

# **ORAL PRESENTATIONS**

### **3D IMAGE ANALYSIS; INVOLVEMENT IN THE PREOPERATIVE CHARACTERIZATION OF OVARIAN MASSES AS BENIGN OR MALIGNANT**

S.Stavros, P. Drakakis, D. Haidopoulos, G. Konomos, A. Rodolakis, S. Mesogitis, D. Loutradis, E. Domali

*University of Athens, Alexandra Hospital, 1st Gynaecology Department, Athens-Greece*

To investigate the potential creation of statistical rules of high predictive value based on ultrasonography of ovarian lesions. Women (n=398), that have been operated based on diagnosis of ovarian lesion, have been recruited; ultrasonic preoperative investigation was organized into 2 steps; first, ultrasonography was performed based on IOTA definitions and second 3D volumes were analysed; 3D image was isolated by the surrounded noise (mc) and was inverted (inverted). Digital information provided by these three still images and volume of inverted image that was accounted automatically via the 3D software were evaluated.

Malignancy is diagnosed in 72% of postmenopausal patients. bloating, menstrual irregularities and deep abdominal pain represent the main reported symptoms (30.0%, 25.0%, and 18.3% respectively). Multilocular-solid (63.3%) or solid appearance (41%) of the mass, presence of septum (54.4%) or solid part (75.4%), and color score 4 raise the probability of malignancy, while Ovarian crescent sign (OCS) and acoustic streaming eliminate it (100%). Descriptive statistics functioned preparatory aiming at the construction of predictive indicators; differentiated correlations of age, vascularity, OCS, log (volume-mc), log (mc), log (inverted) evoked four indicators: T1 (AUC: 0.94, sens:0.96, spec:0.84), T2 (AUC:0.98, sens: 0.96, spec:0.92), T3 (AUC: 0.99, sens: 0.98, spec:0.90), and T4 (AUC:0.96, sens: 0.90, spec: 0.94). ROC curve for LR model incorporating T1/T4 showed AUC: 0.973, sens: 0.833, spec: 0.99 (cut point 0.5). The majority of the cases (361) were successfully predicted. Regarding the 37 remaining cases, 29 were correctly categorized via subjective impression, eliminating in 8 the uncertain cases.

3D inversion software data present functional statistically relationship to digital signal of ultrasonic images; in the future, it might offer predictive results mimicking the subjective feeling of really experienced doctors.

## **SELF-REPORTED DISTRESS IN PATIENTS WITH OVARIAN CANCER: IS IT RELATED TO DISEASE STATUS?**

F.K. Ploos van Amstel<sup>1</sup>, M.A.P.C. van Ham<sup>2</sup>, E.J. Peters<sup>1</sup>, J.B. Prins<sup>3</sup>, P.B. Ottevanger<sup>1</sup>

<sup>1</sup>*Department of Medical Oncology, Radboud University Medical Center, Nijmegen;* <sup>2</sup>*Department of Gynecological Oncology, Radboud University Medical Center, Nijmegen;* <sup>3</sup>*Department of Medical Psychology, Radboud University Medical Center, Nijmegen - The Netherlands*

**Background.** Most patients with ovarian cancer have a poor prognosis and often undergo intensive treatment with surgery and chemotherapy. These patients are therefore at risk for experiencing distress and reduced quality of life. The aim of this study is to investigate distress, self-reported problems and quality of life in relation to disease status. Differences between patients with ovarian cancer with no recurrence/metastases (NOC) and with recurrence/metastases (ROC) are explored. Also, differences were investigated between distressed and non-distressed patients with ovarian cancer.

**Methods.** This cross-sectional study was conducted in 2011 at a university hospital in the Netherlands. Women with ovarian cancer, both during and after treatment, were asked by mail to fill in self-report questionnaires. Distress was measured using the Dutch version of the Distress Thermometer (DT), Hospital Anxiety and Depression Scale- total score (HADS) and Impact of Event Scale (IES). Problems and Quality of Life were assessed with the problem list of the DT, EORTC QLQ C-30 and OV28. Preliminary Results. In total, 104 ovarian cancer patients completed the questionnaires (NOC=59 and ROC=45). Distress was found with the DT in 34% (mean 3.1, SD 2.6), the HADS in 15% (mean 8.6, SD 5.9) and IES in 19% of the patients (mean 17.5, SD 15.5). No significant differences were found in distress and experienced problems between NOC and ROC. The top 3 of most reported problems in both groups were fatigue, impaired physical condition and neuropathy. Distressed (DT $\geq$ 5) patients experienced significantly worse functioning (role, cognitive, emotional, physical and social), more problems and lower quality of life in comparison to non-distressed patients (P<0.01).

**Conclusions.** This study shows that disease status of the ovarian cancer seems less important for distress, the experienced problems and quality of life. In contrast, distressed patients with ovarian cancer experience much more problems, as well with physical as with emotional functioning, and have lower quality of life than non-distressed patients. The physical problems fatigue, impaired physical condition and neuropathy are the most prevailing in patients with ovarian cancer.

## QUALITY OF LIFE IN WOMEN WITH CERVICAL CANCER

R. Grion, A.F. Vaz, L.F. Baccaro, J. Martins, S.C. Esteves, L. Costa Paiva, A. Mendes Pinto Neto  
*Department of Gynecology, Faculty of Medical Sciences, State University of Campinas – UNICAMP, Brazil*

**Purpose:** Cancer of the cervix is the second most common gynecological tumor. Pelvic radiation therapy is one of the most used forms of treatment and it is associated with several side effects that may lead to decrease in quality of life. Studies have evaluated the effects of radiotherapy but there are few data about quality of life before initiating the treatment. Our objectives were to evaluate quality of life and its associated factors in women with cervical cancer before the initiation of radiotherapy treatment.

**Methods:** A cross-sectional study was conducted with 80 women with cervical cancer, aged 18-75 years, referred for radiotherapy at the Women's Hospital of the State University of Campinas – Brazil, from January 2013 to March 2014. The outcome variable was quality of life, assessed using the abbreviated version of the World Health Organization (WHOQOL-BREF) questionnaire. The independent variables were sociodemographic data, health related habits and the characteristics of the neoplasm. Statistical analysis was carried out using frequency distribution, Mann-Whitney test and multiple linear regression.

