaly of the gastrointestinal tract. The majority of meckel’s diverticulum cases is discovered incidentally. There is disagreement about the routine resection of an incidentally discovered asymptomatic meckel diverticulum. In this paper, we present three cases of meckel’s diverticulum encountered during surgical staging of gynecologic cancers.

Methods
Case 1:
During the surgical staging of a 56-year-old woman with endometrial cancer a meckel’s diverticulum with 3.5 cm in length and 2 cm in width at its base was encountered. A 6-cm ileal segment was resected without any perioperative complication.

Case 2:
During the surgical staging of a 64-year-old woman with borderline ovarian serous tumor a meckel’s diverticulum with 3 cm in length and 2 cm in width at its base was detected and resected within a 5-cm ileal segment without any perioperative complication.

Case 3:
During the surgical staging of a 58-year-old woman with endometrium cancer, a concommitant jejunal stromal tumor and a meckel’s diverticulum were detected. Jejunal tumor was excised within a 10 cm jejunal resection. Meckel’s diverticulum was left in situ in order to prevent further morbidity.

Results
Meckel’s diverticulectomy can be performed in patients undergoing surgery for gynecologic malignancies, due to the future risk of confusion of tumoral metastases with probable diverticular complications.

Conclusions
No data exists about elective resection of meckel’s diverticulum performed during cancer surgery in literature. Further studies are needed.
e-Posters: Endometrial Cancer

CLINICOPATHOLOGICAL FEATURES AND PROGNOSTIC FACTORS OF THE UTERINE SARCOMAS: 20 YEARS OF EXPERIENCE AT ÇUKUROVA UNIVERSITY

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Objectives
In this study we aim to evaluate retrospectively the clinical and pathologic features and to investigate the prognostic factors of the uterine sarcoma patients who were treated in our department in the last 20 years.

Methods
The archive files, medical and pathological records of the 132 uterine sarcoma patients who were operated on and regularly followed up in our clinic between March 1991 – March 2011 were reviewed. Clinical features, operation characteristics, pathological findings, adjuvant therapies and follow-up data of the patients and their effects on survival were investigated.

Results
Seventy of the patients were diagnosed with leiomyosarcomas, 33 were with carcinosarcomas, 12 were with endometrial stromal sarcomas, 9 were with undifferentiated endometrial sarcomas, 5 were with adenosarcomas and 3 were with botryoid rhabdomyosarcomas. The average patients’ age was 53.7±12.6 (17-78). About 2/3 of the patients were in the postmenopausal and 1/3 in the premenopausal period. All cases underwent surgery and a procedure of total abdominal hysterectomy + bilateral salpingo-oophorectomy was performed for most of them (88%). The mean duration of follow-up was 36 months (4-198). The 2 and 5 years’ overall survival rates were 65% and 36%, respectively, with a median time of 37 months (95% CI, 28-45). The 2 and 5 years’ disease-free survival rates were 59% and 33%, respectively, with a median time of 29 months (95% CI, 18-40).

Conclusions
As a result of multivariate analysis; while age, stage, lymphovascular space invasion and lymphadenectomy were found to be independent prognostic factors affecting disease-free survival, only stage was detected as an independent prognostic factor for overall survival.
e-Posters: Endometrial Cancer

A CASE OF IMMUNOHISTOCHEMICAL STUDY OF A MALIGNANT MIXED MULLERIAN TUMOR

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Objectives
Our purpose in presenting this case is to report useful information for the diagnosis of this rare combination of tumors.

Methods
A 40-year-old woman gravidae 9, parity 5 curettage 4. The patient was admitted to the medical center in complaining of spotting and vaginal discharge. An endometrial probe curettage (PC) was performed and the pathology result came out to be malignant mixed Mullerian tumor

Results
The patient underwent type 3 radical hysterectomy. Thus a washed abdominal fluid sampling, radical hysterectomy, a bilateral salpingo-oophorectomy and a pelvic and paraaortic lymphadenectomy, omentectomy, appendectomy were performed. The final pathology report revealed Stage IB, grade 3, malignant mixed mullerian tumor. Immunohistochemical staining studies (vimentin, SMA, estrogen, progesterone, LCAHMb-45 and S-100) were applied to the pathological piece. Her radiotherapy treatment was completed. It has been 10 years since diagnosis and operation and no problems or relapses have been encountered yet.

Conclusions
There are two variants of MMT. The homologous variant has stromal cells which looks like endometrial stromal sarcoma, leiomyosarcoma or fibrosarcoma. The heterologous variant has rhabdomyosarcoma and chondrosarcoma as mesenchimal elements. The epithelial component reacts with EMA, cytokeratin and vimentin. In our case the immunohistochemical staining of the tumor reported negative for vimentin, SMA, estrogen, progesterone, LCA, HMB-45 and S-100. Malignant mixed Mullerian tumor cases are really rare and we need more expanded studies for diagnosis and treatment.
SURVEILLANCE FOR ENDOMETRIAL CANCER IN WOMEN RECEIVING TAMOXIFEN

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Objectives
Five years of adjuvant tamoxifen in women with estrogen receptor-positive breast cancer is well established as being excellent therapy with a long-term carryover effect. However, tamoxifen is associated with an increased risk of endometrial malignancy. A strategy for gynecologic surveillance is needed.

Methods
Between 1998 and 2010, women with breast cancer underwent annual gynecologic examination. There were totally 5102 breast cancer patients. Sixty-five percent (3331/5102) had a history of tamoxifen use. We managed these patients not only according to the American College of Obstetricians and Gynecologists committee opinions, but also using transvaginal ultrasonography and endometrial sampling for monitoring women on tamoxifen.

Results
We identified twenty-six patients with a history of breast cancer in whom endometrial cancer developed at Sun Yat-Sen Cancer Center. The majority presented with vaginal bleeding. Eighty percent (21/26) had history of tamoxifen use. The women using tamoxifen had a 2.23 times greater risk of endometrial cancer than did nonusers, especially using for more than 2 years. There were no significant difference in age or pathologic features between tamoxifen users and nonusers.

Conclusions
Patients should be screened before taking tamoxifen. This evaluation, which should include a careful history, pelvic examination, and pap smear, should be repeated annually while the patient is receiving tamoxifen. Although transvaginal ultrasonography is not recommended for routine screening, we perform annual ultrasonography in patients with tamoxifen for more than 24 consecutive months. If endometrial sampling biopsy findings are negative, however, a more aggressive evaluation of endometrium by hysteroscopy and endometrial curettage is needed in the presence of symptoms.
SINGLE-PORT LAPAROSCOPIC EXTRAPERITONEAL PARAORTIC LYMPHADENECTOMY

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Objectives
The aim of this study was to evaluate the feasibility and the safety of single-port extraperitoneal laparoscopic para-aortic lymphadenectomy for patients with gynecologic cancer.

Methods
From July 2012 to January 2013, 7 patients with gynecological cancer underwent a laparoscopic pelvic and para-aortic lymphadenectomy with single port device. An extraperitoneal approach was performed for para-aortic lymphadenectomy using only one 3 cm incision on the left side. To complete the treatment in 6 patients was performed hysterectomy and pelvic lymphadenectomy with conventional laparoscopy.

Results
Aortic dissection was complete in all cases without complications. The median patients age was 63 years (range 48-78 years), and the median patient body mass index was 31 Kg/m² (range 19-38 Kg/m²). The mean of para-aortic nodes was 17 (range 10-25); the mean operative time was 204 minutes (range 120-300 minutes). The mean hospital stay was 4 days (range 3-6 days). No patient encountered postoperative complications.

Conclusions
This study demonstrates the feasibility of single-port laparoscopic extraperitoneal para-aortic lymphadenectomy.
e-Posters: Endometrial Cancer

PRIMARY YOLK SAC TUMOR OF THE ENDOMETRIUM MANAGED WITH CHEMOTHERAPY ALONE

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Objectives
Primary yolk sac tumors of the endometrium are extremely rare. Management is by no means standardized and mirrors management of malignant ovarian germ cell tumors comprising of surgical debulking and adjuvant chemotherapy.

Methods
In April 2011, a healthy 25 year-old G2P0A2 of Haitian origin presented with an eight-month history of menorrhagia. A pelvic examination revealed a large fleshy mass protruding through the cervical canal. Biopsy revealed high grade endodermal sinus tumor. Her Alpha fetoprotein was 3392 ug/L.

Results
The CT, PET and MRI confirmed the uterine origin of this mass as there was evidence that then mass invades the anterior and posterior myometrium and invades circumferentially at the lower uterine segment. Peritoneal deposits were seen in the cul de sac bilaterally and possibly on the left ovary. Hypermeatbolic parauterine, internal and external iliac lymph nodes were present. The patient received 4 cycles of bleomycin, etoposide, and cisplatin. Dramatic response with normalization of alpha fetoprotein. She was followed-up at 3 to 4 month intervals and repeat tumor markers and imaging (MRI) did not detect recurrence. Six months after completing chemotherapy, the patient presented with an unplanned pregnancy. At 6 weeks of gestation, the patient decided for therapeutic abortion due to social reasons. Review of pathology showed products of conception only. At follow-up at the time of this manuscript, the patient remains disease free.

Conclusions
We present the first case primary yolk sac tumor of the endometrium managed with chemotherapy alone.
Mixed Malignant Mullerian Tumour in Mullerian Abnormality with Tamoxifen Use: A Case Report

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Introduction: Mixed mullerian tumours (MMT) are a rare still aggressive type of endometrial cancer. Various reports highlighted the increased risk of developing a MMT with the use of Tamoxifen for breast cancer treatment. There is no link between mullerian abnormalities and MMT yet proven. We present a rare case of MMT associated with an mullerian abnormality in a patient using Tamoxifen.

Case report: A 52-year-old female, with an absent right tube, attended with history of post-menopausal bleeding. She was taking 200mg tamoxifen daily for the last 3 years after a left breast cancer. Clinical examinations revealed a uterine pelvic mass. Pelvic ultrasound showed an endometrial collection of 8.9X2.6X4.3 cm. A total abdominal hysterectomy and left salpingo-oophorectomy with pelvic lymph node and omental sampling was performed. The tumor was a malignant mixed mullerian tumor formed of a polyploidy mass measuring 5 x 4 cm invading the full thickness of the myometrium. Microscopic examination showed pleomorphic cells with atypical mitoses and bizarre tumoral giant cells.

Discussion: Tamoxifen is now routinely used in breast cancer treatment for a maximum period of 5 years due to the increases risk of endometrial cancer [3]. Remarkably in our case an MMMT has developed within 3 years of using tamoxifen in a relatively young patient. We speculate that patients with mullerian abnormalities could be at higher risk of developing MMMT when using Tamoxifen.

Conclusion
We emphasise that Tamoxifen should be used cautiously in high-risk patients for endometrial cancer. Further research is needed to determine the suggested correlation.
e-Posters: Endometrial Cancer

MICROGLANDULAR ADENOCARCINOMA OF THE ENDOMETRIUM: A CASE REPORT

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Objectives
Endometrial microglandular adenocarcinoma (MGA) is an uncommon type of endometrial carcinoma which may be confused with mucinous adenocarcinoma and microglandular hyperplasia (MGH) of cervix and mucinous proliferations of endometrium. We described a case of MGA contains tubal, eosinophilic syncytial and squamous metaplasia in common areas.

Methods
Case report

Results
A 54-year-old obese woman, was referred to gynecology department with postmenopausal vaginal bleeding. Endometrial sampling revealed the formation of closely packed microglandular and mucinous glandular spaces, micropapillary formations and squamous areas. The oval shaped nuclei, commonly with prominent nucleoli, exhibited moderate atypia. Mitoses were rare. Under the suspicion of MGH or MGA, the patient underwent total abdominal hysterectomy, bilateral salpingooopherectomy, sampling from pelvic lymph nodes and omentectomy. Adenocarcinoma with previously noted features observed in only superficial layer of the endometrium. Furthermore, tubal, eosinophilic syncytial and squamous metaplasias were seen in glands. Myometrial invasion was not detected. Immunohistochemically, focal strong Vimentin and CEA positivity was shown. Ki-67 immunoreactivity was observed in 3-4% of neoplastic cells. Alcian blue showed abundant mucinous glandular structures. Finally, the diagnosis was made as FIGO stage 1 and grade 1 tumor of MGA, so adjuvant therapy was omitted.

Conclusions
Microglandular adenocarcinoma is a rare subtype of endometrial mucinous carcinoma which shows microglandular, mucinous and squamous features, so it can be confused with other benign and malignant lesions of the endometrium and cervix. Patient's age, postmenopausal status, histological appearance, immunohistochemistry can be useful for differential diagnosis.
e-Posters: Endometrial Cancer

THE EXPRESSION OF THE RECEPTORS CD 44 AND RHAMM (CD 168) IN ENDOMETRIAL CANCER: AN IMMUNOHISTOCHEMICAL STUDY
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Objectives
The aim of this study was to investigate the expression of the receptors for hyaluronan acid, CD 44 and RHAMM, in tissue samples of endometrial cancer as well as the relation of their expression with clinicopathological parameters.

Methods
We used tissue samples of endometrial cancer from 104 patients who were admitted to the Clinic of gynaecology and obstetrics during the period between the year 2000 and 2006. The expression of CD 44 and RHAMM was analyzed with immunohistochemistry. For the analysis of the CD 44 expression a monoclonal CD 44 antibody was used, while for the analysis of RHAMM expression we used a monoclonal RHAMM antibody.

Results
After we compared CD 44 and RHAMM expression with clinicopathological findings we found a statistically significant correlation with the depth of myometrial invasion, lymph space involvement, FIGO stage of disease and in case of RHAMM expression also a significant correlation with the histological tumour grade. We sorted out a group of 23 (22.1%) patients with a contemporaneously strong CD 44 and RHAMM expression and compared them with the other patients regarding clinicopathological findings. In this group of patients a greater number of cases with deeper myometrial invasion (P=0.024), lymph space involvement (P=0.022) and cytoplasmatic CD 44 expression (P=0.004) was found.

Conclusions
We demonstrated a correlation of CD 44 and RHAMM expression with various clinicopathological findings. For now we can only assume their value as prognostic factors and to assess their exact value as prognostic markers for patients with endometrial cancer further investigations should be done.
TREATMENT OF ENDOMETRIAL CANCER IN CROATIA: RESULTS OF A NATIONAL SURVEY

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Objectives
We investigated the current status of endometrial cancer treatment in Croatia by surveying all gynaecologists who participates in treatment of this disease.

Methods
An anonymous survey containing questions regarding the examinee experience, number of procedures per institution, preoperative analysis, surgical procedures, and indications for lymphadenectomy and adjuvant therapy was sent to all hospital institutions in Croatia.

Results
A total of 70 gynaecologists (66.7%) from 18 institutions responded to the survey. Abdominal total hysterectomy (TAH) was utilized in 427 (75.4%) cases and in 92% with bilateral adnexectomy. Laparoscopy (LAVH, TLH) was used in 64 cases (11.3%). In 334 (59%) cases at least pelvic lymphadenectomy was performed while in 197 (34.8%) cases no lymphadenectomy was performed. We separate examined results from clinical and general hospitals and found that a statistically significant greater number of lymphadenectomies was performed in clinical institutions. Furthermore, gynaecologists from clinical institutions more often requested an intraoperative frozen section analysis.

Conclusions
Results of the present survey showed that lymphadenectomy was used in a small percentage in all types of institutions in Croatia and specially in general hospitals and the same is for the intraoperative assessment of myometrial invasion. Laparoscopic approach was used only in 11% of cases, and interestingly more often in general hospitals. These results represent in part the present status in treatment of endometrial cancer patients in Croatia and this research should be the base for future similar investigations with the intention to determinate the standard surgical procedures to be used for the treatment of endometrial cancer.
FERTILITY-SPARING TREATMENT FOR YOUNG WOMEN WITH ATYPICAL HYPERPLASIA AND EARLY ENDOMETRIAL CANCER WITH HIGH-DOSE MEDROXYPROGESTERONE ACETATE

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Objectives
Fertility-sparing treatment using high-dose medroxyprogesterone (MPA) may be an option for selected young women diagnosed with atypical endometrial hyperplasia (AH) or presumed early endometrial cancer (EC) with no myometrial invasion. The aim of this study was to assess the complete response, pregnancy and recurrence rate in women treated conservatively with high-dose MPA.

Methods
Design: Retrospective observational study
Setting: Gynaecologic Cancer Tertiary Center
Population: young women with AH or presumed stage IA grade 1 endometrioid adenocarcinoma of the uterus and no myometrial invasion that wished to preserve their fertility
Interventions: high-dose medroxyprogesterone acetate (MPA)
Outcomes: primary: complete pathologic response (CR) rate – secondary: spontaneous and assisted pregnancy and live birth rate, disease-free interval, toxicity

Results
We identified a total of 21 women, 17 (81%) had AH and 4 (19%) EC. The complete response rate was 71%. The duration of MPA administration varied across patients. A total of 3 pregnancies and 3 live births were recorded; all of those were conceived spontaneously. Three women were submitted to assisted conception unsuccessfully. All women except one that underwent hysterectomy at the center had invasive endometrioid cancer. There was one case with early myometrial invasion. No women died from the disease.

Conclusions
The data suggest that fertility-sparing treatment with high-dose MPA appears to be safe for selected women. Women should aim to maximize the chances of pregnancy during the period of complete response as the rate of recurrence is high.
e-Posters: Endometrial Cancer

EXPRESSION OF P38MAP KINASE IN EPITHELIAL OVARIAN CARCINOMA

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Objectives
Ovarian carcinoma is the first cause of death of gynecological cancers. In fact, although this is highly sensitive to chemotherapy with platinum compounds, the success rate of treatment is lowered by the high occurrence of relapse.

Great attention has been focused on the metabolic reprogramming that occurs in tumor cells, which show increased levels of glycolysis compared to healthy cells.

p38 is a MAPK, protein that regulates the cell cycle by interfering with the phenomena of apoptosis and autophagy

The objective of our study is the evaluation of p38 and phospho p38 in ovarian cancer in vivo.

Methods
Immunohistochemical analysis of the expression of p38 and pp38 was performed (antibodies to p38 alpha MAP kinase). In particular, we compared the expression between the group of carcinomas and benign tumors, following to carcinomas classification of type I and type II, and the tumor cell grading.

Results
The pp38 is statistically more expressed in the group of carcinomas than in the group of benign tumors. The well differentiated carcinomas have a statistically higher expression of p38 compared to G3 in contrast to pp38 that does not change the expression with the grading.

Conclusions
The increased expression of pp38 in ovarian carcinomas compared to benign tumors confirms that especially carcinomas undergo metabolic reprogramming. Furthermore reprogramming occurs in all carcinomas irrespective histologic type and other characteristics.
e-Posters: Endometrial Cancer

ENDOMETRIAL CANCER: EVALUATION OF PRE AND PER-OPERATIVE ASSESSMENT METHODS OF MYOMETRIAL INVASION.
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Objectives
To compare performance of sonography, MRI and per-operative gross examination of myometrial invasion >50%.

Methods
Retrospective study (2007 - 2011) of patients having sonography, MRI and per-operative gross examination of myometrial invasion. The gold standard was the definitive histopathology. Sensitivity, Specificity, NPV, PPV, kappa and AUC were computed.

Results
56 patients were included. Kappa was 0.76 (95% CI (0.59-0.94) for per-operative gross examination and only 0.28 (0.23-0.53) for sonography and 0.18 (-0.09-0.46) for MRI. Sensitivity (94%), specificity (87%), PPV (76%) and NPV (97%) were higher with intra-operative gross examination. Similarly AUC was significantly higher for gross examination (0.91 (0.83-0.98)) when compared to MRI (0.59 (0.45-0.73)) and sonography (0.66 (0.52-0.79)).

Conclusions
Intra-operative gross examination appears as the most reliable method to assess myometrial invasion >50%.
e-Posters: Endometrial Cancer

THE STAGING I CLINICAL SIGNIFICANCE OF FIGO 2009 AND ITS RELATED FACTORS OF THE ENDOMETRIAL CARCINOMA
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Objectives
To discuss the staging I clinical significance of FIGO 2009 and its related factors of the endometrial carcinoma.

Methods
A retrospective analysis was carried out on 233 cases of FIGO 2009 staging I who admitted to our department from Jan 1998 to Dec 2009 and were carried with complete staging operation, compared with FIGO 1988 staging and their follow-up data were complete. And we analysis 13 death cases with high risk factors.

Results
FIGO 1988 staging IA 41 cases, IB 146 cases, IC 29 cases and IIA 17 cases. The univariate model of IA and IB revealed that histological grade, pathological type, vessel cancer embolus, ER, PR expression and postoperative chemotherapy and postoperative chemoradiotherapy have no obvious statistical difference ( P > 0.05 ); The univariate model of I and IIA revealed that histological grade, pathological type, vessel cancer embolus, myometrial invasion, ER, PR expression and postoperative chemotherapy and postoperative chemoradiotherapy have no obvious statistical difference ( P > 0.05 ), the death causes of I staging patients were pathological grading and pathological types as high risk factors.

Conclusions
FIGO 2009 Endometrial carcinoma stage is more consistent with the patient's clinical status than the FIGO 1988 stage. Postoperative adjuvant therapy should be taken for high risk patients.
THE ROLE OF TRANSVAGINAL SONOGRAPHY IN PLANNING OF SURGICAL TREATMENT IN ENDOMETRIAL CANCER

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Objectives
The aim of this study was to determinate the clinical usefulness of features obtained from transvaginal ultrasound (TVUS) in prediction of lymph node involvement in endometrial cancer.

Methods
Ninety-six consecutive patients with endometrial cancer were enrolled into prospective study. TVUS were subjected to assess extent of the disease to individualize surgical treatment. Two-dimensional US subjective assessment of the largest tumor area (TA), volume of tumor (Spe-Vol) and the minimal tumor free distance into serosa (UTFD) were calculated. Patients were treated according Mayo Clinic surgical protocol. Collected data were correlated to final histopathological findings seeking predictive risk factors of lymph node involvement.

Results
The SPE-VOL and TA were 3.84 cm³ and 3.14 cm², respectively. Averaged UTFD into serosa was 7.3 mm. A total of 12 (14%) patients had metastasis to the lymph nodes. Sensitivity, specificity and negative predictive value of SPE-VOL and TA were 0.615, 0.725, 0.921 and 0.571, 0.80, 0.914, respectively. Best predictive factor of lymph node involvement was obtained from UTFD with AUC ROC of 0.738. Test achieved 0.784 sensitivity and 0.946 NPV with optimal cut-off point of 5 mm. (see Figures).
Conclusions
UTFD is an independent risk factor of lymph node involvement and should be taken into consideration in surgical treatment planning.
FEASIBILITY OF LAPAROSCOPIC EXTRAPERITONEAL BILATERAL PELVIC AND PARAAORTIC LYMPHADENECTOMY IN GYNECOLOGIC MALIGNANCIES: CASE REPORT

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Objectives
In cases of type 2 endometrial carcinomas, lymph node evaluation is an integral part of management and treatment. In our Gynecologic Oncology Unit of the Hospital del Mar, Pelvic and paraaortic lymphadenectomy is done systematically by a transperitoneal laparoscopic approach. However some morbid obese patients have no tolerance to endoscopic surgery. High abdominal pressures require high tidal pressures which sometimes can force conversion to a laparotomic approach, with a significant increase in morbidity.

Methods
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Conclusions
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e-Posters: Endometrial Cancer

CLINICAL MANAGEMENT OF ATYPI CAL POLYPOID ADENOMYOMA OF THE UTERUS. A CLINICOPATHOLOGICAL REVIEW OF 29 CASES

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Objectives
The clinical management of atypical polypoid adenomyoma (APAM) of the uterus remains to be established. We collected APAM cases, reviewed the clinicopathological features, and discussed the clinical management.

Methods
Twenty-nine patients with APAM were identified by searching the tumor registry of the Japan Clinical Oncology Group (JCOG). Clinical information and histological specimens were obtained from 13 institutional members of the JCOG, and a central pathological review was performed.

Results
The mean age of the patients was 38 years (range, 22–58). Squamous metaplasia was present in 19 cases (65.5%), and well-differentiated endometrioid adenocarcinoma coexisted in 5 cases (17.2%). Primary treatment consisted of dilatation and curettage in 9 patients (31.0%), vaginal resection in 2 patients (6.9%), hysteroscopic transcervical resection (TCR) using hysteroscopy in 10 patients (34.5%), and hysterectomy in 8 patients (27.6%). There were recurrences in 5 (23.8%) of the 21 cases in which fertility was preserved, and the recurrent rate was 10% (1/10) in patients those were treated with TCR and 36.4% (4/11) in those the other treatment options were selected. All patients were alive after primary treatment (a mean follow-up period was 39.6 months; range, 1–202).

Conclusions
The clinical outcome of APAM is benign. However, differential diagnosis should be performed because of its histological similarity to invasive endometrial carcinoma and the possibility of coexistence with other endometrial neoplasms. TCR is a recommended diagnostic and treatment option for patients who desire to preserve fertility.
e-Posters: Endometrial Cancer

A COMPARISON OF OPEN SURGERY, ROBOTIC-ASSISTED SURGERY AND CONVENTIONAL LAPAROSCOPIC SURGERY IN MORbidLY OBESE ENDOMETRIAL CANCER PATIENTS

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The intent of this retrospective review was to compare the outcomes of various surgical approaches in the management of morbidly obese endometrial cancer patients.

Methods

Morbidly obese (>40 kg/m²) endometrial cancer patients were managed via open surgery, robotic-assisted surgery or conventional laparoscopic surgery. The surgical procedures were compared to discern any outcome differences with regard to operative time, intra- and postoperative complications, hospital stay and readmission rates.

Results

Sixteen morbidly obese endometrial cancer patients were treated with conventional laparoscopic surgery (CLS; BMI=62.37 kg/m²), 13 were managed via robotic-assisted laparoscopic surgery (RAS; BMI=53.9 kg/m²) and 24 patients underwent an open procedure (OPS; BMI=52.9 kg/m²). The OPS (1.32 hours) patients had a significantly shorter operative duration than the CLS (2.23 hours) and the RAS (2.73 hours) patient groups (p < 0.001); mean estimated blood loss was significantly higher in the OPS (403 cc) group in comparison to the RAS (81 cc) and CLS (209 cc) groups (p=0.002). Moreover, the OPS (4.7 days) patients had a significantly longer hospital stay than the CLS (1.94 days) and the RAL (1.15 days) groups (p=0.002).

Conclusions

The results from the current endometrial cancer study suggest that irrespective of surgical approach, complication rates are reasonable. However, the minimally invasive surgery groups, in contradistinction to the patients treated with an open approach, were associated with lower rates of blood loss and shorter hospital stay albeit longer operative times.
ACCURACY OF MAGNETIC RESONANCE IMAGING IN STAGING OF ENDOMETRIAL CARCINOMA- EXPERIENCE FROM A TERTIARY CARE CENTRE IN DEVELOPING COUNTRY

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Objective
To evaluate accuracy of MRI in staging of endometrial carcinoma, and comparison with surgery and histopathologic findings.

Setting

Methods
52 patients with diagnosis of endometrial carcinoma were referred to radiology department for preoperative staging by MRI and undergone surgery.

Results
The MRI was found to be 79% sensitive, 85% specific and 80% accurate for staging endometrial carcinoma while PPV and NPV were 97% and 66% respectively.

Conclusion
Magnetic resonance imaging is a good, safe, accurate and non invasive imaging modality in staging of endometrial carcinoma. It can be used as a first line radiological investigation in patients with endometrial carcinoma for treatment planning.
e-Posters: Endometrial Cancer

ISOLATED FALSE POSITIVITY OF MEDIASTINAL LYMPH NODES ON FDG-PET/CT IN PATIENTS WITH ENDOMETRIAL CANCER: CASE REPORT

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Objectives
Mediastinal staging with Positron-Emission Tomography (PET) and histopathological evaluation (HE) in patients with non-small cell lung cancer (NSCLC) has been well described. Data are lacking on HE of isolated mediastinal PET positivity in endometrium cancer. However, false-positive results in nodal staging have been shown in coexistent inflammatory or infectious diseases, and as a consequence, the debate continues over the nodal staging algorithm with combinations of PET/CT and invasive procedures.

Methods
These two cases are the first to report the outcomes of endometrium cancer patients with isolated mediastinal PET positivity verified by HE.

Results
Case 1: 63 year old patient with stage IB, grade 2 endometrial cancer underwent PET scan 8 months after the completion of treatment due to suspected recurrence. Hypermetabolic lymph node (LN) were detected in mediastinal and right supraclavicular fossa (SCF) with SUVmax values of 7.2 and 8.6 respectively. Biopsy of the SCF LN revealed granulomatous lymphadenitis and no adjuvant treatment was delivered. She is alive with no evidence of disease at 30 months.

Case 2: 56 year old patient with previously stage IC, grade 2 disease presented a hypermetabolic LN in mediastinum (SUVmax: 8.3). Biopsy resulted in caseation granulomatous lymphadenitis. She is in remission at 48 months.

Conclusions
Both cases were initially assessed as metastatic disease. If not for the HE, both would be given chemotherapy, resulting in unnecessary toxicity. PET/CT results should be evaluated carefully, knowing in individuals at risk of granulomatous diseases, it may mimic malignancy.
RELATIONSHIP BETWEEN BODY MASS INDEX AND OUTCOMES OF WOMEN WITH ENDOMETRIAL CANCER
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Objectives
The aim of this study was to evaluate the outcome of surgery in function of the body mass index (BMI) of patients

Methods
The study cohort consisted of consecutive women undergoing surgery for endometrial cancer in our institution between January 2000, and september 2012. Individual records of all patients were reviewed and analyzed. Patient BMI was categorized as underweight, normal, overweight and obese.

Results
A total of 192 patients were evaluated. Patients were followed for one to 153 months with a mean of 52.56 months. The mean BMI and the range of each of the BMI categories was 16.97 kg/m² (14-18), 22.97 kg/m² (20-24.9), 27.61 kg/m² (25.7-29.4), 37.34 kg/m² (30-71)

Women with higher BMI were more frequently affected by hypertension (8.3%, 31.43%, 58.13% and 59.7% respectively, p=0.0004) and diabetes (16.67%, 4.3%, 13.9% and 29.85% respectively, p=0.02). Women with normal BMI had more frequently postmenopausal replacement therapy than the other categories (p=0.02). In the obese group there were significantly higher peroperative blood loss (p=0.01), more wound abces (p=0.05), more eventration (p=0.02) and more reinterventions for complications (p=0.03) and much less positive lymph nodes (p=0.03) . There were no statistically significant differences in surgical approaches (p=0.37), in histological types (p=0.33), myometrial invasion (p=0.69), grade (p=0.92), lymphovascular invasion (p=0.98), FIGO stages (p=0.36), no increased conversion to laparotomy due to increased BMI, and no differences in overall 5-years survival (p=0.54)

Conclusions
Our study demonstrate a survival equivalency for obese and nonobese women even though obese women showed less positive lymph nodes.
IS ENDOMETRIAL CURETTAGE ENOUGH TO DIAGNOSE ENDOMETRIAL CANCER? PRESENTATION OF 7 CASES
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Objectives
Endometrial cancer is the most common gynecologic malignancy. Most women with endometrial cancer are diagnosed at an early stage with uterine-confined tumours. Endometrial sampling is the gold standard for evaluation and diagnosis for endometrial neoplasia. Endometrial carcinoma is surgically staged according to the 2010 FIGO classification system. Extrrafascial hysterectomy with bilateral salpingo-oophorectomy with pelvic and paraaortic lymph node dissection is the standard staging procedure for endometrial carcinoma. Frozen section of the area of deepest invasion may provide additional information, but studies comparing results of frozen section with final pathology have not reported consistently high concordance, especially in low-stage and low-grade disease.

Methods
We are presenting 7 cases, whose hysterectomy specimens were benign in spite of biopsy proven endometrium adeno carcinoma and undergone unnecessary cancer staging procedure. All seven patients' endometrial curettage samples were consulted to our pathology department for second opinion and all confirmed ad endometrial adeno cancer.

Results
We encountered several intra and post operative complications as surgical wound infection, wound dehiscence and gastrointestinal tract injury in addition to prolonged hospital stay.

Conclusions
Although the main route of spread for endometrial cancer is through lymphatic dissemination, the role of lymphadenectomy for women with early stage endometrial tumours is controversial. Some gynecological oncologists advocate selective lymph-node sampling in women at high risk for nodal metastases (with high grade or deeply invasive tumours) whereas others recommend comprehensive surgical staging at the time of hysterectomy in all women diagnosed with endometrial adeno carcinoma.
e-Posters: Endometrial Cancer

UTERINE SARCOMA – EXPERIENCE FROM A TERTIARY CARE CENTER
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Objectives
We intend to assess the clinicopathological features in retrospective manner and to share our experience with literature for these rare neoplasms.

Methods
Institutional cancer registry database was reviewed for breast cancer cases recorded within a 5-year period between 2006 and 2012. Patients who were evaluated and treated in gynecological oncology unit were included in the study.

Results
33 patients were detected from cancer registry database of our oncology unit with the diagnosis of uterine sarcoma. 21 of cases with the diagnosis of leiomyosarcoma, 5 of cases with the diagnosis of carcinosarcoma, 4 of cases with endometrial stromal sarcoma and 3 of cases with mixed sarcoma diagnosis. Median age of patients was 51.8 years. All patients underwent primary surgery and they were treated according to their stage of primary malignancies.

Conclusions
Uterine sarcomas are rare neoplasms in gynecologic oncology. Because of this rarity of disease there is no exact guideline for this kind of malignancies' treatment process. Sharing data of uterine sarcomas can be useful for development of treatment guidelines.
LAPAROSCOPIC DIAPHRAGMATIC PERITONECTOMY: VIDEO PRESENTATION OF PARTIAL LIVER MOBILIZATION AND DIAPHRAGMATIC STRIPPING TECHNIQUE.

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Objectives
To share our experience from our first case of laparoscopic partial liver mobilization and laparoscopic diaphragmatic stripping/peritonectomy technique.

Methods
A 71 years old patient with adenocarcinoma of the endometrium consented to laparoscopic management.

Results
Complete excision of the falciform and the round ligament from the liver and the anterior abdominal wall, as presented in the video (https://youtu.be/_xhzVoOtjGg), in our observation offers: i) mobilization and lowering of the liver without handling it, facilitated by the increased intraabdominal pressure, gravitational dropping ii) inspection of all the peritoneal folds of the upper abdomen aided by 30° degree or flexible scopes, iii) dissecting the two folds of the falciform ligament (embryologic plane of dissection?) from the sternal diaphragmatic aponeurosis/central tendon offers access to both domes simultaneously, iv) a medial to lateral dissection/stripping seems easier to perform and may be safer, instead of the recommended laparotomy technique that is lateral to medial from costal margins to midline v) may spare dissection of the triangular, coronary ligaments and bare area of the liver vi) offers the possibility of abandoning a planned laparotomy debulking with minimal trauma to the patient.

Conclusions
Laparoscopic diaphragmatic peritonectomy is technically feasible, and to the best of our knowledge, this is the first case report for endometrial cancer. The proposed laparoscopic partial mobilization of the liver, in order to assess the possibility of a successful planned diaphragmatic procedure, is an alternative approach that can precede planned cytoreductive surgery avoiding subxiphoid incisions, sternal and subcostal extension of a midline laparotomy.
EXPRESSION PROFILING OF ENDOMETRIAL CANCER REVEALS COMMON GENE PROGRAM FEATURES AMONG ES AND OTHER GYNECOLOGICAL PRE-MALIGNANT AND CANCER CELL TYPES.

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e-Posters: Endometrial Cancer

Objectives

Novel gene expression technologies are revealing specific pathogenetic patterns of endometrial carcinoma (EC) cells. To this end, we systematically investigated the expression profiles of EC using the Affymetrix platform.

Methods

A total of 8 samples from 5 EC patients covering early and advanced stages of EC undergoing surgical management, and from 3 matched healthy controls were used. Functional analysis was based on Gene Ontology, Database Annotation and IPA software.

Results

Computational analyses identified 1880 differentially expressed genes (DEGs) between EC and controls. Further categorization revealed upregulation of apoptosis-related genes, and downregulation of most transcriptional factors involved in core developmental processes. A significant overlap was encountered in gene signatures from the recently identified region of squamocolumnar junction (SJ), considered to be implicated in cervical cancer. Based on the latter finding and in view of our studies in vulvar carcinoma (VC), a direct comparison of the profiles between the EC vs VC series, revealed a significant overlap of 223 DEGs regulating apoptotic and transcriptional pathways. Utilizing recent findings on profile similarities between cancer and ES, we detected a significant enrichment in the Myc (66 genes) and the Polycomb (25 genes) modules operating in ES cells. Finally, recent genomic classification on EC by TCGA, revealed that our data correlate mainly with the expression profile of POLE and MSI subcategories.

Conclusions

Conclusively, these data lead us to propose common properties among the EC, ES, VC and pre-malignant (SJ cells), where the Myc and Polycomb modules along with genomic features are important for the pathogenesis of endometrial carcinomas.
THE SIGNIFICANCE OF GRADE 2 ENDOMETRIOID ADENOCARCINOMA OF THE UTERUS: LOW GRADE OR HIGH GRADE?
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Objectives
Grade 1 endometrioid cancers are considered low risk, while grade 3 cancers are associated with nodal metastases/higher stage. There is currently no consensus on management of grade 2 lesions. Furthermore, pre- and postoperative histology correlation can be poor, putting patients at risk of under- or over-treatment. Our hypothesis is that grade 2 cancers require complete surgical staging, given their not insignificant rate of upgrading to a high grade lesion, and their correlation with high grade features.

Methods
We retrospectively reviewed preoperatively identified grade 2 cancers surgically managed between 2006-2009. Data collected included preoperative imaging, surgical staging, histologic correlation, and adjuvant treatment.

Results
Sixty-eight patients were identified. Mean age was 62.8 years. Most patients had a preoperative ultrasound (95.0%), while 11.7% had multiple imaging. Pelvic lymph nodes (PLN) were dissected in 95.4%, while 23.4% had para-aortic lymph nodes (PALN) removed. Nodes were positive in 12.9% and 13.3% of PLN and PALN specimens, respectively. Positive nodes were found in a variety of histologic subtypes. Postoperative pathology correlated in 51.5% of cases (correlation ρ = 0.65). The remainder were grade 1 adenocarcinoma (N=27), grade 3 adenocarcinoma (N=5) and carcinosarcoma (N=1). Twenty-eight (45.2%) patients had a final stage greater than I.

Conclusions
This cohort demonstrates a moderate correlation of pre- and postoperative histology and a heterogeneous subgroup of patients with positive lymph nodes. The optimal surgical management of patients with grade 2 endometrioid adenocarcinoma remains unclear; this data however supports the use of complete surgical staging to appropriately triage patients for adjuvant therapy.
EMOTIONAL DISTRESS IN ENDOMETRIAL CANCER PATIENTS: A PROSPECTIVE LONGITUDINAL EVALUATION

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Objectives
This is a prospective, longitudinal study evaluating the Anxiety and Depression levels in a large series of endometrial cancer (EC) patients over a follow-up period of 24 months from diagnosis.

Methods
One hundred thirty-two EC patients with FIGO Stage I-IIIC treated with radical surgery at our Institution were enrolled. Patients received the Hospital Anxiety and Depression Scale (HADS) questionnaire at baseline and 3, 6, 12 and 24 months after surgery. Patients experiencing recurrence/progression of disease were withdrawn from final evaluation. Anova for repeated measures was used to analyze scoring changes over time and to identify predictors of poor HADS scores.

Results
Median age was 67 years (range, 41–87 years). Most tumors (81.5%) were endometrioid histotype; 113 (85.6%) patients showed at diagnosis FIGO stage I-II of disease and 19 (14.4%) cases FIGO stage III. Sixty-four (48.5%) women received adjuvant treatments including radiotherapy, chemotherapy and chemoradiation. Nor age, neither FIGO stage or other clinicopathological factors correlated with Anxiety and Depression levels. No statistically significant changes over time were observed for Depression levels. A slight statistically significant improvement over time compared to baseline levels was observed for Anxiety levels. In multivariate analysis: unemployed/retired status was identified as predictor of poor recovery of Anxiety levels (p=0.032).

Conclusions
Although, it was documented a statistically significant decrease of Anxiety levels in the whole series, the recovery from borderline/pathological levels was less relevant in unemployed/retired women; thus identifying a specific subset of EC patients to whom address psychosocial interventions.
ENDOMETRIAL ADENOCARCINOMA IN PATIENTS WITH LYNCH SYNDROME: IMMUNOHISTOCHEMISTRY FOR P53 PROTEIN AND MLH1, MSH2, MSH6 AND PMS2 PROTEINS

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Objectives
Lynch syndrome is associated to deficiency in mismatch repair (MMR) system. Expression of p53 is associated with poor prognosis. The aims was to evaluate the expression of p53 in groups 1 and 2 (Lynch syndrome and sporadic) and to identify the expression of mlh1, msh2, msh6 and pms2.

Methods
Patients with endometrial carcinoma who underwent primary surgical treatment. IHC was used for screening of Lynch syndrome in patients at risk (N= 48) and IHC analyses for p53 protein in all patients (N= 131). The study was approved by the Ethics Committee of Universidade Federal de Ciencias da Saude and of Hospital de Clinicas.

Results
The expression of p53 in groups 1 and 2 was 34.8% and 51.9% (P = 0.06). In eleven (25.6%), the results showed loss of expression of MMR proteins. Two cases showed loss of mlh1, two cases showed loss of msh2, three cases showed loss of msh6, and three cases showed loss of pms2. Simultaneous loss of mlh1 and msh6 expression in one case. Among 32 patients with suspected Lynch syndrome and normal expression of MMR proteins, six (two under 50 years) had families meeting the Amsterdam criteria, 14 (three under 50 years) had families meeting the Bethesda guidelines, nine were younger than 50 years and three had a first-degree relative with Lynch syndrome-related tumor.

Conclusions
Lynch-syndrome tumors showed a lower rate of p53 expression than sporadic tumors, with a borderline significant difference. The valid percentage of IHC results suggestive of Lynch syndrome among the suspected cases was 25.6% (11/43).
DIGITALLY GUIDED ENDOMETRIAL SAMPLING: AN ALTERNATIVE TO ANAESTHESIA FOR THE ASSESSMENT OF INCREASED ENDOMETRIAL THICKNESS IN HIGH OPERATIVE RISK PATIENTS

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Objectives
A number of different approaches have been advocated to obtain a definitive histological diagnosis in patients with an increased endometrial thickness. Beyond surgical procedures such as dilatation and curettage and outpatient hysteroscopy, there have been alternatives for endometrial sampling in the outpatient setting. The majority of studies in this area have looked at comparison of different endometrial sampling equipment with most finding relatively little difference between the various approaches. Few studies have looked at alterations in technique away from those advocated by the medical device companies.

Methods
We describe a novel technique that is extrapolated from the approach used in obstetrics to perform artificial rupture of membranes in the minimally dilated cervix. This technique uses a bimanual approach to identify the external os and pass a Pipelle™ curette in to the endometrial cavity.

Results
Several high risk surgical candidates unable to tolerate hysteroscopic examination have had biopsies obtained in this way with no adverse outcomes.

Conclusions
Digitally guided endometrial biopsy has a rare role in women who are unable to be appropriately assessed without resorting to general or regional anaesthetic. It is not an alternative for most women presenting with postmenopausal bleeding as the lower genital tract is not visualised but could be a safer option for those with a high risk of complications from surgical intervention who need assessment of their endometrial cavity.
THE USE OF BIOMARKERS HE4 AND CA125 FOR PREDICTION OF THE MYOMETRIAL INVASION, TUMOR SIZE AND THE CHOICE OF THE THERAPY OF ENDOMETRIAL CARCINOMA

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Objectives
So far used biomarker CA125 has for the diagnosis of endometrial cancer a very low sensitivity and specificity. It is reported that only 10-20% of patients in the early stage and 25% of asymptomatic patients with recurrent disease has increased the value of CA125.

Our aim was to determine whether a combination of histological examination, sonographic findings and biomarker CA125 together with the HE4 can preoperatively predict intra or extraterine spread of the tumor and thus better plan surgical treatment and its extent.

Methods
In patient with the evidence of endometrial carcinoma, tumor markers CA125 and HE4 are examined. In the final evaluation is correlated the value of tumor markers with: myometrial invasion of the tumor, its size, histological type and grade according to FIGO, the presence of LVSI and the lymph nodes involvement.

Results
Currently, there is no marker for the screening of endometrial cancer, for monitoring of the treatment, for follow-up, or used as a predictor of intra or extraterine spread of the cancer. For those purposes we still use monitoring of clinical symptoms, gynecological examination and imaging studies, particularly ultrasound. Our results show that the correlation of CA125 and HE4 with stage of the disease reaches the Spearman correlation coefficient CA125 / r = 0.6120 p = 0.0002 / a HE4 / r = 0.5047, p = 0.0027 /.

Conclusions
In our study, we have demonstrated that the current examination of HE4 and CA125 significantly improves the sensitivity and specificity for detection of endometrial cancer.
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SURGICAL-PATHOLOGIC STAGE II ENDOMETRIAL CARCINOMA: NO RISK TO HAVE POSITIVE PELVIC LYMPH NODES?
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Objectives
To know if the invasion of cervical stroma by endometrial cancer is linked to an increased percentage of positive pelvic lymph nodes in patients with surgical stage II (FIGO 2008).

Methods
In 172 patients with endometrial carcinoma, all histologies (endometrioid 148, papillary serous 18, clear cells 6) submitted to radical hysterectomy type A or B with bilateral salpingoophorectomy and systematic pelvic lymphadenectomy we found 18 patients (10.5%) with histologic study in strict stage II. Of this group, 72.2% (13/18 patients) had also aortic lymphadenectomy up to the renal veins.

Results
In the group of 18 patients stage II we obtained an average of 23 pelvic lymph nodes (range 11-41), all negatives. All 18 patients had endometrioid histology, 2 of them with a minor percent of clear cells carcinoma and 5 with lymphovascular space invasion positive. Thirteen patients (72.2%) with aortic lymphadenectomy (mean lymphnodes resected 11, range 3-25), had also all lymph nodes negatives.

Conclusions
According to this study, in surgical-pathologic endometrial carcinoma stage II, the risk of positive pelvic lymph nodes is negative.
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RECURRENCES IN CARCINOMA ENDOMETRIUM- LESSONS LEARNT. EXPERIENCE FROM A CANCER INSTITUTE IN SOUTH INDIA

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Objectives

To evaluate the pattern of recurrence of all cases of carcinoma endometrium treated at our Institution during a 5 year period and to look at whether risk factors based on uterine histology and age could help us make decision regarding adjuvant treatment

Methods

The hospital records were searched to identify all patients treated for endometrial cancer at Amrita Institute of Medical Sciences from January 2004 till December 2008. Data collected included patient's age, details regarding initial diagnosis, surgery and adjuvant treatment, details of recurrence and treatment taken.

Results

We stratified all 131 patients into low, intermediate and high risk groups based on their age, myometrial invasion, grade and cervical/adnexal involvement. There were 40 patients in the low risk group, 61 in the intermediate and 30 were high risk. There were 3 recurrences (7.5%) in the low risk group, 5 (8.2%) in the intermediate risk group and 9 (30%) in the high risk group. The recurrences in low risk group who had not received adjuvant radiation was in vault whereas in intermediate group failures were predominantly peritoneal (intermediate: 3 peritoneal and 2 distant) while in the high risk group the failures were predominantly distant (high risk: 6 distant and 3 nodal). All low risk patients who recurred were salvaged with radiation therapy.

Conclusions

Risk stratification based on age and uterine factors will help to decide adjuvant treatment in endometrial cancer. High risk patients failed in the distant sites and addition of chemotherapy might help these group.
e-Posters: Endometrial Cancer

Concordance of colorectal polyps with ovarian and endometrial cancer

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Abstract

Background and Aim
Patients with endometrial or ovarian cancer have an increased risk of breast or colon cancer. The aim of this study was assessing the individual and age-related characteristics of patients with a combination of these malignancies.

Methods
This study is a descriptive and retrospective study. We reviewed the hospital records of patients who had endometrial or ovarian cancer had admitted at the Rasol Akram, Akbar abadi and Firozgar academic hospitals in Tehran, Iran at 2010-2011. Colon polyp’s were examined by immunohistochemistry assay. Data analysis was done by SPSS 18.

Results
100 cases participated in this study. Five patients had colon polyps. The mean age, weight, BMI were 50.21± 9.582, 65.9± 6.554, and 26.07 ± 2.824, respectively. Total of 5 cases with colon polyp had positive familial history of ovarian cancer.

Conclusions
More attention should be paid to colorectal cancer patients’ family histories with respect to ovarian and endometrial cancer, especially if the patient is premenopausal. This might help to identify women at risk of getting colorectal cancer later in life.
THE CHANGING SURGICAL MANAGEMENT OF ENDOMETRIAL CANCER

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Objectives
We undertook a large audit involving nearly 450 cases of endometrial cancer operated in Derby, a cancer centre, between 2007-2012. We specifically investigated the uptake of minimal access surgery and audited against national standards (NICE IPC 356, 2010) about operating time, complication rates, demography (age and histology of cancer)

Methods
We identified 393 cases operated at Derby retrospectively, utilising the Derby MDT data base. We identified clinical questions and national auditable standards. We trialled our collection form before auditing histology, imaging; operative technique e.g. laparoscopy or laparotomy; operative time; estimate blood loss; length of stay; complications; conversion rates to laparotomy; readmissions.

Results
Patients' age of presentation, proportion of different histology types are same as the national trend. 79.1% of endometrial sampling was by hysteroscopy, 24.4% by Pipelle. Use of laparoscopy has increased from 0% in 2007 to over 50%. There was comparable operating time for laparoscopy versus laparotomy (Mean 98.6 vs 107.8 minutes). The trend suggests the laparoscopy operating time is becoming shorter. Mean hospital stay after laparoscopy is 2 days, 5.1 days for open procedures. Mean estimated blood loss for laparoscopic procedures is 219.1ml, compared to 346.4ml for open methods. 7.2% laparoscopies were converted to laparotomy. Overall complication rate - 20.0% for laparoscopy, 21.3% for open. Readmission rates - 10% and 7% respectively.

Conclusions
We are treating endometrial cancer more with laparoscopy which involves shorter hospital stays, lower estimated blood losses, comparable surgical time and lower complication rates. These are all keeping with the national standards, in some respect even better.
THE DIAGNOSTIC ROLE OF LYMPHADENECTOMY IN EARLY ENDOMETRIAL AND CERVICAL CANcer

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Objectives
To investigate the diagnostic role of lymphadenectomy in early endometrial and cervical cancer.

Methods
We conducted retrospective analysis of 64 cases of pelvic lymphadenectomy in early endometrial (endometrioid adenocarcinoma stage IA) and cervical (squamous cell carcinoma stage IA1-IA2) cancer that involved surgery in Odessa National Medical University Hospitals in 2010-2012. We compared operation time, complications rate, number of removed lymph nodes, and frequency of lymphorrhea and lymphocele formation after abdominal and laparoscopic pelvic lymphadenectomy.

Results
Among 64 cases of pelvic lymphadenectomy 32 patient was operated laparoscopically (1st group), 32 by abdominal access (2nd group). There were no differences in age, clinical stage, hystologic type, body mass index in two groups. Operation time (180,3±22,2) min and (167,9±17,3) min, number of removed lymph nodes (from 6 till 11), rate of complications (1 case in each group), were similar in both groups. Positive pelvic lymph nodes were detected in 2 cases in 1st group (6,3 %) and 3 cases in 2nd group (9,4 %). We used postoperative drainage after lymphadenectomy during 5-7 days untill the amount of lymphorrhea had markely diminished (less than 70-80 ml). Lymphocele formation were detected in 2 cases in 1st group and 4 cases in the 2nd group of patients. There were no differen?es for recurrency disease and survival rate in two groups.

Conclusions
There were no significal diagnostic role of lymphadenectomy in early endometrial end cervical cancer. Laparoscoiopic lymphadenectomy demonstrate the same results as abdominal one with tendency of decreasing rate of lymphocelete formation.
THREE CASES OF CLEAR CELL ENDOMETRIAL CANCER
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Background
Uterine clear cell carcinoma is a rare form of endometrial cancer, representing 1-5.5% of all primary endometrial cancers. It is characterised by aggressiveness and a high recurrence rate.

Aims
To describe the cases of endometrial clear cell carcinoma treated at East Tallinn Central Hospital from 2007 to 2012.

Methods
The hospital electronic database and patients’ records were searched to identify and describe the histologically confirmed cases of clear cell endometrial cancer.

Results
Among 195 endometrial cancer patients operated on from 2007 to 2012 there were three cases of clear cell endometrial cancer (1.5%). At the time of diagnosis, the patients were 64, 68 and 79 years old. For two of them, the presenting symptom was vaginal bleeding; one was referred by a family doctor because of an abnormal PAP smear. In one case, clear cell cancer was histologically diagnosed in the curettage material, and for two patients the diagnosis was confirmed by examination of a surgical specimen. The FIGO stages were established as IA, IIIC, and IVA. All three patients underwent radical surgery followed by chemotherapy: doxorubicin and cisplatin in one case, and carboplatin and paclitaxel in two cases. One patient died two months after the operation due to generalisation of the cancer; one patient had a cancer recurrence in the lungs within two years. The third patient has been recurrence-free during six months postoperatively.

Conclusions
As an aggressive cancer with a high recurrence rate, uterine clear cell carcinoma should always undergo postoperative chemotherapy. However, the prognosis remains poor.
e-Posters: Endometrial Cancer

A CLINICAL AND PATHOLOGICAL STUDY OF DEDIFFERENTIATED ENDOMETRIAL CARCINOMA
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Objectives
Dedifferentiated carcinoma (DC) is an uterine malignant tumor that contains both low-grade endometrioid carcinoma and undifferentiated carcinoma. Until now, most publications about DC were individual case reports and only one paper of Asia population which was just from our lab. Now we made in depth investigation on pathological features of DC in order to guide accurate treatment and to assess prognosis.

Methods
Eight cases of DC from Jan, 2011 to Dec, 2012 in Tianjin Central Hospital of Gynecology & Obstetrics were analyzed in pathological and clinical characteristics.

Results
We found the average age of the patients was 53.9 years old and the common pathological features in these cases were large sizes of the tumor (average 6.5cm³), presence of the myometrial invasion (8/8 cases) and focal squamous metaplasia. In these cases, the percentage of the undifferentiated component was 30-80%. But intravascular tumor emboli (confirmed by CD31 immunostaining) were identified in all cases. Follow-up results (4-24 months) showed that one patient died after 12 months of the initial operation and the other one occurred distant metastasis in 3 months after surgery.

Conclusions
The recognition of DC is extremely important, since it has a worse prognosis when compared with FIGO grade 3 endometrioid carcinoma.
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ACCURACY OF D&C IN THE PREOPERATIVE DIAGNOSIS OF GRADE 1 ENDOMETRIAL ADENOCARCINOMA
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Objectives
Preoperative tumor grade and histologic subtype, along with the gross inspection of the depth of myometrial invasion intraoperatively, are commonly used to determine the type of surgery for endometrial cancer. This study was carried out to evaluate the accuracy of dilation and curettage (D&C) in the preoperative diagnosis of grade 1 endometrial adenocarcinoma in women surgically treated in our Department.

Methods
We retrospectively reviewed the medical charts and the pathology reports of our Hospital. All women had undergone D&C under general anesthesia in various hospitals. Following the diagnosis of endometrial cancer, the extent of surgery was left at the discretion of the primary surgeon. At least, a total hysterectomy and bilateral salpingo-oophorectomy was performed within 1 month after the D&C.

Results
Grade 1 endometrial adenocarcinoma was preoperatively identified in 34 women. Their mean age was 60.4 years. Histologic examination of the hysterectomy specimen confirmed the tumor grade in 26 of them (76%). The remaining 8 cases (24%) were upgraded as moderately differentiated tumors (grade 2). In 6 of them, the D&C and hysterectomy specimens were evaluated in different pathology laboratories. Histologic findings consistent with grade 3 endometrial adenocarcinoma, serous or clear cell adenocarcinoma and carcinosarcoma were not recognized in any woman.

Conclusions
In line with the existing literature, the preoperative diagnosis of grade 1 endometrial adenocarcinoma following D&C does not accurately correlate with the final tumor grade. Inter- and intra-observer variability, tumor heterogeneity and sampling limitations may account for the observed discrepancy.
e-Posters: Endometrial Cancer

PREOPERATIVE LEUKOCYTOSIS AMONG PATIENTS WITH ENOMETRIOID ENDOMETRIAL CANCER: INCIDENCE AND PATHOLOGIC CHARACTERISTICS

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Objectives
It has been recently shown that preoperative leukocytosis among endometrial cancer patients is independently associated with larger tumor size and increased risk of death. We aim to present the incidence of preoperative leukocytosis in a population with endometrioid subtype treated in our University Department, along with their pathologic features.

Methods
Data were retrospectively retrieved from the medical charts and the pathology reports of our Hospital. Participants underwent at least a total hysterectomy and bilateral salpingo-oophorectomy. White blood cells count (WBC) was measured within the last 7 days before surgery. Leukocytosis was defined as WBC count ≥10,000 per μl.

Results
Preoperative leukocytosis was noted in 6 out of 87 women with uterine endometrioid adenocarcinoma scheduled for surgery. Their mean age was 62.3 years. Half of the patients had grade 2 and half grade 3 adenocarcinoma. Myometrial invasion <50% was evident in 1 and ≥50% in 2 cases. Cervical stromal or serosal involvement was recognized in 1 and 2 participants, respectively. Lymphovascular space invasion was identified in 3 specimens. Pelvic/para-aortic lymph nodal metastases complicated 3 cases, while no lymph nodes for pathologic examination were available in 2 women.

Conclusions
Preoperative leukocytosis was observed in 6.9% of our study population. Based on GOG clinicopathologic criteria, 83.3% of our patients with elevated WBC count prior to surgery had high-intermediate or high-risk disease. Further research is needed to elucidate the relationship between preoperative leukocytosis and endometrial cancer clinical course, as well as the mechanisms that underlie it.
ROBOTIC SENTINEL LYMPH NODE DETECTION (RSLND) FOR PATIENTS WITH ENDOMETRIAL CANCER (EC)

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Objectives
Lymphadenectomy as part of the staging for EC patients is controversial. SLND is being evaluated to determine which patients would benefit from adjuvant therapy and to limit morbidities associated with a full nodal dissection. The purpose of this study is to evaluate diagnostic accuracy and detection rate of RSLND as part of the surgical staging for EC.

Methods
A retrospective database of all patients who underwent intraoperative lymphatic mapping followed by RSLND as a part of their procedure was reviewed. Cervical injection methylene blue was used in all cases. SLN was initially examined by routine H&E and, if negative, ultrastaging by immunohistochemistry (IHC).

Results
Between 4/2011 and 6/2013, 119 patients with endometrial cancer underwent RSLND. The median age was 62 (25-87); median BMI was 32 (18-76). Out of 119 patients, only one patient underwent RSLND with fertility preservation; 118 patients underwent robotic hysterectomy and surgical staging with RSLND. None of the cases were converted to an open procedure. At least 1 SLN was detected in 86% (102/119) of the patients. Bilateral SLN were detected in 51% (61/119). Positive nodes were identified in 8% (9/119) of the patients. Of those with SLN(+), 44% (4/9) were by ultrastaging (IHC) alone. No patients had positive regional nodes without SLN(+). The negative predictive value of a SLN(−) was 100%.

Conclusions
This cohort represents one of the largest series of RSLND for EC. RSLND using methylene blue cervical injection can identify a SLN in most patients with EC. IHC ultrastaging improves detection of node positive disease when compared to traditional pathologic evaluation.
MALIGNANT MIXED MESODERMAL TUMOR IN GROUND ADENOMATOUS POLYP. CASE PRESENTATION.

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Objectives
To present the importance and incidence of malignant mixed mesodermal tumors

Methods
82-year-old patient is admitted in our Department with vaginal bleeding over 20 days. The ultrasound examination revealed hyperplastic endometrium with uneven texture. The CT scan showed a hyperintense 3 cm mass into the uterine cavity. No other pathological elements were found. The patient was submitted to diagnostic curettage, where the biopsy showed pieces of malignant neoplastic tissue with differential diagnosis of descending order of probability malignant mixed mesodermal tumor, endometrium sarcoma of a high degree of malignancy, and leiomyosarcoma. A total abdominal hysterectomy was decided to be performed with bilateral salpingo-oophorectomy, pelvic lymphadenectomy and epiploectomy. Biopsy of the material revealed carcinosarcoma on endometrial adenomatous polyps. The tumor invaded superficially the myometrium. The lymph nodes were not infiltrated.

Results
The most common symptom of carcinosarcoma is postmenopausal vaginal bleeding, presented in 80%-90% of the cases. The tumor may increase in size and claim the uterine cavity. The myometrium is filtered in various degrees in most cases. Carcinosarcomas quickly metastasize in pelvic lymph nodes and paraaortal nodes. The most common dispersal areas are the pelvis, the lymph nodes, the peritoneal cavity, the lungs and the liver.

Conclusions
The most important factor that affects prognosis of carcinosarcoma is the size of the tumor. Tumors of stage 1 which are contained inside the uterus have a 5-year survival rate 70% after surgical staging, radiation and chemotherapy. Survival dramatically decreases in stages 2-3 with extension into the cervix, the vagina or parametrium.
CA ENDOMETRII AND MMP-2

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Objectives
Persistent and prolonged estrogenic stimulation is a well-known risk factor in the causation of endometrial cancer. Some data indicates that the estrogen is attributed to targeting the expression of matrix metalloproteinases (MMPs), which are essential proteases involved in invasion and migration of cancer cells. The aim of this study was to determine and compare the expression of MMP-2 in endometrial cancers and benign endometrium.

Methods
This study included forty eight postmenopausal women referred for hysterectomy??At the Department of Gynecology and Obstetrics, University Clinic Hospital Split, Croatia, between May 2011 and October 2012. To avoid the error we have included in the study postmenopausal women with low estrogen levels. After Ethical Committee approval and informed consent, they were divided in two groups: twenty four with endometrial cancer and 24 with benign diseases. Immunohistochemical expression of MMP-2 was performed on formaline fixed and paraffin embedded sections of the endometrial tissue of women with and without endometrial cancer. Stained tissue samples were evaluated as positive and unstained samples as negative.

Results
Immunohistochemical expression of MMP-2 was performed in samples of endometrial carcinomas (N = 24) and benign endometrium (N = 24). A significant increase in MMP-2 immunohistochemical expression was seen in endometrium from women with endometrial cancer (P = 0.009).

Conclusions
Our study showed elevated MMP-2 immunohistochemical expression in endometrium of endometrial carcinoma compared to benign endometrium. These data suggest that MMP-2 may be marker of endometrial cancer and may play a key role in endometrial tumor progression.
SIGNIFICANCE OF PERINECROTIC EXPRESSION OF CA9 AND GLUT-1 IN ENDOMETRIAL CANCER

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Objectives
The objective of this study was to evaluate the prognostic value of CA9 and Glut-1, that are major factor of hypoxia induced pathway, in endometrial cancer.

Methods
The tissue samples from endometrial cancer were obtained, together with routine histopathological specimens, during surgical operations carried out at Pusan National University Hospital. We studied 129 patients with endometrial cancer who underwent surgical resection. A series of endometrial cancer was immunostained for CA9 and Glut-1 and the results were correlated with histopathological and clinical parameters.

Results
Expression of CA9 and Glut-1 were observed in the cell membrane and cytoplasm and the staining was most prominent in hypoxic and peri-necrotic regions. Perinecrotic expression of CA9 and Glut-1 showed positive correlations with histologic grade, clinical disease stage, myometrial invasion, lymph node metastasis, tumor size, and tumor necrosis. They also are correlated with disease recurrence, including local recurrence and metastasis. In patients with endometrial cancer, perinecrotic and necrosis-related expression of CA9 and Glut-1 are important prognostic factors.

Conclusions
The expression of CA9 and Glut-1 in endometrial cancer suggests that these isozymes could represent potential targets in endometrial cancer therapy. The expression pattern of CA9 and endometrial cancer suggests that it could also serve as a useful histopathological marker protein for hypoxia in endometrial cancer.
INTRATUMORAL ANDROGEN CONCENTRATIONS IN ENDOMETRIAL CARCINOMA TISSUES

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Objectives
We previously reported that androgen may play an important role in the progression of endometrial cancer. In addition, androgen receptor is expressed in a majority of endometrial carcinoma tissues. Among the enzymes involved in biologically active androgen synthesis, both 17β-hydroxysteroid dehydrogenase 5 (androstenedione into testosterone) and 5α-reductase [testosterone into 5α-dihydrotestosterone (DHT)] were expressed in endometrial carcinoma tissues. Although in situ androgen synthesis may play an important role in progression of endometrial cancers, intratumoral concentration of androgens has not been clarified.

Methods
In this study, we examined the concentrations of androstenedione (biologically weak precursor), testosterone, and DHT (potent androgen) in endometrial carcinoma and nonpathological endometrial tissues. And we also examined those of serum in each case. Thirty-one tissues of endometrioid adenocarcinoma (G1; 12 cases, G2; 10 cases, G3; 9 cases), 4 of serous adenocarcinoma and 5 of normal endometrium were available for liquid chromatography/electrospray tandem mass spectrometry to study intratumoral androgen concentrations. The ethics committee at the Tohoku University School of Medicine approved the research protocol.

Results
We found that a DHT level in tissues of endometrioid adenocarcinoma G1 was higher than all the other types, although there was no significant change in DHT levels measured in serum of each endometrial carcinoma case. We detected lower concentrations of all androgens in tissues of serous adenocarcinoma compared with those of all the others.

Conclusions
Therefore, androgenic actions may be involved in the malignancy of endometrial carcinoma.
ADJUVANT CHEMOTHERAPY AND VAGINAL VAULT BRACHYTHERAPY FOR STAGE 1 PAPILLARY SEROUS OR CLEAR CELL ENDOMETRIAL CANCER

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Objectives
To assess and compare adjuvant chemotherapy followed by either high-dose-rate vaginal vault brachytherapy (VBT) alone or VBT combined with pelvic external beam radiotherapy (EBRT) for FIGO stage 1 serous or clear cell (CC) endometrial cancer.

Methods
Between 2006 and 2012, 85 women with stage 1 serous or CC endometrial cancer were evaluated post-operatively for adjuvant treatment at our hospital. Patients declining or not completing adjuvant treatments were excluded. Twenty-five women received 4-6 cycles of carboplatin/paclitaxel followed by EBRT and VBT. Thirty-two women received 6 cycles of carboplatin/paclitaxel followed by VBT. Loco-regional control and toxicities were assessed during follow-up.

Results
At 2-year follow-up, there were no vaginal recurrence and only one patient developed a distant recurrence in the EBRT group. The pelvic recurrence rate was 7.7%(n=1) for patients treated with VBT alone and 5.9%(n=1) for those treated with EBRT and VBT, (p=ns). Only one patient had grade 3 toxicity (chronic gastrointestinal(GI) toxicity in the EBRT+VBT group). Acute grade 1-2 GI toxicities were less frequent in the VBT group compared to the EBRT+VBT group (p=0.008). Acute and late grade 1 urinary toxicities tend to be less frequent in the VBT group (16%vs.42.9%, ns and 25%vs.50%, ns, respectively). Grade 1 vaginal toxicity was similar in both groups. No grade 2 urinary or vaginal toxicities were reported.

Conclusions
According to this study, VBT alone seems to be as effective as EBRT and VBT for stage 1 serous and CC endometrial cancer treated with surgery and adjuvant chemotherapy. Furthermore, less GI toxicities were seen in the VBT group.
FROM LAPAROTOMY TO LAPAROSCOPY IN ENDOMETRIAL CANCER TREATMENT

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Background
The first laparoscopic procedure for endometrial cancer treatment was performed at East Tallinn Central Hospital (ETCH) five years ago. From 2007, when 95% of endometrial cancer patients were laparotomised, the proportion of laparoscopic surgery has steadily risen.

Aims
To describe the surgical treatment for endometrial cancer at ETCH, 2011-2012

Methods
The hospital electronic database was searched regarding operations for endometrial cancer in 2011 and 2012. The patients’ characteristics, blood loss during surgery, duration of operation and hospitalisation were compared in the laparoscopy and laparotomy groups.

Results
In 2011 from 30 endometrial cancer operations, one-third (10) were laparoscopic. In 2012, the number of laparoscopic operations increased to 22, which formed 55% of all performed operations (40). For laparoscopic surgery, the patients with preoperatively determined FIGO IA-B stages with no known high-risk indicators were selected. Patients who underwent laparoscopy did not differ significantly from laparotomised patients neither by age nor BMI. There were also no statistically significant difference in duration of the procedure between the operation groups (median duration for laparoscopy 145, for laparotomy 155 minutes, p=.675). Blood loss during surgery was smaller for laparoscopy compared to laparotomy (median 100 vs. 250 ml, p=.000). Median duration of hospitalisation was 7 days for laparoscopy and 10 days for the laparotomy group (p=.000).

Conclusions
Since 2007, gynaecologists have mastered laparoscopic surgery and this method is established in the treatment of endometrial cancer patients at ETCH. The procedure takes no longer than the laparotomy; it reduces blood loss during an operation and duration hospitalisation.
e-Posters: Endometrial Cancer

ANAALYSIS OF ISOLATED PARAAORTIC LYMPH NODE INVOLVEMENT IN PATIENTS WITH ENDOMETRIAL CANCER
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Objectives
We aimed to determine the incidence and sites of isolated paraaortic lymph node (PaLN) involvement in the setting of negative pelvic nodes in completely surgically staged EC patients.

Methods
We identified all cases that had comprehensive staging surgery, including PPaLND up to the renal vessels, for EC between 2005 and 2012 retrospectively and analyzed the clinicopathologic characteristics of patients with isolated PaLN involvement.

Results
276 EC patients were surgically treated at our institution between 2005 and 2012. 137 (49.6%) had comprehensive staging surgery including PPaLND. Only 5 (3.6%) had positive PaLN with negative pelvic nodes. Median age of these patients was 59 (range, 31-74). Of the 5 cases, 1 had synchronous ovarian cancer, 1 had tubal metastasis, and 1 had cervical involvement. Four of 5 cases had endometrioid histology and one had non-endometrioid. Four of 5 cases had 50% or greater myometrial invasion. In 3 of 5 cases the site of PaLN metastasis was inferior pre-caval region, and in 1 of 5 was inferior pre-aortic region. Only 1 case had an isolated PaLN involvement above the inferior mesenteric artery. Follow-up data were reported for 4 patients. Median follow-up time was 45 (34-62) months. None of cases recurred, and all are alive with no evidence of disease.

Conclusions
However, pre-operatively identified tumor grade and intraoperatively assessment of myometrial invasion in patients with EC is somewhat problematic. We suggest that 3.5% chance of isolated PaLN involvement is high enough to consider performing systematic PPaLND for all patients.
SURVIVAL ANALYSIS OF PELVIC LYMPHADENECTOMY ALONE COMPARED TO COMBINED PELVIC AND PARA-AORTIC LYMPHADENECTOMY IN PATIENTS WITH ENDOMETRIOID TYPE ENDOMETRIAL CANCER

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Objectives
To determine whether the addition of para-aortic lymphadenectomy to pelvic lymphadenectomy improves survival in patients with endometrioid type endometrial cancer (EC).

Methods
A single tertiary-center, retrospective analysis was conducted in a total of 186 EC patients who surgically treated with pelvic lymphadenectomy alone (PLND) (n=97) or combined pelvic and para-aortic lymphadenectomy (PPaLND) (n=89) between January 2005 and August 2012. Adjuvant treatments were prescribed based on the Gynecologic Oncology Group (GOG) risk of recurrence analysis. The primary endpoint of the study was overall survival (OS). Secondary endpoints were progression-free survival (PFS) and time-to-progression (TTP).