**Results:** The mean age of the women was 48.1 ( $\pm$  13.5) years. Thirty-four women (42.5%) were postmenopausal, 57.5% were white and 55% had clinical stage IIIB. Some of the clinical and sociodemographic data are shown in table 1. In the final statistical model, having a more advanced clinical stage ( $p = 0.04$ ) and lower family income ( $p = 0.04$ ) were associated with worse quality of life in the physical domain of the questionnaire. In the psychological domain, use of any medication ( $p = 0.02$ ) was associated with worse quality of life. Regarding the environment domain, having a more advanced clinical stage ( $p = 0.04$ ) and lower family income ( $p < 0.01$ ) were associated with worse quality of life. Having higher schooling ( $p = 0.03$ ) and no smoking ( $p < 0.01$ ) were associated with better overall quality of life. Not having undergone surgery before radiotherapy ( $p = 0.01$ ) and having higher schooling ( $p < 0.01$ ) were associated with worse general health. No smoking ( $p = 0.01$ ) was associated with better general health.

**Conclusions:** Quality of life before the initiation of radiotherapy treatment was associated with a set of factors. Advanced clinical stage, lower family income, and smoking are some of the factors associated with poorer quality of life before radiotherapy. This information is useful to identify women who need more support and attention during the course of therapy for cervical cancer.

*Acknowledgments: Funding by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) number 2012/09215-7*

## Clinical and sociodemographic data (n=80)

Characteristics	%
<b>Color</b>	
White	57.5
Non-white	42.5
<b>Menopausal status</b>	
Premenopausal	57.5
Postmenopausal	42.5
<b>Marital status</b>	
With partner	48.8
Without partner	51.2
<b>Smoking</b>	
Yes	15.6
No	84.4
<b>Schooling</b>	
≤ 8 years	56.2
> 8 years	43.8

## **ISOLATION AND MOLECULAR CHARACTERIZATION OF OVARIAN CANCER SELF-RENEWING SPHEROIDS: ROLE IN CHEMORESISTANCE MECHANISMS**

L. Zanotti<sup>1</sup>, L. Tassone<sup>1</sup>, C. Romani<sup>1</sup>, E. Bandiera<sup>1</sup>, R.A. Tassi<sup>1</sup>, P. Todeschini<sup>1</sup>, E. Bignotti<sup>1</sup>, G. Damia<sup>2</sup>, F. Ricci<sup>2</sup>, M. Ragnoli<sup>3</sup>, V. Zizioli<sup>3</sup>, G. Tognon<sup>3</sup>, F.E. Odicino<sup>3</sup>, A. Gambino<sup>3</sup>, E. Sartori<sup>3</sup>, S. Pecorelli<sup>3</sup>, A. Ravaggi<sup>1</sup>

<sup>1</sup>*“A. Nocivelli” Institute of Molecular Medicine, Division of Gynecologic Oncology, University of Brescia, Brescia, Italy;* <sup>2</sup>*Department of Oncology, Istituto di Ricerche Farmacologiche “Mario Negri” – IRCSS, Milan, Italy;* <sup>3</sup>*Department of Obstetrics and Gynecology, University of Brescia, Brescia, Italy*

**Purpose and Background.** The aim of the study was to investigate the molecular phenotype of a model of ovarian cancer stem cells and to evaluate the implications in prognosis and treatment of ovarian carcinoma (EOC). EOC is the leading cause of gynecological cancer-related death in the developed world. The vast majority of initially responsive diseases eventually relapse. This may be explained by the existence of a subpopulation of self-renewing malignant progenitors, called cancer stem cells (CSCs), considered to be responsible for tumor progression, relapse, metastases and therapeutic resistance, as already proposed for other tumors.

**Methods.** Eleven EOC cell lines were placed in serum-free DMEM/F12 medium, 20 ng/ml EGF, 10 ng/ml bFGF, 5 µg/ml insulin and B27 supplement, in low adherence conditions. The cell lines able to generate self-renewing spheres were then evaluated by FACS analysis for the expression of surface markers of EOC CSCs: CD24, CD44, CD117 and CD133. Total RNA was extracted from the spheres and the parent cell lines. After reverse transcription, quantitative real time PCR was performed for the principal genes implicated in stemness and epithelial to mesenchymal transition (EMT) on a custom PCR array. Three endogenous controls (GAPDH, HPRT1, GUSB) were used for normalization. For chemotherapy resistance assay, both spheres and the corresponding differentiated cell line were treated with different concentrations of six anticancer agents (cisplatin, paclitaxel, doxorubicin, etoposide, trabectedin and PS341). The control group was represented by untreated cells. Proliferation and cytotoxic effects were monitored by MTS assay and optical density reading at 490 nm, after 96 hours.

**Results.** Four EOC cell lines were able to propagate in serum-free medium to generate self-renewing spheres for at least six months. The majority of these spheres did not show differences in expression of the surface markers investigated, in comparison with the differentiated parent cells. Spheres deriving from only one cell line, showed a significantly different staining from the differentiated ones. The percentage of CD117 and CD133 positive cells in spheres and parent cells were respectively 18% and 4.5%. The spheres exhibited an overexpression of stem cell genes (SHH, NOTCH, SOX2, NANOG, ALDHA1), EMT genes (SNAI1, VIM) and a membrane efflux transporter (ABCG2). The results of cytotoxic assays revealed generally a greater resistance of spheres to chemotherapeutic drugs, compared with differentiated cells. The differences of the calculated IC50 were statistically significant, except for trabectedin.

**Conclusions.** The isolation of an “in vitro” model of cancer stem cell could represent a useful tool to better understand chemoresistance mechanisms in EOC. Successful translation of findings at the molecular level could allow the identification of new targets for future innovative treatment regimens.

## **PARAMETRIAL BOOST DOES NOT REPLACE OPTIMAL BT TREATMENT IN 102 PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER (LACC)**

A. Doupagne<sup>1</sup>, F. Kridelka<sup>2</sup>, M. De Cuypere<sup>2</sup>, F. Goffin<sup>3</sup>, K. Delbecque<sup>4</sup>, C. Gennigens<sup>5</sup>, F. Lakosi<sup>6</sup>, A. Kakkos<sup>2</sup>, J. Hermesse<sup>6</sup>

<sup>1</sup>University of Liege, Faculty of Medicine (student), Liege, Belgium; <sup>2</sup>Obstetrics & Gynaecology, University of Liege - CHU Liege, Liege, Belgium; <sup>3</sup>Obstetrics & Gynaecology, University of Liege - CRH Citadelle, Liege, Belgium; <sup>4</sup>Anatomopathology, University of Liege - CHR Citadelle, Liege, Belgium; <sup>5</sup>Medical Oncology, University of Liege - CHU Liege, Liege, Belgium; <sup>6</sup>Radiotherapy, University of Liege - CHU Liege, Liege, Belgium

**Aims.** We report 102 patients with LACC, treated by concomitant cisplatin-based chemoradiotherapy (CCRT) and brachytherapy (BT). We focus on the identification of variables that can predict late morbidity and recurrence.