Results
Median follow-up time was 39 months (IQR 38.14-47.13 months) for PLND group, and 37 months (IQR 31.88-41.06 months) for PPaLND group. There were no statistically significant differences in either OS, PFS or TTP. The estimated 3-year OS, PFS and TTP for patients with low or low-intermediate risk by lymphadenectomy groups were: PLND 100%, 98.7%, and 98.7%, PPaLND 100%, 100%, and 100%, respectively. The estimated 3-year OS, PFS and TTP for patients with high or high-intermediate risk by lymphadenectomy groups were: PLND 92.3%, 81.3%, and 81.3%, PPaLND 90.7%, 77.1%, and 80.9%, respectively. There were also no statistically significant differences in 3-year OS, PFS and TTP regardless of GOG risk of recurrence between the lymphadenectomy groups (98.4%, 95.3%, and 95.3% for PLND, and 94.9%, 87.1%, and 89.4 for PPaLND).
Conclusions
The combination of pelvic and para-aortic lymphadenectomy does not provide any survival advantage.
SELECTION OF HOUSEKEEPING GENES FOR MICRORNA EXPRESSION STUDIES IN ENDOMETRIOID ENDOMETRIAL CANCER TISSUES

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Objective
Background. microRNAs comprise a family of small, non-coding RNAs, which regulate gene expression at the posttranscriptional level. Multiple studies implicated important roles of microRNAs in various malignancies including endometrioid endometrial carcinoma (EEC). qPCR is widely used in the studies investigating microRNAs expression. Relative quantification of microRNAs expression requires proper normalization methods and housekeeping genes, also called endogenous controls, are widely used for this purpose. The aim of this study was experimental identification of stable endogenous controls for normalization of microRNA qPCR expression studies in EEC.

Methods
Methods. Expression of twelve candidate endogenous controls (miR-16, miR-26b, miR-92a, RNU44, RNU48, U75, U54, U6, U49, RNU6B, RNU38B, U18A) was investigated in tissue samples obtained from 45 patients (30 EEC, 15 normal endometrium) using qPCR. Stability of candidate endogenous controls was evaluated using NormFinder, geNorm, Bestkeeper and equivalency test.

Results
Results. RNU48, U75 and RNU44 were identified as stably and equivalently expressed between malignant and normal tissues. Both NormFinder and geNorm indicated that those three snRNAs were optimal for qPCR data normalization in EEC tissues.

Conclusions
In conclusion, we suggest that average expression of those snoRNAs could be used as a reliable endogenous control in microRNA qPCR studies in endometrioid endometrial cancer. In addition to identifying suitable endogenous controls in EEC, our study presents an appropriate strategy for validation of candidate reference genes for any microRNA qPCR study.
SHOULD OMENTECTOMY BE A PART OF SURGICAL STAGING IN PATIENTS WITH ENDOMETRIOID ADENOCARCINOMA OF THE UTERINE CORPUS?

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Objectives
The purpose of the study was to determine the prevalence of omentum metastasis in endometrioid adenocarcinoma and to correlate risk variables with this spread.

Methods
A retrospective analysis of patients with endometrioid adenocarcinoma who underwent omentectomy in addition to staging laparatomy was performed.

Results
Omentum metastases were noted in 11 of the 322 patients with endometrioid adenocarcinoma (3.4%). In 6 (54.5%) of these cases, the disease in the omentum was clinically evident while in 5 (45.5%) cases, microscopic disease was present. Among the patients with omental metastasis, 8/11 (72.7%) had deep myometrial invasion, 10/11 (90.9%) had lymphovascular space invasion, 8/11 (72.7%) had grade 3 tumors, 4/11 (36.3%) had cervical stromal involvement, 6/11 (54.5%) had adnexal involvement, 8/11 (72.7%) had positive peritoneal cytology and 5/11 (45.5%) had positive lymph nodes. Multivariate analyses showed that there was a significant correlation between omentum metastasis and positive peritoneal cytology, adnexal involvement, and grade 3 tumor ($P=0.028$, $P=0.001$, $P=0.01$, respectively). There was no statistical relationship between omentum metastasis and lymphovascular space involvement, deep myometrial invasion and lymph node metastasis ($P=0.087$, $P=0.97$, $P=0.92$, respectively).

Conclusions
Grade 3 endometrioid adenocarcinomas, especially those that are complicated by deep myometrial invasion, have a pattern of intraabdominal spread similar to more aggressive endometrial cancers, with frequent involvement of the omentum. Overall, we conclude that 37.5% (3/8) of patients who had a grade 3 tumor and omentum metastasis stage IV disease would have been missed if a staging operation similar to that employed for ovarian cancer had not been performed.
e-Posters: Endometrial Cancer

PREDICTION OF STAGING AND RELIABILITY OF FROZEN/SECTION IN PATIENTS WITH A PREOPERATIVE DIAGNOSIS OF GRADE 1 ENDOMETRIOID TUMOR IN ENDOMETRIAL CANCER

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Objectives
To investigate the likelihood of the detection of the necessity of staging preoperatively with the use of clinical parameters and the reliability of frozen/section (FS).

Methods
219 patients were included who were operated between 1996-2010 with a diagnosis of grade 1 endometrioid adenocarcinoma in probe curettage.

Results
The mean age of the patients was 60.1 years and ranged between 35-84 years. Sixty-nine (31.5%) patients were staged intraoperatively according to the FS criteria. Among the clinical characteristics, only age and body mass index (BMI) predicted staging preoperatively. The probability of staging increased as age increased and BMI decreased. The concordance between preoperative diagnosis and FS was 89.5%. The wrong diagnosis regarding grade, depth of myometrial invasion, tumor type and cervical invasion in FS was clinically significant and it effected the decision of staging in 10 patients. Three of these 10 patients were staged because of the existence of other high risk factors. In conclusion only 7 patients (3.2%) who acquired staging surgery were missed in FS.

Conclusions
In the present study, it was shown that preoperative clinical parameters couldn’t predict the patients who should be staged. Additionally, FS was found to have high accuracy rate in this patient group. Patients with a preoperative diagnosis of grade 1 endometrium cancer should be operated in centers where FS is utilized and oncologic staging surgery could be performed.
e-Posters: Endometrial Cancer

THE IMPORTANCE OF AGE AND MENAPOUSAL STATUS IN ENDOMETRIAL COMPLEX HYPERPLASIA WITH ATYPIA

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Objectives

Endometrial cancer is detected in the 20-62% of the hysterectomy materials of the operated patients with a preoperative diagnosis of complex hyperplasia with atypia (CHA). In this study, the effect of menapousal status on the intraoperative and postoperative pathology results of the patients operated with a preoperative diagnosis of CHA was assessed.

Methods

111 patients diagnosed in our center between January 1993-March 2013 were included.

Results

The mean age of the patients was 53 years. Cancer was detected in the PB of 52 patients. Among these, 50 patients had stage IA disease and 48 patients had endometrioid tumor. While tumor was limited to endometrium in 22 patients, depth of myometrial invasion was ≥1/2 in only one patient. There was no patient with grade 3 disease and only one patient had grade 2 tumor. The histopathological results of 40 patients and 52 patients were upgraded in frozen/section (FS) and paraaffin block(PB), respectively. The patients with a PB result of cancer were older (p< 0.0001) and the probability of detection of cancer in PB increased as age increased. In 31.1% of the premenapousal patients and 66% of the postmenapousal patients, PB revealed cancer (p <0.0001). The results of FS and PB were concordant in the 60% of the patients. This concordance was 51% and 70% in the premenapousal and postmenapousal patients, respectively (p=0.041).

Conclusions

In the patients operated with a preoperative diagnosis of CHA, the probability of detection of cancer in PB increases with increasing age and menapousal period. The reliability of FS is limited in younger and premenapousal patients.
IS PRE-OPERATIVE RISK ASSESSMENT IN LAPAROSCOPIC TREATMENT OF PRESUMED LOW RISK ENDOMETRIAL CANCER EFFECTIVE?

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Objectives
To compare pre- and postoperative data on histopathology, FIGO stage and short-term complication rates in laparoscopic treatment of presumed low-risk endometrial (pre) malignancy.

Methods
Pre- and post-operative histopathology was reviewed by two expert gynaecopathologists. Post-operative FIGO stage and grade were compared with preoperative diagnosis. Complications were registered according to standard Dutch guidelines.

Results
In 24.1% of cases (28/116) histopathology was upgraded on the definitive hysterectomy specimen; In 3.5% (4/116) upgrading to high-risk grade 3 EC was observed. In 11.1% (9/81) of EC cases a postoperative FIGO stage IG3, II or III EC was diagnosed, one case revealing unexpected extra-ovarian serous FIGO stage IIIa G3 carcinoma. In 24.1% of cases (28/116) histopathology was upgraded on the definitive hysterectomy specimen; In 3.5% (4/116) upgrading to high-risk grade 3 EC was observed. In 11.1% (9/81) of EC cases a postoperative FIGO stage IG3, II or III EC was diagnosed, one case revealing unexpected extra-ovarian serous FIGO stage IIIa G3 carcinoma.

Conclusions
A clinical relevant inconsistency between pre- and postoperative data on histopathology and FIGO stage was observed in 11.1% of EC cases. A more extensive pre-operative risk analysis of histopathological, clinical and potentially tumour biological markers of presumed low-risk EEC appears indicated to guide a more effective, individualized surgical treatment planning, especially for the morbid obese.
e-Posters: Endometrial Cancer

CLINICOPATHOLOGICAL FACTORS ASSOCIATED WITH PARA-AORTIC LYMPH NODE METASTASIS IN ENDOMETRIOID ENDOMETRIAL ADENOCARCINOMA: A CONSECUTIVE STUDY OF 689 PATIENTS

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Objectives
To evaluate the correlations between various clinicopathological findings and para-aortic lymph node metastasis (PALNM) in endometrioid endometrial adenocarcinoma (EEA).

Methods
We performed a retrospective analysis of 689 consecutive patients with EEA who were surgically staged from Jan 2006 to Dec 2011. Correlations between various clinicopathological factors and PALNM were assessed by univariate and multivariate analyses.

Results
Among the 689 eligible patients, 61 (8.9%) had lymph node metastases. Of these, 30 (49.2%) had only pelvic lymph node metastasis (PLNM) and 21 (34.4%) had metastases that involved both pelvic and para-aortic lymph nodes. The other 10 (16.4%) patients had PALNM without PLNM (defined as isolated PALNM). The incidence of PALNM and isolated PALNM in the study cohort were 4.5% and 1.5%, respectively. Univariate analysis showed that poor differentiation, tumor diameter (TD) ≥ 2 cm, deep myometrial invasion (DMI), cervical invasion, corneal or fundus-localized tumors, adnexal invasion, lymph-vascular space invasion (LVSI), serum CA125 ≥ 35 IU/ml, positive peritoneal washings and PLNM were significant factors for PALNM. Multivariate analysis revealed that only adnexal invasion, serum CA125 ≥ 35IU/ml and PLNM were independent factors for PALNM. Regarding isolated PALNM, DMI, cervical invasion, adnexal invasion, LVSI, serum CA125 ≥ 35IU/ml and positive peritoneal washings were significantly involved in PALNM, but only adnexal involvement and LVSI were identified as significant independent factors by multivariate analysis.

Conclusions
Adnexal invasion, elevated serum levels of CA125 and PLNM are significant independent factors for PALNM, but only adnexal involvement and LVSI are significant independent factors for isolated PALNM.
e-Posters: Endometrial Cancer

PARA-AORTIC LYMPHADENECTOMY SHOULD BE CARRIED OUT IN PATIENTS WITH CLINICALLY EARLY-STAGE NON-ENDOMETRIOID CARCINOMA: A STUDY OF 56 CONSECUTIVE PATIENTS
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Objectives
To evaluate the rate of para-aortic lymph node metastasis (LNM) among patients with clinically early-stage non-endometrioid carcinoma, and the correlation between para-aortic LNM and various clinical-pathological findings.

Methods
We retrospectively reviewed the medical records and pathological findings of 56 consecutive patients with non-endometrioid carcinoma who were surgically staged.

Results
The median number of lymph nodes harvested was 21 (range, 10-39) and 6 (range, 4-29) for pelvic and para-aortic regions, respectively. LNM was identified in 19 patients, pelvic LNM alone in 2 (10.5%) patients, both pelvic and para-aortic LNM in 10 (52.6%) patients, and para-aortic LNM alone in 7 (36.8%) patients. Univariate analysis showed that deep myometrial invasion, adnexal invasion, lymph-vascular space invasion, positive peritoneal washings, a corneal or fundus-localized tumor, and pelvic LNM were significantly associated with para-aortic LNM and/or isolated para-aortic LNM, but only pelvic LNM and a corneal or fundus-localized tumor were significant independent factors for para-aortic LNM and isolated para-aortic LNM, respectively.

Conclusions
Due to the lack of preoperative and intraoperative methods to correctly assess the clinical-pathological factors associated with para-aortic LNM and the high risk for para-aortic LNM in patients with non-endometrioid carcinoma, para-aortic lymphadenectomy is necessary for such patients.
A RETROSPECTIVE ANALYSIS OF DOCETAXEL-CISPLATIN CHEMOTHERAPY (DP CHEMOTHERAPY) FOR RECURRENT ENDOMETRIAL CANCER

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Objectives
There is poor evidence for the treatment methods and effective chemotherapy regimens for recurrent endometrial cancer. We treated 21 patients with recurrent endometrial cancer who received docetaxel-cisplatin (DP) chemotherapy as 2nd or 3rd line chemotherapy.

Methods
We reviewed 21 patients who were diagnosed as recurrent endometrial cancer and underwent DP chemotherapy from 2002 to 2012 at our institution. The patients who were underwent radiation as adjuvant therapy were excluded. Docetaxel 70mg/m² and cisplatin 60mg/m² were administered by intravenous injection every 3 weeks. Response rate (RR) was evaluated by WHO criteria. Adverse effect was evaluated by CTCAE ver 4.0. Median age at the start of DP chemotherapy was 62 years old, and median follow-up period was 30.3 months.

Results
RR was 57.1%. RRs were different according to the recurrence sites. RR was more than 60% at vaginal stump, lung, and liver, while RR was lower at lymph node and peritoneal dissemination. Grade 3 or 4 adverse effects occurred as leukopenia (81.0%), neutropenia (81.0%), anemia (9.6%), diarrhea (14.3%), general fatigue (14.3%), liver dysfunction (4.8%), peripheral neuropathy (4.8%), and hyponatremia (4.8%). Five-year progression-free survival (PFS) was 7.1% and median PFS was 7.5 months. Treatment-free interval (TFI) ≥6 months group had significantly better PFS than TFI <6 months group (p=0.01). Platinum-free interval (PFI) ≥6 months group tended to have better PFS than PFI <6 months group (p=0.09).

Conclusions
DP chemotherapy was fully feasible for recurrent endometrial cancer patients.
SYNCHRONOUS ENDOMETRIAL ADENOCARCINOMA AND PRIMARY PERITONEAL SEROUS CARCINOMA

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Objectives
Two or more primary tumors that occur in a patient closely in time are termed as synchronous tumors. Synchronous pelvic tumors are rarely seen. They constitute 0.7-1.8% of all gynecologic malignancies. Here, we describe a woman with endometrioid endometrial adenocarcinoma and primary peritoneal serous carcinoma.

Methods
A 58-old-woman with postmenopausal bleeding was undergone laparatomy with the biopsy results indicating endometrium adenocarcinoma. The ovaries were in normal appearances. There were common implants on peritoneal surfaces. In final pathologic evaluation of histerectomy and peritoneal biopsy samplings, a concomitant endometrioid stage 1a, grade 1 endometrial carcinoma and primary peritoneal serous carcinoma was reported. Abdominal fluid washing specimen was resulted as positive for serous carcinoma. The patient was submitted for standart chemotherapy for peritoneal cancer.

Results
The most frequently observed form of synchronous pelvic tumor is coexistence of low stage and low grade ovarian and endometrial cancers. Synchronous ovarian and endometrial cancers exhibit favorable survival outcomes as compared with single primary ovarian cancers. Authors explained this event by favorable characteristics associated with synchronous tumors, including younger age at diagnosis, earlier stage of disease, and better grade of disease.

Conclusions
Despite to similar pathophysiologic, clinical and therapeutic features of ovarian and primary peritoneal cancers no report is available about coexistence of endometrial and primary peritoneal cancer.
e-Posters: Endometrial Cancer

MIR-200B REDUCES THE EXPRESSION OF TIMP2 IN HEC-1A CELLS OF ENDOMETRIAL CANCER

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Objectives
Mir-200b showed the most significant change in our microRNAs array. The TIMP2 that was the target gene of mir-200b was predicted by TargetScan 5.0. The influence of mir-200b on TIMP2 was investigated.

Methods
Mir-200b mimic was transfected into HEC-1A, the influence of mir-200b on TIMP2 at mRNA and protein level was validated by luciferase assays, quantitative real-time PCR, western blotting and ELISA.

Results
The expression of TIMP2 at mRNA and protein level was reduced by mir-200b.

Conclusions
He expression of TIMP2 in vitro could be regulated directly by mir-200b, which contributes to explore the functions of mir-200b in tumor invasion and metastasis.
ANALYSIS OF D2-40 AND CXC R4 STATUS IN CARCINOSARCOMA (CS) OF THE UTERUS.
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Objectives
Carcinosarcoma (CS) of the uterus is a highly aggressive tumor. Because of their rarity and poor clinical outcome, investigations into the expression of potential therapeutic targets are limited. D2-40 staining has been reported to be useful for both identifying lymphatic vessel invasion (LVI) and counting lymphatic vessel density (LVD) in various cancers. CXCR4 is an independent of the VEGFR pathway in promoting lymphagenesis. The aim of this study was to clarify the expression of D2-40 and CXCR40 staining in patients with CS.

Methods
A total of 18 patients with CS underwent total abdominal hysterectomy at our institution between 2009 and 2011. Immunohistochemical staining of D2-40 and CXC R40 was performed. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results
There were no significant differences found in D2-40 and CXCR4 expression in patients with CS and LM. 72% percent of patients with CS had high expression of CXCR4 comparing to 58% in LM (p=0,29). 28% patients with CS had high expression of D2-40 comparing with only 11% in LM (p=0,26). High expression of D2-40 and CXC40 didn’t correlate with OS.

Conclusions
CXCR4 and D2-40 have limited prognostic value in carcinosarcoma of the uterus.
ANALYSIS OF CD31 AND CD34 STATUS IN CARCINOSARCOMA (UCS) OF THE UTERUS.

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Objectives
Carcinosarcoma (CS) of the uterus is a highly aggressive tumor. Because of their rarity and poor clinical outcome, investigations into the expression of potential therapeutic targets are limited. Angiogenic activity of the tumor may be measured by expression of vascular development markers - CD31 and CD34. The aim of this study was to analyze angiogenic activity of CS tumors.

Methods
Fresh tissue blocks of CS of the uterine corpus were collected from 18 patients who had undergone total abdominal hysterectomies at our institution between 2009 and 2011. Immunohistochemical staining of CD31 and CD34 was performed. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results
There were no significant differences found in CD31 and CD34 expression in patients with CS and LM (10.66 vs 17.518 for CD31 and 11.39 vs 16.71 for CD34). LM presented significantly higher expression of CD31 and CD34 comparing to CS (respectively p=0.048, p=0.013). Intensity of CD31 and CD43 expression in CS fresh tissue didn’t correlate with OS.

Conclusions
CD31 and CD34 expression in carcinosarcoma fresh tissue is lower than that observed in leiomyoma and have no impact on overall survival.
e-Posters: Endometrial Cancer

ANALYSIS OF D2-40 AND CXCR40 STATUS IN UNDIFFERENTIATED STROMAL SARCOMA (USS) OF THE UTERUS.

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Objectives

Undifferentiated stromal sarcoma (USS) of the uterus is a highly aggressive tumor. Because of their rarity and poor clinical outcome, investigations into the expression of potential therapeutic targets are limited. D2-40 staining has been reported to be useful for both identifying lymphatic vessel invasion (LVI) and counting lymphatic vessel density (LVD) in various cancers. CXCR4 is an independent of the VEGFR pathway in promoting lymphangiogenesis. The aim of this study was to clarify the expression of D2-40 and CXCR40 staining in patients with USS.

Methods

A total of 12 patients with USS underwent total abdominal hysterectomy at our institution between 2009 and 2011. Immunohistochemical staining of D2-40 and CXC R40 was performed. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results

There were no significant differences found in D2-40 and CXC R4 expression in patients with USS and LM. 90% percent of patients with ESS had high expression of CXCR4 comparing to 58% in LM (p=0,32). 30% patients with ESS had high expression of D2-40 comparing with only 11% in LM (p=0,38). High expression of D2-40 and CXC 40 didn’t correlate with OS.

Conclusions

There is no role of D2-40 and CXCR4 as a prognostic factors in patients with undifferentiated stromal sarcoma.
e-Posters: Endometrial Cancer

PROGNOSTIC IMPORTANCE OF MMP-9 AND IL-8 IN THE UTERINE SARCOMA.

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Objectives
Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of the extracellular matrix and the cancer metastasis; however, there is no report regarding this factor in uterine sarcoma.

Methods
Histopatological material and blood samples of 29 patients with uterine sarcoma were collected. 17 carcinosarcomas (CS), 12 undifferentiated stromal sarcoma (USS) were studied. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results
Within our patients the highest expression of MMP-9 was found in USS (p<0.001). The MMP-9 expression in USS was found to be 40 times higher than in LM and 30 times higher than in CS. The level of circulating MMP-9 was also higher in patients with CS and USS (p=0.05) when compared to leiomyomas. IL 8 level was found to be the highest in CS and no significant differences were found when comparing with LM group (p=0.28). Higher intensity of MMP-9 expression was positively correlated with greater mortality (p=0.002). No influence of blood circulating MMP-9 and IL-8 on patient’s survival was found.

Conclusions
Although level of MMP-9 and IL 8 in uterine sarcoma are higher than in leiomyoma there are no correlations of these cytokines with patient’s survival.
ANALYSIS OF CD31 AND CD34 STATUS IN UNDIFFERENTIATED STROMAL SARCOMA (USS) OF THE UTERUS.

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Objectives
Undifferentiated stromal sarcoma (USS) of the uterus is a highly aggressive tumor. Because of their rarity and poor clinical outcome, investigations into the expression of potential therapeutic targets are limited. Angiogenic activity of the tumor may be measured by expression of vascular development markers - CD31 and CD34. The aim of this study was to analyze angiogenic activity of USS tumors.

Methods
Fresh tissue blocks of USS of the uterine corpus were collected from 12 patients who had undergone total abdominal hysterectomies at our institution between 2009 and 2011. Immunohistochemical staining of CD31 and CD34 was performed. Control group was constituted from 17 patients with leiomyomas (LM) of the uterine corpus.

Results
There were no significant differences found in CD31 and CD34 expression in patients with USS and LM (13,89 vs 17,518 for CD31 and 13,6 vs 16,71 for CD34). LM presented higher but not significantly higher expression of CD31 and CD34 compared to USS (p=0,264, p=0,260 respectively). Intensity of CD31 and CD43 expression in USS fresh tissue didn’t correlate with OS.

Conclusions
Although this study confirmed that CD31 and CD34 is expressed in undifferentiated stromal sarcoma it is required to search for other targets differentiating with leiomyoma.
SURGICAL MANAGEMENT OF ADNEXAL TORSION IN OUR CLINIC

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Objectives
Adnexal torsion is more frequently seen in reproductive age. But adnexal masses in menopausal patients are more likely to be malignant. Our aim was to evaluate the surgical results of patients with diagnosis of adnexal torsion in our clinic.

Methods
Two hundred thirty patients with diagnosis of adnexal torsion that presented to our clinic between January 2005 and December 2012 were included in this retrospective analysis. Data regarding age, gravidity, parity, size of mass, operation time, and duration of hospitalization were recorded and compared between the patients that had laparoscopy to those who had laparotomy. The pathological results of patients also were recorded.

Results
One hundred eight patients were treated laparoscopically while 122 patients had laparotomy. The most frequent presenting symptom was pelvic pain (94%). Laparoscopy group consisted of young patients with low parity, operation and hospital stay time was shorter in laparoscopy group. Velocity loss in Doppler ultrasonography was noted in 80.6% of the patients. Of the laparotomy group 52 postmenopausal patients had hysterectomy and bilateral salpingo-oophorectomy, staging surgery was done for 28 of them. The pathological finding was found to be malignant in 8 and borderline serous tumor in 6 patients.

Conclusions
Laparoscopy is preferred for young patients who want to preserve their fertility. Because of high risk of malignancy in postmenopausal ovarian masses presenting with torsion; frozen section should be used. If not possible or not conclusive, staging surgery is more appropriate especially if there is suspicion of malignancy.
COMPARATIVE INHIBITORY EFFECT OF CAMMELLA SINENSIS (GREEN TEA) AQUEOUS NON-FERMENTED, FERMENTED AND SEMI FERMENTED EXTRACTS AGAINST H. PYLORI: STUDY ON PREGNANT WOMEN IN KARACHI.

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Objectives
The growing problem of antibiotic resistance by the organism in Pakistan thus demands the search for novel compounds, especially from natural sources as in this study.

Methods
In this study, a total of 400 biopsies were collected from the patients of gastro-duodenal pathology who were referred for endoscopy in a public sector hospital in Karachi, Pakistan. All these biopsies were processed for detection of H. pylori by two rapid Helicourease – indigenously developed rapid urease detection kits, culture and polymerase chain reaction (PCR). The 5% aqueous extract of fermented, semi fermented and non-fermented Green tea was prepared and their antibacterial potential was explored against 35 clinical isolates of H. pylori agar well diffusion technique.

Results
A total of 120, clinical H pylori isolates were successfully cultured and identified by rapid and molecular methods. The most significant activity was obtained in non-fermented green tea with an average zone of inhibition along with MIC was around 32 mm (MIC 120-150 ?g/ml), semi fermented product showed 28 mm (MIC 140-200 ?g/ml) showed and fermented one showed 32 mm (MIC 120-200?g/ml).

Conclusions
In conclusion, our results indicated that all processed forms of green tea extracts possessed some variable level of anti H. pylori activity. But non fermented that is freshly plucked green tea leaves with out any industrial treatment have profound effect with least MIC and thus considered as a suitable and safe candidate for the eradication of H.pylori particularly drug resistant species.
PREVALENCE OF ASCUS AND COMPARISON OF METHODS FOR MANAGEMENT OF PATIENTS IN ALBANIA POPULATION

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Objectives
To determine clinical significance and prediction of neoplasia among patients with (ASCUS) on Pap smear.

Methods
Out of a total of 1321 patients who underwent Pap smear over a year, 52 patients with report of ASCUS were followed up for 2 years. Those women were invited for a repeated examination 6 months later. At that occasion, a smear sample was collected and used for cytological examination and a concomitant HPV test, further management with colposcopy was decided.

Results
Women with an ASCUS diagnosis showed a normal cytology and a negative HPV test in 13.5% of the cases, abnormal cytology and a positive HPV test in 48% of the cases; in 21% of the women, the HPV test was positive, whereas cytology was normal; and in 17% of the women, the HPV test was negative, whereas cytology was abnormal (ASCUS or more). Hpv test was positive in 70% of ASCUS cases. HPV high risk were detected in 28% of HPV test positive and in 100% of cases diagnosed in CIN 3. Oncogenic types detected were 33, 16, 18, 52, 68, 51, 31, 56.

Conclusions
Patients with second time ASCUS should be meticulously followed up as a large number of them may have a underlying persistent disease. As the HPV tests have a higher sensitivity than the cytological screening, it is suggested that an HPV test in conjunction with a diagnosis of ASCUS can be employed to more efficiently select women, to whom further follow up is recommended. Colposcopy can be reasonably deferred till the second Pap smear.
ENDOMETRIAL BIOPSY AND MRI AS PRE-OPERATIVE PREDICTORS OF INVASIVE DISEASE IN ENDOMETRIAL CANCER: EXPERIENCE FROM TWO UK CENTRES

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Objectives
Pre-operative endometrial sampling is used to identify endometrial cancers that are at higher risk of invasive disease. Current UK radiological guidelines recommend triaging women at risk of high grade disease to undergo preoperative MRI Pelvis. Pre-operative staging is often used to triage high risk patients to include pelvic lymphadenectomy as part of primary surgery. Our aim was to assess the sensitivity and specificity of endometrial sampling and MRI pelvis in predicting invasive disease.

Methods
Retrospective analysis of electronic patient records at two centres. Women diagnosed with endometrial carcinoma who underwent primary surgery were identified. Endometrial biopsy was categorised as low risk (grade 1 endometrioid) and high risk (all others). Final histology was grouped into Type I (Endometrioid G1/2) and Type II (endometrioid G3, serous, clear cell, carcinosarcoma). Preoperative histology and MRI staging were compared with final histology and staging.

Results
A total of 247 cancers were analysed, of which 80 had pre-operative MRI. MRI pelvis gave sensitivity of 66%, specificity 81%, and diagnostic accuracy 74%, in predicting myometrial invasion. This is comparable with published national averages.

Initial histology showed sensitivity of 75%, specificity 58%, and diagnostic accuracy 63% in predicting type of endometrial cancer. Pre-operative histology to predict stage of disease of ≥1b showed sensitivity of 66%, specificity 61%, and diagnostic accuracy 63%.

Conclusions
Our results show pre-operative endometrial sampling is a poor predictor of subtype of endometrial cancer. MRI Pelvis should not be reserved for women who have higher grade cancers on initial histology, because we have shown this frequently underestimates disease severity.
e-Posters: Diagnostics

MALIGNANT MIXED MÜLLERIAN TUMOR OF THE FALLOPIAN TUBE OF THE HOMOLOGOUS TYPE – CASE REPORT
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Objectives
Malignant mixed Mullerian tumor (MMMT) of the female genital tract is uncommon and extremely rare in the fallopian tube.

Methods
We report a case of primary MMMT of fallopian tube in a 55 year-old nulligravida woman presenting a pelvic mass and postmenopausal bleeding.

Results
On physical examination, was found a voluminous pelvic mass, mobile and painful with approximately 20cm. There was no clinical evidence of ascites or adenopathy.

The pelvic magnetic resonance imaging revealed a pelvic mass right adnexal poorly-defined, solid-cystic, which seemed in dependence of the ovary, with 21x10 cm. In preoperative study, the only tumor marker high was the CA-125.

The patient underwent laparotomy, which revealed a mass within the right Fallopian tube, measuring 20x30 cm in size, involving the small bowel loops and with metastases in omentum.

A total of abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and also segmental bowel resection, were made.

The final pathologic diagnosis was MMMT, and cytologic sampling of the fluid was reported as malignant cytology.

The patient was categorized as International Federation of Gynecology and Obstetrics FIGO Stage IIIC.

The patient keeps stable, and will start adjuvant chemotherapy.

Conclusions
Prognosis is poor. Surgery is the treatment of choice, although chemotherapy may have of some benefit.
THE RELATIONSHIP BETWEEN THE OVARIAN VOLUME AND SERUM CA-125 LEVELS
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Objectives
The aim of this study was to investigate the relationship between ovarian volume and serum CA-125 levels.

Methods
Serum CA-125 levels and ovarian volume were compared among the cases with benign ovarian neoplasms, primary epithelial ovarian cancer (EOC), controlled ovarian hyperstimulation and ovarian hyperstimulation syndrome (OHSS). Also, the correlation between CA-125 levels and ovarian volume were evaluated in the presence of peritoneal fluid and/or peritoneal carcinomatosis.

Results
Although ovarian volume was not different among the groups, CA-125 levels were higher in the cases with EOC than with benign ovarian tumors (p=0.001). Baseline CA-125 levels were not found to have increased while ovarian volume went up with controlled hyperstimulation in the infertile group (p=0.555). However, uncontrolled hyperstimulation of the ovaries and the presence of peritoneal fluid caused an increase in the levels of CA-125 (p=0.001). There was no correlation between ovarian volume and CA-125 levels in the cases with malignant ovarian tumors (r=0.083).

Conclusions
The results of this study have confirmed that CA-125 is a peritoneal marker and increased ovarian volume with benign ovarian neoplasms or controlled hyperstimulation does not increase CA-125 levels in the same way. The presence of peritoneal carcinomatosis and/or peritoneal fluid seems to be an important factor for high CA-125 levels in the patients with EOC.
OFFICE HYSTEROSCOPY IN PATIENTS WITH POSTMENOPAUSAL BLEEDING
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Objectives
Dilatation and Curettage was the standard method for the management of women with postmenopausal bleeding in Albania. Only recently hysteroscopy is used as diagnostic tool for detecting intrauterine pathologies. The aim of this study is to review our experience in using hysteroscopy for diagnosis of endometrial cancer in women with postmenopausal bleeding.

Methods
We retrospectively studied 40 consecutive office hysteroscopies in patients referred to our clinic for postmenopausal bleeding.

Results
The mean age of examined patients was 58.4 ages. In 36 cases hysteroscopy showed an abnormality. We found 6 cases with endometrial cancer. In 16 patients hysteroscopy revealed endometrial atrophy. We found 11 endometrial polyps in 8 patients. In 6 patients hysteroscopy showed an endometrial hyperplasia. In all cases histopathology confirmed the diagnosis.

Conclusions
Office hysteroscopy is a well-tolerated, safe and highly accurate diagnostic tool for examination of women with postmenopausal bleeding.
e-Posters: Diagnostics

VALUE OF COLOR DOPPLER SONOGRAPHY IN DETECTING OVARIAN MALIGNANCY
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Objectives
The aim of this study is to assess the efficacy of color Doppler ultrasonography in differentiation between benign and malignant ovarian tumors and to study the correlation between Doppler indexes PI, RI and histopathology results.

Methods
37 patients with complex ovarian tumors were included in the study in the period of time 2009 - 2011 at the University Hospital "Queen Geraldine". A color Doppler ultrasonographic examination was performed prior surgery. The data of ultrasonographic morphology and Color Doppler were compared with results of histopathology.

Results
The analysis of the data showed a significant correlation between RI and Histopathology (p=0.002). There is an important statistical correlation between PI and Histopathology (p=0.003). There isn't any important statistical correlation between the age of patients and the histopathologic results p=0.881. RI showed a specificity of 12.5% and a sensitivity of 40%. PI showed a specificity 12.5% and a sensitivity of 60%.

Conclusions
Color Doppler ultrasonographic examination provides additional information regarding ovarian tumor malignancy. There is a significant correlation between PI, RI and histopathologic results.
HPV DNA AND MRNA IN PREGNANT WOMEN AND THEIR NEONATES.
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Objectives
To estimate HPV infection in pregnant women and possibilities of HPV transmission to the child.

Methods
The study was conducted in 2012 in the university clinic in Krakow, Poland. The clinical material were cells samples of uterine cervix of 107 delivering women and exfoliated cells from the mouth of the 112 infants for the presence of HR HPV DNA and mRNA E6/E7 HPV.

Results
In 22,4% and 4,7% of delivering women HR HPV DNA and mRNA E6/E7 HPV were found respectively. In 7,8% and 2,3% of placenta HR HPV DNA and mRNA E6/E7 HPV were found respectively. In neonates HR HPV DNA was wound in 2,3% while mRNA HR HPV in 1,8%.

Conclusions
The study confirms that the incidence of HPV infection is slightly higher in pregnant women comparing to the general population. The risk of vertical transmission is relatively low. The expression of mRNA E6/E7 HR HPV is extremly low and rare phenomenon.
IMMUNOHISTOCHEMICAL ANALYSIS OF P16 EXPRESSION IN UTERINE SMOOTH MUSCLE TUMORS

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Objectives
In the uterus, p16 overexpression in uterine leiomyosarcomas compared with leiomyomas has been reported but the clinical significance has not been well established. In the present study, we examined the expression of p16 in various uterine smooth muscle tumors by immunohistochemical method and analyzed the expression of p16 and various clinico-pathological parameters including prognosis.

Methods
Specimens of tissues were also obtained from those 59 patients with uterine smooth muscle tumors, including 29 leiomyomas, 13 STUMPs, and 17 leiomyosarcomas. The prevalence of p16 expression in various uterine smooth muscle tumors was examined and investigated the association between p16 expression and various clinico-pathological parameters including prognosis in LMS.

Results
The prevalence of p16 expression of LM, STUMP, and LMS tumors were 10.3%, 38.4%, and 76.4%, respectively. The prevalence of p16 were significantly higher in LMS group compared to groups with LM or STUMP tumors. In LMS groups, IHC scores of p16 were significantly higher in the groups with more advanced stage, with higher mitotic activity, and with recurrent groups. High expression of p16 in LMS was linked to shorter disease-free and overall survival.

Conclusions
In the present study, we found statistically significant higher levels of p16 in LMSs compared to other group. Our results suggest that p16 may be useful marker in the differential diagnosis of uterine smooth muscle tumors. In LMS tumors, p16 expression is significantly higher in the group with more advanced stage, with higher mitotic change, and with recurrent diseases. These results may suggest that over-expression of p16 in LMS may be associated with poor prognosis.
e-Posters: Diagnostics

ULTRASOUND CHARACTERISTICS OF UTERINE SARCOMAS
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Objectives
Unfortunately, uterine sarcomas are often diagnosed incidentally at surgery or by histologic examination. A better sonographic preoperative differentiation of uterine masses may reduce morbidity and mortality.

Aim of the study is to find sonographic characteristic of uterine sarcomas.

Methods
Retrospective analysis of sonographic images of uterine sarcomas diagnosed between 2001 and 2012. Following criteria were described: maximum tumor diameter ($D_{\text{max}}$), echogenicity (homogenous, mixed), presence of a capsule, and degree of vascularity by power Doppler (circular or complex).

Results
Twenty six patients were analyzed, 16 with carcinosarcomas (CS), 5 leiomyosarcomas (LS), 4 uterine stromal sarcomas (USS), 1 undifferentiated endometrial sarcoma (ES), and 1 adenosarcoma (AS). At sonography only 3 tumors showed a classical capsule. Homogenous echogenicity was found in 11 cases, and mixed in 12. 3 tumors were hypoechoic. $D_{\text{max}}$ was not different between groups (CS 72.73mm; LS 59.6mm; USS 52mm; ES 95mm; AS 80mm). Leiomyosarcomas and endometrial stromal sarcomas had always a solid aspect, while carcinosarcomas had a solid aspect just in 3 cases. A complex and suspect degree of vascularity was found in 91% of CS, in 50% of USS and in all LS, ES and AS.

Conclusions
In contrast to myomas, uterine sarcomas are characterized by a lower prevalence of a capsule and a higher rate of suspicious vascular pattern. Combined with patient age and clinical manifestation, these sonographic pattern may help during preoperative counseling.
NEW LABORATORY MARKERS IN THE DIAGNOSIS OF ENDOMETRIAL CANCER – THE PILOT STUDY

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Objectives
Calgizzarin (S 100A-11), AIF-1, and TFF are proteins which, in addition to their physiological functions in the body interfere significantly in carcinogenesis. Their abnormal values in serum could therefore indicate pathological changes in the endometrium. The objective of this study was to verify the effectiveness of diagnostic determination of AIF-1 TFF, TFF-2, TFF-3 and S100A-11 in the diagnosis of endometrial carcinoma.

Methods
In total, 44 women undergoing diagnostic hysteroscopy were included in the study. Blood samples of fourteen patients with endometrial cancer and 30 women with benign endometrial findings (polyps, atrophy) were taken preoperatively. Sera specimens were tested for levels of S100A-11 (BioVendor, DSX) TFF-1 (BioVendor, DSX), TFF-2 (BioVendor, DSX), TFF-3 (BioVendor, DSX), AIF-1 (BioVendor, DSX) and Ca-125 (Siemenes, Centaur XP).

Results
Patients with carcinoma had significantly higher values of S100 A-11 and TFF-3 in sera (S100 A-11 7.2 vs. 4.2 ng / ml, P <0.01; TFF-3 1.0 vs. 2.7 ng / ml, P <0.05). There was no difference in values of Ca 125, TFF-1, TFF-2 and AIF-1 between both groups. Linear regression model with stepwise regression included only as a diagnostic marker of choice S-100 A11.

Conclusions
Results of this pilot study reveal a possibility to use S100 A-11 and TFF-3 as a potential markers in patients with endometrial cancer. The recruitment of additional patients is ongoing.
DISTRIBUTION OF HPV-DNA TYPES IN TURKISH WOMEN

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Objectives
Persistent infections with carcinogenic human papillomavirus (HPV) types are well-recognized causes of cervical cancers. Thus, HPV genotype detection is helpful procedure in reducing cervical cancer incidence. We aimed to study the types of HPV in cervical cytology specimens and distribution according to the ages of Turkish women.

Methods
Cervical swab samples were obtained in 920 women, aged ≥30 years, undergoing routine cervical screening in Tepecik Educational and Research Hospital between June-September 2012. To identify HPV genotypes, cervical samples were analyzed by 4800 Cobas System real-time PCR (Roche Diagnostics, USA) for HPV-DNA types 16, 18 and the other 12 high risk HPV (HR-HPV) types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68).

Results

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HPV-DNA 16</th>
<th>HPV-DNA 18</th>
<th>HR-HPV Multipl</th>
<th>HPV TYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-40</td>
<td>12</td>
<td>1</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>41-50</td>
<td>3</td>
<td>22</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>61-70</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>2</td>
<td>56</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 1: Distribution of HPV-DNA types according to age
Of total 920 patients, 83 (8.92%) tested positive for HPV-DNA. Among HPV-DNA positive women, 67.5% were infected with HR-HPV types, followed by HPV-16 19.2%, HPV-18 2.4%, and multiple HPV genotypes 9.6%. HPV-DNA 16 and 18 most often detected between 30-40 years of age (Table 1).

Conclusions
Pap testing combined with HPV-DNA detection would be efficient strategy for cervical cancer screening. Also, data of HPV-types for local populations will be useful for vaccination strategies.
COMPARISON OF TRANSVAGINAL 3D SONOHYSTEROGRAPHY WITH OUTPATIENT HYSTEROSCOPY IN THE EVALUATION OF ABNORMAL UTERINE BLEEDING.

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Objectives
To compare transvaginal 3D sonohysterography and outpatient hysteroscopy with regard to diagnostic accuracy and procedure time in abnormal uterine bleeding. Design A prospective randomized controlled cohort study Setting A teaching hospital in London Population A group of 49 women with abnormal uterine bleeding from varied ethnic backgrounds were recruited of which 44 completed the study. Subjects with pregnancies, pelvic infections, large uteruses, suspicious or diagnosed pelvic malignancies and who did not meet the criteria for day case surgery were excluded

Methods
Patients were randomized to two groups: Group 1 had hysteroscopy followed by sonohysterography while Group 2 had sonohysterography followed by hysteroscopy Main Outcome Measures Diagnostic accuracy and procedure time of sonohysterography in comparison to hysteroscopy.

Results
A total of 44 patients completed the study. The average age of the study population was 44.8 and the mean parity was 1.8. Nulliparas represented 34.03% of the study population and the average duration of symptoms were for 14.8 months

Conclusions
In the investigation of women with abnormal bleeding in an outpatient setting both hysteroscopy and sonohysterography are comparable in the diagnosis of intracavity lesions and procedure time. Though the development of sonohysterography is a significant advance in gynaecologic investigation and there is a case for incorporating it in gynaecologic scanning services. Therefore in terms of patient acceptability, post-operative complications, visualizing the adnexae and determining myometrial extension sonohysterography scores over hysteroscopy.
TWO CASES OF TROUSSEAU’S SYNDROME WITH REPEATED THROMBOSIS DESPITE STRICT ANTICOAGULANT THERAPY.
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Objectives
Occasional reports have appeared recently. However, it is very difficult to manage when Trousseau’s syndrome is actually encountered.

Methods
We had the two cases with the management of Trousseau’s syndrome in our department and in these cases, it was impossible to perform surgery because of repeated thrombosis in spite of careful management.

Results
(Case 1)
The patient was a 52-year-old, who had a history of cerebral infarction 3 years ago but she had completely recovered. We thoroughly examined for a chief complaint of lower abdominal pain and we diagnosed of an intrapelvic tumor. The patient had experienced four cerebral infarctions, two episodes of deep vein thrombosis and one episode of pulmonary embolism before she died. She died by her cancer on the 135th day of illness. Ovarian carcinoma was diagnosed at autopsy.

(Case 2)
The patient was a 67-year-old. She had an intrapelvic tumor of 12 cm in diameter. The patient’s general condition subsequently gradually deteriorated, and she died on the 78th day of illness. Before she died, she experienced two cerebral infarctions and two episodes of deep vein thrombosis of the lower limbs.

Conclusion
In Trousseau’s syndrome, thrombosis comes from a result of hypercoagulability due to a malignant tumor and makes the rapid deterioration of the patient’s condition. The attention is focused on the changes of peripheral blood D-dimer as a predictor of thrombosis. Anticoagulant therapy must be continued with careful management.
e-Posters: Diagnostics

LEIOMYOMA OF THE ROUND LIGAMENT PRESENTING AS AN ADNEXAL MASS IN A PATIENT WITH A HISTORY OF Hysterectomy

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Although the tumors of the round ligament are rare, the most frequently seen ones are leiomyomas. A 52 year old woman with the complaint of pelvic tenderness applied to our outpatient clinic. In her medical history, she had underwent total abdominal hysterectomy for uterin leiomyoma 15 years before. Physical examination revealed a firm, left sided pelvic mass and uterine vault prolapse. Ultrasonography and computed tomography demonstrated an eight centimeter in diameter solid mass arising from the left adnexal region with increased vascuarity and blood flow velocities obtained by doppler examination suggesting a malignant tumour. Laparotomy and frozen section were performed for the suspected mass. During exploration the uterus was negative seconder to the previous operation, both ovaries were normal and a highly vascularised solid mass arising from the left round ligament was observed. This mass was completely removed and diagnosed as leiomyoma on frozen section. Then the patient underwent abdominal sacrocolpexy for the treatment of vault prolapse. Despite adnexal masses are more frequently seen causes of pelvic masses in women, leiomyomas should be kept in mind in the differential diagnosis of adnexal masses even in patients with the history of hysterectomy.
18F-FLUORODEOXYGLUCOSE UPTAKE AND CLINICOPATHOLOGICAL FEATURES OF RECURRENT OR METASTATIC ENDOMETRIAL STROMAL SARCOMA (ESS).

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²Obstetrics and Gynecology, Hyogo College of Medicine, Nishinomiya, Japan

Objectives
Maximum standardized uptake value on FDG-PET was evaluated as a predictive surrogate marker in developing treatment strategies for recurrent or metastatic ESS.

Methods
Clinical information was obtained from records of patients with recurrent or metastatic endometrial stromal sarcoma who underwent surgery or biopsy following PET/CT. Pathological features—including estrogen receptor, progesterone receptor, and Ki-67 expression—were immunohistochemically evaluated. We classified lesions as ‘PET-positive’ if the maximum standardized uptake value was ≥3.0.

Results
Among 8 recurrent and 1 metastatic ESS patients, 4 (44%) had PET-positive. Two PET-positive patients were estrogen receptor negative and the 5 PET-negative patients were estrogen receptor positive (p = 0.073). The Ki-67 index was ≥10% in the 4 PET-positive patients, but <5% in the 5 PET-negative patients (p = 0.003). Three patients with PET-positive tumors received more aggressive treatment (e.g., cytotoxic chemotherapy and additional surgery) than did those with PET-negative tumors. One patient who died of disease had PET-positive tumors, was negative for estrogen and progesterone receptors, and had a 20% Ki-67 index.

Conclusions
FDG uptake was associated with tumor biology of recurrent or metastatic ESS. PET/CT was useful for developing treatment strategies for recurrent or metastatic ESS.
ANALYSES OF ATYPICAL GLANDULAR CELLS RE-DEFINED BY THE 2006 BETHESDA SYSTEM: HISTOLOGIC OUTCOMES AND CLINICAL IMPLICATION OF FOLLOW-UP MANAGEMENT.

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Objectives
To evaluate the histopathology and the long-term follow-up outcome of women who had atypical glandular cells on Pap smears.

Methods
All women with atypical glandular cells (AGC) who underwent colposcopic and histopathologic evaluation between January 2005 and October 2010 were reviewed. Patient data were examined up to October 2012, allowing for at least two years of follow-up for all patients.

Results
Forty-four women with AGC Pap test underwent histologic follow-up during the study period. Overall, upon reclassification of smears, 35 (79.5%) cases were diagnosed with AGC “not otherwise specified” (NOS) and 9 (20.5%) with AGC “favour neoplasia”. Seven out of 9 patients (77.7%) with AGC “favour neoplasia” had significant pathology. On the other hand, only 11 out of 35 cases (31.4%) with AGC “NOS” had significant pathology. Significant correlation was found between AGC “favour neoplasia” smears and a significant pathology (P: 0.01). Of the 44 patients, 18 (40.9%) had significant pathology. Eight patients (18.2%) had low grade cervical intraepithelial neoplasia (CIN 1), 4 (9%) had high-grade cervical intraepithelial neoplasia (CIN 2 / 3), 1 (2.2%) had microinvasive squamous cell carcinoma of uterine cervix, 1 (2.2%) had cervical adenocarcinoma in situ, 1(2.2%) had cervical adenocarcinoma, 1 (2.2%) had endometrial adenocarcinoma, and 2 (4.5%) had endometrial hyperplasia.

Conclusions
Reporting AGC in our population is clinically significant due to the high prevalence of underlying preinvasive and invasive diseases (40.9%). The subtypes of the AGC category are significant predictor of such lesions.
THE USE OF HYSTEROSCOPY IN CASE OF ENDOMETRIAL PATHOLOGY
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3Faculty of Medicine, Riga Stradins University, Riga, Latvia
4Institute of Anatomy and Anthropology, Riga Stradins University, Riga, Latvia

Objectives
Hysteroscopy is suitable for more accurate diagnostic of endometrial pathology [Kalampokas, 2012]. Using hysteroscopy, suspected diagnosis more likely corresponds to the histological results [Gan, 2013]. D&C without hysteroscopy is not recommended in case of endometrial polyps or in women in menopause [Lee, 2011]. The aim was to compare the use of hysteroscopy for diagnostics of endometrial pathology, for instance, in two clinics in Germany and in Latvia.

Methods
421 patients with histological proved endometrial pathology treated in Riga Hospital No.1 in 2007-2010 were observed retrospectively. The data about these patients were compared to the patients in Charité Universitätsmedizin in Berlin for the same period of time.

Results
Mean age of patients is 44.8 years (SD ± 8.9). D&C was combined with hysteroscopy only in 6.7% of cases in Latvian hospital. The indication was incompletely removed polip in out-patient department or recurrence of endometrial pathology. In German hospital 90% of patients underwent hysteroscopy. Hysteroscopy was not chosen only in case of severe bleeding or if hysterectomy was planned due to another indication.

Conclusions
Frequency of use of hysteroscopy is measurable differently in Latvian and German clinic. There are very different indications for use and no-use of this diagnostic method. Considering global literature data and experience in German hospital, hysteroscopy should be recommended for more frequently use in Latvia, especially as a diagnostic tool.
COMPARISON BETWEEN SCORING SYSTEM AND SUBJECTIVE EVALUATION OF ADNEXAL MASSES BY TWO INDEPENDENT ULTRASOUND EXAMINERS WITH A DIFFERENT LEVEL OF EXPERTISE: TRAINING ASPECTS.

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2Department of Statistics Faculty of Management, University of Gdansk, Sopot, Poland

Objectives
To compare predictive performance in transvaginal ultrasound (TVU) of variously experienced ultrasonographers using score-based and subjective methods in assessment of adnexal masses, and to determine which method may have greater value for TVU training.

Methods
142 TVU examinations were performed in 71 patients (median age - 53) with a suspected malignant adnexal mass after outpatient referral to our unit over 17 months. The score was based upon sonomorphologic index by novice examiner and skilled examiner who used pattern recognition. Each mass was classified as a being benign or malignant. The TVU data was introduced to database and analyzed with respect to the survival associated with pathological findings. Statistical analysis was used to identify which ultrasound examiner assigned tumors more accurately to malignant or benign groups. Training aspects were expressed by comparison of accuracy of diagnoses over the time.

Results
Ovarian malignancy was found in 49 cases and 22 were benign. Statistical values were (scoring vs. subjective): sensitivity: 85.7% vs. 94%, specificity 77.2% vs. 64%, positive likelihood ratio 3.759 vs. 2.58 and negative likelihood ratio 0.185 vs. 0.096. Inter-observer agreement was 69% (Scott’s pi = 0.149) (95% CI -0.068685 - 0.393276). No statistically significant difference was achieved by experienced and novice ultrasound examiners in defining tumor character (p > 0.05).

Conclusions
In some subset of patients, if the ultrasound equipment is good enough, result of examination may be similar regardless of the time spent on examination and examination’s deftness. The examinations should be done on the training device. We can either simplify training or let doctors gain experience in their field.
MANAGEMENT OF MALIGNANT PLEURAL EFFUSION. EXPERIENCE IN OUR CENTER
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Objectives
Ovarian cancer patients suffer different complications, mainly malignant pleural effusion (MPE) and intestinal occlusion (IO). We describe the prevalence of MPE, treatment and the evolution in our Center.

Methods
Observational retrospective study of patients that suffered ovarian cancer and MPE or IO between 2008-2011. Characteristics: 12 patients, mean age: 62 years (37-84).

Results
MPE: 9 patients- Thoracocentesis was performed to every patients, with improvement of symptoms in 100%. Pleurodesis was not performed after first thoracocentesis. 6 patients relapsed, and we performed pleurodesis in them, being effective in 66 % of patients. Talc was the treatment with the pleurodesis. We lose patients and we don't know median survival (in our country live a lot of United Kingdom patients that move to original country when they begin with bigger problems).

IO: 5 patients (2 patients had both problems). 4 patients’ received medical treatment (nasogastric sounding and parenteral nutrition) and surgery was performed in one. Fatal evolution happened in 3 of the patients dying secondary to several complications.

Conclusions
MPE and IO are typical complications of ovarian cancer that should be treated definitively at the time of initial diagnosis to provide a better evolution and better control of symptoms.
e-Posters: Palliative Care

REGIONAL ONCOLOGIC INSTITUTE IASI - PALLIATIVE CARE UNIT, ONE YEAR EXPERIENCE IN PALLIATIVE TREATMENT OF GYNECOLOGICAL CANCER
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²1st Department of Oncologic Surgery Gynecologic Oncology Unit, Regional Institute of Oncology, Iasi, Romania

Objectives
This paper intends to present a retrospective data analysis obtained from women diagnosed with gynecologic cancer and hospitalized in the Palliative Care Unit.

Methods
Using the Regional Institute of Oncology Iasi - Palliative Care Unit dataset, information was collated for 382 patients hospitalized from April 2012 to April 2013.

Results
From 166 women (43.5% of patients), 40 (24%) have been diagnosed with primary cervical cancer, ovarian cancer and/or breast cancer. Data analysis revealed that 25 patients had breast cancer, 5 patients had ovarian cancer and 10 had endometrial cancer. The age was between 35 and 82 years with the mean age of 62.4 years. Most patients received opioid therapy and other palliative procedures. Death occurred at 19 patients (47.5%).

Conclusions
Providing palliative care can be a very powerful experience. Providing care and support to a terminally ill woman and her caregivers can be physically and emotionally demanding. Being available to offer care and support to an ill woman and her family is vital and helpful in itself. The most important thing is that palliative care leads to improved quality of life in patients diagnosed with cancer.
e-Posters: Palliative Care

**BENEFIT OF PALLIATIVE CHEMOTHERAPY AND HOSPICE ENROLLMENT IN LATE-STAGE OVARIAN CANCER PATIENTS**

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**Objectives**
The ideal timing for transition to best supportive care (BSC) for ovarian cancer patients is not clear. We retrospectively assessed the survival benefit of continuing chemotherapy and hospice enrollment in late-stage ovarian cancer patients.

**Methods**
Eligibility criteria included platinum and taxane treatment, clinical progression within 6 months of the last platinum dose, and progression during chemotherapy.

**Results**
Of the 54 eligible patients (median overall survival [OS] after first becoming refractory [1st Ref], 96 days), 22 received chemotherapy (Chemo group), 2 received radiation therapy, and 30 were not treated. The remaining 18 patients (BSC group) were compared with the Chemo group. The Chemo and BSC groups had similar background characteristics, except for the rate of consultation with a regional palliative care physician before or within 1 week of 1st Ref (9% vs. 50%, respectively). Median OS was significantly longer in the Chemo than in the BSC group. Response rate to chemotherapy was 9.0%. In multivariate analysis, chemotherapy (hazard ratio [HR] 0.288, p = 0.006) and hospice enrollment (HR, 0.274, p = 0.013) were prognostic of survival after 1st Ref.

**Conclusions**
Chemotherapy after 1st Ref can be offered and hospice enrollment during the terminal stages is encouraged for recurrent ovarian cancer patients.
COULD SENTINEL NODE MAPPING OF GROIN LYMPH NODES CAUSE EXTRANODAL METASTASES IN VULVA CANCER?

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Objectives
Complete groin nodes lymphadenectomy in vulva cancer carries a substantial risk of short and long-term morbid sequelae, making sentinel lymph node (SLN) mapping a valid alternative in patients with squamous cancer of diameter <4cm and non-suspicious lymph nodes. Sentinel nodes are mapped according to the combined technique of radioscintigraphy using technetium-labelled colloid and blue dye. We describe early extranodal recurrence in two patients undergoing SLN mapping.

Methods
Both patients had lymph node metastases at their original dissection. We question whether rapid lymph flow promoted by injection of colloid and dye could cause retrograde flow of cancer cells along the lymphatics draining from the pubis to the groin and extravasation of cancer cells into the dermis because these metastases arose anterior to the pubis and medial to the groin. These recurrence sites were more mediocephalad than would be expected for skin bridge metastasis.

Results
CT imaging shows the metastases are within the dermis. No lymphatic tissue was identified around these subcuticular deposits of cancer on histopathological examination. Body wall extension occurs in recurrent vulva cancer but we had never seen such an early recurrence when full inguinofemoral lymphadenectomy without SLN was the standard approach.

Conclusions
These two cases raise a caveat in the application of SLN mapping in vulva cancer. The risk may be higher in cases with metastasis to lymph nodes because the afferent channels to the lymph nodes may be already blocked by tumour.
e-Posters: Vaginal and Vulvar Cancer

MELANOMA GENITAL- AN ANOTHER PROGNOSIS FACTOR?
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Objectives
The primary melanoma of the urogenital tract in the woman is a rare pathology with a poor prognosis. We present our experience in the management of genital melanoma in order to identify prognostic factors and optimal treatments.

Methods
Between April 1992 and Mars 2012, 10 patients with a primary genital melanoma were referred in our department. 5 patients presented a vulvar melanoma, 4 a vaginal melanoma and only one cervical melanoma. The median dimension of the lesion was 34 mm and the median depth of invasion was 10.1 mm. The AJCC stage of the patients ranged from IB to IIIC. 6 cases were the classic dark-blue flat melanoma and the other 4 cases were an atypical amelanotic tumor. The wide local surgery was performed in 4 patients. A radical surgery was performed in 5 patients. In the large cervical melanoma, radiotherapy was performed as first-line treatment. In 8 patients a regional lymph node staging was performed. Adjuvant treatment was realized in 5 patients.

Results
At that time, 2 patients are alive without recurrence. The others 8 patients experienced a rapid recurrence. The median disease free survival was 6 months. The recurrence was metastatic without sign of local relapse. The different prognostic factors were analyzed. The disease free survival could be linked a clinical presentation (Breslow thickness and morphology of lesion) associated to the early diagnosis.

Conclusions
In our series, the most important prognosis factor are the tumor thickness and the morphology of lesion. These rare lesions should be treated in experienced centers in order to improve their prognostic.
e-Posters: Vaginal and Vulvar Cancer

BASAL CELL CARCINOMA OF THE VULVA
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Objectives
Describe a case of basal cell carcinoma of the vulva, diagnosed in cercical pathology unit ASSIR L’Hospitalet (Barcelona, Spany)

Methods
Clinical case woman of 67 years in which he outlines the history of hysterectomy for genital prolaspso, and exeresis seven basal cell carcinomas of location on the face, shoulder and armpit.

Complaint:
vulvar itching, long-lasting more than 6 month’s with vulvar injury refractory to treatment whith topical antifungal / corticosteroid.

Vulvar Exploration:
right labia majora injury about 4 cm, snorkel whith areas pink, hypopigmented and pearlescent. To palpation is noted indurated area, suggestive of infiltrative injury.

Vulvoscopy:
In right labia majora we observe an injury of 4x3 cm, whith areas of leukoplakia hiperkeratosis and small vascular dilatations. (photo)

Punch biopsy was performed (punch 4 mm)

Results
pathological anatomy reports an infiltrative basal cell carcinoma

Treatment: bilateral vulvectomy

Conclusions
Basal cell carcinoma is a rare neoplasm, representing less than 1%

On the conducted literature review have been reported only 250 cases of localized basal cell carcinoma of the vulva
Its etiology is not completely known and has been associated with many factors: advanced age, chronic inflammation, local trauma, radiation, immunodeficiency, although the main factor involved is the UV RADIATION DISTANCE (cause of case study).
The recurrence rate is high, up to 25% and are related to incomplete surgical excision, so the postoperative follow-up is essential. The basal cell carcinoma vulva has a good prognosis. TO CONSIDER WE RECOMMEND THAT: ALL LONG ITCH VULVAR EVOLUTION HAS TO MAKE A VUVULVOSCOPIA AND PRACTICE A BIOPSY OF INJURY
e-Posters: Vaginal and Vulvar Cancer

THE IMPORTANCE OF GroIN LYMPHADENECTOMY IN CLINICALLY StAGES IB AND II VulVAR CANCER
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Objectives
We analyzed the prevalence of inguino-femoral lymph nodes metastases in clinically early stages of vulvar cancer.

Methods
Twelve patients with IB-II FIGO stages vulvar cancer with no clinically and imagistic evidence of nodes metatases were treated in our clinic during a 25 months period (January 2011-February 2013). The surgical procedures consisted in radical vulvectomy plus uni- (2 patients) or bilateral (10 patients) inguino-femoral lymphadenectomy (depending on the primary lesion localization). In 2 patients we performed also a distal urethral resection (10-15 mm), in 4 a partial colpectomy and in one a unilateral extraperitoneal pelvic lymphadenectomy.

Results
The final pathological result was squamous carcinoma in 11 patients and carcinosarcoma in one. The prevalence of positive lymph nodes was 50% (6 out of 12 patients, between 1 and 5 positive nodes per groin, two bilateral and 4 unilateral). The median number of harvested lymph nodes was 10.7 per groin (between 7 and 27). Seven patients developed some wound complications (infections, dehiscence, lymphocele etc.), but all were solved. Till now, ten patients are alive and with no evidence of disease, one died of disease and one had a groin relapse and follows radiotherapy.

Conclusions
The prevalence of groin metastases in stages IB-II vulvar cancer is high. A thorough inguino-femoral dissection seems necessary, despite the high incidence of wound complications.
VULVAR HOOD FLAP RECONSTRUCTION FOR IMPROVING QUALITY OF LIFE FOLLOWING SURGICAL EXTERPATION OF VULVAR CANCER

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Background
Post-oncologic-vulvar reconstruction has profound long-term impact on the quality of life. While several algorithmic approaches address important issues of recovery of sexual function they do not effectively address simple day-to-day challenges that most patients face silently: the disruption of the vulvar mucosa – leading to chronic dryness, mucosal irritation, ulcerations, vulvar itching and pain. Anatomically these problems are a result of: ablation of the natural mucocutaneous junction; and mucosal eversion wherein the inflexible newly reconstructed skin-edge of the flap pulls the more pliable mucosal edge outwards leading to exposure mucositis. Postoperative radiation only further aggravates these problems.

Aim
Create operative technique named the Vulvar Hood Flap (VHF) that restores anatomic muco-cutaneous boundaries, mitigates mucosal eversion and improves overall comfort.

Methods
We have used this operative technique on 5 patients who underwent complete vulvectomy for recurrent vulvar dysplasia and/or vulvar cancer.

Results
The VHF is an effective addition to conventional flaps used for vulvar reconstruction. Operative steps include: Preoperative marking of additional medial-margin of 2cm; Thinning-out the medial edge of 1.5cms for creation of the hood; Meticulous inset of multiple layers and approximation of the vulvar-mucosal edge to the skin-edge of the VHF. Patients reported a normal sensation of their vulva without the usual irritation following surgery.

Conclusions
The VHF offers several benefits: (a) restores anatomic muco-cutaneous boundaries, avoids mucositis and maintains sensation; (b) safe, effective and easy - adds only 20 minutes to the operative-time; (c) universally applicable refinement to a variety of conventional flaps commonly used in vulvar-reconstruction.
PROGNOSIS OF 51 PATIENTS WITH PRIMARY MALIGNANT MELANOMAS OF THE CERVIX AND VAGINA

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Objectives
Primary malignant melanomas of the uterine cervix and vagina are rare neoplasms with very poor prognosis. This article aims at investigating the clinicopathologic characteristics, treatment and prognosis of primary malignant melanomas of the cervix and vagina.

Methods
The clinical data of 51 patients of primary malignant melanomas of the cervix and vagina treated at Fudan University Shanghai Cancer Center between December 1998 and July 2011 were reviewed.

Results
The 2-year and 4-year progression-free survival (PFS) rate was 32.8% and 13.1%, respectively (median PFS, 15 months). The 2-year and 4-year overall survival (OS) rate was 67.2% and 39.8%, respectively. Twenty-nine (56.9%, 29/51) patients had a recurrence. The common sites were vaginal stump / pelvis (11 patients, 44%), lung (4 patients, 16%), liver (4 patients, 16%), bone (3 patients, 12%) and vulva (3 patients, 12%). Larger tumor size and lymphovascular space invasion were the independent predictors of poor overall survival (P<0.05). Pelvic lymph nodes metastases was associated with shorter PFS (P=0.05). Thirty-eight patients had adjuvant therapy after surgery. Among them, those who received combined immunotherapy and chemoradiotherapy achieved longer median time to progression (TTP) (17 months) compared with patients who had chemotherapy alone (9 months) or immunotherapy alone (11 months).

Conclusions
Primary melanomas of cervix and vagina have a very poor prognosis. The multidisciplinary treatment of combining surgery, chemoradiotherapy, and immunotherapy can improve the patients' prognosis.
e-Posters: Vaginal and Vulvar Cancer

SQUAMOTRANSITIONAL CELL CARCINOMA OF THE VAGINA: CASE REPORT AND REVIEW

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Objectives
Primary squamotransitional cell carcinoma (STCC) is a rare variant of squamous cell carcinoma. The authors aim to present a case of a STCC of the vagina and compare to those cases previously described.

Methods
Case report and literature review on Pubmed using as keywords "squamotransitional cell carcinoma"and "vagina".

Results
A 75-year-old Portuguese women presented with a 3 cm lesion in the middle third of the vagina, near the external urethral orifice. She had a previous total hysterectomy for benign disease and no vaginal cuff or vulvar lesions were identified. A biopsy was performed and the tumor qualified as a STCC. Staging evaluation concluded that the tumor was limited to vagina. A partial vaginectomy was performed and because one of the surgical margins had 1,5 mm she was proposed to adjuvant radiotherapy.

Conclusions
We present the eighth known case of a STCC of the vagina. First described by Rose et al in 1998, STCC of the vagina occurred mainly in the anterior vaginal wall and in older women (mean age: 68-year-old) with a previous hysterectomy. Because of its rarity, the clinical, treatment and long-term follow-up are poorly known. As in our case, others authors recommend radical surgery followed by adjuvant therapy based on histological and staging results.
e-Posters: Vaginal and Vulvar Cancer

MODIFIED GLUTEAL FOLD ADVANCEMENT V-Y FLAP FOR VULVAR RECONSTRUCTION AFTER SURGERY FOR VULVAR MALIGNANCIES.

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Objectives
To assess the feasibility and complications of the modified V-Y advancement gluteal flap in the vulvo-perineal reconstruction among women operated for vulvar malignancies.

Methods
From December 2008 to April 2012 women who underwent radical surgery for invasive vulvar cancer were considered for the study. Patients after demolitive procedure were submitted to reconstructive step (Group A) consisting of bilateral or monolateral V-Y advancement fascio-cutaneous flap, from gluteal fold. Surgical results were compared to those of an historical group of patients (Group B) with same characteristics but non-submitted to reconstructive step.

Results
Twenty-nine patients were considered for the study and submitted to radical surgery followed by V-Y Flap. Surgical results were compared to those of 78 patients submitted to demolitive surgery only. There were no differences in terms of clinical characteristics between two groups. The average length of hospital stay was 7 and 10 days, respectively for group A and B (P<0.05). Mean operating time was higher in group A, minutes 210 vs 120 (P<0.05). Among women with tumor size bigger than 4 cm (27 group A, 30 group B), Group A had lower complication rate (dehiscence 11 % vs 40 %; p<0.05)

Conclusions
VY flap is easily reproducible, safe and can be harvested in a single surgery session. It could be able to reduce hospital stay and, in patients with huge loss of substance, could reduce rate of complications.
EXPRESSION OF VITAMIN D RECEPTOR IN SQUAMOUS EPITHELIAL VULVAR CANCER AND VULVAR INTRAEPITHELIAL NEOPLASIA

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Objectives
The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. The aim of this study is to evaluate whether vulvar cancer express the vitamin D receptor and when the vitamin D receptor is expressed whether it is upregulated compared to benign vulvar lesions. Furthermore the expression of VDR in precursor lesion is examined.

Methods
The expression of VDR in benign vulvar lesions (n=47), vulvar intraepithelial neoplasias (n=20) and vulvar cancer (n=20) was determined by immunohistochemistry using the Remmele score and by western blot.

Results
The vitamin D receptor is expressed in benign vulvar lesions and in vulvar cancer. Comparing benign lesions with malignant lesions the expression of VDR is upregulated in vulvar cancer.

Conclusions
Vulvar cancer and vulvar intraepithelial neoplasias may be a target for antiproliferative treatment with vitamin D analoga.
EVALUATION OF 25OHD3 IN SERUM OF PATIENTS WITH VULVAR CANCER AND BENIGN VULVAR LESIONS

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Objectives
The antiproliferative effects of calcitriol is mediated via the vitamin D receptor. In previous studies we could show that the VDR is expressed in vulvar cancer and seemed to be upregulated. The aim of this study is to evaluate whether the serum levels of 25OHD3 in patients with vulvar cancer and in patients with benign vulvar lesions are similar or whether they are different. Low serum levels of 25OHD3 in patients with vulvar cancer could indicate a role of 25OHD3 in carcinogenesis of vulvar cancer.

Methods
The level of 25OHD3 in serum was determined in patients with vulvar cancer (n=20) matched with patients with benign vulvar lesions (n=20).

Results
The level of 25OHD3 in serum was not significantly lower in patients with vulvar cancer compared with patients with benign vulvar lesions.

Conclusions
So far, there is no evidence that serum levels of 25OHD3 play a role in carcinogenesis of vulvar cancer.
EVALUATION OF SENTINEL LYMPHNODE BIOPSY IN VULVAR CANCER

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Objectives
The value of sentinel lymph node biopsy in vulvar cancer with clinically unsuspect inguinal lymphnodes had been determined.

Methods
126 patients with vulvar cancer and sentinel lymphnode biopsy in the years 2004 to 2010 had been evaluated. The inclusion criterions were T1 stage or size < 4 cm and cN0. Lymph node detection was only performed with blue dye.

Results
The mean age was 65,4 years. The median follow-up was 8,4 years. The local inguinal recurrence rate after sentinel lymph node biopsy was 2.5%. The detection rate was 95%.