**Methods.** Between 2006 and 2013 102 consecutive patients with FIGO stage 1B1 N+ or  $\geq$  1B2 LACC were treated by CCRT-BT. Staging lymph node dissection was performed in 61 patients. The total dose of external beam radiation therapy (EBRT) was respectively 50,4 Gy (n=71) and 60 Gy (n=31) when a parametrial tumor boost was delivered without interstitial BT. Dose delivered by BT varied accordingly from 25 to 35 Gy. Past medical history including abdominal surgery, smoking, diabetes and age were recorded. Univariate analysis of factors linked to CCRT-BT responsible for Grade I/II and Grade III/IV morbidity was performed.

**Results.** With the a medium follow-up of 22 months, recurrence was observed in 27 patients. It was associated with two factors : tumor size  $\geq$  6 cm (OR=0,29 ; p=0,017) and BT dose <35 Gy (OR=4,61 ; p=0,0014). The Grade III/IV late toxicity profile was the following : 11 gastrointestinal, 4 genitourinary and 10 vaginal. No correlations were found between any medical factors or radiation dose and techniques, and late toxicity.

**Conclusion.** Decreasing BT dose even if compensated by EBRT has an unfavorable impact on rate of recurrence. These conclusions await confirmation on larger series of patients with prospective evaluations.

## **ROBOTIC SURGERY IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER AFTER NEOADJUVANT CHEMOTHERAPY: SURVIVAL OUTCOMES**

G. Siesto, F. Romano, G. Musicò, N. Palma Iedà, C. Bulletti, D. Vitobello

*Department of Gynecology, Cancer Center, IRCCS, Humanitas Clinical and Research Center, Rozzano, Milan - Italy*

**Aim:** To evaluate the survival outcomes of consecutive patients with locally advanced cervical cancer (LACC) who underwent comprehensive robotic surgery after neoadjuvant chemotherapy (NACT).

**Materials and Methods:** Since 04/2009, consecutive patients with LACC (FIGO stages IB2-IIB) were submitted to robotic surgical staging after 3 cycles of NACT. Comprehensive surgical staging was offered regardless patient's age, BMI, medical and surgical history. Clinical objective tumor response was assessed according to the Response Evaluation Criteria in Solid Tumor, whereas pathologic responses were defined according to the criteria of the European study SNAP01. Univariate analysis using Kaplan-Meier life table method with log-rank test and multivariate analysis using Cox's proportional hazard model with hazard ratio (HR) and its 95% confidence interval were performed to jointly examine the relative importance of variables as potential clinical-pathological prognostic factors affecting progression-free (PFS) and overall survival (OS).

**Results:** During the study period, 31 patients meeting the inclusion criteria were managed. The median (range) age and BMI were 46.9 (28.6–75.5) years and 23.2 (17.5–37.1) kg/m<sup>2</sup>, respectively. Overall, 27.5 (range 12–58) lymph nodes were retrieved. According to the final pathologic examination 6 (19.4%) women had positive pelvic lymph nodes, whereas 15 (48.4%) patients achieved Optimal Pathologic Response (OPR) which included complete pathologic response (PRC) or microscopic (<3 mm) residual disease (pPR1). After a median follow-up of 29.0 (range 2.1–60.4) months, 6 (19.4%) patients recurred and 5 (16.1%) died of disease. OPR [0.1 (0.02–0.7);p=0.01], positive nodal status [52.2 (5.7–481.9); p=0.0005], Grade 3 [5.5 (1.1–28.1);p=0.004], lympho-vascular space invasion [17.4 (2.4–12.1);p=0.01] and NACT with 3 agents (vs 2 agents) [0.05 (0.004–0.5);p=0.009] were all associated to PFS at univariable analysis (Log-Rank test). Positive nodal status [11.2 (2.1–61.1);p=0.005] was the only independent predictor of PFS at multivariate analysis. OPR [0.1 (0.02–0.8);p=0.02], positive nodal status [45.8 (3.6–575.0); p=0.003], lympho-vascular space invasion [15.2 (1.6–144.7);p=0.02] and NACT with 3 agents [0.02 (0.001–0.2);p=0.002] were all associated to OS at univariable analysis. Positive nodal status [7.6 (1.2–49.4);p=0.03] and NACT with 3 agents [0.2 (0.02–0.8);0.03] resulted as independent predictors of OS at multivariate analysis.

**Conclusions:** Nodal status represents the strongest predictor of survival in women with LACC. Similarly, NACT including 3 agents (TIP and TEP regimens) warranted better overall survival than those achieved by other schedules.

## THE INCIDENCE AND CLINICAL SIGNIFICANCE OF THE MICRO-METASTASES IN THE SENTINEL LYMPH NODES DURING SURGICAL STAGING FOR EARLY ENDOMETRIAL CANCER

D. Ferraioli<sup>1</sup>, N. Chopin<sup>1</sup>, F. Beurrier<sup>1</sup>, N. Carrabin<sup>1</sup>, P. Mathevet<sup>2</sup>

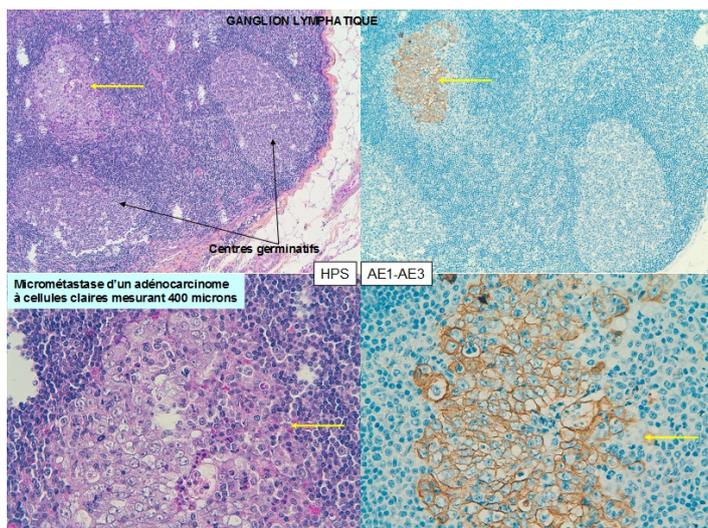
<sup>1</sup>*Cancer Center Leon Berard, Gynaecology Dpt, Lyon - France;* <sup>2</sup>*Lausanne Hospital, Gynaecology Dpt, Lausanne - Switzerland*

**Introduction:** The status of regional node remains one of most important factor to guide adjuvant therapy in endometrial cancer (EC). In selected patients, the sentinel node biopsy could be proposed. Pelvic recurrence occurs in up to 15% of patients with early stage EC and histologically negative pelvic lymph nodes (LN). The recurrence could be linked to the false negative LN or to the presence of micrometastases (MM). The prognostic significance of detecting MM in LN during EC staging is still controversial. This retrospective case-control study (ratio 1:2) performed in the oncological gynecology department (Hospital Femme Mere Enfant –Lyon, France) between December 1998 and June 2012 reports the incidence and the clinical significance of MM detected during ultrastaging of negative sentinel LN of patients treated for EC.