Conclusions
Sentinel lymph node biopsy in patients with vulvar cancer and clinically unsuspect inguinal lymph nodes is a safe procedure.
ADENOID CYSTIC CARCINOMA OF THE BARTHOLIN’S GLAND: REPORT OF TWO CASES

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Objectives
Although vulvar carcinomas are the 4th most common malignancies of female genital tract, adenoid cystic carcinoma of the Bartholin's gland (ACCBG) is a rare malignancy and there have been 73 cases of ACCBG in the literature.

Methods
We present 2 cases of ACCBG. First patient was 59 y.o., presented with Bartholin's gland swelling and vulvar pain, underwent Bartholin's gland excision with a pathology report of ACC. Patient had modified radical vulvectomy and ipsilateral lymphnode dissection. Her pathology reports revealed, ACC existing in the medial border of surgical margin of right vulva and 3 reactive lymphnodes. Second patient was 62 y.o., she came to our clinic with biopsy report of ACCBG. She underwent wide local excision and ipsilateral lymphnode dissection, pathology report was 2*2 cm ACC with tumor free margin of more than 2 cms, 5 reactive lymphnodes.

Results
There is no consensus on optimal management of ACCBG, surgery is the main treatment. Operations from wide local excision to radical vulvectomy and bilateral lymphnode dissection are performed. Here we performed modified radical vulvectomy to patient with observed big lesion and wide local excision to other patient with a small lesion with ipsilateral lymphadenectomy to both. Although we performed modified radical vulvectomy to our first patient, her surgical margin was positive for ACC and she received pelvic and conformal boost radiotherapy.

Conclusions
Main treatment of Vulvar ACC is surgery and extend of surgery depends on tumoral mass. Surgical margins 1 cm free of ACC is enough for the treatment, radiotherapy lessens recurrence in margin positive patients.
LYMPHANGIOMA CIRCUMSCRIPTUM OF THE VULVA: A RARE CASE REPORT

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Objectives
Lymphangioma circumscriptum (LC) is a rare, benign disorder of the lymphatics located in the deep dermal and subcutaneous tissues. It is a localized group of thin walled and translucent vesicles resembling frog spawn. LC is considered primary if it is present at birth or it develops in early childhood, or secondary or acquired if it is caused by impaired lymph flow.

Methods
We report an unusual case of vulval lymphangioma circumscriptum in a young woman without an obvious cause.

Results
A 23-year-old woman presented with vesicles in the vulvar region, watery discharge, itching, lower-limb lymphoedema, edema and papules of the bilateral labia majora, oozing clear serous fluid and pain in the area. She had taken various antifungal and antibacterial for her problem without any benefit. In addition, she was initially diagnosed with condyloma acuminata and prescribed imiquimod 5% cream. This did not improve the lesions or the symptoms. Considering the clinical course of the disease she underwent a diagnostic punch biopsy of the vulvar skin with a suspicion of vulvar warts. The diagnosis of LC was confirmed. She was treated with electrocoagulation. Therewere no signs of LC-recurrence during a follow-up of 14 months

Conclusions
Lymphangioma circumscriptum of the vulva is a rare disease that poses a diagnostic challenge, the risks of which are misdiagnosis and mistreatment. There is no standard therapy for the management of LC. The most common procedures are abrasive therapy, sclerotherapy, electrocoagulation and surgical resection.
SUCCESSFUL TREATMENT OF RECURRENT LANGERHANS’ CELL HISTIOCYTOSIS OF THE VULVA WITH LENALIDOMIDE

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Objectives
Langerhans cell histiocytosis (LCH) of the female genital tract is rare. First-line treatments include surgery, radiotherapy, chemotherapy, thalidomide and local treatment. We describe a case of vulvar LCH in which the disease recurred locally after prolonged treatment with thalidomide and was successfully treated with lenalidomide.

Methods
N/A

Results
A 33-year-old Ethiopian woman initially presented with a nodular lesion on her left vulva. The lesion was biopsied with pathology consistent with LCH. A metastatic workup did not reveal any evidence of disease beyond the vulva. The patient was treated with radiotherapy to the vulva. She later developed recurrent disease in the vulva and subsequently underwent a wide local excision. Her malignancy quickly recurred locally and was treated with radiotherapy with only limited control. She underwent a wide radical vulvar excision with symptom control for 3 months, after which she experienced recurrence and underwent systemic treatment with thalidomide. Within 2 months of starting thalidomide therapy, the patient experienced resolution of symptoms and vulvar lesions. She remained symptom-free for nearly 6 years while on thalidomide therapy but then presented to our institution with symptoms of local recurrence. Vulvar biopsy confirmed LCH. Scans were performed which revealed no evidence of metastatic disease. We subsequently started lenalidomide therapy and achieved marked improvement in symptoms with no current evidence of disease.

Conclusions
Thalidomide has been described in the literature as an effective first-line treatment and maintenance option in primary vulvar LCH. We describe the use of lenalidomide as an alternative and well tolerated therapy in the relapsed setting.
THE MANAGEMENT OF CHRONIC VULVAL DISORDERS IN PRIMARY CARE

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Objectives
A survey was planned to evaluate the management of these women in primary care.

Methods
A questionnaire based survey was conducted among the General practitioners (GPs) in Shropshire, England.

Results
A total number of 62 GPs responded to the survey.

45 GPs (73%) saw less than 5 patients per month with recurrent vulval symptoms.

75% of the GPs thought pruritus vulva was the commonest presentation and 7(11%) thought lump or thickening of vulva is the commonest. When asked about examination, 66% always examined their patient while the rest didn’t. When enquired about the reasons for not examining, 51% said they are satisfied from the history. During investigations only 4 (6%) thought of doing vulval skin biopsy and for that also they didn’t have facilities.

With regard to recurrent pruritus vulvae, 95% of GPs thought of Lichen Sclerosis as a diagnosis but only 51% thought VIN or vulval cancer can be a differential diagnosis. Most of the GPs (83%) identified Vulvodynia as a neuropathic pain. However none thought vulval neoplasia can present in this manner.

35(56%) of them said they would treat them further with anti-microbials and steroids before referring them to secondary care.

27(43%) of GPs never had any formal training in management of vulval disease and 45(72%) believed they need more training in dealing with these women.

Conclusions
This questionnaire survey offers insight to the scale of the problem in primary care. It also highlights that in most instances women were inappropriately managed due to lack of awareness and education among GPs.
WAYS OF PRESERVING FERTILITY OF GENITAL CANCER PATIENTS IN BELARUS
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Objectives
Feasibility of preserving fertility is one of the important issues of the concept «cancer patient life quality». It is most burning as far as female genital cancer is concerned, in the setting of the ovaries and/or the uterus being subject to curative treatment.

Investigation of the potentials for preserving fertility of female genital cancer patients, based on the data of N.N. Alexandrov National Cancer Centre from 2000 through 2012.

Methods
A technique for photodynamic therapy with Photolon for CIN II-III (168 cases) was developed, tested and assessed. Complete recovery was achieved in 92.8% of the patients. Seven of them were subsequently pregnant, three women terminated their pregnancies on their own accord, and four gave birth to healthy babies.

Results
The following organ-sparing operations were performed at our Centre: radiowave and knife conization of the cervix for CIN III (487 cases), amputation of the cervix for CIN III and T1A1, B0N0M0 (87 cases), trachelectomy for T1A, B1N0M0 cervical cancer (11 cases), one-sided excision of borderline ovarian tumor (284 cases).

Transposition of ovaries was done in 27 cases of surgical and radiation treatment of cervical cancer.

Conclusions
Cryoconservation of ovarian tissue is not used, although in Belarus experience has been gained in sperm cryoconservation and other auxiliary reproductive technologies, with several thousand babies being born with their application over the past 17 years.

Our country has reached the point of necessity to assess the efficacy of current techniques for preserving fertility and developing a scientific lead securing conservation of female genetic material.
ADENOID CYSTIC CARCINOMA GLANDULAE.BARTHOLINI: CASE REPORT WITH REVIEW OF LITERATURE

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Objectives
Adenocarcinoma gland Bartholini’s is a very rare tumor accounting 2-7% of all cancers of the vulva and less than 1% of all genital malignant diseases. The literature describes 61 cases. Basic features are slow to grow, expanding locally and sometimes gives distant metastasis. There is no agreement what is the optimal treatment for this type of carcinoma.

Methods
We will show the case we treated with local incision. 60 year old patient complained of the elevated tumor marker CEA (16,2) detected by random. She already did gastrointestinal exam. At gynecological examination can be seen enlarged Bartholini’s gland about 2 cm to the left side. We did not suggest any treatment. After 6 months the patient noticed increasing Bartholini’s gland about 6 cm. We did local removal of the lesions.

Results
Hystopathology confirmed that this is a Bartholini’s gland adenocarcinoma. The tumor was removed in its entirety with healthy edge. CT, MRI of the pelvis were normal and CEA dropped in 1,6. Regular monitoring of patients after 6 years of treatment show that she is without any problem and recurrence.

Conclusions
This indicates that the primary adenocarcinoma Bartholini’s in the early stages can be treated with only wide local excision, but monitoring of tumor marker is essential because it can be indicator of recurrence or distant metastasis.
DERMATOFIBROSARCOMA PROTUBERANS OF THE VULVA

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Objectives
Dermatofibrosarcoma is a rare cutaneous malignancy that can sometime arise in the vulva.

Methods
We report a patient submitted to posterior hemyvulvectomy for a large dermatofibrosarcoma protuberans of the vulva.

Results
A 39-years-old woman was referred to our Unit with diagnosis of a 5x7 peduncolated vulvar lesion. Pathologic examination of an incisional biopsy gave diagnosis of dermatofibrosarcoma protuberans and the patient was submitted to posterior hemyvulvectomy with plastic reconstruction of the vulvar defect. Post-operative course was uneventful and the patient was discharged on the 6th post operative day. Ten months after operation the patient had no sign of recurrent disease.

Conclusions
Plastic reconstruction is necessary in the management of wide dermatofibrosarcoma protuberans of the vulva.
RISK FACTORS FOR ERYSIPelas AFTER PRIMARY SURGICAL TREATMENT IN PATIENTS WITH VULVAR CARCINOMA

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Objectives
Vulvar carcinoma is treated surgically in the majority of patients, with an overall good prognosis. Over the past years surgical procedures are changed and the introduction of the sentinel node (SN) procedure has reduced a substantial number of inguinal lymph node dissections (LND). Yet, the surgical treatment of vulvar carcinoma still causes severe morbidity. It is known that many patients present with erysipelas after surgical treatment of vulvar carcinoma, sometimes repeatedly. So far data on prevalence of erysipelas are limited. The aim of the present study was to determine the prevalence of erysipelas after surgical treatment for vulvar carcinoma and identify risk factors.

Methods
All patients (n=116) with primary vulvar carcinoma who underwent a surgical procedure in the Dutch Comprehensive Cancer Centre South region between 2005 and 2012 were included. Patients with FIGO stage IA and IV were excluded. Clinical and histopathological data were analysed retrospectively with Chi-Square and non-parametric tests.

Results
A total of 23/116 (20%) patients suffered from one or more episodes of erysipelas. Patients after LND were at significantly higher risk compared to SN, 36% (n=12) and 14% (n=11) respectively (p=0.008). Additionally, patients with diabetes tended to have a higher prevalence of erysipelas when compared to patients without diabetes, 28% versus 18%. There was no correlation with BMI.

Conclusions
Erysipelas after surgical treatment for vulvar carcinoma is frequently observed. Patients who underwent an inguinal LND have an increased risk of 36% to develop erysipelas. Patients with diabetes tend to have a higher risk, whereas no correlation was observed with BMI.
BASAL CELL CARCINOMA OF THE VULVA IN 37 YEARS OLD WOMAN: A CASE REPORT

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Objectives
Basal cell carcinoma occurring on location unexposed to sun, especially in the perianal and genital regions, is very rare and account for less than 5% of vulvar cancer cases. It usually affects white women over 70 years of age.

Methods
Case report

Results
A 37 years old caucasian woman was referred to our department with a reddish lesion on the right labium majus. The lesion measured 25mm x15mm. She reported a 2-year history of vulvar discomfort and itching. The probatory excision revealed a basal cell carcinoma. The radical wide excision was performed and the final histology confirmed the diagnosis of basal cell carcinoma with all margins free of disease. The patient recovered without complications and there was no recurrence within 14 months of follow-up.

Conclusions
Basal cell carcinoma of the vulva is a very rare disease. As the lesions in these sites, especially in younger women, sometimes seem innocuous, biopsy of all suspected lesions is advisable, especially in middle-aged women.
LOWER LIMB LYMPHEDEMA IMPACTS QUALITY OF LIFE IN WOMEN WITH VULVAR CANCER SUBMITTED TO SURGICAL TREATMENT

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Objectives
Vulvar cancer is relatively uncommon, however the incidence has been increasing over the past decade in women younger than 50 years. Standard treatment for early stage vulvar cancer is wide local excision with uni and bilateral lymphadenectomy via separate incisions. Morbidity after vulvectomy and lymphadenectomy is high, the main cause being the lymphedema. Lymphedema causes major repercussions in the quality of life of these women, generating physical, emotional, and social inconvenience.

Methods
Twenty-eight vulvar cancer patients submitted to vulvectomy and inguino-femoral lymphadenectomy and 28 healthy age-matched women (control group) were prospectively evaluated. The LLL occurrence and severity were determined by Miller Clinical Evaluation. Quality of life was assessed by the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire (EORTC QLQ-C30). The differences between groups and correlations were assessed by Student's t, Chi-square, and Spearman-rho tests. Significance level was set at 5%.

Results
The occurrence and severity of LLL were higher in women with vulvar cancer compared to the control group (p<0.001 and p=0.003, respectively). There was no association between stage, adjuvant treatment, laterality and complications with LLL severity. Patients with advanced age and higher body mass index presented more severe LLL (p=0.04). The physical, cognitive, emotional, social, fatigue, pain, sleep, and financial issue domains of quality of life were associated with the LLL severity (p<0.05).

Conclusions
Patients submitted to vulvectomy and inguino-femoral lymphadenectomy for vulvar cancer present higher risk of developing LLL, which negatively impacts their quality of life.

**e-Posters: Vaginal and Vulvar Cancer**

**REPERCUSSIONS FROM VULVECTOMY AND INGUINAL LYMPHADENECTOMY ON URINARY FUNCTION AND QUALITY OF LIFE IN WOMEN WITH VULVA CANCER**

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**Objectives**

Cancer of the vulva represents about 5% of all gynaecological tumours. Women submitted to surgical treatment for cancer of the vulva can present sexual and urinary disorders, and difficulties accepting their body shape. Depression, drop in libido and orgasms, reduced sexual satisfaction, and changes in body shape lead to psychological vulnerability for these women. Despite surgical techniques for treating cancer of the vulva improving survival indices, the impact of these procedures on pelvic floor functions are still uncertain.

**Methods**

Observational, prospective, transverse study of 28 women undergoing surgical treatment for cancer of the vulva and 28 healthy women (control group), matched for age. Their urinary function and sexual performance were assessed using the International Consultation on Incontinence Questionnaire - Short Form (SF-ICIQ) and Female Sexual Function Index (FSFI) questionnaire. The following statistical tests were used: chi-squared, Student’s t', and Mann Whitney-U tests. Differences or correlations with p<0.05 were considered significant.

**Results:**
Correlation was seen between sexual quality of life and age (p=0.01) and stable partnership (p=0.02). The following variables did not influence urinary function: BMI, menopause, and cancer of the vulva. There was correlation between age and urinary function (p=0.01) and deliveries (p=0.01).

Conclusions
Women undergoing surgical treatment for cancer of the vulva have no worsening in quality of sexual life or urinary function.
e-Posters: Vaginal and Vulvar Cancer

PRIMARY BREAST-LIKE CARCINOMA OF THE VULVA – 2 CLINICAL CASES

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Objectives
Breast-like carcinoma of the vulva is a rare pathology, with about 25 cases reported in the literature. The presence of mammary tissue in the vulva was first described in the 19th century, with different pathologic findings encountered in this topography. Two cases of vulvar breast-like carcinoma are presented.

Methods
Case Report

Results
Case 1 – 62 year-old woman, admitted in 2006 after excision of a vulvar lesion. Pathologic examination revealed a moderately differentiated carcinoma. Immunohistochemistry was positive for estrogen and progesterone receptors and cytokeratin 7 and negative for GDCF-8,5 and erbB-2. A diagnosis of breast-like carcinoma with origin in ectopic mammary tissue was established. The patient underwent lymph node dissection, with 1 metastasized node in 12 excised. Staging was T1bN1aM0, FIGO stage IIIA. Chemotherapy with FAC6, followed by radiotherapy and hormone therapy were instituted.

Case 2 – 78 year-old patient, with history of malignant melanoma of the right hallux treated surgically in 2010. In October 2012 a vulvar lesion was identified in the medium third of the right labium minus. Biopsy showed a breast-like infiltrative adenocarcinoma which expressed estrogen and progesterone receptors but not GCDFP-15, p63 and erbB-2. In January 2013, the patient was submitted to a resection with lymph node dissection. Staging was T1aN1bM0, FIGO stage IIIA. The patient underwent adjuvant chemotherapy with FEC3-D3 followed by radiotherapy and hormone therapy.

Conclusions
Although the presence of ectopic mammary tissue in the vulva is rare, the possibility of a primary carcinoma with origin in this tissue should be considered in the differential diagnosis of suspicious vulvar lesions.
USE OF NEUTRAL ARGON PLASMA IN GROIN NODE DISSECTION FOR VULVAR MALIGNANCY- A REVISED TECHNIQUE

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Objectives
Vulvar malignancy is the fourth most common malignancy accounting for less than 5% of all gynaecological tumours worldwide. Surgical in the form of wide local excision or radical vulvectomy with or without bilateral groin node dissection (BGND) is known to cause significant post-operative morbidity. Immediate post-operative complications include breakdown and lymphocyst formation in more than 50% of cases.

Following a recent pilot RCT where the PlasmaJet® (PJ) system was used following BGND with encouraging results, the technique was revised.

Aim
Potential and safety of PJ in reduction of groin lymphocyst formation in patients undergoing BGND.

Methods
A 43 year old lady was referred with a vulval lesion. Wedge biopsy reported a well differentiated squamous cell carcinoma to a depth of at least 1.2 mms. Following an amendment to the ongoing trial where the device was used following BGND, the PJ device was used throughout the procedure for dissection and following the procedure for 5 minutes on the groin bed to destroy lymph vessels and channels on one side only. Drain outputs were documented daily until removal and found to have reduced output on the PJ side.

Results
Our case suggests that use of PJ appears to reduce daily lymph drain outputs and lymphocyst formation. Ischaemia rates and wound infection were lesser on the PJ side. Length of stay unaffected as the patient acted as her own control.

Conclusions
The previous randomised trial has now been amended to incorporate the new technique and explore this further.
ROLE OF FIBRIN GLUE FOLLOWING GROIN NODE DISSECTION FOR VULVAR MALIGNANCY IN REDUCING WOUND COMPLICATIONS- A SYSTEMATIC LITERATURE REVIEW

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Objectives
Seroma formation following lymph node dissection is common. Vulvectomy and bilateral groin node dissection (BGND) is the preferred surgical treatment for early stage vulvar cancer increasing survival. However significant post-operative morbidity has been reported in > 50% of cases.

Aim
Evaluation of randomised controlled trials (RCT) reporting fibrin glue/sealant use following BGND for any malignancy.

Methods
Systematic review of RCTs undertaken to evaluate the role of fibrin sealants in reducing post-operative drainage and lymphocyst formation following BGND.

Results
Four trials fulfilled inclusion criteria. 2/4 studies involved melanoma patients. 1/4 was for women with vulvar cancer and one study included patients undergoing both groin as well as axillary node dissection. 274 participants from 4 groin studies. Tisseel was used in 2/4 studies, VH fibrin sealant and Tissuecol were each used in one study. Drains were removed when output was less than 30-50mls over 24hours. Volume of drain output was significantly reduced in one study (762 vs 89mls) on fibrin sealant use. Time to drain removal was significantly increased on fibrin use in 1/4 (26 vs 31days). 2/4 studies did not report any statistical significance. Hospital stay was not considered significant in any of the 4 studies. Assessment of lymphedema was performed in 2/4 studies but not considered significant.

Conclusions
Current evidence on the role of fibrin sealant following BGND is not supportive of its use and fails to influence drain outputs, seroma formation or post-operative morbidity.
e-Posters: Vaginal and Vulvar Cancer

SENTINEL LYMPH NODE BIOPSY IN VULVAR CANCER
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Objectives
Determine the importance of sentinel lymph node biopsy in the staging and treatment of vulvar cancer, avoiding more aggressive procedures, which are associated with increased morbidity and mortality.

Methods
We report the case of a patient of 70 years old was referred to our clinic for indurated and ulcerated lesion in right vulvar side. As past medical history, she presents a heart failure, which is followed by the Cardiology Unit of our hospital and insulin-dependent diabetes mellitus.

The examination showed an ulcerated lesion of 3 cm. in right labia majora, without palpable inguinal lymph nodes. It was biopsied and diagnosed with squamous cell carcinoma of the vulva. We performed a comprehensive study extension, all tests being negative. Given these findings the patient was diagnosed with Stage IB vulvar cancer.

The patient was scheduled for radical vulvectomy + biopsied sentinel lymph node, which was conducted without incident obtaining two negatives sentinel nodes.

Results
Proper treatment of vulvar cancer comprises highly radical surgery, is mainly governed by the location of the lesion.

The most important prognostic factor is lymph node involvement, so it is necessary a correct evaluation of the inguinal nodes, as it is the first tumor draining station.

Conclusions
Today, the technique of sentinel lymph node biopsy can reliably assess inguinal lymph node without being required more aggressive procedures such as inguinal lymphadenectomy.
LAPAROSCOPIC EXENTERATION IN RECURRENT CERVICAL CANCER. VIDEO PRESENTATION.

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Objectives
Pelvic exenteration is an ultra-radical surgical procedure, which involves resection in block of the tumor and pelvic organs affected. Although laparotomy is the most used technique we describe a laparoscopic approach that be performed in our hospital.

Methods
We display a video presentation of the surgical procedure

Results
A 46 years old woman, treated of a vaginal squamous cell carcinoma, stage IA, with external radiotherapy and interstitial brachytherapy for pelvis, who after 24 month, presented a local recurrence of 5 cm that compromised vagina, cervix, parametrium, bladder and mesorectal fat with imprint on anterior rectum. Surgical treatment was indicated, after exclude metastasis.

We performed a laparoscopic infralevator total pelvic exenteration, with radical cystectomy and urethrectomy, radical hysterectomy with double anexectomy, vaginectomy complete resection of sigma-rectum-anus and central resection of levator ani muscle. Urinary derivation by Bricker right ileostomy and digestive derivation with left colostomy. The pelvic defect was corrected with a biological mesh and musculo-cutaneous flap bilateral gracilis, with creation of neovagina.

Postoperative complications were superficial ischemia of gracilis flap, treated with debridement and pelvic abscess treated by CT-guided percutaneous drainage and urokinase.
Conclusions

Laparoscopic approach is possible in selected cases which requiring pelvic exenteration. The main advantages are the reduction of intraoperative and postoperative morbidity, with lower surgical stay, although the technique is complex and involves a longer operating time and learning curve.
e-Posters: Vaginal and Vulvar Cancer

PELVIC EXENTERATION IN RECURRENT GYNECOLOGIC CANCER. EXPERIENCE OF LA PAZ UNIVERSITY HOSPITAL. MADRID.
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Objectives
Pelvic exenteration (PE) is an ultraradical surgery consisting of an en-bloc resection of pelvic organs that is mainly applied as a salvage procedure for recurrent gynecologic tumors. Urinary and digestive diversion and soft-tissue reconstruction, such as neovagina creation, may be performed. The surgery is carried out with a curative intention, aiming the excision of the tumor with microscopic free margins. Associated morbidity is close to 50% due to urinary and digestive anastomosis and plastic reconstructive complications, with a global perioperative mortality of 5%.

Methods
A retrospective analysis of all patients treated with PE for recurrent gynecologic cancer at our unit from 2003 to 2012 was performed.

Results
Nine patients underwent PE due to gynecologic cancer (3 cervical, 2 endometrial, 2 vaginal, 2 vulvar and 1 ovarian). All patients had received primary treatment. Six patients (33%) underwent total PE, two (22%) anterior and one (11%) posterior. Bricker’s urinary diversion was performed in all cases. Reconstructive technique was performed with vascularized tissue flaps. Postoperative complications were related to the urinary diversion in 44% of cases, reconstructive technique 33% and infection 22%. Two patients died in the postoperative period from a septic shock and seven are alive (four disease free). Survival rate ranges from 6 to 108 months.

Conclusions
Despite the high morbidity and mortality rates of PE, it is a feasible and, in the majority of cases, the last chance after cancer recurrence. It may be applied with curative intent in selected patients.
ONLY BONE METASTASIS OF PRIMARY VAGINAL CANCER
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Objectives
The primary vaginal cancer accounts for 2% of gynecologic malignancies. Bone involvement is a rarity diagnosed (1).

Methods
Review of a case diagnosed in our department presentation and treatments given.

Results
Sixty year old woman with double oophorectomy and hysterectomy at age 30 for benign disease was diagnosed in May 2010 of G3 vaginal carcinoma FIGO stage I. She received RT + BT between April and June 2010, with complete response. In September 2010 right nephrectomy was performed with chromophobe renal cell carcinoma pT1a pNx. In September/2012 left arm Rx showed a lytic lesion treated with osteosynthesis and radiotherapy with a pathological report of metastatic carcinoma G3. The immunohistochemistry was positive for AE1-AE3, CK7, synaptophysin, CK20, CD99, and negative for CD45 and chromogranin. The tumor was morphologically and by immunohistochemistry similar to the vaginal tumor. The total-body CT scan (7/12/12) showed two pulmonary nodules (Upper lobe of the right lung: 3mm and Lower lobe of the left lung: 14mm), suspected metastasis and bone scan humerus fracture. PET: Expansile lytic lesion of malignant metabolic behavior in proximal / middle of the left humerus and associated surgical inflammatory changes.

With diagnosis of vaginal carcinoma with isolated bone relapse, stage IV, Carboplatin-Paclitaxel and Zoledronic acid started in February 2013. To date she has received three of six cycles without relevant toxicity.

Conclusions
Vaginal cancer is a rare tumor, and bone metastasis unusual migration site.
SEBACEOUS CARCINOMA OF THE VULVA: A CASE REPORT
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Objectives
Sebaceous glands are abundant and prominent on the vulva, however, sebaceous carcinomas of the vulva are quite rare.
We present a case of Sebaceous carcinoma of vulva in a fifty-two year old lady. This was treated with Wide local excision of vulva.

Methods
The patient presented initially with a left vulval cyst and excision biopsy showed it to be a Epidermoid cyst. She presented with a recurrence, 2yrs post-surgery. Vulval excision was done and histopathology revealed Grade 3 Sebaceous Carcinoma with incomplete excision. MRI was performed and no lymph node involvement was seen. Wide local excision was then performed and no residual or metastatic disease was detected on microscopic examination of the surgical specimens. Histology did not reveal any VIN or other pathology.

Results
Patient is being followed-up in the clinic with no signs of recurrence.

Conclusions
Sebaceous carcinoma of vulva is very rare and our search showed only 7 published case reports. Sebaceous carcinomas have been reported in association with internal malignancies and subsequently described as Muir–Torre syndrome. Radical surgery and ipsilateral lymphadenectomy is an option but with its own complications including lymphodema, which can be debilitating. Due to their rarity there is no standard treatment protocol. It remains to be seen whether wide local excision with good follow-up is a better option than radical surgery.
BENEFIT OF RADICAL SURGERY (PELVIC EXENTERATION) FOR THE MALIGNANT MELANOMA OF VAGINA.
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Objectives
Malignant melanoma of the vagina is a rare tumor and has a poor prognosis. Wide local excision with adjuvant radiotherapy is recommended in the literature. The aim of this study is to reevaluate the usefulness of radical surgery for the management of vaginal melanoma.

Methods
Six patients with vaginal melanoma were observed from 2006 to 2012 in our hospital. Four patients underwent radical surgery included vulvectomy; three total pelvic exenteration (PE), one radical hysterectomy (RH) and total vaginectomy (TV) + vulvectomy. Two patients underwent usual surgery; RH+TV only or wide local excision. All patients received adjuvant dacarbazine based chemotherapy and/or INF-alpha therapy. We analyzed pathological and prognosis factors.

Results
All patients had multifocal diseases. Lymph node metastases were observed in two patients. Three of four patients who underwent radical surgery, were alive without recurrence (12, 24, 40 months). One patient had systemic recurrences at 8 months and died of disease at 12 months. In usual surgery, even local control was difficult. The first who underwent wide local excision had upper vaginal recurrences at 4 months, is still alive with disease at 23 months. The second RH+TV only had a mucosal recurrence near the urethra at 8 months and died with systemic disease at 14 months.

Conclusions
Our findings suggest radical surgery such as PE is recommended for the local control in patients with vaginal melanoma and might improve prognosis of this disease.
VULVAR MELANOMA - CASE REPORT
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Objectives
Vulvar melanoma is the second most frequent vulvar neoplasm although it accounts for only 3-5% of female melanoma. These are more frequent in postmenopausal women, in their 6th decade of life, over the labia minora or clitoris and possibly extending to the urethra or vagina. Usually being asymptomatic, the diagnosis is based on inspection when a hyperpigmented and exophytic lesion is found. However, genital pruritus, haemorrhage or enlarged inguinal nodes may be noted.

The prognosis depends on the lesion size and its depth (better when <1mm); ulceration, melanosis and advanced age usually indicate poor prognosis.

Methods
A 73 year-old female bedridden patient was referred for large hyperpigmented vulvar lesion, with no palpable inguinal lymph nodes.

Results
An incisional biopsy was performed and confirmed the clinical diagnosis of melanoma; intra-operatively, the sentinel lymph node was biopsed (negative) and so a wide excision of the mass was performed. The patient showed no relapse at 6 months of follow-up.

Conclusions
Although rare, vulvar melanoma is highly lethal, offering a 22-54% 5-year survival rate. Differential diagnosis include seborrheic keratosis, nevocellular nevus and lentigus. The mainstay of treatment is now the excision with surgical margins of 1 to 3cm, being the existence of palpable enlarged lymph nodes and indication for radical vulvectomy. Sentinel lymph node biopsy offers relevant prognosis related information. This case-report shows the importance of pelvic examination of dependent or bedridden elderly women, as vulvar tumors may grow into large masses on account of these women's incapacity of performing an early, self-diagnosis.
e-Posters: Vaginal and Vulvar Cancer

SINGLE CENTER EXPERIENCE WITH 18 INVASIVE VULVAR CANCER
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Objectives
Vulvar cancer is the fourth most common gynecologic cancer following endometrium, ovary and cervix. Diagnosis is often made by excisional biopsies of suspected lesion. Recommended management is appropriate surgical staging. Surgical staging consists of excision of the lesion with clear surgical margins and inguino-femoral lymph node dissection. The most important predictor of overall survival is lymph node status. Staging procedure has to be individualized to optimize total excision of the lesion with clear surgical margins with the most conservative method to minimize post operative morbidity and obtain long term psychosexual wellbeing. We are presenting our experience with 18 vulvar cancer cases.

Methods
We examined our two years experience with vulvar carcinoma retrospectively. The aim of the study is to determine demographic characteristics of the patients, to determine a correlation between tumor size, histological subtype, status of surgical margins and inguino-femoral lymph nodes.

Results
Patient’s age was between 36 and 85 years. The mean age was 64.389. 15 patients had complete surgical staging with lymph node dissection, 3 patients didn’t require lymph node dissection because of T1a tumor. We found correlation between tumor size and lymph node metastasis, invasion depth and lymph node metastasis, but correlations were not statistically significant.

Conclusions
The most important predictor of overall survival is lymph node status. Tumor size and invasion depth is the most important predictor of the lymph node metastasis. That’s why early diagnosis and liberal biopsies from suspected vulvar lesions is the key point of the management of invasive vulvar carcinoma.
DIFFICULTY OF TREATMENT OF VERRUCOUS CARCINOMA OF THE VULVA: POSSIBILITIES OF RECURRENCE

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Objectives
Evaluation of radical vulvectomy as the treatment of verrucous carcinoma of the vulva in order to prevent relapses, considering the non efficacy of neo adjuvant or adjuvant chemotherapy and radiotherapy

Methods
We present a case of a 82 years-old woman, that recurred vulvar verrucous carcinoma 8 times, after underwent to the excision of vulvar lesions with free margins. Then, it was decided to radical vulvectomy followed by closure of the incision through the rotation of bilateral gluteal fold flap.

Results
Patient recovered with good healing of extensive surgical wound, without dehiscence. She did not developed any lesion for two years, until again showed verrucous recurrence in topography of the clitoris (picture 1A, 2A and 3A)
Conclusions
Aggressive radical surgical treatment as total vulvectomy did not avoided the possibility of recurrence of verrucous carcinoma of the vulva. Maybe the best strategy is to remove the vulvar lesion with free margin as many times as necessary.
e-Posters: Vaginal and Vulvar Cancer

PREDICTIVE FACTORS FOR FIRST RECURRENCE OF VAGINAL INTRAEPITHELIAL NEOPLASIA AFTER TREATMENT WITH CO2-LASER VAPORIZATION

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Objectives
To investigate predictive factors for first recurrence of vaginal intraepithelial neoplasia (VAIN) after treatment with CO2-laser vaporization.

Methods
The medical records of all consecutive patients treated for VAIN with CO2-laser vaporization at Sant’Anna Hospital of Turin, from 1995 through 2011, were retrospectively reviewed. A multivariate Cox Proportional Hazard model was performed to evaluate the potential predictive value of different clinical features.

Results
The retrospective study included 285 patients: 110 were affected by VAIN 1 (38.6%), 136 by VAIN 2 (47.7%) and 39 by VAIN 3 (13.7%). With a median follow up of 60 months, the incidence of VAIN first relapse was 25% (71/285); median time to first recurrence was 7 months for VAIN1, 6 for VAIN2, and 4.3 for VAIN3. Clinical features suggesting to be VAIN first relapse predictive factors were: age >=45 years (versus <45) (HR 1.7, 95%CI 1.0-2.8 p=0.04), VAIN grade2-3 (versus grade1) (HR 1.3, 95%CI 0.8-2.1 p=0.2), vaginal vault site at first diagnosis (versus other sites) (HR 4.2, 95%CI 1.5-11.8 p=0.005), previous hysterectomy (HR 3.4, 95%CI 1.8-6.5 p=0.0001), nulliparity (HR 1.4, 95%CI 0.8-2.2 p=0.15) and HPV co-infection (HR 2.1, 95% CI 1.1-4.0 p=0.01). Predictive factors that retained their value in the multivariate model were: nulliparity (HR 1.8, 95%CI 1.0-3.2 p=0.05); age (HR 2.1, 95%CI 1.0-3.5 p<0.01); HPV co-infection (HR 2.6, 95%CI 1.2-4.7 p=0.003).

Conclusions
Our study suggests age, high grade VAIN, previous hysterectomy, and nulliparity and HPV co-infection as risk factors for VAIN first recurrence: these features should be taken into account in the follow-up planning.
MANAGEMENT OF VULVAR CANCER: RETROSPECTIVE EXPERIENCE OF THE RADIATION ONCOLOGY UNIT OF FLORENCE

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Objectives
Vulvar cancer (VC) accounts for about 4% of all gynecological cancers. Surgery represents the gold standard treatment, but radiotherapy is frequently required. We retrospectively analyzed our experience with patients affected by VC, focusing on radiotherapy aspects.

Methods
We collected data regarding patients affected by VC from 1983 to 2010. A total of 87 patients treated with curative intent were included in our study: 37 with adjuvant intent, 22 with radical intent and 28 with salvage intent at the time of local relapse. Median age was 72 years. Mean dose for EBRT was 52.7 Gy for vulva (range 46-64); 53 Gy for inguinal region (range 22-66) and 49.6 Gy for pelvis (range 38-58). Mean dose for EBRT in radical setting was 54 Gy for vulva (range 30-66); 52.7 Gy for inguinal region (range 36-64) and 48 Gy for pelvis (range 36-54). Four patients and 17 patients received brachytherapy respectively in an adjuvant (mean dose 53 Gy) and in a radical/salvage setting (mean dose 57 Gy).

Results
Median DFS was 9.3 months: in adjuvant setting was 15 months, in radical setting was 6 months and in salvage setting was 7 months. Local control was achieved in 51 (58%) patients: 24 (47%) in adjuvant and 27 (53%) in radical and salvage setting. 3-year and 5-year OS was 40.2 and 29.8% respectively.

Conclusions
Radiotherapy is an effective and well tolerated treatment in VC. Postoperative RT showed a better local control than the treatment at the time of relapse.
**e-Posters: Vaginal and Vulvar Cancer**

**PROGNOSTIC SIGNIFICANCE OF TUMOR SIZE IN SQUAMOUS CELL CARCINOMA OF THE VULVA: THE ONCOLOGIC HOSPITAL OF BUENOS AIRES EXPERIENCE**

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**Objectives**

To evaluate the tumor size significance in patients with locoregional vulvar cancer which may be radically resected.

**Methods**

Retrospective study including 105 cases of invasive vulvar squamous cell carcinoma with preoperatively tumor size > 2 cm, between 01/1995 - 01/2012. They underwent radical vulvectomy or local wide excision with bilateral inguino-femoral lymphadenectomy. FIGO Stages IA and IV were excluded. Tumor size was stratified in: > 2-3.99 cm; 4-5.99 cm; 6-7.99 cm and ≥ 8 cm. Comparison between groups, age, histological grade, stage, lymph node status, OS- DFS, and follow-up were also considered.

**Results**

Age: 67 years (36-83). Follow-up: 21 months (3-120). 2-year OS and DFS were 48% and 40% respectively. Eighty three patients (79%) had recurrent disease. Time to relapse: 12 months. A significant difference was seen in the OS analysis comparing tumors >2-3.99 cm to 4-5.99 cm (P =0.004) and 4-5.99 to 6-7.99 cm. No significant difference was observed comparing tumors 6-7.99 to ≥ 8 cm (P = 0.647). The risk for failure to survive was 2.8 times higher for patient's tumor size between 4-5.99 cm (hazard rate [HR] = 2.85); 16 times for 6-7.99 cm (HR = 16.0) and 20.1 times for ≥ 8 cm (HR = 20.1), compared with tumor size >2-3.99 cm.

**Conclusions**

Tumor size and stage were an independent prognostic factors for DFS and OS. A clear cut-off value in tumors ≥ 6 cm. could be established, being important to tailor the treatment for patients with bulky primary tumors.
PECULIARITIES OF RELAPSE IN VULVAR CANCER PATIENTS, DEPENDING ON TUMOR GRADE AND LOCALIZATION

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Objectives
Vulvar cancer is a rather rare disease, presenting about 2-5 % among all gynecological malignancies.

Methods
There was conducted retrospective study of 19 patients with vulvar cancer stage IA – IVA (T1-3N0-2M0). All the patient underwent treatment in Grigoriev Institute of medical radiology during the period of 2001 - 2005.

Results
Clinical data analyze showed, in the most part of our patients tumor was localized at large labii - in 11 (57.9 %) patients.

The tumor size less than 3? m in diameter was detected in 11 of 19 (57.9 %) vulvar cancer patients.

In the most part of patients was detected high-grade squamous cancer (G1) - in 16 (84.3 %) patients. Metastatic affection of regional lymphatic nodes was in 5 of 19 (26.3 %) patients.

The relapse of disease was appeared in 5 patients (26.3) %. Among them, in 4 (80.0 %) patients, the primary tumor was localized at large labii. Among 3 patients, in whom the tumor was localized at region of clitoris, at follow-up of 60 month there was not noticed any sign of relapse.

In 3 of 5 (60 %) patients with relapsed disease, the primary tumor size was more than 3??, that considered to be a worse prognostic factor.

In all 5 (100 %) patients with relapsed disease there was detected high-grade tumor (G1).

Conclusions
The relapse of disease was localized in the most cases at place of primary tumor – region of large labii and tumor size was more than 3?? . There was not revealed any influence of tumor grade on relapse-rate.
TUMOR SIZE OF 4 CM HAS PROGNOSTIC SIGNIFICANCE IN NODE NEGATIVE VSCC CASES BUT THIS CAN’T BE EXPLAINED BY THE DIFFERENCES IN LOCAL IMMUNE SURVEILLANCE.

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Objectives

The largest cohort study to date which evaluated the effect and prognostic performance of the new FIGO vulvar cancer staging system has suggested that lesion size (4 cm) in node negative cases is an important prognostic variable. Immune escape is a crucial feature of cancer progression and could explain the difference in survival between small and big tumors. Previously we have analyzed immune surveillance in 76 vSCC cases by evaluating tumor infiltrating lymphocytes (TILs) and indoleamine 2,3-dioxygenase (IDO). AIM: To compare the host immune reaction against tumors <4 <4 cm vs. >=4 cm in node negative cases.

Methods

Data on TILs: CD8+, CD4+, FOXP3+, CD56+, GZB+ and IDO expression as well as clinicopathological features were extracted from our previous studies. Prognostic significance of 4 cm was tested in node negative cases. The mean number of infiltrates and level of IDO expression were compared between the two groups (<4 cm vs. >=4 cm). Differences in TILs and IDO expression are summarized in table.

| pT<4 cm | pT>=4 cm | P UMW/Fisher*
|-------|-------|-----------
| CD4+ | 5,2 | 3,8 | 0,726
| CD8+ | 37,2 | 28,9 | 0,873
| FOXP3+ | 14,9 | 14,9 | 0,966
| CD56+ | 2,9 | 2,7 | 0,44
| GZB+ | 2,8 | 2,9 | 0,987
| IDO+/− | 3/26 | 3/14 | 0,64*

Conclusions

There is no difference in immune surveillance between lesions < 4 cm and >= 4 cm in node negative vSCC patients. Prognostic ability of 4 cm tumor size needs to be further analyzed.
e-Posters: Vaginal and Vulvar Cancer

RISK FACTORS FOR SHORT- AND LONG-TERM COMPLICATION AFTER GROIN SURGERY IN VULVAR CANCER.

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Objectives

The cornerstone of treatment in early-stage squamous cell carcinoma (SCC) of the vulva is surgery, predominantly consisting of wide excision with elective uni- or bilateral inguinal-femoral lymphadenectomy. This strategy is associated with a good prognosis, but also with impressive treatment-related morbidity. The focus of this study was to determine risk factors for the short-term and long-term complications after groin surgery.

Methods

Between 2009 and 2011, 44 consecutive patients underwent a bilateral inguinal-femoral lymphadenectomy as a part of their surgical treatment for vulvar cancer. The clinical and histopathological data were retrospectively studied.

Results

44 patients primarily treated with modified radical vulvectomy or hemivulvectomy and complete uni- or bilateral inguinal-femoral lymphadenectomy using separate or en bloc groin incisions (n = 72) were included. One or more complications after groin dissection were observed in 15 of the 44 (34.1%) of the patients. The main complications were wound breakdown (13.3%) and lymphocyst formation (20.0%). In 21 of 72 (29.1%) groin dissections, one or more complications were documented. The presence of vein thrombosis, varices and BMI were not significant risk factors for the occurrence of complications. The occurrence of diabetes and higher drain production on the last day of drain in situ were significantly related to the early/late-complication: (p value respectively 0.018 and 0.02).

Conclusions

Our analysis shows that patient characteristics, and postoperative management influence short- and/or long-term complications after inguinal-femoral lymphadenectomy in vulvar SCC patients. Further research of postoperative management is necessary to analyse possibilities to decrease the complication rate of inguinal-femoral lymphadenectomy. New strategies for prevention of chronic lymphedema are needed.
VALIDATION OF THE FIGO 2009 STAGING SYSTEM FOR CARCINOMA OF THE VULVA.
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Objectives
The 1988 International Federation of Gynecology and Obstetrics (FIGO) vulvar cancer staging system failed in 3 areas: stage 1 and 2 had similar survival, stage 3 represented a heterogeneous group of patients and the number and morphology of positive nodes were not taken into account. The objective of this study was to compare FIGO 1988 and 2009 staging system for carcinoma of the vulva in terms of patient distribution and efficacy in predicting prognosis.

Methods
Medical records of 89 patients treated for vulvar cancer between 2009 and 2011 were retrospectively analyzed. Data included patients' characteristics and clinical details. We recorded the original 1988 FIGO stage, reviewed all patients' histopathology information, and restaged all patients to the 2009 FIGO staging system. Data were analyzed using the Kaplan-Meier method to compare relapse-free survival and overall survival.

Results
Data from 52 patients with primary vulvar carcinoma were eligible. The median follow-up time was 47.1 months (range, 2-144). Five-year overall and disease-free survival for the entire group was 74.3% and 63.1%, respectively. Stage migration was observed. FIGO 2009 stage II has become rare, with only 5 of 112 patients allocated to stage II. Stage III has been broken down into 3 substages, thus creating differences in relapse-free survival and overall survival. Prognosis of patients with stage IIIC disease is poor.

Conclusions
The FIGO 2009 staging system for vulvar carcinoma successfully addresses some concerns of the 1988 system. Especially, it identifies high-risk patients within the heterogeneous group of lymph node positive patients.
e-Posters: Vaginal and Vulvar Cancer

SENTINEL LYMPH NODE DETECTION IN EARLY STAGE VULVAL CARCINOMA
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Objectives
To determine the accuracy of sentinel lymph node (SLN) detection in early stage vulval carcinoma and to report reliability and safety of this procedure.

Methods
For period of 2 years we recruited women undergoing surgery for clinical I-II stage vulval carcinoma. All women had a preoperative biopsy confirming the depth of invasion greater than 1mm. SLN detection was performed using combined method (Tc-99 m and methylene-blue dye). The SLNs were ultrastaged when they were negative on routine histological examination.

Results
Among 8 women undergoing SLN detection, SLN was detected in 8 women (100%) with combined method. The median SLN count was 2 nodes (range 1-6) of 8 women; 2(25%) had inguinofemoral lymphonodectomy and 6 (75%) had the SLN only removed. There were no false-negative SLNs. 3 (37,5%) had positive nodes on final histology.

Conclusions
SLNs detection is safe and accurate in assessing lymph node status in women with vulval cancer undergoing staging. The combined method for SLN detection has the best detection rate. Routine ultrastaging of negative SLN improves the detection of nodal metastases.
FERTILITY PRESERVATION AND CONSERVATIVE TREATMENT OF ENDOMETRIAL CANCER: REVIEW OF THE LITERATURE.
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Objectives
Endometrial cancer is the most common cancer of the female genital tract. Since 2008 there has been an increase in incidence. A significant number of patients with endometrial cancer are pre-menopausal. Three main factors influence the prognosis: histological subtype, depth of invasion and lymph node involvement. Surgery remains the gold standard of treatment for this cancer.

Methods
20% of all women will be diagnosed with endometrial cancer before menopause. 5% of them will develop the disease before the age of 40. As the number of younger women with endometrial cancer increases, fertility-sparing treatment is receiving more attention between clinicians and patients. Endometrial cancer in women of reproductive age poses a therapeutic dilemma for clinicians, especially for women who wish to preserve their fertility. In those women appears as a well-differentiated endometrioid adenocarcinoma and an estrogen-dependent tumor. The prognosis in cases with no myometrial invasion, is excellent.

Results
A recent review suggests that only well-differentiated early-stage EC patients (Stage IA, grade 1) without myometrial invasion or extraterine involvement should be selected for conservative therapy; however, some researchers reported that patients with grade 2 lesions or myometrial invasion have successfully undergone fertility-sparing treatment.

Conclusions
Conservative management of early stage, low-grade endometrial cancer with hormonal therapy has allowed many women to complete childbearing before definitive treatment with hysterectomy. There is always a dilemma concerning the type, dose, duration, and the route of progestin administration. Further prospective studies with larger numbers are needed to delineate more clearly the efficacy of fertility-sparing concerning the Endometrial cancer.
Objective

Ideal surgical management of borderline ovarian tumors (BOT) affecting women of reproductive age remains controversial. Laparoscopic fertility sparing techniques and advances in assisted reproductive techniques (ART) allow women to retain their reproductive potential. We present two cases of advanced stage borderline ovarian tumors (BOT) in young women, both successfully managed laparoscopically with fertility sparing cytoreductive surgery, thus allowing preservation of future reproductive potential.

Methods

Two nulliparous women 19 and 22 years old underwent laparoscopic unilateral oophorectomy and biopsy-based staging for ovarian mass (stage IIIa BOT). They both opted for fertility-sparing laparoscopic management. Case 1 underwent secondary platinum-based chemotherapy and subsequent laparoscopic completion oophorectomy, omentectomy, pelvic lymphadenectomy with uterine preservation. Seven years follow up was performed, and underwent successful assisted reproduction (ART) treatment. Case 2 had secondary laparoscopic partial contralateral oophorectomy, infragastric omentectomy, preserving a near-complete ovary and uterus, and initiated appropriate follow up.

Results

Both laparoscopic operations were completed without conversion to laparotomy. Histopathology confirmed seropapillary BOTs with non-invasive implants on ovary/omentum/parietal peritoneum. Peritoneal washings were positive, lymph nodes negative. The first patient had successful reproductive outcome with IVF; gave birth to twins at 7 years and remains well with no evidence of recurrence.

Conclusions

Advanced stage BOTs can be successfully managed laparoscopically. Fertility sparing laparoscopic surgery emerges as a feasible and safe option for women of reproductive age. Efficacy of such laparoscopic operations is enhanced by the meticulous application of oncological principles and by the thoughtful awareness of the technique’s inherent limitations.
Objectives
During recent years the increase incidence rate of gynecological malignancies in reproductive age patients who had no time to implement reproductive function has been registered. In majority cases special treatment results in partial or full deprivation of fertility as a result of the high ovarian sensitivity to chemotherapy and radiation therapy. Cryopreservation and autotransplantation of ovarian tissue appear to become the method of fertility preservation.

Aim: The aim of the research was to evaluate the ovarian reserve and develop policy of treatment of patients with gynecology malignancies with the purpose of cryoconservation of ovarian tissue for further realization of reproductive function.

Methods
10 patients of reproductive age (< 35 years) have been treated in National Cancer Institute from 2010 to 2012 year with diagnosis IB – IIB stage cervix cancer. Panhysterectomy type 3 has been executed in 9 patients, radical abdominal trachelectomy – in 1 patient. Ovarian tissue obtained after laparotomy was placed in aseptic terms in container with special medium at a temperature +20-25 ° C and after that it was transported to Institute of Cell Therapy for following investigation, cryopreservation and further preservation. Currently, all the patients are placed under dynamic surveillance. There is no evidence of the disease.

Results
As a result, cryoconservation of ovarian tissue can be fulfilled with the aim to realize the delayed reproductive function.

Conclusions
This method does not require the delay of the treatment, ovarian stimulation and can be accepted for the needs of patients with gynecological malignancies.
LAPAROSCOPIC TRACHELECTOMY IN CERVICAL CLEAR CELL ADENOCARCINOMA

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Objectives
Adenocarcinoma represents about 5-10% of all tumors in this location and within these, the clear cells account for 4-9%. This type of tumor affects mainly postmenopausal women, but also occurs in young women with a history of prenatal exposure to diethylstilbestrol (DES).

Methods
A case of clear cell adenocarcinoma of the cervix in a woman of childbearing age, unrelated to intrauterine exposure to DES, which wished to preserve fertility for which he was treated with radical vaginal trachelectomy and pelvic lymphadenectomy.

Results
A 28 year old woman, nulliparous, went to our center with a high squamous intraepithelial lesion and positive HPV in cytology.

During exploration, a 2 cm exophytic lesion was observed that was biopsied, that was informed as an adenocarcinoma of clear cells.

A diagnostic conization was performed showing an anatomic-pathologic result of clear cells of 20x15 mm with stromal infiltration of 3 mm, free margins, without lymphovascular invasion (FIGO IB1). The patient was willing to preserve her fertility so a radical trachelectomy with selective biopsy of the sentinel lymph node was performed, that was negative.

The follow up included gynecologic exploration, vulvoscopy, colposcopy, tumoral markers and gynecologic ultrasound every 3 month and Magnetic resonance every 6 month without incidence. After 18 months of follow up the patient is asymptomatic and looking for pregnancy.

Conclusions
The treatment of women with cervical cancer in early stages may include fertility preservation. Larger studies are needed on controversial histologic types such as clear cell adenocarcinoma, but the final decision must always correspond to the correctly informed patient.
THE WAYS OF PRESERVING FERTILITY IN GENITAL CANCER PATIENTS IN BELARUS

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Objectives
Preservation of fertility and its feasibility are important factors of the future quality of life of patients after cancer therapies. It is most acute issue in gynecological cancer patients where the ovaries and/or the uterus are being subject to treatment. The objective of this study was to investigate the potential for preserving fertility in female genital cancer patients in Belarus.

Methods
We analyzed patient database (2000-2012) maintained by the N.N. Alexandrov National Cancer Centre.

Results
The following organ-sparing operations were performed at our Centre: radiowave and knife conization of the cervix for cervical intraepithelial neoplasia (CIN) III (487 cases), amputation of the cervix for CIN III and T1A1,B0N0M0 (87 cases), trachelectomy for T1A,B1N0M0 cervical cancer (11 cases), one-sided excision of borderline ovarian tumor (284 cases). Transposition of ovaries was done in 27 cases of surgical and radiation treatment of cervical cancer.

Photodynamic therapy with Photolon for CIN II-III (168 cases) was developed, tested and assessed. Complete recovery was achieved in 92.8% of the patients. Seven of them subsequently achieved pregnancy, three women elected to terminate their pregnancies; four gave birth to healthy babies.

Conclusions
Cryopreservation of ovarian tissue and oocytes is not yet being used in Belarus. This approach is of interest to women whose reproductive potential is threatened by cancer therapy, including gynecologic cancers, hematologic malignancies or breast cancer. Our country has reached the level of health care when we need to assess the efficacy of current techniques for preserving fertility and secure the option for conservation of female genetic material for future cancer patients.
SUCCESSFUL DELIVERY AFTER PREGNANCY ACCOMPANIED BY TREATED DUCTAL INVASIVE BREAST CANCER – A THERAPEUTIC DEMEMLA

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Objectives
As women in western countries delay childbearing, it has been hypothesized that the incidence of breast cancer diagnosed during pregnancy will increase. Breast cancer in pregnancy is rare with an incidence of 1:3 000 to 1:10 000 and is the second most common after cervical cancer. This is a case report of a 32-year old patient, her first full term pregnancy and successful vaginal delivery, with right breast cancer diagnosed in the fourth month and treated

Methods
This is a case of a first desired pregnancy in a patient who rejected to abort it in the fourth month of her pregnancy after invasive ductal breast cancer had been diagnosed by Tru-Cut biopsy – Ca ductale invassivum HG II, NG II with DCIS present, cribriform type, Er 7, Pr 7, HER 1+, Ki 67 low (10%). US revealed multiple right breast cancer Bi RADS 4C with left axillary and neck limphadenopathy. She was treated by Neo Adj HT.

Results
She was under intensive surveillance and gave birth to a full-term female baby 2800/49/34, Ap 9/10 at Ob/Gyn University clinic ‘Narodni front’.

Conclusions
Since two lives are at risk, the need for prompt treatment presents a clinical dilemma of considerable magnitude. Breast cancer during pregnancy put the health of the mother in conflict with that of the fetus. The aim is to give optimal treatment to the mother to maximise the chances of survival, whilst minimising the risk of harm of the fetus.
FERTILITY AND PREGNANCY OUTCOME IN A PATIENT WITH PREVIOUS LAPAROSCOPIC SURGERY FOR BILATERAL OVARIAN MATURE CYSTIC TERATOMAS.

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Objectives
Mature cystic teratoma (MCT) is the most common benign ovarian tumor in young women. Bilateral localization is observed in some 10-15% of cases; incidence of malignant transformation is estimated to be 0.17-2%. MCT can be surgically treated by laparoscopic ovarian cystectomy with fertility sparing and a recurrence rate about 3-4%. Some cases will require assisted reproduction technology.

Methods
We report on bilateral ovarian MCT in a woman treated by laparoscopic cystectomy with subsequent spontaneous pregnancies.

Results
The patient underwent surgery for MCT of the left ovary at the age of 27. An ovarian MCT occurred 7 years later in the right ovary. Both teratomas were confirmed at histology. Four years later she got pregnant spontaneously. At about 5 weeks of gestation she underwent emergency surgery for peritoneal haemorrhage in a suspected left fallopian tube ectopic pregnancy. At histology a decidual reaction at tubal surface was seen, but no chorionic villi were found. She had spontaneous abortion a month later. Histology showed decidua and chorionic villi. One year later a spontaneous uterine pregnancy was carried to term. The pregnancy evolution was normal, but she had a post-partum haemorrhage. One month after delivery she underwent surgery for placental residual.

Conclusions
The management of MCT in women of childbearing age poses unique challenges given the potential impact on fertility. Future fertility is of major concern among these women; therefore, the surgical management must focus on preserving ovarian tissue. Available data indicate that in these patients fertility and pregnancy outcome is very good.
e-Posters: Fertility / pregnancy

PERSISTENT ADNEXAL MASSES MANAGED SURGICALLY AT PREGNANCY: A CASE SERIES

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Objectives
The aim of this study is to evaluate the outcomes of adnexal masses diagnosed and managed surgically at pregnancy.

Methods
We retrospectively reviewed the hospital records and present nine cases with adnexal masses persisted beyond 14 weeks of gestation and underwent surgery at pregnancy.

Results
The mean age of patients was 27±5.29 years old. Gestational ages at the time of surgery ranged from 14 to 22 gestational weeks. All of the cases underwent salpingo-oophorectomy. Pathological diagnosis confirmed mature cystic teratoma, cystadenoma, borderline tumor and corpus luteum in four (44%), two (22%), two (22%), one (11%) of cases respectively. On the follow up period five (55%) cases delivered vaginally and one (11%) case by cesarean section at term respectively. All of the newborns were healthy. One (11%) of the cases aborted after surgery and two (22%) pregnancies are still in the follow up period.

Conclusions
Surgery for adnexal masses persisted beyond the first trimester is safe in the second trimester of gestation. Neither antenatal nor neonatal outcomes are effected adversely by surgery.
CANCER AND FERTILITY NEEDS ASSESSMENT: A SURVEY AMONG PATIENTS AND HEALTHCARE PROVIDERS

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Objectives
Due to increasing survival rates after cancer therapy, patients will experience side-effects like in-/subfertility. The purpose of this cross-sectional, retrospective study is to investigate knowledge, needs and preferences in fertility counselling and fertility preservation (FP) among patients receiving cancer treatment and their physicians.

Methods
Male and female patients between 18 and 44 years who received cancer treatment possibly affecting fertility, their GPs and their specialists in the Mid-Netherlands were invited to fill out a questionnaire regarding knowledge and attitudes towards cancer, fertility issues and FP.

Results
Out of 632 patients, 130 responded (20.6%). Fifty-one out of 93 specialists responded (54.8%) and 40 out of 290 general practitioners responded (13.8%). Specialists acknowledged the importance of FP in cancer consultations. Seventy-nine percent of the specialist and 40% of the GPs stated they discuss FP before start of treatment. Patients reported the counselling rate on fertility issues and FP was respectively 57.5% and 55.8%, without difference in counselling rate between younger and older patients. Patients were unaware about most fertility issues and FP techniques. Specialists were less likely to offer FP in patients older than 40 years (48.9%) and patients with poor prognosis (51.1%). Forty-one percent of the GPs stated they did not discuss FP because this was not their responsibility. Knowledge regarding FP varied among specialists, GPs and patients.

Conclusions
Although physicians acknowledge the importance of fertility counselling and FP in cancer patients, patient reported counselling rates were low. Patients had little knowledge about FP techniques. Improvements in counselling are required.
e-Posters: Miscellaneous

VAGINAL AND VESTIBULAR RECONSTRUCTION FOLLOWING RADICAL CYSTECTOMY AND URETHRECTOMY : A NEW TECHNIQUE

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Objectives
Reconstruction of the vagina and anterior vestibule following radical excision for urethral or bladder cancer is challenging. We present a novel technique applied in a nonhysteretomised patient in which the uterus was used for reconstruction with a satisfactory outcome.

Methods
A 53 year old patient with squamous cancer of the proximal urethra underwent radical cystectomy and urethrectomy with excision of the entire anterior vaginal wall and the anterior vestibule (Figure 1). The posterior wall of the uterus was elevated as a flap by incising the lateral margins along a line posterior to the insertion of the uterine vessels (Figure 2). The endometrium was excised with a wire electrical loop. The uterus was swung into anteversion and the cut end of the posterior lower uterine segment was advanced to the mucosa of the vestibule (Figure 3). The body of the uterus was apposed to the posterior wall of the vagina with a series of interrupted polyglycolic sutures (Figure 4). The sutures were continued anteriorly to appose the skin of the anterior vulva to the neovestibule. The serosa of uterus was ablated with natural argon plasma.

Results
Satisfactory reconstruction was achieved.

Conclusions
We conclude that the anteverted uterine flap is a viable option for vaginovestibular reconstruction in radical urological surgery when the uterus is preserved.
INHIBITION OF EXPRESSION OF POLYSIALIC ACID IN KELLY NEOBLASTOMA CELL LINE BY NON-POLAR CONSTITUENT/S OF ASHWAGHANDA HERB

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Objectives
Several studies demonstrated the re-expression of embryonic polysialic acid (PSA) on NCAM in progressive stages of metastatic tumours (1, 2). Kelly human neuroblastoma cell line was utilised as a model of tumour with high expression of PSA. For inhibiting PSA with no cytotoxicity, the model was treated with extracts of Withania somnifera (ashwagandha), a popular Indian anticancer herb (3, 4).

Methods
ELISA was applied on 96-well flat bottom plates. Anti PSA-NCAM monoclonal and biotinylated IgG were used as primary and secondary antibodies, respectively. Water soluble 2,2-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) peroxidase substrate was used. Ashwagandha roots were extracted in water (W), ethanol (E), DMSO (D), hexane (H) and chloroform (C). H and C residues were re-suspended in D, where others in corresponding solvents. ELISA was performed in parallel to MTT.

Results
W and E were neither cytotoxic nor inhibiting PSA. At first two concentrations, D has no cytotoxicity and over-expressing PSA. At highest concentration, D is cytotoxic and E was not, where both reduce PSA (figure 1.A). Apart from first two concentrations of H, treatments of cells with other suspensions exert cytotoxicity correlated with reduction in PSA. At first two concentrations, H suspension has no cytotoxicity with PSA reduction of ≈ 83 and 70 %, respectively (figure 1.B).

Conclusions
Non-polar constituent/s of ashwagandha have inhibition potential on PSA expression with no cytotoxicity.
RECURRENT AND METASTATIC UTERINE LEIOMYOSARCOMA: SINGLE INSTITUTION EXPERIENCE

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Objectives
Uterine leiomyosarcoma (ULMS) is a rare uterine malignancy but it is an aggressive tumor with high mortality, regardless of initial stage. Because of its low incidence, there is no agreement on standard treatment. We describe our series.

Methods
We retrospectively identified 13 patients (pts) who received chemotherapy and/or surgery for recurrent or metastatic ULMS at our institution from July 2007 to April 2013. We analysed patient characteristics and treatments received.

Results
Median age at diagnosis was 55 years (range 50-61). Nine pts (70%) were postmenopausal. Surgical FIGO Stages were I:6pts(46%), II:2pts(15%), III:2pts(15%) and IV:3pts(24%). Eleven pts (85%) underwent initial surgery (1 with pelvic and 1 with pelvic-paraortic lymphadenectomy). 6 pts (45%) received adjuvant radiotherapy. 2pts (15%) received adjuvant chemotherapy (adriamycin/iphosphamide). The main site of recurrence was lung, followed by peritoneum and soft tissue. Three patients underwent metastasectomy (1 patient once, 1 patient twice and 1 patient 5 times). All patients received at least 1 palliative chemotherapy regimen (3pts one, 7pts two, 1pt three, 1pt four and 1pt five). Chemotherapy regimens were Docetaxel/Gemcitabine, Adriamycin/Iphosphamide, Trabectidin, Temozolamide, Dacarbazine and Adriamycin.
Median Survival from 1st line chemotherapy to end of follow-up was 21 months (range 16-25). Overall survival from diagnosis in our series was 55 months (4-106).

Conclusions
ULMS include a broad spectrum of diseases where some selected patients can benefit from chemotherapy and or surgery at recurrence. Further studies with these treatment modalities are needed to define their role jointly or separately and which is the best treatment sequence, mainly for isolated metastasis.

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ADJUVANT THERAPY DOES NOT IMPROVE OUTCOMES IN STAGE I LEIOMYOSARCOMA OF THE UTERUS

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Objectives
To evaluate the impact of adjuvant therapy for stage I uterine leiomyosarcoma (LMS).

Methods
Clinicopathological data of cases with stage I uterine LMS from 1996 to 2010 were retrieved from the computerized database of Hacettepe University Hospital. The Kaplan-Meier method was used to estimate survival and progression-free survival, and survival differences were analyzed by the log-rank test. Cox regression analysis was performed to account for the potential influence of confounding factors.

Results
We evaluated the outcomes of thirty-five patients with histologically proven stage I LMS. The median age at diagnosis was 50 years. All patients underwent surgical treatment and twenty patients (57.1%) received adjuvant therapy. Twelve of these patients (34.3%) received adjuvant chemotherapy, three (8.6%) received adjuvant pelvic irradiation and five (14.2%) received adjuvant chemotherapy with pelvic irradiation. The median follow-up duration was 34 months (range, 3-231 months). Twenty-three (65.7%) patients recurred during follow-up. The median progression-free survival and median overall survival of patients were not different between patients who received and did not receive adjuvant therapy. 2-year progression-free survival rates were lower for patients who received adjuvant therapy (51%) than for those who did not (77%). Cox regression analysis did not demonstrate any significant impact of the factors studied, including age, menopausal status, tumor size, mitotic count, lymphadenectomy, hysterectomy, and oophorectomy and adjuvant therapy.

Conclusion
Adjuvant therapy for surgically treated LMS confined to uterus did not influence progression-free survival and overall survival.
INCIDENTALLY DIAGNOSED EXTRASKELETAL EWING’S SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOR (PNET) OF THE RETROPERITONEUM IN A PATIENT OPERATED FOR AN ADNEXAL MASS: A CASE REPORT

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Objectives
To report a very rare extraskeletal occurrence of Ewing’s sarcoma (ES)/primitive neuroectodermal tumor (PNET) that was encountered during surgical exploration for an adnexal mass.

Methods
A 33-year-old woman was referred to our institution for evaluation of an adnexal mass suspicious for a malignancy. Preoperative pelvic ultrasonography revealed a left sided pelvic mass with predominantly solid components measuring 12x9 cm. Serum CA19-9 was elevated (41U/ml), whereas CA125 was in the normal range (11U/ml). Surgical exploration revealed a left sided 9x7 cm ovarian mass with macroscopical features resembling a mature cystic teratoma. A 15x12 cm retroperitoneal mass was discovered incidentally, which was located under the left psoas muscle. The muscle was incised and the mass was extirpated. The operation was concluded and the patient recovered uneventfully.

Results
On final pathological analysis, left ovarian mass was reported as a mature cystic teratoma, and the retroperitoneal mass was reported as an extraskeletal ES/PNET. Immunohistochemically, the retroperitoneal mass was diffuse positively stained with CD-117, CD-99 and Vimentin. The patient was referred to medical oncology and radiation oncology departments for further treatment.

Conclusions
ES/PNET is very rarely encountered in the female genital tract, and is classified as a subtype of Ewing’s sarcoma. Preoperative clinical and radiologic findings are generally non-specific. Diagnosis is generally concluded after immunohistochemical examination. As there are very few cases reported in the literature, a standard treatment approach is not established. Surgical resection of the mass, followed by adjuvant treatment in terms of chemotherapy and/or radiotherapy is the current practice in these cases.
WHAT TYPES OF GYNECOLOGICAL CANCER ARE EXPECTED IN WOMEN UNDER THE AGE OF 40? LONG TERM FOLLOW-UP STUDY ON 461 PATIENTS

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Objectives
To describe what types of gynecological-cancer are most frequently diagnosed in women <40, as well as their epidemiological characteristics and survival-rates.

Methods
Medical records dated from January 1990-December 2011 were reviewed. All cases of preinvasive-disease from the genital tract and gestational trophoblastic disease were excluded. Survival rates were analyzed by using the Kaplan-Meier technique.

Results
461 patients were included. The mean follow-up period was 93.7 months. Cervix was the most frequently identified primary site, in 46.6% of patients, followed by ovary in 41.7%. Uterine cancer was diagnosed in 6.7% of patients, vulvar cancer in 1.1% and other types in 3.9%. The most frequently found histological types were: squamous-cell for cervix (73%), borderline-tumors for ovary (59%), adenocarcinoma for uterus (71%) and squamous-cell for vulva (80%). Most tumors were diagnosed at an early-stage; however, CC was diagnosed at an advanced-stage in 43% of cases. Surgical treatment was applied to 77.2% of patients, 43% of them with fertility-sparing surgery; 24.8% of them achieved pregnancy. After treatment, 33.6% of menopausal patients received HRT. OS-rates at 5 and 10-years were 78.4 and 76.7% respectively. The 5-year OS rates were 72.7% for CC, 88% for ovarian cancer, 85.2% for uterine cancer and 100% for vulvar cancer (p<0.0001).

Conclusions
Cervical and ovarian cancers were the most common types of gynecological-cancer in women <40. CC was frequently diagnosed at an advanced-stage and was associated to the lowest survival-rates. Physicians should be aware of the importance of initiating screening programs in this population according to the guidelines for each country.
EFFICACY OF FIBRIN SEALANT FOLLOWING INGUINAL LYMPHADENECTOMY: A SYSTEMATIC REVIEW

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Objectives
Inguinal lymphadenectomy is an integral part of surgical management of vulval, penile cancers and melanoma. The procedure is associated with a high incidence of groin wound complications. Several strategies have been explored with a view to minimising groin morbidity. The aim of this systematic review is to appraise the efficacy of fibrin sealant in minimising groin wound complications.

Methods
Boolean combination of terms were deployed in our search strategy. Medline, EMBASE and CINAHL databases were searched with English language and human subject restriction. Abstracts of 99 citations were reviewed and four full text articles met the inclusion criteria. Data was extracted by two investigators. Quality assessment using Cochrane guidelines was performed.

Results
Three studies reported on melanoma patients and one on vulval cancer cohort. 310 participants were included in the studies. In the melanoma cohort, there was no significant difference in terms of a portfolio of postoperative complication; in the vulval cancer group, the fibrin group demonstrated significantly fewer cases of post operative infections. In one study, interventional group required longer duration of groin drainage. No significant difference was found in terms of wound reoperation rate, amount of drainage or lymphodema. The studies are at high to moderate risk of bias.

Conclusions
The current evidence base does not support the use of fibrin sealant to minimise complications following inguinal lymphadenectomy.
e-Posters: Miscellaneous

**T-CELL/HISTIOCYTE-RICH B-CELL LYMPHOMA PRESENTING AS PELVIS LYMPHADENOPATHY**

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**Objectives**

T-cell/histiocyte-rich B-cell lymphoma (TC/HRBCL) is a rare subtype of diffuse large B-cell non-Hodgkin's lymphoma (DLBCL) with characteristic morphologic and immunophenotypic features, often misdiagnosed as Hodgkin's lymphoma and peripheral T-cell lymphoma. It represents less than 2% of all DLBCLs. Diagnosis may be difficult, as it may appear similar to other lymphoid diseases.