**Patients And Methods:** 93 patients affected by type I and II EC were submitted to surgery with sentinel lymph node (SLN) mapping. The inclusion criteria were: primary surgery with SLN mapping and bilateral pelvic LN dissection (LND), detection of at least one SLN and any grade of type I and II EC. Dual labelling method was used to detect SLN. SLNs were subjected to histological frozen section and then, with non-SLNS, routine staining was realized. Negative SLNs were subjected to ultrastaging researching MM. The patients that had a loco-regional or distant relapse represented the cases of our series (CS). The patients without loco-regional or distant recurrences were the cases-control (CC) and they were matched (1:2 ratio) according to age, FIGO stage and histo-pathologic features.

**Results:** 93 women with preoperative stage I EC underwent surgical staging with SLN mapping and biopsy followed by systematic bilateral pelvic LND. 10 patients presenting a relapse represented CS. In the remaining patients without recurrence, 20 CC were individualized. SLN was bilateral in 6 out of 10 patients (60%) for CS and in 11 out of 20 patients for CC (55%). The detection rate of SLN per hemipelvis was of 17 out of 20 hemipelvis (85%) and of 33 out of 40 hemipelvis (82.5%) for CS and CC respectively. The median detection rate of SLN per total hemipelvis was of 50/60 (83.3%). Two SLN of CS arm were positives at frozen section. One of eight patients of CS arm with negative SLNs was positive for MM by immunohistochemistry analysis. In the small study the prognostic significance of MM remains still unknown because their incidence is very low and is not statically possible to analyze.

**Conclusion:** LN status is one of the most important hysto-pathologic features to determine the adjuvant treatment. SLN technique, as alternative at LND, could be use proposed in early EC and in the patients with important comorbidities. MM in SLN could be researched and, if considered as probable prognosis factor, could be help to modulate the following treatment. The large multicenter study must be performed to clarify the optimal method of research of SLN in EC and the significance of MM in the LN.



## **FERTILITY SPARING SURGERY IN CERVICAL CANCER - FOLLOW UP PRAGUE EXPERIENCE**

L. Rob<sup>1</sup>, H. Robova<sup>1</sup>, M. Pluta<sup>1</sup>, M.J. Halaska<sup>1</sup>, J. Matecha<sup>1</sup>, J. Lisy<sup>2</sup>, P. Skapa<sup>3</sup>

<sup>1</sup>*Department of Obstetrics and Gynecology, 2nd Medical Faculty, Charles University in Prague, University Hospital Motol;* <sup>2</sup>*Department of Radiology, 2nd Medical Faculty, Charles University in Prague, University Hospital Motol;* <sup>3</sup>*Department of Patology and Molecular Medicine, 2nd Medical Faculty, Charles University in Prague, University Hospital Motol - Czech Republic*

**Introduction:** Two protocols of follow-up in women after fertility-sparing surgery with cervical cancer with different risk of recurrence are presented.

**Methods:** We included 70 women with tumor < 20 mm after lymphadenectomy and trachelectomy (LAP I) and 28 women with tumor > 20 mm that underwent neoadjuvant chemotherapy followed by fertility-sparing surgery (LAP III) with minimal follow-up of 24 months (24-180). First check after 2 months from surgery include clinical examination and colposcopy, after 6 months we perform clinical examination, HPV-HR, PAP-smear, expert colposcopy and ultrasonography (cervical length and structure). We recommend pregnancy. Then until 5th year colposcopy and PAP-smear are done every 6 months and ultrasonography and HPV-HR yearly.

LAP III protocol include women with higher risk for local recurrence. The follow-up is the same, only MRI is added in 6 months and then yearly 3x.

**Results:** LAP I: Fertility was spared in 62 women. Two istmic recurrences (3.1%) 14th and 18th month were detected, one died (1.6%). In one woman (1.6%) with squamous cancer adenocarcinoma as duplicity was diagnosed 28 months after trachelectomy. She died of disease (1.6%). HPV-HR positivity was detected in 20 (32.2%) and persistent HPV-HR in 9 (14.5%) women. Abnormality in PAP-smear was found 32 cases (51.6%) but pre-cancer lesion was confirmed only in 10. Hysterectomy was performed in 10 women (16.1%). LAP III: Fertility was preserved in 20 women. Four (20%) recurrence were detected during follow-up (16-108 months), three were istmic and one distant. Two women died (10%).

**Conclusion:** HPV-HR testation brings more important prognostic information than PAP-smear. PAP-smear evaluation needs experiences. Early detection of local recurrences is important because curability is high. Ultrasonography and MRI is important part of follow-up in risky women.

## **EMBRYONAL RHABDOMYOSARCOME AFTER IN UTERO EXPOSITION TO CHEMOTHERAPY: A CASE REPORT AND REVIEW OF LITERATURE**

A. Surbone, C. Ahtari

*Lausanne University Hospital, Obstetrics and Gynaecology Department, Lausanne - Switzerland*

**Introduction:** Malignant cancer occurs about 1 in every 1000 pregnancies. Maternal and fetal safety of chemotherapy (CT) during pregnancy plays a key role in the therapeutic choice; one concern is the possibility of chemo-induced tumors in the newborn.

**Case Report:** A 33 years old pregnant woman was diagnosed with a squamous cells cervical carcinoma at 22 weeks (w) of gestational age (GA). At 26 w MRI showed frank local progression to a FIGO 2B radiological stage. A neoadjuvant chemotherapy (NACT) by Cisplatin/Paclitaxel (CDDP/PTX) permitting to delay the delivery until 34 w was proposed to the couple. The patient received 1 cycle at 28 w with a 50% mass reduction and a second cycle at 31 w, having stabilized the disease. A fetal lung maturation was administered at 28 w. At 34 w a cesarean section coupled to pelvic-aortic lymphadenectomy and ovarian transposition was performed, since the patient refused hysterectomy. The newborn had an excellent adaptation with an APGAR score of 9/10/10 and weighted 2040g. Her evolution was good except for a transient respiratory distress, hyperbilirubinemia and hypoglycemia due to prematurity. All the other hematologic, hepatic, renal and otologic tests were normal. At 10 and 18 months her development and health were normal. Then, she was lost to follow up. When 5 years old, she consulted the Emergency Room because of a strong abdominal pain. The MRI and CT revealed a heterogeneous retroperitoneal mass that was biopsied revealing an embryonal rhabdomyosarcome (ER) compressing the left ureter and metastatic to the left inguinal vein. The child is actually following her second CT regimen with a partial response and an improved general status.