**Methods**

A 69-year-old white woman presented to our center complaining of urinary incontinence symptoms, during the last decade with haematuria or vaginal bleeding. The abdominal ultrasound did not reveal pathological findings. TVS revealed 2 masses (7x4.5cm and 4.8x2.2cm) in front of the bladder and behind the right iliac artery. MRI confirmed the presence of an extend lymphadenopathy of the right pelvis. Laboratory exams, revealed no signs of malignancy except from CA 15-3, CA 19-9 and CA 125 which were above normal values. The patient underwent uterus curettage and excision of a lymph node from the right inguinal region.

**Results**

The histological examination revealed granulomatous lesions with necrotic changes and atypia. Further investigation was performed in a specialized hematological center. The final histological examination revealed T-cell/histiocyte-rich B-cell lymphoma. The patient is being followed up with hematological and imaging examinations, in regular basis, in a good clinical condition.

**Conclusions**

TC/HRBCL is a rare morphologic variant of DLBCL with distinct clinical and pathologic features. TC/HRBCLs are difficult to be recognized without immunohistochemistry. Is charachterized by: 1) diffuse nodular pattern of growth; 2) small proportion of large CD20 positive neoplastic cells 3) prominent component of both reactive T cells and histiocytes; and 4) a very few reactive, small B cells.
GYNECOLOGIC MALIGNANCY IN WOMEN WITH MULLERIAN ANOMALIES: REPORT OF FOUR DISTINCT CASES

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Objectives
To present behaviors of gynecologic tumors in the presence of Mullerian anomalies.

Methods
Four women who had Mullerian anomalies with gynecologic malignancy were diagnosed since 2010 in our center. Medical records of these women reviewed retrospectively.

Results
There were one bicornis unicollis and three didelphic uterine anomaly. Case one with uterus bicornis unicollis anomaly was 41 years old lady with 105x85 mm well-differentiated endometrioid adenocarcinoma of the right ovary with the right uterine horn involvement without myometrial invasion. Case two with didelphic uterine anomaly was 52 years old women with well-differentiated right cervical endometrioid adenocarcinoma without left cervical involvement. Case three with didelphic uterine anomaly was 30 years old women with well-differentiated cervical mucinous adenocarcinoma with both cervical involvement. Case four with didelphic uterine anomaly was 49 years old women with serous gynecological tumor of unknown origin. There were 8x5x4 cm right ovarian tumor with deeply invaded bilateral uterine cavity and endocervical canal. Presenting symptoms of these patients were abdominal fullness followed by pelvic pain. CA 125 levels were elevated in whole cases. Two of these patients had no preoperative diagnosis of Mullerian anomaly possibly due to large tumor mass on routine ultrasonography. There was no urinary system anomaly in these cases.

Conclusions
The incidence of Mullerian anomalies is not well defined. In the presence of suspicion MRI is advised for diagnosis. Presence of such anomalies may cause variation of surrounding structures and effects disease spread with unknown lympho-vascular connections in gynecologic malignancies, which mandates attention during surgery.
STAGE DETERMINATION OF THE SECOND TUMOR IN CASES OF PRIMARY MULTIPLE GYNECOLOGICAL CANCER

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Objectives
The aim of the study was to estimate the stage determination of the second tumor in cases of gynecological cancer.

Methods
Primary multiple malignant tumor in 1869 cases of gynecological cancer as a first tumor in Bulgaria during the period 1993-2010 according data from Bulgarian National Cancer Registry were analyzed.

Results
The most frequent second tumor was: cancer of the breast (511 cases), colon-rectum (289 cases), lung (98 cases), bladder (79 cases) and stomach (51 cases). The second tumor was in more advanced stage than the first tumor. The second tumor was in: stage I- 25,6%, stage II- 20,9%, stage III-15,6%, stage IV-13,1%, and unknown stage in 24,9% cases. Cervical cancer in 453 cases, endometrial cancer in 422 cases were found. When the first tumor is cervical cancer, the second one was found in stage I in 27,4%, and the rest stages were 18,5%, 13,5%, 15,7% and 24,9% respectively. When the first tumor is endometrial cancer, the second one was found in stage I in 26,4%, and the rest stages were 22,1%, 16,4%, 11,5% and 23,5% respectively. When the first tumor is ovary cancer, the second one was found in stage I in 22,5%, and the rest stages were 19,7%, 16,4%, 13,5% and 28,0% respectively.

Conclusions
Our results indicated late diagnosis of the second tumor with worst prognosis after the treatment the gynecological cancer. We recommend target search of a second tumor at follow-up period of the patients with gynecological cancer.
A HUGE OVARIAN FIBROID OF 35 KILOGRAMS IN ELDERLY WOMAN OF 65 YEARS ADMITTED IN MEDICAL EMERGENCY WARD, A RARE PRESENTATION - A CASE REPORT

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Objectives
The objective of this case presentation is to show how a longstanding and huge ovarian tumour invites serious medical problems like respiratory and nutritional ailments forcing the woman to seek emergency medical care, if remain untreated of primary disease for long, in an ill-structured health care system in rural India.

Methods
Mrs DB, menopausal since 10yrs, presented with a huge ovarian mass with ascites, respiratory distress and severe nutritional deficiency, landed up in medical emergency. After being treated for medical problems, she was prepared for surgery in gynaecology ward. A 35 kg ovarian fibroid was removed from left ovary with right ovary and uterus being absolutely normal. No enlarged lymph nodes noted in abdomen. TAH and BSO performed and tissue sent for histopathological and ascitic fluid for cytological examination. She was kept in ICU in immediate post-operative period which was uneventful.

Results
She was transfused with two units of whole blood and two units of albumen and was shifted back to ward after 48 hours. The cytological report showed no malignant cells and histopathology showed ovarian fibroid with myxomatous degeneration. Her recovery was a little slow and left hospital after two weeks.

Conclusions
A huge ovarian tumour of 35 kgs or similar, which is rare in present day gynaecology, apart from being a surgical problem, can be associated with many serious and life threatening medical issues like respiratory and nutritional etc, putting a lot of economic burden to the family as well as to the nation.
e-Posters: Miscellaneous


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Objectives
The purpose of this study is to statistically compare the mean ages of the patients with gynecologic cancer in our hospital during the 1998-2012 interval.

Methods
The data was collected from the Histopathology Exams (HPE) registers.

Results
Gynecologic cancer was discovered in 1752 cases; there were 1020 cases of cervical cancer, 556 cases of uterine cancer, 118 cases of ovarian cancer, 51 cases of vulvar cancer and nine cases of vaginal cancer. The mean ages were 53,21±13,21 years for cervical cancer (age range 22-87 years), 61,92±9,55 years for uterine cancer (age range 32-88 years), 51,66±14,22 years for ovarian cancer (age range 18-77 years), and 69,24±9,29 years for vulvar cancer (age range 39-84 years); vaginal cancer was not considered because of the non-normal distribution of the age groups. The age groups with the most patients were: 41-50 years for cervical cancer (293 cases or 28,73%), 51-60 years for uterine cancer (207 cases or 37,23%), 51-60 years for ovarian cancer (34 cases or 28,81%), and 71-80 years for vulvar cancer (24 cases or 47,06%). After performing Student’s test, the statistically significant differences were: cervical vs uterine (p<0.0001), cervical vs vulvar (<0.0001), uterine vs ovarian (<0.0001), uterine vs vulvar (<0.0001), and ovarian vs vulvar (p<0.0001). Cervical and ovarian cancer mean ages were not significantly different (p=0.23).

Conclusions
The mean ages of the patients with different types of gynecological cancer was similar to that in literature.
e-Posters: Miscellaneous

VULVAR AND VAGINAL CANCER IN THE "DR. SALVATORVUIA" CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 1998-2012 PERIOD
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Objectives
This paper intends to present the frequency of vulvar cancer in our hospital during the 1998-2012 interval.

Methods
The data was collected from the Histopathology Exams (HPE) registers.

Results
Vulvar cancer was discovered in 51 cases, representing 2.91% of all genital cancers, and vaginal cancer in nine cases, representing 0.51% of all genital cancers (1752 cases). Most cases (58 or 96.66%) were represented by carcinomas, while one patient had a carcinoma combined with sarcoma (1.67%) and another had a vulvar hemangiosarcoma (1.67%). The mean age of the group was 68.92±9.42 years (age range 39 to 84 years); the mean ages for vulvar and vaginal cancer were 69.24±9.29 (age range 39 to 84 years) and 67.11 years, respectively (age range 51 to 81 years).

Conclusions
Vulvar and vaginal cancer, although less frequent, is diagnosed late in many cases, thus making treatment less effective.
RADIOTHERAPY IN GYNECOLOGICAL CANCERS: ANALYSIS OF TREATMENT RESULTS AND PROGNOSTIC FACTORS

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Objectives
To evaluate treatment results and prognostic factors women with gynecologic cancer undergoing radiotherapy in a newly established tertiary gynecologic oncology and radiation oncology unit.

Methods
78 patients with gynecological malignancy receiving curative radiotherapy (RT) between June 2010-January 2013 were retrospectively evaluated.

Results
33, 44 and 1 patient were treated for cervical cancer, endometrial cancer and endocervical canal tumor respectively. Median age was 56 (34–83). Mean follow-up period was 23.9±1.4 months. At time of diagnosis 18 patients were premenopausal (23.1%) whereas 60 were (74.9%) postmenopausal. 31 endometrial cancer patients were received adjuvant RT while 9 receiving adjuvant chemotherapy and RT. Five of the patients with recurrent endometrial cancer received RT after salvage surgery. Sixteen patients with locally advanced cervical cancer treated with definitive chemoradiotherapy. Ten patients (30.3%) operated for cervical cancer were applied adjuvant RT whereas 6 patients (18.2%) received adjuvant chemoradiotherapy. The patient with endocervical canal tumor received adjuvant chemoradiotherapy. The median overall survivals were 26.3 and 21.1 months for patients with endometrial and cervical cancer respectively. In regression analyses for EC patients there were a relation between the overall survival and local recurrence (p=0.046), tumor diameter (p= 0.030) and stage (p= 0.036); on the other hand no relation was observed for lymphovascular invasion (LVSI) (p=0.711) and myometrial invasion (p=0.684). For cervix cancer there was an association between lymph node positivity and progressin free survival.

Conclusions
Despite shorter follow-up, classical prognostic factors rules for endometrial and cervical cancer but we could not observe same trends for LVSI and myometrial invasion in EC.
PARAAORTIC PARAGANGLIOMA (ECTOPIC PHEOCROMACITOMA) ARISING IN AN ENDOMETRIUM CANCER PATIENT MIMICKING LYMPH NODE METASTASIS

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Objectives
Paragangliomas are rare tumors arising from chromaffin cells in autonomic nervous system. They are most frequently located in paraaortic region. Most cases are functional, with increased level of catecholamine or its metabolites. 1/5 of reported cases were associated with familial neoplasm syndromes such as neurofibromatosis-1. Nonfunctioning cases are very rare incidental tumors without hypertension.

Results
Case: A 50 year old postmenauposal woman was referred due to incomplete surgery diagnosed as endometrial cancer by final pathologic examination after total abdominal hysterectomy and bilateral salpingooopherectomy. Myometrial invasion was <1/2. Her past medical history was unremarkable except for a history of left adrenal adenoma. Her blood pressure was 110/60 mmHg and pulse rate was 90/ min. Patient underwent pelvic and paraaortic lymph node dissection to complete surgery. During paraaortic lymph node dissection a 5cm of highly vascular lymph node was detected at the right low paraaortic region. Aberrant small vascular structures were observed around the lesion which bled during dissection. Frozen section examination revealed nonspecific malign tumoral lesion. Final pathologic examination revealed positive immunostaining for chromogranin, synaptophysin, and s-100. Pheochromacitoma arising in ectopic adrenal tissue namely a ‘paraganglioma’ was diagnosed. There was no hypermetabolic activity at this localization on the preoperative PET-CT. There was no nodal lymphatic involvement with stage1a tumor according to the FIGO 2009 classification.

Conclusions
Total excision and systemic evaluation are the basis of curative treatment for paragangliomas due to potentially malignant nature. Moreover, clinicians should be aware of unexpected findings unrelated to primary disease during retroperitoneal surgery.
**LAPAROSCOPIC MODIFIED MCCALL CULDOPLASTY FOR THE CORRECTION OF UTEROVAGINAL PROLAPSE IN PATIENTS WITH CONCOMITANT GYNECOLOGIC TUMORS.**

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**Objectives**

Concomitance of uterovaginal prolapse and genital malignancies are not rarely observed in the clinical practice and this association leads to important surgical consequences. The laparoscopic management of pelvic tumors and pelvic floor defects is progressively gaining importance and popularity over laparotomy or even vaginal route. The objective of the study is to evaluate feasibility and safety of a novel approach for the concomitant endoscopic treatment of gynecologic tumors and uterovaginal prolapse.

**Methods**

Series of cases in which women with severe uterovaginal prolapse associated to gynecologic tumors undergone to laparoscopy for the oncologic treatment in parallel with a modified McCall culdoplasty.

**Results**

In our series of 4 cases, we achieved successful completion in all patients, without conversion to laparotomy. Average operative time, blood loss and length of hospitalization were favorable. Based on the comparative POP-Q measurements and the evaluation of the satisfaction rates of the patients, this strategy can be objectively and subjectively considered appropriate for the correction of an uterovaginal prolapse.

**Conclusions**

The modified laparoscopic McCall culdoplasty is a viable and safe alternative to the simultaneous correction of a uterine prolapse and genital cancer treatment. We believe that the routine use of this innovative technique may significantly improve the quality of live of a number of women affected simultaneously by uterovaginal prolapse and gynecologic tumors. Further studies are needed to confirm the oncological safety of the technique.
SUBCUTICULAR SUTURE FOR SKIN CLOSURE REDUCES WOUND COMPLICATIONS IN OPERATION FOR GYNECOLOGIC MALIGNANCIES

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Objectives
Wound disruption and surgical site infection (SSI) are potential complications of surgeries for gynecologic malignancies that require a wide incision and many hours to complete. Some reports suggest that buried sutures have a more protective effect than skin staples against incisional SSI following digestive surgery. It is not clear, however, if this is also the case for surgery for gynecologic malignancies. In the present study, we evaluated risk factors for wound disruption and SSI in patients receiving surgery for gynecologic malignancies.

Methods
This retrospective single-institution study included patients receiving surgery for gynecologic malignancies between 2007 and 2012. Logistic regression analysis was used to evaluate univariate and independent multivariate associations with the risk factors for the occurrence of wound disruption or SSI.

Results
317 patients were identified. 23 (7.3%) patients had wound disruption and 8 (2.5%) had SSI. In univariate logistic analysis, factors significantly associated with the possibility of wound disruption were body mass index, collagen disease, subcutaneous thickness measured by magnetic resonance imaging, and skin staples. Multivariate analyses performed with wound disruption as the endpoint revealed collagen disease, subcutaneous thickness, and skin staples as an independent predictor. Factors significantly associated with the possibility of SSI were subcutaneous thickness, and skin staples in univariate analysis, and subcutaneous thickness and skin staples were independent factors in multivariate analysis.

Conclusions
Subcutaneous skin closure following surgery for gynecologic malignancies has protective effects against wound disruption and SSI.
CARCINOSSARCOMAS: A CASE SERIES
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Objectives
Uterine sarcomas are rare uterine tumors and in the literature carcinossarcomas are the most common of these neoplasms. Also known as malignant mixed Mullerian tumors they have low overall survival rates, poor prognosis, tend to recurrence, and most of all there is no established treatment.
In the Federal University of Sao Paulo, in the last 3 years, we observed different rates and clinical characteristics for these tumors.

Methods
Assessment and clinical data examination of all patients with uterine corpus malignancy from January 2010 until April 2013 in our database and a literature review.

Results
Incidence rate of this malignancy in the time period described is of approximately 18% carcinossarcomas of all uterine tumors instead of the usual 4% in literature. Our survival rate is now and only 16% of the patients died thus far.
Regarding the treatment, it was individualized case by case considering the small amount of trials and RCT concerning uterine sarcomas. 33% were treated with exclusive chemotherapy, 16% treated with chemotherapy followed by radiotherapy, 33% treated with a sandwiched chemotherapy/radiotherapy scheme.

Conclusions
Our best results, considering disease-free survival, were obtained with the chemo-radiotherapy association.
CARCINOMA OF THE FALLOPIAN TUBE PRESENTING AS AXILLARY PALPABLE MASS
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Objectives
Primary tubal carcinoma is a rare gynecological malignancy. Patients generally present with initial non-specific symptoms of abdominal mass, pain, vaginal bleeding or discharge. In this report we present a case with primary tubal carcinoma whose initial diagnose was palpable axillary lymphadenopathy.

Methods
CASE REPORT. A 61 years old woman was firstly admitted to medical oncology with palpable left axillary lymph node. Pathological examination of lymphadectomy showed metastatic serous carcinoma includes diffuse micropapillary architecture. Physical examination of mammography and toracal CT, endoscopy and colonoscopy didn’t reveal specific pathology. Subsequently PET CT scan detected a 4x5 cm in diameter lobulated left adnexial – iliac mass with increased glycolytic activity (SUV Max: 13,8). Serum CA 125 level was 307 U/mL. Exploratory laparotomy revealed a 4 cm left adnexial mass originated from the distal end of left fallopian tube and extended to sigmoid colon. The meso of sigmoid colon was minimally invaded with the tumor. Uterus bilaterally ovaries and right fallopian tube were all normal. Frozen section of tumor revealed primary adenocarcinoma of left fallopian tube. Total abdominal hysterectomy, bilaterally salpingoophorectomy, pelvic and paraaortic lymphadenectomy, omentectomy and segmenter sigmoid colon resection and primary anastomosis were performed. Postoperative term was uneventful.

Results
Figure 1, 2 and 3 shows strong nuclear staining for EMA, WT-1 and CA-125, respectively that indicated metastatic serous cancer in sections from axillary lymph node.

Conclusions
Spreading through the central lymphatic duct may be possible way of spreading tubal carcinomas to the supradiaphragmatic lymph nodes without paraaortic lymph nodes involvement.
e-Posters: Miscellaneous

MALIGNANCIES RESEMBLING A VAGINALLY PROLAPSED LEIOMYOMA: REPORT OF SIX CASES
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Objectives
To identify malignancies that initially presented with a mass resembling a vaginally prolapsed leiomyoma at our institution.

Methods
We conducted a retrospective chart review of malignant cases that initially presented with a vaginal mass prolapsed from the cervix, within a five-year period (January 2008-January 2013) at Zekai Tahir Burak Women’s Health Training and Research Hospital in Ankara, Turkey.

Results
Six cases were identified within the study period. Clinical features are presented in Table 1.

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Age</th>
<th>Symptom</th>
<th>Tumor size</th>
<th>Final pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>Vaginal bleeding</td>
<td>7 cm</td>
<td>Low grade Endometrial stromal sarcoma</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>Abdominal pain</td>
<td>3 cm</td>
<td>Non-Hodgkin Lymphoma</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
<td>Postmenopausal vaginal bleeding</td>
<td>2 cm</td>
<td>Squamous cell carcinoma of cervix</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>Postmenopausal vaginal bleeding</td>
<td>4 cm</td>
<td>Cervical adenosarcoma</td>
</tr>
<tr>
<td>5</td>
<td>51</td>
<td>Postmenopausal vaginal bleeding</td>
<td>4.5 cm</td>
<td>Serous psammomatous adenocarcinoma</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>Pelvic pain + postcoital bleeding</td>
<td>6 cm</td>
<td>Uterine mesenchymal tumor</td>
</tr>
</tbody>
</table>

Conclusions
Various malignant diseases may present with a vaginal mass that grossly appear as a vaginally prolapsed leiomyoma. Non-genital malignancies such as non-Hodgkin lymphoma may also present in this clinical context. Careful evaluation and taking multiple biopsies are essential before intervening in such cases.
FACTORS AFFECTING HIGH-RISK HUMAN PAPILLOMAVIRUS PERSISTENCE AFTER COLD KNIFE CONIZATION PROCEDURE

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Objectives
To determine the clinical, surgical and pathological variables that influence Human papillomavirus (HR-HPV) persistence in patients who had undergone cold knife conization (CKC) for cervical intraepithelial neoplasia (CIN).

Methods
The study was conducted on CKC cases performed between January 2007 and January 2012, who had a positive HPV test preoperatively and was diagnosed with CIN after the procedure. The effects of patient age, HPV type, excised tissue dimensions (width and depth) , post-excisional surgical margin positivity on HR-HPV persistence one year after the initial procedure were assessed.

Results
A total of 253 patients underwent CKC within the study period. Among these, 176 cases (69.6%) were positive for HR-HPV before CKC. Biopsy results revealed CIN in 131 cases, which were included in the study. Mean patient age was 39.1±10.3 (range, 20-71). Most common HPV types were HPV-16 (n:78, 47%) and HPV-18 (n:15, %9). Mean width and depth of the specimen were 30.6±5.9 and 16.1±5.7 mm, respectively. Surgical margins were positive in 20 cases (15.3%). HPV persistence was observed in 20 cases (15.3%). Mean patient age, specimen width and depths were similar between HPV persistent and non-persistent groups (p>0.05). Presence of positive surgical margins after the initial procedure, HPV type did not have an association with HR-HPV persistence (p>0.05).

Conclusions
None of the assessed factors had an association with HR-HPV persistence in our study. Future studies are needed to clarify the risk factors for HR-HPV persistence in patients treated with CKC for CIN.
e-Posters: Miscellaneous

PRIMARY TUBAL CARCINOMA IN A 51-YEAR-OLD POSTMENOPAUSAL WOMAN - A CASE REPORT

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Objectives
An asymptomatic 51-year-old patient, pluriparous, 5 years after menopausis, was admitted to our clinic due to a small tumour mass in the left adnexal region, detected by a routine transvaginal US, 30 mm in diameter, with solid and cystic components, and tumour blood flow with a low resistance index (0.40). Ca 125 slightly elevated (58 iu/l).

Methods
Her weight, blood pressure and sugar level were normal. Also laboratory findings, chest X ray, PAP smear, abdominal US showed no abnormalities. Having suspected an ovarian tumour she was subjected to exploratory laparotomy.

Results
The left tube was dilated in the ampullar and fimbrial area to the length of about 3 cm, and filled with a cauliflower-like tumour mass. Left ovary appeared normal, as well as the uterus and right adnexa and other abdominal organs and peritoneum. Small amount of peritoneal fluid was found, collected and sent for a cytology.
Total hysterectomy with bilateral salpingo-oophorectomy was performed, infracolic omentectomy and pelvic lymphadenectomy. Final pathology showed primary adenosquamous cell carcinoma of the left fallopian tube, limited to the tube, grade 2. FIGO stage was considered as Ic. After the surgery, the patient received six courses of adjuvant chemotherapy with single-agent carboplatin.

Conclusions
This is a rare malignant tumour, out of all carcinomas of the female genitalia, it accounts for 0.3% to 1%, most frequently detected in stage III (49%), with poor prognosis. The five-year survival is approximately 35%, but ranging up to 70% for Stage I.
Four years later our patient still shows no signs of recurrence.
e-Posters: Miscellaneous

LAPAROSCOPIC TRANSPOSITION OF OVARIES WITH EXTRA-PERITONEAL TUNELLING,
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Objectives
The need for ovarian transposition arises in gynaecological and other pelvic cancers such as rectal cancers and sarcoma prior to radiotherapy treatment. Preservation of ovarian function prevents the long-term physical and psychological sequelae of oestrogen deficiency and importantly preserves oocytes for potential biological parenthood through surrogacy. The standard intraperitoneal approach to transposing ovaries leaves the patient with a bridge/ovarian pedicle running from the pelvic brim to the peritoneum of the anterior abdominal wall. Vascular obstruction within this bridge can result in thrombosis leading to ovarian failure. Small bowel loops can herniate through the space between the vascular bridge and the abdominal wall.

Methods
We would like to demonstrate our surgical technique of laparoscopic transposition of ovaries. We create an extra-peritoneal tunnel through which the ovaries are swung laterally and cephalad and then returned to the peritoneal cavity through a fenestration in the peritoneum in the mid-axillary line 8-10 cm above the anterior superior anterior supine.

Our technique involves the following steps:

Step-1: Bilateral salpingectomy.
Step-2: Transecting the ovarian ligament
Step-3: Mobilisation of the ovary with its vascular pedicle above the pelvic brim.
Step-4: Creating a peritoneal tunnel on the lateral abdominal wall
Step 5: Swinging the ovarian pedicle through the tunnel and delivering the ovary back to the peritoneal cavity through a peritoneal fenestration.
Step 6: Suturing the ovary to the peritoneal edge with monofilament nonabsorbable suture.

Results
NA

Conclusions
This technique retains the ovarian vessels in the extraperitoneal space with less traction on the vascular pedicle.
EXTRAABDOMINAL FIBROMATOSIS ARISING FROM VAGINAL STUMP
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Objectives
We report a case of fibromatosis arising from vaginal stump in a 64-year-old woman.

Methods
The patient was referred to our clinic with a hyperechogenic mass on stump by transvaginal ultrasonography, but with normal cytology. She undergone hysterectomy for uterine myoma 15 years earlier. Magnetic resonance imaging revealed a tumor between anterior aspect of vaginal stump and bladder wall, and we surgically resected the mass with single-port laparoscopy.

Results
Histopathological evaluation confirmed out clinical suspicion of extraabdominal fibromatosis.

Conclusions
Fibromatosis is a benign fibrous tumor arising from musculoaponeurotic structure of the entire body. It characterized by infiltrative growth and frequent recurrence, however, unlike sarcoma, it never metastasis. Majority of them occur in anterior abdominal wall, and rare in pelvic cavity, especially extremely in case of primarily arising from vaginal stump. So, we report this case of fibromatosis with a brief review of other reports and literature.
e-Posters: Miscellaneous

PRIMARY EXTRANODAL HODGKIN’S LYMPHOMA PRESENTING AS A PELVIC MASS: A RARE CASE REPORT

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Objectives
To report a case of primary pelvic Hodgkin's lymphoma mimicking a gynecologic malignancy.

Methods
A 75-year-old woman presented with the symptoms of lower abdominal pain and vaginal bleeding. On bimanual examination an ill-defined large pelvic mass was detected. A computed tomography scan revealed large heterogenous mass extending into right parametrial and perivesical tissues and grade two hydronephrosis in the right kidney. There was no enlarged lymph node found in abdomino-pelvic and thoracic CT scan. Serum CA 125 level was slightly elevated to 44.7 U/L. While a cervical cancer was suspected and biopsies taken, a diagnosis was not made and she refused further diagnostic workup. After one and a half year later, she was readmitted to hospital with the symptoms such as fatigue, fever and night sweats. On diagnostic laparoscopy, there was a 100x75 cm retroperitoneal mass which extended from behind the symphysis pubis upward (Figure). The uterus and adnexa were normal. The biopsy was taken from the mass.

Results
Final histopathology revealed a Hodgkin's lymphoma. The clinical stage was determined according to Ann Arbor staging system. Her stage was defined as 4E. Although chemotherapy was started, her medical condition got worse and she died after first cycle of chemotherapy.

Conclusions
This report indicates that, gynecologist should have high level of suspicion for malignant lymphomas in pelvis, as this disease can arise adjacent to gynecologic organs. Laparoscopy might be the gold standard for differential diagnosis of suspicious pelvic masses.
e-Posters: Miscellaneous

THE VALUE OF RANDOM BIOPSIES, OMENTECTOMY AND HYSTERECTOMY IN OPERATIONS FOR BORDERLINE OVARIAN TUMOURS
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Objectives
Borderline ovarian tumors (BOT) are traditionally treated surgically like malignant ovarian tumors, with hysterectomy, omentectomy and multiple peritoneal biopsies in addition to removal of the ovaries. Normal looking tissues are often removed as part of staging. The aim was to evaluate how often the surgeon could identify disease spread during operations for BOT.

Methods
The macro- and microscopic findings in a cohort of these patients from Department of Obstetrics and Gynaecology, Odense University Hospital (OUH), Odense, Denmark were reviewed. Women treated for BOT at OUH from 2007 to 2011 were included. Data were extracted from electronic journal files. Intra-operative assessment of tumor spread (macroscopic disease) was compared with the microscopic evaluation of removed tissues.

Results
75 patients were eligible for this study, 59 (79%) were stage I, 9 (12%) stage II and 7 (9%) stage III. The histologic subtypes were serous (68%), mucinous (31%) and Brenner type (1%). Radical surgery was performed in 62 (83%) patients. 52 (69%) received complete staging. The surgeon could usually identify tumor spread from the appearance of the contralateral ovary and the peritoneum with sensitivities of 88% and 69% and specificities of 90% and 93% respectively. The macroscopic assessment of the uterine surface, omentum and lymph nodes was not as good a predictor of microscopic disease. During follow-up 4 patients (5%) relapsed with no relation to surgical radicalism or the extent of staging procedures.

Conclusions
Ovaries and peritoneal surfaces with a macroscopically normal appearance very rarely contain a microscopic focus of BOT.
ROBOT ASSISTED GYNAECOLOGIC PROCEDURES IN MORBIDLY OBESE PATIENTS

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Objectives
The study aims to evaluate perioperative morbidity in morbidly obese women undergoing robot-assisted surgery for malignant and benign conditions in gynaecology.

Methods
Between February 2011 and March 2013, 123 patients underwent elective pelvic robotic surgery for a gynecologic procedure at a tertiary referral center for gynaecology and gynaecologic oncology. Perioperative morbidity was analyzed descriptively in the subgroup of morbidly obese patients with a body mass index (BMI) of ≥40?kg/m².

Results
A total of 17 patients were considered morbidly obese. 9 patients had the diagnosis of a malignant gynaecologic disease whereas 8 patients had a benign condition. The median BMI was 49 with a range from 40 to 70. Procedures carried out included hysterectomy, adnexectomy, pelvic +/- paraaortic lymph node dissection, omentectomy, and myomectomy. Intraoperatively no visceral organ injury or bleeding complication was observed. One patient required conversion to laparotomy due to inadequate exposure for systematic lymph node dissection. Postoperatively two patients required secondary surgery due to vaginal cuff bleeding and trocar site bowel herniation, respectively. Further postoperative complications included one vaginal cuff hematoma and one patient with wound healing complications after secondary laparotomy.

Conclusions
Overall our results suggest that robot assisted procedures in gynaecology and gynaecologic oncology can be performed with acceptable morbidity in morbidly obese patients.
THE BENEFIT OF CANCER FOLLOW-UP FOR SURVIVAL: SINGLE INSTITUTION EXPERIENCE STUDY

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Objectives
The aim of our study was to compare the survival differences between asymptomatic and symptomatic patients at the time of relapse.

Methods
Retrospective cohort analysis. Women were routinely followed-up with the combination of symptom enquiry, physical examination, and laboratory and imaging techniques. Survival curves were calculated using the Kaplan-Meier method. Mean times were compared using the log-rank test and medians were compared with Wilcoxon-Rank test.

Results
All women treated for vulvar, cervical, endometrial and ovarian cancer at our institution between 2003 and 2012 were included in this study (59 patients with vulvar, 216 with cervical, 311 with endometrial and 177 with ovarian cancer). We identified 21 patients with recurrent vulvar cancer (13 symptomatic and 8 asymptomatic at the time of recurrence), 45 patients with recurrent cervical cancer (33 symptomatic and 12 asymptomatic), 50 patients with recurrent endometrial cancer (37 have symptomatic and 13 patients asymptomatic), 57 patients with recurrent ovarian cancer (23 symptomatic and 34 asymptomatic). There were no statistically significant differences between the mean time of survival after recurrence diagnosis between symptomatic and asymptomatic patients: in vulvar cancer 23,9 versus 29,2 months, p=0,181, in cervical cancer 13 versus 10,6 months, p=0,379, in endometrial cancer 22,2 versus 27,5 months, p=0,265 and in ovarian cancer 18,9 versus 18,4 months, p=0,861.

Conclusions
There were no survival differences between asymptomatic and symptomatic patients at the time of relapse. We need more effective follow-up programmes as to survival benefit for the patients with vulvar, cervical, endometrial and ovarian cancer.
Robotic Retroperitoneal Surgery Advantages and Disadvantages

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Objectives
Paraortic lymph node dissection is one of the possible diagnostic procedures in the management of endometrial or advanced cervical cancer. It is the best way to establish radiation field, surgical removed nodes are affected in 26.1% of PET negative nodes. The indication of robotic assisted retroperitoneal access for node dissection is still controversial, mainly due to the complexity of the procedure and the time needed.

Methods
10 patients underwent robotic assisted retroperitoneal lymphadenectomy. We describe our proposal for port placement as well as surgical aspects. We place the 12mm balloon trocar for optics, 2 finger above and medial to the antero-superior iliac spine. We put a robotic 8 mm trocar below the balloon trocar, as caudal as safe insertion allows. Assistant trocar is located on a conventional position. We locate a second robotic arm as high as possible between the anterior axillar line and midclavicular line (with robotics we can approach the axillar line and safely avoid peritoneal recessions).

Results
Mean operative time was 333 minutes, mean number of lymph nodes retrieved was 16.3 (15-18). No patients presented intra or post-operative complications, required transfusion, or reoperation. We found some disadvantages in the surgery, the unavailability of advanced sealing devices for our model (DaVinci S), that makes more difficult the excision of left infrarenal nodes, the constrained operating field in retroperitoneal access, the loss of haptic perception and the cost.

Conclusions
We found little advantages in doing paraortic lymphadenectomy with retroperitoneal access although it is a safe and feasible technique.
e-Posters: Miscellaneous

ANALYSIS ON THE STATISTICS OF THE ARTICLES PUBLISHED IN THE KOREAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

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Objectives
Our purpose was to assess the statistical analysis in studies published in the Korean Journal of Obstetrics and Gynecology, as well as documentation of appropriateness in applying statistics.

Methods
All papers from January through December 2001 issues in the Korean Journal of Obstetrics and Gynecology were reviewed in terms of the application of statistics. Each paper was given a rating for the thoroughness of the listing of applied statistics and a rating for the appropriateness of statistical usage, when possible.

Results
Of the 370 available articles, 162 consisted of studies void of statistics, 4 of which required statistics or claimed significance without the use of statistics. Therefore 208 articles were included in the final analysis. Of 147 articles presenting descriptive statistics, 25 articles (17.0%) could be classified as having appropriate usage of statistics. The most common statistical methods included Student’s t-test. The choice of statistical method was considered to be suitable in 78 of the 183 (42.6%) articles presenting statistical inferences. Most papers were noted to have one or more statistical errors.

Conclusions
Most of the articles contained examples inappropriately used statistics. This finding warrants a policy of statistical review to be instituted.
EXPERIENCE OF PRETREATMENT APPROACHES WITH SINGLE PORT LAPAROSCOPIC SURGERY IN GYNECOLOGIC CANCER: A PILOT STUDY

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Objectives
The purpose of this study is to evaluate the feasibility and safety of pretreatment single port access (SPA) laparoscopy in patients with uncertain gynecologic malignancy.

Methods
We report our experience with 9 patients who underwent SPA laparoscopic surgery followed by chemotherapy or concurrent chemoradiation therapy. Single port channel system consists of the Alexis wound retractor (Applied Medical, CA, USA) and a 7 and 1/2 surgical glove. In terms of postsurgical medical treatment, 6 cases received neoadjuvant chemotherapy, 2 cases received palliative chemotherapy and 1 case received concurrent chemoradiation therapy based upon widely acceptable criteria.

Results
Out of 9 patients, diagnostic peritoneal excision was performed for 7 patients with ovarian cancer, right salpingo-oophorectomy and peritoneal excision for one patient with peritoneal cancer and pelvic lymph node debulking for one patient with locally-advanced cervical cancer (Figure). Median operation time and postoperative hospital stay were 21 minutes (range, 18 to 42 min) and 3 days (range, 3 to 5 days), respectively. Median time interval between the end of procedure and the start of medical treatment was 8 days (range, 7 to 14 days). There were no perioperative complications.

Conclusions
This pilot study of pretreatment SPA surgery in gynecologic cancer is feasible and safe compared with conventional laparoscopy. Single port laparoscopic surgery can be a therapeutic option for pretreatment intervention in women with advanced gynecologic cancer who are required to receive medical therapy.
EXPERIENCE WITH PRIMARY NON-GERM CELL GYNAECOLOGIC MALIGNANCIES IN YOUNG WOMEN IN A GYNAECOLOGICAL ONCOLOGY CENTRE.

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Objectives
To describe the epidemiologic characteristics of non-germ cell gynaecological malignancies (NGCGM) in patients 30 years or younger over a 23 year period.

Methods
We searched the pathology database and electronic and medical records to identify patients.

Results
We identified 48 patients with NGCGM. Eleven patients were diagnosed in 1990-2000, 26 patients in 2001-2010 and 11 patients from 2011 till date. 16 patients were 25 years or younger and 32 patients were in the 26-30 age group. The most common gynaecological site in the 25-year age group was ovary (10 out of 16 patients), followed by cervix (3 out of 16 patients), then vagina (2 out of 16 patients) and one endometrium. The two vaginal cancers were rhabdomyosarcomas. The most common site in the 26-30 year age group was cervix (17 out of 32 patients), followed by ovary (15 out of 32 patients). Four patients had Krukenberg cancers of the ovary in the 26-30 age group compared to one patient in the 25 year group. The first presentation of three patients to us in the 25-year age group was with a recurrent tumour. All cervical cancers except one were screen-detected, the exception was a clear cell carcinoma. In ovary, mucinous cystadenocarcinoma of the intestinal type was the most common followed by serous cystadenocarcinoma.

Conclusions
NGCGM cancer is rare in young patients. While all but one cervical cancer was screen detected it is of concern that routine cervical cancer screening is now not recommended before the age of 25.
RETROSPECTIVE ANALYSIS OF TRABECTEDIN INFUSION IN AN OUTPATIENT SETTING BY PERIPHERALLY INSERTED CENTRAL VENOUS CATHETERS (PICC): A MULTICENTRIC ITALIAN EXPERIENCE.

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Objectives
A central venous catheter (CVC) is highly recommended for T administration. However, CVC put patients at risk of catheter-related complication and have a significant budget impact. The most frequently used CVC are subcutaneously implanted PORT-chamber catheters (PORT), while PICC are relatively new. We evaluate the cost efficient ratio between the use of PORT and PICC.

Methods
We reviewed data about CVC use in trabectedin treated pts in 6 Italian centers.

Results
Data on 102 trabectedin treated patients (22 with sarcoma, and 80 with ovarian cancer) were recorded. In 45 pts T was infused by a PICC, inserted by trained nurses with an ultrasound-guided technique at the bed-side, while in 57 pts a PORT, requiring a day surgery procedure in the hospital by a surgeon, was used. Device’s dislocations and infections were reported in 4 pts, equally distribute between pts with PORT or PICC. Thrombosis occurred in a single patient with a PORT. Complications requiring devices removal were not reported during any of the 509 cycles of therapy (median 5; range, 1-20). Nor PICC misplacement nor early malfunctions were experienced during T infusion. Cost efficient ratio favor PORT over PICC, but only when the device is used for more than 1 years. Pts showed a good acceptance of PICC, but data on quality of life have not been specifically collected.

Conclusions
Our data suggest that T infusion by PICC in an outpatient setting is safe and well accepted, with a preferable cost efficient ratio than PORT in pts requiring a short standing of the device.
HOW OLD IS "TOO OLD" FOR HYSTERECTOMY?

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Objectives
With the persistent aging of the population, we encounter the issue of complex abdominal surgeries in the elderly more often. Most of the data regarding perioperative morbidity and mortality deals with younger women. Hence, the Data on the operative problems of women older than 75yo is scant.

Objective – To compare operative results of women older than 75 who had abdominal versus vaginal hysterectomy, and try to characterize the risk factors for morbidity and mortality among this age group.

Methods
A retrospective analysis of hysterectomy results at Hadassah-Hebrew University Medical Center, a tertiary referral center during the years 2000-2011.

We analyzed the pre-operative, operative and post-operative data for each patient and the outpatient follow up for further information regarding morbidity and mortality according to its definition by the ICD9.

Results
135 patients above the age of 75 were included: 65 had abdominal/laparoscopic hysterectomy and 70 had vaginal hysterectomy. The mean age was similar between the groups (78) as well as the WHO performance scale. There was no statistical difference in the rate of complications between the groups (15% vs. 30% p=0.59). Univariate analysis showed that the number of comorbidities (above 1.8), duration of operation (above hour and a half) and length hospital stay (above 13 days) influenced the morbidity but not the age of the patient (p=0.947).

Conclusions
- The patient's age is not a risk factor for operative or postoperative morbidity. Hence if the patient s in good overall medical condition she should receive the optimal treatment regardless her age.
DESMOPLASTIC SMALL ROUND CELL TUMOR IN WOMAN IN REPRODUCTIVE AGE

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Objectives
Desmoplastic small round cell tumor (DSRCT) is a rare and highly aggressive mesenchymal tumor. DSRCT mainly develops in adolescent and young adults. We want to present DSRCT in women in reproductive age as case report.

Methods
A 37-year-old woman, gravid 2, para 2, presented a distended abdomen with ascites and loss of weight. A clinical examination and magnetic resonance imaging demonstrated a massive tumor in the abdomen with unknown origin, 30 cm in diameter and a lot of implants on peritoneal surface. On the right side on the skin surface near inguinal canal was an enlarged lymph node which was taken as the pre-operative sample. The specimen showed a rhabdomyosarcoma with unknown origin. The cytology of ascites showed malignant cells with unknown origin also. The gynecology oncology team agreed for neo adjuvant chemotherapy for three cycles and after evaluation of the tumor size.

Results
The size of the tumor was unchanged and we decided to do an operation. During the surgery, debulking operation was performed. Residual disease was on the head of the pancreas and right glandular suprarenalis. After the operation we agreed for 3 more cycles of adjuvant chemotherapy with the same drugs. Three weeks after the surgery patient got bowel skin fistula and she got fourth cycle of chemotherapy.

Conclusions
There are some new procedures in the treatment of DSRCT but without evidence of clinical utility. Patients with successful surgical debulking and chemotherapy appear to have the best outcome. Techniques such as HIPEC or IMRT needs to be clearly defined.
A REVIEW OF GYNECOLOGIC ONCOLOGY CASES ABOVE 65 YEARS OLD WITHIN A 6-YEAR PERIOD IN A TERTIARY REFERRAL HOSPITAL IN ANKARA, TURKEY

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Objectives
Gynecologic malignancies are generally encountered in second half of lifetime. Geriatric period is a term defined for patients above 65 years of age. Many systemic problems create a barrier for the clinician in the treatment process in oncology practice.

Methods
Institutional cancer registry database was reviewed for all malignant cases that were managed in our center’s gynecologic oncology department within a 6-year period and patients above 65 years of age determined and examined.

Results
A total of 1646 malignant cases were identified during a six year period. 304 of patients were above 65 years old. Endometrial cancer including sarcoma was diagnosed in 147 (48.6%) cases, ovarian cancer in 65 (21.3%) cases, cervical cancer in 40 (13.1%) cases, vulvar cancer in 16 (5.2%) cases, tubal cancer in 5 (1.6%) cases, primary peritoneal carcinoma in 11 (3.6%) cases, vaginal cancer in 6 cases (1.9%), breast cancer metastasis in 5 cases (1.6%), gastrointestinal cancer in 5 cases (1.6%), urinary bladder cancer in 1 cases (0.3%), lymphoma in 1 cases (0.3%), liposarcoma in 1 cases (0.3%) and malignancy of unknown primary in 1 cases (0.3%).

Conclusions
In tertiary referral centers, various gynecologic oncological malignancies are encountered. Elderly is a period that malignancy incidence increases. Many systemic diseases increase not only the risk of surgery and anesthesia but also chemo- radiotherapy and healing process. For early diagnosis and better clinical results routine gynecological examination and effective screening is crucial.
INCIDENTAL DETECTION OF A TUMOR WITH GASTROINTESTINAL ORIGIN ON THE SURFACE OF LEIOMYOMA

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Objectives
Metastatic adenocarcinoma to the uterus from gastric cancer is rare, and the clinicopathologic features of this metastasis are unclear.

Methods
47 years old patient was admitted to our clinic with a complaint of abdominal pain. In her medical history admission to a gastroenterology clinic with same complaint about 3 months ago was detected. Imaging studies including endoscopy of upper gastrointestinal system revealed no pathology except a subserous myoma in 6 cm diameter. She was referred to our clinic with diagnosis of myoma uteri

Results
Patient was underwent laparatomy for myomectomy in our clinic. Intraoperative investigation revealed a subserous myoma 6 cm. in diameter which is located subserously in the fundus of the uterus. Because the frozen section investigation revealed benign histo-pathology no further process was performed. Final pathologic investigation showed metastasis of adenocarcinoma with signet-ring cells and extracellular mucin in the surface of myoma. Pathology report denoted the primary of the metastasis as gastric origin.

Conclusions
Metastasis of gastrointestinal system adenocarcinomas to genital system is usually seen in overy. Single uterine metastasis of signet-ring cell tumors are extremely rare. Simple myomectomy is sometimes a burden for a gynecologic oncologist but it should be kept in mind that even if these kind of metastasis like in our case are extremely rare, the clinician should always be alert about these rare conditions.
A REVIEW OF GYNECOLOGIC ONCOLOGY CASES BELOW 40 YEARS OLD WITHIN A 6-YEAR PERIOD IN A TERTIARY REFERRAL HOSPITAL IN ANKARA, TURKEY

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Objectives
Gynecologic oncology is a medical discipline with high rate of evolution. With the introduction of technological, technical and medical improvements, many surgeries that were once associated with high morbidity and mortality are carried out with low incidence of complications. Gynecologic cancer diagnosis in reproductive period can be catastrophic for the patient and his family as well.

Methods
Institutional cancer registry database was reviewed for all malignant cases that were managed in our center’s gynecologic oncology department within a 6-year period and patients below 40 years of age determined and examined.

Results
A total of 1646 malignant cases were identified during a six year period 312 of cases were below 40 years of age. Among these young reproductive patients cervical cancer in 162(%52) cases, ovarian cancer in 87(%28) cases, endometrial cancer including sarcoma was diagnosed in 35(%11) cases, gastrointestinal cancer in 11(%3.5) cases, vulvar cancer in 7(2.2%) cases, breast cancer in 3 cases, (0.9%) primary peritoneal carcinoma in 2(2.3%) cases, breast cancer metastasis in 2(0.6%) cases lymphoma in 1 cases(0.3%) and malignancy of unknown primary in 2 cases(0.6%) 50 of 87 ovarian cancer patients were epithelial in origin and 37 of them were non epithelial origin.

Conclusions
In tertiary referral centers, various gynecologic oncological as well as non-gynecologic malignancies are encountered. Multidisciplinary approach is crucial especially in cases with non-gynecologic tumors However overall survival is seemed to be the most important goal of the treatment, preservation of reproductive capacity should be the other challenge for the oncologist.
THE IMPACT OF NUTRITIONAL PROFILE ON THE MORBIDITY AND LENGTH OF HOSPITAL STAY IN GYNECOLOGICAL CANCER PATIENTS.

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Objectives
The aim of the study was to assess the preoperative nutritional status (NS) and to investigate the association with clinical outcomes and time of hospitalization, in surgical treated patients.

Methods
In a retrospective cohort study, 190 women who underwent surgical treatment of breast or gynecological cancer at a university hospital, in the period of August 2003 and April 2005, had their preoperative body mass index (BMI), nutritional subjective global assessment (SGA) and physical status (ASA) evaluated and the frequency of perioperative complications, blood transfusion, admissions to the ICU and length of hospital stay recorded. Statistical analysis consisted of: uni or multivariate Cox regression for factors associated with complications and polotomic logistic analysis for factors associated with length of stay, being adopted the significance level of 5%.

Results
Mean age was 53.48±13.9; 18.3% of the patients were ASA1, 65.1% were ASA2 and 16.6% were ASA3-4; 22.1% presented BMI ≥ 30kg/m2 e 77.9 presented BMI < 30kg/m2. According to SGA 75.3% were euthrophic and 24.7% malnourished. The physical status and the duration time of anesthesia were related to the admissions to the ICU (p= 0.005 and p= 0.0001, respectively). The length of hospital stay correlates with physical status (ASA), duration time of anesthesia and staging of disease (p= 0.0001, p= 0.0004 and p= 0.0039 respectively). Malnutrition diagnosed by SGA was associated with an increase of 12 times in the risk of occurrence of two or more complications in the intraoperative period (p= 0.025).

Conclusions
These results suggest that nutritional profile should be assessed in ASA 3-4 patients routinely.
RETROSPECTIVE REVIEW OF CASES WITH GYNAECOLOGICAL CARCINOSARCOMA; A CLINICO-PATHOLOGICAL STUDY
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Objectives
Introduction: Gynaecological carcinosarcomas (MMMT—malignant mixed Müllerian tumours) are highly aggressive, rare, biphasic tumours. Recurrences occur in over half of patients after primary surgical and adjuvant therapy.
Introduction: Gynaecological carcinosarcomas (MMMT—malignant mixed Müllerian tumours) are highly aggressive, rare, biphasic tumours. Recurrences occur in over half of patients after primary surgical and adjuvant therapy.

Aim: To review our Centre experience with different Gynaecological carcinosarcomas with regards to demographics, presentation, cancer site and type, management and outcome for these women.

Methods
Study methodology: We identified the cases from the cancer database during the study period of four years from 2009 to 2012, at the Gynaecological Oncology Centre at Wolverhampton (GOCW). Relevant information collected from case notes and electronic databases.

Results
Results: A total of 31 cases were identified during this period. Age ranged from 21 to 98 years, with a mean of 65 years. Abnormal vaginal bleeding was the most common presentation. The primary site of cancer was from uterus in majority, and 5 cases from ovary and 1 from cervix. Primary site was unknown in two women who presented at advanced stage. 42% of uterine carcinosarcomas had laparoscopic hysterectomies. 10% women needed primary bowel surgery. 5% were unsuitable for primary surgery due to advanced presentation. 2/3rd of women completed adjuvant therapy in the form of chemo or radiotherapy. 25% of women sadly died within one year of diagnosis. 22% developed recurrence within two years of primary treatment.

Conclusions
Conclusions: The GOCW experience with Gynaecological carcinosarcomas is in keeping with previously published data. A multidisciplinary approach is essential for optimal individualised management of these rare tumours.
LEEP CONIZATION AND POSITIVES MARGINS, EXPERIENCE IN A SOUTHERN SECTOR HOSPITAL IN SANTIAGO OF CHILE

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Objectives
To describe the results using cold knife conization after an loop electrosurgical excision procedure (LEEP) that results with positive microscopic margins.

Methods
We retrospectively analyzed records of 167 patients who underwent at LEEP in the Parroquial Hospital of San Bernardo, Santiago, Chile, who were treated and followed during 2011 and 2012.

Results
Of 167 patients who underwent at LEEP, 110 (65.9%) had negative and 57 (34.1%) had positive resection margins. Of the 57 patients with positive margins 28 (49.1%) were treated with a cold knife conization, while the rest of the patients were followed up. Residual disease was found in 13(46.4%) patients which 9 (69.2%) had negative and 4 (30.8%) had positive microscopic edges. These last 4 patients subsequently underwent hysterectomy. Regarding 9 patients with negative microscopic margins, 1 patient was treated with hysterectomy because she had history of ovarian cancer while the remaining 8 patients were not performed additional procedures.

Conclusions
LEEP is a feasible procedure in an outpatient clinic. Of those who had positive margins and went for a second cone, 46% had residual disease after a new cone biopsy. According with our series, we justify a new procedure after a LEEP conization with positive edges to ensure resection of the entire disease.
CHYLOUS ASCITIES AND LYMPHOCESTS: COMPLICATIONS OF LAPAROSCOPICAL PELVIC AND PARA-AORTIC LYMPHADENECTOMY. A CASE REPORT MANAGEMENT.


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Objectives
To present the medical treatment of chylo ascities and the laparoscopic management of lymphocyst in a patient after a laparoscopic surgery in a Fallopian tube carcinoma.

Methods
We report a case of a 61-year-old woman with a high grade fallopian tube adenocarcinoma with presurgical stage IV. After chemotherapy was taken to the operating room for a complete oncological laparoscopic surgery (hysterectomy and BSO, pelvic and para-aortic lymph node dissection and omentectomy).

The seventh day after surgery developed chylous ascities (drain loss of 400ml/24 h) treated with conservative measures: maintenance of a tube drain in abdominal cavity, octreotide and total parenteral nutrition up to 5 days decreasing the drain loss to <50 ml/24 h.

On postoperative day twenty one, the patient presented fever and was diagnosed by TC scan of two aortic and one right pelvic lymphocysts. Despite five days antibiotic treatment, the temperature did not descend and therapeutic laparoscopy was performed including adhesiolysis and lymphocyst aspiration.

Six days after the second surgery, the patient was discharged in good condition.

Results
We presented the videos of the two laparoscopic surgeries: the transperitoneal para-aortic lymphadenectomy and the lymphocysts remove.

Conclusions
Chylous ascites is a very infrequent postoperative complication after retroperitoneal surgical procedure. The treatment is primarily conservative, including the use of a low-fat diet, medium chain triglyceride intake, paracentesis, total parenteral nutrition, and somatostatins.

Lymphocysts are a possible complication after oncology surgery and, although they are usually asymptomatic, could produce pain or fever. Laparoscopic drainage could be an adequate treatment in symptomatic lymphocysts.
e-Posters: Miscellaneous

CASE REPORT: A RARE FINDING OF A SYNCHRONOUS ADENOCARCINOMA AND LEIOMYOSARCOMA OF THE UTERUS.
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Objectives
We report a case of well differentiated endometrioid adenocarcinoma of the endometrium and Grade I leiomyosarcoma in a 44y.o. Caucasian woman. (Negative family history, Menarche 10y., Nulliparous, regular gyn. examinations-Pap smears, Appendicectomy, left Salpingo-Oophorectomy due to serous cyst torsion at 14y).

Methods
In 2007 a curettage due to metrorragia revealed an endometrial polyp, followed by a second curettage in 2/2008 which showed complex atypical hyperplasia. Despite progesterone treatment p.o. and later IUD, no regression was observed (curettage 10/2008).

In 4/2009 she was referred to our Gyn-Onc Dept after an intrauterine biopsy, revealing Uterine Adenocarcinoma.

Pre-op assessment for uterine malignancy led to Hysterectomy, right Adnexaectomy and bilateral Pelvic lymphadenectomy.

Intraoperative pathological gross examination revealed a circumscribed intramural nodule with a greatest dimension of 25 mm and the frozen section revealed superficial myometrial invasion. Day 5 post-op the patient was discharged in good condition.

Results
Pathological examination showed: 1)centrally to the uterus a well differentiated endometrial endometrioid carcinoma (Ø 18mm, 4mm invasion), ER and PR positive and 2)a totally intramural Grade I leiomyosarcoma (Ø25mm).

The leiomyosarcoma displayed necrosis, more than 10 mf/hpf and expressed ER. Adnexal examination revealed salpingitis and insignificant ovarian findings. All 12 pelvic lymph nodes were negative for metastases. The patient has N.E.D. 48 months after a regular follow up (Clinical, laboratory, imaging findings).

Conclusions
SEXUAL HEALTHCARE IN CANCER PATIENTS: AWARENESS AND ROLE PERCEPTIONS OF RADIATION THERAPISTS.

A. turner

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Objectives
Cancer patients report dissatisfaction with care they receive in relation to changes effecting intimacy and relationships. Health care professionals (HCPs) describe barriers in providing support in these areas due to lack of time, training, education and privacy. Radiation therapists (RTs) play a key role in cancer care but there is little evidence of their role in sexual healthcare. This project investigated awareness levels and role perceptions of RTs in sexual health issues related to cancer patients receiving radiation therapy.

Methods
A mixed methods approach was used for this investigation. Quantitative data was collected via an online questionnaire developed from the literature. 284 RTs from two large cancer centers were eligible to participate; 84 responded (29%). Two focus groups were conducted with 15 volunteer RTs to validate questionnaire data and further explore the topic. Content analysis was employed to identify themes from the qualitative data.

Results
RT respondents acknowledge the complexity of sexual health issues; 85% recognized that issues can occur across all cancer sites. 92% agreed that sexual health is important for quality of life. Barriers identified to RT provision of sexual healthcare are similar to other HCPs i.e. environment, time, lack of training and education.

Conclusions
Barriers to RT involvement in sexual healthcare may be resolved through training and education. Provision of private space for patient education may provide a more conducive environment for sexual healthcare interactions. Involvement of RTs in sexual health care may increase services for cancer patients and improve patient satisfaction in this domain.
e-Posters: Miscellaneous

ROBOTIC PARAAORTIC LYMPHADENECTOMY AND COMPLEX ONCOLOGICAL PROCEDURES. LEARNING CURVE, ADVANTAGES AND DISADVANTAGES.
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Objectives
Complex oncological procedures are increasingly performed robotically in hospitals where this resource is available. We analyze our learning curve and surgical advantages and disadvantages.

Methods
There are included all robotic oncological pelvic and aortic lymphadenectomies performed from November 2011 to April 2013. There were multiple oncological surgeries including ovarian, cervical and endometrial cancer. Cervical cancers were advanced staging cases and all endometrial cancers were more than IB FIGO stages or with lymphovascular space involvement, those, according to our institutional protocol, require aortic lymphadenectomy.

Results
16 patient underwent robotic assisted lymphadenectomy (RAL), mean body mass index was 31.66 (23.6-41.5). There were 10 retroperitoneal, 5 transperitoneal and 1 conversion to open surgeries. We obtained 22.3 nodes per patient, 12.8 (6-25) pelvic nodes and 11 (4-21) paraortic nodes. Mean time operative time, skin to skin, was 328 minutes (270-410).
Many advantages were found in robotic surgery such as better equipment precision, high definition 3D optics and downsizing of movements. It allows surgeon to improve the inter-aortocave node excision in the trans and the retro peritoneal access and the latero-aortic node dissection in the transperitoneal approach. However, the lack of trocar versatility, the greater size and number of ports, the more laborious omentectomy, the worse intestinal movement and the constrained retroperitoneal access add some difficulties. Surgical time is increased due to docking time, des-docking time and downtimes.

Conclusions
RAL is a feasible and available technique for those who are used to oncological laparoscopy. The closer view and dissection of the structures facilitates its feasibility.
THE TREATMENT OF PARANEOPLASTIC NEUROLOGICAL SYNDROMES IN GYNECOLOGICAL AND BREAST TUMORS. WHAT MAY WE LEARN FROM AVAILABLE REPORTS?

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Objectives
Paraneoplastic neurological syndromes (PNS) in females are frequently related to gynecological and breast neoplasms. It is not clear how surgery or immunotherapy based management influence patient’s prognosis. We examined multiple studies in an attempt to determine the relationship between immunotherapy, tumor treatment and the outcome in PNS females.

Methods
We analyzed the reports of PNS in gynecological and breast tumors. The studies were located via a search of PubMed databases. Clinical manifestation, onconeuronal antibodies, immunotherapy, PNS outcome and death were considered. We have identified 42 studies (64 patients). Efficacy outcome of the applied treatment was defined as “no improvement”, “stable”, “partial”, “improvement” of PNS. Cox proportional-hazards regression, multiple regression and logistic regression analyses were performed with the use of licensed MedCalc software.

Results
Cox proportional-hazards regression analysis in the model including effects of intravenous immunoglobulins (IVIG), steroids, plasma exchange, cyclophosphamide, surgery and chemotherapy on patients death showed that only tumor excision influenced survival (P=0.0176). Among cancer therapy, surgery was also the only effective treatment (P=0.0219). If the model included IVG, plasma exchange and steroids, only the last treatment was effective (P=0.0109). In logistic regression analysis we have identified age as the factor negatively (P=0.0352) and the diagnosis of gynecological tumor (P=0.0417) as the factor positively affecting the outcome in the model including IVIG, steroids, plasma exchange and cyclophosphamide treatment.

Conclusions
The analyzed reports indicate the beneficial effect of surgery on the outcome of PNS. Steroids may improve an outcome in PNS patients.
e-Posters: Organisation of Gynaecologic Cancer Care

GYNECOLOGICAL CANCER INCIDENCE AND SURVIVAL IN BULGARIA FOR PAST 20 YEARS

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Objectives
In Bulgaria, there are over 3300 diagnosed with gynecological cancer annually. The aim of the study was to estimate the incidence, mortality and survival for the past 20 years.

Methods
Gynecological cancer in Bulgaria during the period 1993-2009 according data from Bulgarian National Cancer Registry were analyzed. Age-standardized incidence and mortality rates per 100 000 persons were estimated by Joinpoint regression. Life table method for gynecological cancer survival was used.

Results
Cervical cancer incidence was increased from 795 in 1993, to 1072 in 2009, with age-standardized rates from 14,0 in 1993 to 18,7 in 2009 per 100 000. The mortality was increased from 4,8 to 5,4 per 100 000. Endometrial cancer incidence was increased from 943 to 1278, with age-standardized rates from 13,8 to 17,3 per 100 000. The mortality was increased from 2,4 to 2,9 per 100 000. Ovary cancer incidence was increased from 657 to 862, with age-standardized rates from 10,6 to 13,0 per 100 000. The mortality was increased from 4,6 to 5,2 per 100 000. Survival for all states was increased: from 49,7% to 54,5% for cervical cancer, from 66,6% to 69,0% for endometrial cancer, and from 35,4% to 40,3% for ovary cancer.

Conclusions
Our results indicated the difference between gynecological cancer incidence and mortality in Bulgaria and other European countries. The economic problems and health politic in Bulgaria are the most important cause of absence the early detection and adequate treatment of the gynecological cancer.
FERTILITY PRESERVATION IN ONCOLOGIC PATIENTS AND REFERRAL CANCER CENTRE: A MODEL OF ORGANISATIONAL SET UP

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Objectives
Cancer occurring in reproductive age accounts for approximately 10% of all diagnosed cancers.
The trend of postponing childbearing in the last two decades and increased survival of oncologic patients lead to an increasing number of women requiring fertility preservation.
Gonadal shielding, ovarian transposition, oocytes/ embryo cryopreservation are standard fertility preserving therapies. Oocytes cryopreservation, which has been recently recognized a standard practice in oncologic patients, can be combined with ovarian tissue cryo-banking, with a small, but clinically relevant, reported number of successful pregnancies.

Methods
We present our organizational set up dedicated to the service of fertility preservation born inside Humanitas Cancer Centre (Rozzano, Milano).
Our Institute offers counseling and cryopreservation to male and female patients since 2010. The experience of these years and the coexistence, probably unique, in the same Institution of several oncologic referral departments and one of the larger infertility units in our country, running over 3000 ART treatments a year, has stimulated us to create a more structured lay-out coordination into the activities of our Cancer Center.

Results
This project has been carried out by multidisciplinary team composed by Oncologists, Gynecologists expert in Reproductive Medicine and in Oncology and Psychologists with the aim of providing accessibility to fertility sparing techniques, multidisciplinary management and special follow up program to women affected by cancer during childhood and reproductive age

Conclusions
Our organization guarantees the possibility of providing adequate information and integrated multidisciplinary approach prior, during and after oncologic treatment to every patient potentially eligible for fertility preservation.
e-Posters: Quality of Life after Treatment of Gynaecologic Cancer

THE EFFECT OF ORAL EVENING PRIMROSE OIL ON MENOPAUSAL HOT FLASH: A RANDOMIZED CLINICAL TRIAL
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Hot flash is the most common vasomotor symptom with a great concern to women seeking medical treatment. Although, the efficacy of estrogen, as hormone replace therapy (HRT), in hot flash well established, is not recommended in women with history of breast or endometrial cancer, thromboembolic disease, active liver disease. Therefore, an effective and safe alternative to HRT is required. The aim of this study was to compare efficacy of evening primrose oil (EPO) with placebo in improvement of menopausal hot flash.

Methods
In a 6-week randomized clinical trial, a total of 56 menopausal women aged 45-59 years selected. The patients asked for their hot flash characteristics and responded to HFRDIS (hot flash related daily interference scale) questionnaire before and after the intervention. The participants were randomly assigned to take two capsules per day of placebo or EPO (500 mg oral soft gel) for continuous 6 weeks. The improvement in hot flash was compared between two groups.

Results
The improvement in hot flash frequency, severity, duration were 39%, 42%, 19%, in EPO group vs 32%, 32%, 18% in placebo group, respectively. Although, only hot flash severity was significantly better in EPO group vs placebo group (p< 0.05), all 3 characters of hot flash were ameliorated in first arm (not significant). All HFRDIS score were significantly improved in two groups, but in social activities, relations with others, and sexuality were significantly superior to placebo group (p< 0.05).

Conclusions
The severity of hot flash might be decreased using EPO as non-hormonal treatment, larger studies needed.
e-Posters: Quality of Life after Treatment of Gynaecologic Cancer

HORMONE REPLACEMENT THERAPY IN REHABILITATION OF PATIENTS WITH GYNAECOLOGICAL MALIGNANCES
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Objectives
Over the last few years the number of patients with gynecological malignancies in reproductive and premenopausal age has been permanently increasing. In majority of cases radical treatment results in termination of ovarian function and development of postovariectomy syndrome.

The aim of the study was to follow the degree of postovariectomy syndrome after radical treatment and evaluate efficacy of hormone replacement therapy (HRT) in patients with gynecological malignancies.

Methods
The results of HRT were analyzed in following groups of patients: 35 patients with endometrial cancer, 53 patients with cervical cancer after surgical treatment (or surgical treatment + irradiation); 15 patients with ovarian cancer after complex treatment.

The group of patients included people of the age range from 23 to 53. The duration of treatment after an operation lasted 6.7 ± 1.2 months. Transdermal HRT was prescribed to patients during 3-4 months after operation following by ordering the tablets. The duration of the treatment amounted from 3 months to 5 years. The evaluation of HRT effectiveness was made according to modified menopausal index. All patients before surgical treatment had menstruation before surgical treatment.

Results
Vegetative-vascular disorders of different levels have been diagnosed in every patient at the beginning of observation. HRT was found to be effective in correction of the menopausal symptoms. Urogenital disorders (dryness in vagina, dysuric phenomenon) appeared to be decreased by 65-70%.

Pronounce psycho–emotional disorders in patients were decreases by 60-63% as compared with control group.

Conclusions
Prescription of HRT in patients with gynecological malignancies supports increased quality of life.
SEXUAL ACTIVITY AND FUNCTION IN PATIENTS WITH GYNECOLOGICAL MALIGNANCIES AFTER COMPLETED TREATMENT


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**Objectives**

Sexual activity (SA) and function (SF) after completion of treatment are central for quality of life (QoL) in women affected by gynecological cancers. Aim of this study was to analyse the SA, SF and QoL of women with primary cervical-, endometrial- or vulvar cancer compared to patients with breast cancer.

**Methods**

In a multicenter cross-sectional study, women, aged 18-70 years, were surveyed at least 12 months after completion of primary therapy for cervical-, endometrial- or vulvar cancer. A cohort of breast cancer patients served as control. Data was collected through validated questionnaires.

**Results**

Patients in the gynecological cancer group (GCG) (n=77) and the breast cancer group (BCG) (n=186) were of similar age (median 55 vs. 56.5 years) and menopausal status (90.5% vs. 88.6%). 41.3% of the patients in the GCG were sexually active and 45.8% in the BCG. The most common reason for sexual inactivity in the GCG was 'the presence of a physical problem' (40.9% vs. 37.8%) whereas in the BCG 'low interest in sex' was most common (44.9% vs. 34.1%). Overall, there was a better SF in the GCG with a trend towards higher sexual satisfaction (p=0.09), significantly more pleasure (p=0.02) and less discomfort during intercourse (p=0.03). QoL and overall health were not significantly different between the two groups (EORTC-QLQ-C30 score 68.25 vs. 67.50) and comparable to populations without cancer.

**Conclusions**

The high number of sexually inactive women indicates that women suffer from persistent functional problems after therapy of gynecological malignancies. However, women who regain sexual activity after completed treatment have a very good overall SF.
QUALITY OF LIFE IN ELDERLY WOMEN WITH GYNECOLOGICAL CANCER

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Objectives
Quality of life in elderly women with gynecological cancer was studied. From 2007 till 2012, 368 patients with gynecological cancer at age 70 years old and older were treated at the department of gynecological oncology in National Cancer Hospital, Sofia. 297 of them were at the age group of 70-79 years old and 71 patients were more than 80 years old.

Methods
A prospective method was applied to this study. Most common comorbidities are as follows: hypertension (60% of the cases), ischemic heart disease (15% of the cases), varices of the lower limbs (12% of the cases), cerebrovascular incidents (5% of the cases) or accompanying cancer with other localisation (8% of the cases).

Results
More than 50% of the patients were diagnosed with advanced stages of gynecological cancer. No cases of surgical related death was registered among the patients.

Conclusions
Gynecological cancer is in itself serious diagnose, but in combination of elderly and multiple comorbidities becomes a challenge in complete treatment.
DEPRESSION, ANXIETY AND SEXUAL DYSFUNCTION IN WOMEN WITH BREAST CANCER
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Objectives
With the improvement of the prognosis of breast cancer, long term effects of the disease and treatment is becoming increasingly important. Breast cancer related psychological, emotional and sexual problems have a long term impact on the quality of life. The purpose of this study was to examine the feasibility of questionnaires such as the Hospital Anxiety and Depression Scales (HADS) and Female Sexual Function Index (FSFI) to identify breast cancer patients who are at risk to develop one of these problems. Furthermore, the significant relationship was studied between the socio-demographic or clinical measures and the risk to develop a depression, anxiety or sexual dysfunction.

Methods
A cross-sectional study of the breast cancer patients treated at the Ghent University Hospital Breast Clinic between February and June 2010. The prevalence's were measured by the HADS and FSFI. A Fisher's exact test was used to study the significant relationship.

Results
The prevalence of depression was 15.8%, of anxiety was 27.5% and of sexual dysfunction was 62.9%. A significant relationship was found between the risk for depression and reduced sexual activity (p≤0.02) and anxiety (p≤0.001). Additionally we found that therapy induced menopause and a hormonal substitution therapy stop, increase the risk of developing an anxiety disorder.

Conclusions
A substantial percentage of breast cancer patients was at risk for depression and anxiety, a majority suffered from sexual dysfunction. HADS and FSFI can be used as a reliable instrument to detect the breast cancer patients who are at risk to develop depression, anxiety or sexual dysfunction.
Objectives
There is a progressive focus on understanding the unmet needs of cancer survivors. Treatments for gynaecological cancers can cause significant long-term morbidity. This is often not reported at routine hospital follow-up after cancer treatment. We undertook a service improvement exercise aimed to demonstrate the burden of gastrointestinal (GI) and bladder morbidity and compare patient reported outcome measures to clinical details recorded within the medical records.

Methods
We identified two specific cancer populations within our regional cancer network (population 1.5 million):

1. Assess GI toxicity in patients with cervix or endometrial cancer treated with pelvic radiotherapy
2. Assess bladder function in patients with cervix cancer treated with radical hysterectomy (without adjuvant radiotherapy)

We identified patients who had completed treatment between 2009-2012. Patients were sent a postal questionnaire including a Patient Reported Outcome Measure (PROM) specific to GI toxicity and bladder function respectively. We also undertook a review of the medical records specifically assessing the reporting of post-treatment morbidity.

Results
There was a 43% response rate to the postal questionnaire (38/90 GI toxicity and 21/48 bladder function). Of the patients reporting significant GI toxicity or bladder dysfunction in a PROM this was not elicited or reported in the medical records in 55% and 60% of cases respectively.

Conclusions
Standard hospital based follow-up alone after cancer treatment fails to identify and manage morbidity associated with cancer treatment. We advocate the routine use of PROM to determine the unmet needs of cancer survivors so that patients can be directed into appropriate management pathways.