The mother, who initially refused a radical hysterectomy, accepted it 6 months later but refused any adjuvant radiotherapy. She is disease-free at 5 years.

**Discussion:** The endpoint of NACT is the control of the neoplastic disease until fetal viability. There are only 3 reported cases of second malignancies in children exposed to CT in utero. We report a new case of ER after in utero exposition to PTX and CDDP; it is difficult to ascribe casualty to an individual agent, but it is known that CDDP distributes to third spaces and amniotic fluid may act as a reservoir. In literature about 77% of CDDP-exposed pregnancies report adverse pregnancy outcomes (APO) and first-trimester exposure result in a 17% of congenital malformations. The overall frequency of APO in PTX-exposed pregnancies is 13%, without congenital malformations. ER has already been related to X-ray exposure in pregnancy.

**Conclusion:** The therapeutic choice in cancer during pregnancy needs to be carried out within a multidisciplinary team and parents need exhaustive information about actual risks and possible long-term consequences in offspring. Further long-term follow up and comparison with appropriate control groups are still needed to address the risk of late complications after in utero exposition to CT.

## CONSERVATIVE TREATMENT IN PATIENTS WITH ATYPICAL ENDOMETRIAL HYPERPLASIA FROM A SINGLE CENTRE

M. La Russa<sup>1</sup>, A. Jeyarajah<sup>1</sup>, I. Biliatis<sup>1</sup>, N. Singh<sup>2</sup>, A. Faruqi<sup>2</sup>, A. Rosenthal<sup>1</sup>

<sup>1</sup>Gynaecological Oncology department, Barts Health NHS Trust; <sup>2</sup>Pathology department, Barts Health NHS Trust

**Background:** Atypical Endometrial Hyperplasia (AEH) is a common premalignant endometrial lesion that can affect women in their reproductive age as well as older women with severe comorbidities. Conservative management of AEH with high dose progestins has been reported to have excellent results in terms of both regression and fertility outcomes in young women. In addition, it can be effective in treating older patients not fit to undergo hysterectomy. The aim of this study was to report results of conservative management of AEH in a tertiary Gynaecological Oncology centre.

**Methods:** Retrospective cohort study of all women diagnosed with AEH from 2004-2012. Patient characteristics and histopathology were retrieved from case files and electronic database. Patients with AEH were given large doses of oral progestogens (medroxyprogesterone, Megestrol acetate, Norethisterone) and/or Mirena IUS, and underwent the first endometrial biopsy 3-6 months after diagnosis. Progression, persistence, partial response and complete response were defined.

**Results:** 60 patients with AEH were diagnosed during the study period. Median age was 51 years (range 25-77). Forty patients had primary hysterectomy (64.5%), while the remainder had conservative management either for fertility preservation (15/60 25%) or due to severe comorbidities (5/60 8.3%). 15 (72.7%) of 20 patients managed conservatively achieved complete or partial response (13 and 2 respectively) adequate to commence fertility treatment. The remaining 5 (27.3%) failed to respond adequately to commence fertility treatment or had progressive disease resulting in hysterectomy. In two of them only Grade 1 Endometrial Cancer was detected in the hysterectomy specimen. Median treatment duration was 17.5 months (range 3.73-43.67 months). There was no significant difference in the rate of complete response in relation to mode of treatment (4/4, 100% for Mirena only, 5/7, 71.4% for oral treatment only and 4/9, 44.4% for combined treatment), however due to small numbers, we were unable to reject the null hypothesis. Five premenopausal women attempted to conceive. One had a first trimester miscarriage and another one had a normal pregnancy and delivered at term.

**Conclusions:** Progestogen treatment with Mirena, oral or combination are all effective in the management of atypical endometrial hyperplasia. It may be used for young women wishing to preserve their fertility or older women who cannot undergo hysterectomy.



## **STRATIFIED CANCER FOLLOW-UP LEADS TO A LARGE REDUCTION IN VISITS AND COSTS IN THE NETHERLANDS: A SIMULATION STUDY**

S.M.E. Geurts<sup>1</sup>, J.P.C. Grutters<sup>1</sup>, F. de Vegt<sup>1</sup>, K.K.H. Aben<sup>1,2</sup>, V.E.E.P. Lemmens<sup>2,3</sup>, J. A. Witjes<sup>4</sup>, L.A. Kiemeny<sup>1,4</sup>, L.F.A.G. Massuger<sup>5</sup>, V.C.G. Tjan-Heijnen<sup>6</sup>, J.A.A.M. van Dijck<sup>1</sup>, A.L.M. Verbeek<sup>1</sup>

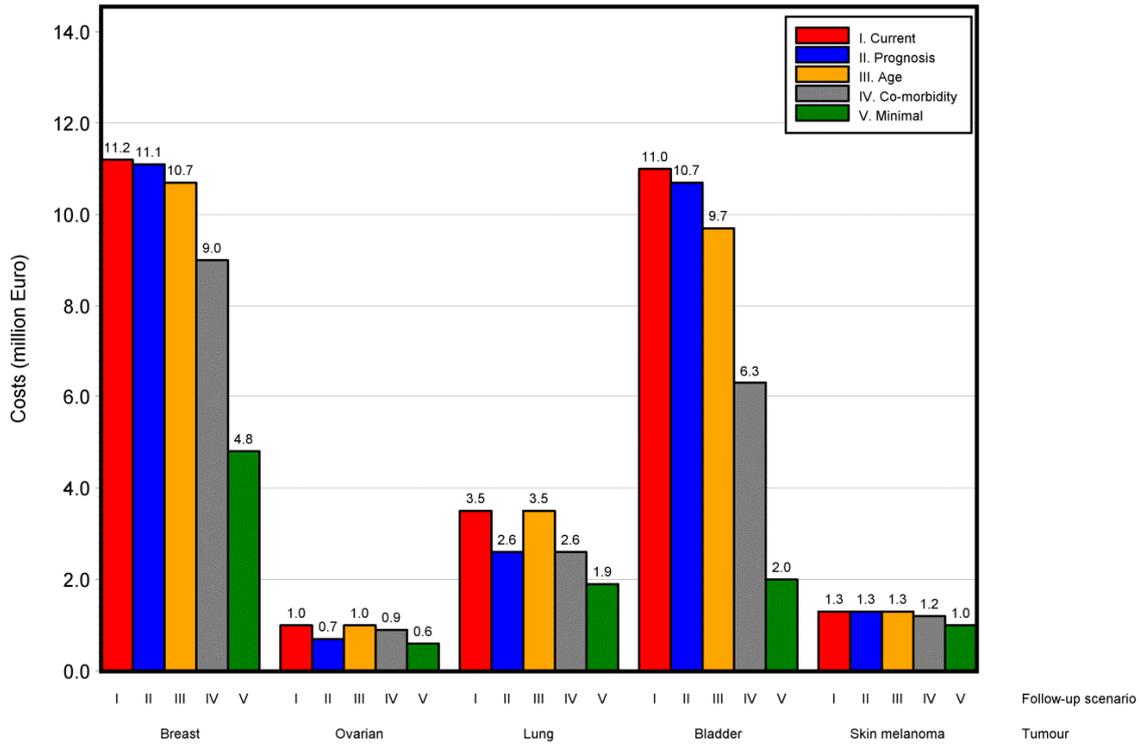
<sup>1</sup>Department for Health Evidence, Radboud university medical center, Nijmegen; <sup>2</sup>Comprehensive Cancer Centre the Netherlands, Utrecht; <sup>3</sup>Erasmus MC University Medical Center Rotterdam, Department of Public Health; <sup>4</sup>Department of Urology, Radboud university medical center, Nijmegen; <sup>5</sup>Department of Obstetrics and Gynecology, Radboud university medical center, Nijmegen; <sup>6</sup>Department of Medical Oncology, GROW – School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht - The Netherlands

**Purpose.** To calculate the reduction in routine follow-up visits and cost savings by offering minimal follow-up to patients with a small likelihood of benefit from routine follow-up for five common cancer types: ovarian, breast, lung and bladder cancer, and skin melanoma.

**Materials and methods.** We simulated (1) current follow-up in all patients, (2-4) minimal follow-up in three patient subgroups and current follow-up in the other patients and (5) minimal follow-up in all patients. The three patient subgroups were advanced stage cancer(2), age 80+ years(3) and at least one life-shortening co-morbidity(4). Current follow-up was defined as follow-up according to the Dutch tumour-specific guideline recommendations. Minimal follow-up consisted of routine visits for two years without any routine tests. The number of routine visits and cost calculations were based on the follow-up schedules, the overall survival rates and the distributions of patients across the subgroups. Patient, tumour and mortality data from 214,173 patients diagnosed in the period 2003-2009 were derived from the Netherlands Cancer Registry. Costs for routine visits and tests were derived from the Dutch Healthcare Authority.

**Results.** For ovarian cancer, the yearly reductions in the number of visits and costs in the Netherlands for scenarios (2-5) compared with (1) were 2,051(-20%), 165(-2%), 1,245(-12%) and 3,541(-35%) visits, and €0.3M (-28%), €0.02M (-2%), €0.1M (-17%) and €0.4M (-46%), respectively (Figure 1). For the five cancer types together, the yearly reductions in the number of visits and costs in the Netherlands for scenarios (2-5) compared with (1) were 4,000(-2%), 5,000(-2%), 24,000(-11%) and 66,000(-29%) visits, and €1.6M (-6%), €1.8M (-6%), €8.0M (-29%) and €17.7M (-63%), respectively.

**Conclusion.** For ovarian cancer, minimal follow-up in patients with advanced stage cancer has the potential to reduce the number of visits by 2,000 and the costs of routine visits and tests by €0.3M. We anticipate that part of this reduction is already achieved in the Netherlands as a response to the results of the MRC OV05/EORTC 55955 trial by Rustin et al (Lancet 2010). For the five cancer types studied, stratified follow-up can reduce annual costs by €1.6-€8.0M in the Netherlands. Equivalent numbers are €54-€271 million in the United States and €52-€258 million in Europe.



## **DURING THE SOUTH EAST SCOTLAND GYNAECOLOGICAL ONCOLOGY MULTIDISCIPLINARY MEETING: IS THE TIME ALLOCATED TO THE INDIVIDUAL PATIENT FOR DISCUSSION ADEQUATE?**

P. Giamougiannis, G. Walker, C. Martin

*Royal Infirmary of Edinburgh, Gynaecological Oncology Department, Edinburgh - United Kingdom*

**Introduction:** Multidisciplinary teams (MDTs) are defined as a group of people of different health-care disciplines, who meet together at a given time (whether physically in one place or by video or tele-conferencing) to discuss a given patient. Each professional is able to contribute independently to the diagnostic and treatment decisions about the patient.

MDTs are designed to improve communication, coordination and decision making between healthcare professionals in considering the treatment options for oncology patients. Having adequate protected time for MDT meetings has been emphasised as important for effective outcomes, as has having adequate time to discuss individual patients.

**Aim:** To identify whether enough time is allocated to each patient for discussion during the course of the South East Scotland gynaecological oncology multidisciplinary meeting (MDM).

**Methods:** A prospective study over 27 consecutive gynaecology oncology MDMs during a 6 month period between 28/3/13 and 26/9/13.

**Results:** In total 715 patients were discussed, an average 26 patients per meeting with an average discussion time of 3 minutes and 4 seconds per patient. The average time per meeting was 1 hour 28 minutes. The average time for discussion per patient is similar to the average time in gynaecology oncology MDMs across the UK, however the time per patient clearly becomes less as the meeting progresses and is markedly decreased for the last patient discussed. This is confirmed by the finding that more patients are discussed in the final third of the MDM compared to the first two thirds.

**Recommendations:** Extending the time of the meeting by 30 minutes or setting a maximum number of patients for discussion at each MDM (for instance 25) could ensure that adequate discussion time is available for all patients, thus avoiding the obvious substandard discussion of the last few patients.

## **FOLLOW-UP OF ENDOMETRIAL CANCER PATIENTS – A RANDOMIZED CONTROLLED TRIAL COMPARING SELF-REFERRAL WITH CONVENTIONAL FOLLOW-UP**

M.M. Mathiesen<sup>1</sup>, P.T. Jensen<sup>1</sup>, D.G. Hansen<sup>2</sup>, O. Mogensen<sup>1</sup>

<sup>1</sup>*Odense University Hospital, Dpt. of Gynecology, Odense,* <sup>2</sup>*University of Southern Denmark, Research Unit of General Practice, Odense - Denmark*

**Purpose:** Recently the rationale for performing follow-up examinations in cancer survivors has been challenged. According to retrospective studies in endometrial cancer patients recurrence of disease is detected regardless of follow-up examinations due to symptoms. Consequently, follow-up examinations do not improve survival. Little is known of the psychological impact of follow-up examinations. On one hand follow-up is associated with a sense of security, on the other hand it may serve as a reminder of disease and thus induce anxiety. The objective of the study is to compare hospital-based follow-up examinations with instruction in self-referral in stage I endometrial cancer patients. It is hypothesized that the intervention will reduce fear of recurrence and improve quality of life and cost-utility.

**Methods: Design:** A multi-center randomized controlled trial. Women treated for stage I endometrial cancer at Odense University Hospital, Aalborg University Hospital and Aarhus University hospital between April 2013 and April 2015 will be included in the study. Randomization is done following FIGO staging, and those with high risk histology and/or scheduled for adjuvant oncologic treatment are excluded. Women allocated to the control group attend regular follow-up examinations at the department of Gynecology and Obstetrics for three years following discharge. Women in the intervention group are carefully instructed in symptoms that require examination by a physician. They are given a contact person at the department of Gynecology that they can consult with questions and in case of symptoms. Consequently, examination in the intervention group is initiated by the patient in case of symptoms or distress. Both groups are free to consult their general practitioner at any time. The primary end-point is fear of recurrence as measured by a validated multi-scale questionnaire: Fear of Cancer Recurrence Inventory (FCRI). Further, quality of life, unmet needs, and disease-free survival will be assessed. Finally, a cost-utility analysis will be performed.

**Results and conclusions:** As inclusion is on-going, results will not be available for the meeting, but a description of the methods and progress will be presented. Findings may greatly impact on future follow-up offers for endometrial cancer patients.

## **PATIENTS' AND CARERS' PERSPECTIVES AND PREFERENCES FOR GYNAECOLOGICAL CANCER FOLLOW UP AFTER TREATMENT IN WALES: A HEALTH ECONOMICS PERSPECTIVE**

L.J. Budd<sup>1</sup>, V. Morrison<sup>2</sup>, N.S.A. Stuart<sup>3,4</sup>, S.C. Leeson<sup>3</sup>, R. Whitaker<sup>4</sup>, N.H. Williams<sup>4</sup>, S. Tien Yeo<sup>1</sup>, R. 'h Aslam<sup>4</sup>, R. Tudor Edwards<sup>1</sup>

<sup>1</sup>*Centre for Health Economics and Medicines Evaluation, Bangor University;* <sup>2</sup>*School of Psychology, Bangor University, UK;* <sup>3</sup>*Betsi Cadwaladr University Health Board (BCUHB);*

<sup>4</sup>*North Wales Organisation for randomised Trials in Health, Bangor University - UK*

**Purpose:** There are no NICE guidelines and no consensus regarding the most effective and cost-effective follow up after treatment for gynaecological cancer. As a result, differing follow up care protocols are implemented. The NHS is striving to improve cancer outcomes, ensuring that outcomes are based on patients' and carers' needs. The aim of the research is to explore patients' and their informal caregivers' perspectives and preferences for endometrial, cervical, and ovarian cancer follow-up after treatment.

**Methods:** Four related studies are being undertaken:

1. The biopsychosocial and economic outcomes of female cancer follow up after treatment: A mixed method systematic review of national policy, effectiveness, cost effectiveness, patient, carer and health care professional views.
2. Gynaecological cancer follow-up after treatment: What attributes do patients and their informal caregivers' value? This focus group study will facilitate the design of the discrete choice experiment (DCE), a health economics stated preference method. Patients are currently being recruited purposefully from the follow up clinics within Betsi Cadwaladr University Health Board (North Wales, UK), to ensure representative sampling. Sufficient focus groups will be conducted until data saturation is reached. The results will be analysed using the Framework approach.
3. Patients' and Carers' preferences for different models of Gynaecological cancer follow-up after treatment: a discrete choice experiment (DCE). A DCE is a health economics stated preference method. The findings from the systematic literature review and focus group study will influence the design of this all Wales DCE (sample size 200 patients and their caregivers). The inclusion of a hypothetical willingness to pay attribute will demonstrate how much participants are willing to pay for a trade in one level of care (e.g. consultant) compared to another (e.g. specialist nurse).
4. The hypothetical allocation of follow up care resources: a patient, carer and health care professional perspective. The findings from the systematic literature review and focus group study will influence the design of an all Wales survey (sample size 200 patients and their caregivers, and 75 health care professionals).

### **Results**

1. The systematic literature review is ongoing.
2. Participants are currently being recruited for the Focus Group study which is due to take place in August 2014.
3. Recruitment for the DCE will commence in Spring 2015.
4. Recruitment for the resource allocation survey will commence in Spring 2015.

**Conclusion:** Knowledge and understanding of patients' and their informal caregivers' perspectives and preferences for gynaecological cancer follow-up could help reduce the inefficiencies in the provision of health care services within limited NHS resources.

## **HIGH-RISK ENDOMETRIAL CANCER: DISCORDANCE BETWEEN PREOPERATIVE AND FINAL SURGICAL DIAGNOSIS IS A RISK FACTOR FOR POOR ONCOLOGIC OUTCOMES**

A. Di Cello<sup>1</sup>, F. Zullo<sup>1</sup>, A. Lucia<sup>1</sup>, E. Rania<sup>1</sup>, V. Zuccalà<sup>2</sup>, R. Venturella<sup>1</sup>, A. Sacchinelli<sup>1</sup>, M. Rocca<sup>1</sup>, R. Cirillo<sup>1</sup>, M. Morelli<sup>1</sup>

<sup>1</sup>*Unit of Obstetrics and Gynaecology, ‘Tommaso Campanella’ Cancer Center of Germaneto, Department of Experimental and Clinical Medicine, ‘Magna Graecia’ University, Catanzaro, Italy*

<sup>2</sup>*Unit of Pathology, Faculty of Medicine, Health Science Department, ‘Magna Graecia’ University - Catanzaro, Italy*

**Study’s purpose:** In high-risk endometrial cancer (EC) it is crucial to have a reliable preoperative diagnosis in order to address patients to the best surgical approach. Aim of our work has been to evaluate the discordance between pre- and post-operative pathologic diagnosis and to correlate this discordance to the oncologic outcomes.

**Methods:** Data from 447 patients, surgically treated for EC, were retrospectively reviewed and stratified into low or high-risk class based on the definitive surgical pathology. The discordance between pre- and post-operative diagnosis was evaluated. High-risk patients were sub-categorized into two groups according to the “discordant” or “concordant” diagnosis, and compared for oncologic outcomes. The effect of several variables on survival was measured. In order to assess whether the sub-optimal treatment in those high-risk patients preoperatively misdiagnosed as low-risk might worsen the prognosis, a sub-analysis of data was performed. The impact of extensive surgery on the OS was evaluated measuring the difference in OS between high-risk EC patients which have been submitted to extensive surgical staging and those undergone to standard surgery. To evaluate the prognostic value of FS performed for pelvic lymph nodes and myometrial infiltration (MI) evaluation, the difference in OS between high-risk EC patients in which FS was performed and patients in which FS had not been made, was evaluated.

**Results:** A discordant diagnosis rate of 32.1% was observed for high-risk ECs. Among 109 high-risk patients, a significant difference in 5-years overall survival (OS; 70.2 vs. 86.8%;  $p=0.029$ ), disease specific survival (DSS; 72.5 vs. 88.2%;  $p=0.039$ ), recurrence free survival (RFS; 62.6 vs. 82.5%  $p=0.024$ ) between patients with “discordant” and “concordant” diagnosis was observed. Stage, discordant diagnosis, not-performing the extensive surgical staging and lack of chemotherapy, significantly reduced the OS. The implementation of an extensive surgical staging improved the OS in high-risk patients (71.9 vs. 89.4%;  $p=0.01$ ) while the use of FS for pelvic lymph nodes and myometrial evaluation has not able to significantly improve the prognosis (84.0 vs. 81.4%;  $p=0.70$ ).

**Conclusions:** Patients with high-risk EC have an important discordance rate between pre- and post-operative pathologic diagnosis and this aspect significantly worsens their oncologic outcomes. The use of FS for pelvic lymph nodes and MI evaluation is not always discriminant for deciding what is the best management of high-risk patients. Furthermore, FS does not provide any additional information about the genetic profile of EEC G3, which seems to be the main prognostic factor for choosing the best surgical and adjuvant treatment.

# POSTERS

**BORDERLINE OVARIAN TUMORS AND DIAGNOSTIC DILEMMA OF INTRAOPERATIVE DIAGNOSIS: COULD PREOPERATIVE HE4 ASSAY AND ROMA SCORE ASSESSMENT INCREASE THE FROZEN SECTION ACCURACY? A MULTICENTER CASE-CONTROL STUDY**

S. Gizzo<sup>1</sup>, R. Berretta<sup>2</sup>, M. Noventa<sup>1</sup>, G.B. Nardelli<sup>1</sup>, T. Silvio Patrelli<sup>2</sup>

<sup>1</sup>*Department of Woman and Child Health, University of Padua, Padua;* <sup>2</sup>*Department of Surgical Sciences, University of Parma, Parma - Italy*

**Objective:** to evaluate the usefulness of pre-operative He4 serum assay and ROMA score assessment in improving the accuracy of histological BOTs FS diagnosis in pre- and post-menopausal women.

**Methods:** retrospective-multicenter case-control study on women with unilateral pelvic ovarian mass who underwent intra-operative FS analysis and received a diagnosis of serous or mucinous BOTs at FS or/and at subsequent permanent histology. For all the patients the Pathologists were aware of pre-operative clinical and instrumental information. For Group\_A patients Pathologists obtained also information about pre-operative He4, CA125 values and ROMA score, while for Group\_B patients pre-operative CA125 value was given only.

**Results:** the comparison between Group\_A and Group\_B in terms of FS accuracy showed that consensual diagnosis was obtained in 62.8% versus 58.6% [p:n.s.], under-diagnosis was detected in 25.6% versus 41.4% [p<0.05] and over-diagnosis was detected in 11.6% versus 0% [p<0.01].

The major risk factors for low FS accuracy resulted menopausal status (OR:2.13), laparoscopic approach (OR:2.18), mucinous histotype (OR:2.23), grade 1 tumour (OR:1.30), 1st FIGO stage (OR:2.53). Ultrasound detection of papillae (OR:0.29), septa (OR:0.39) atypical vascularization (OR:0.34), serum He4 assay (OR:0.39) and ROMA score assessment (OR:0.44) resulted protective factors for FS underdiagnosis.

**Conclusions:** giving information to the Pathologist attempting FS evaluation of pelvic mass about serum markers assay in combination with ultrasound features may potentially reduce the rate of under-diagnosis despite it seems to increase the over-diagnosis rate when BOTs is suspected at FS histology. Independently from FS, fertility sparing surgery is suggested when women have future fertility desire.

## **ARYLESTERASE ACTIVITY OF PARAOXONASE 1 IN PATIENTS WITH PREMALIGNANT LESION OF THE CERVIX**

D. Butorac<sup>2</sup>, M. Grdić Rajkovića<sup>1</sup>, I. Čelap<sup>3</sup>, S. Kačkov<sup>4</sup>, T. Miletić<sup>5</sup>, A. Hulina<sup>1</sup>,  
T. Žanić Grubišića<sup>1</sup>

<sup>1</sup>*Department of Medical biochemistry and Hematology, Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb;* <sup>2</sup>*Clinic of Gynecology and Obstetrics, Clinical Hospital Center Sestre milosrdnice, Zagreb;* <sup>3</sup>*Clinical Institute of Chemistry, Clinical Hospital Center Sestre milosrdnice, Zagreb;* <sup>4</sup>*Medical biochemistry laboratory, Polyclinic Bonifarm, Zagreb;* <sup>5</sup>*Polyclinic “Aviva Zagreb, Croatia*

Paraoxonase 1 (PON1) is an enzyme which is associated with high density lipoprotein (HDL) in serum. PON1 possesses paraoxonase, arylesterase and lactonase activity and hydrolyze different kinds of substrates. Also, PON1 has antioxidant/antiatherogenic activity, and it removes carcinogenic radicals of lipid peroxidation in human body. It was established earlier that patients with premalignant lesions of cervix have increased lipid peroxidation and changes in antioxidative system, which points importance of oxidative stress in early phase of carcinogenesis. We carried out this study in order to determine PON1 arylesterase activity in patients with premalignant lesions of the cervix.

Study included 65 women [38 (32-46) years] with a biopsy confirmed diagnosis of cervical intraepithelial neoplasia (CIN), 18 patients had CIN1, 23 had CIN2 and 24 had CIN3. 109 healthy volunteers [37 (29-42) years] without any cervical or other disease were enrolled in the study as a control group. Concentration of HDL cholesterol and apolipoprotein AI (apoAI) were determined by commercially available reagents. PON1 arylesterase activity was assayed spectrophotometrically with phenylacetate as a substrate. We standardized PON1 arylesterase activity according to the concentration of HDL-cholesterol and apoAI.

PON1 arylesterase activity was significantly reduced in group of patients with premalignant lesions of the cervix ( $53 \pm 20$  kU/L vs  $75 \pm 18$  kU/L;  $P < 0,001$ ). PON1 arylesterase activity standardized on the concentration of HDL ( $36 \pm 28$  kU/mmol vs  $41 \pm 35$  kU/mmol;  $P = 0,004$ ) and on the concentration of apoAI [ $28 (23 - 35)$  kU/g vs  $42 (35 - 51)$  kU/g;  $P < 0,001$ ] were lower in the group of patients with premalignant lesion of cervix compared to the healthy volunteers.

Diagnostic accuracy of PON1 arylesterase activity in discriminating between healthy subjects and patients with premalignant lesion of the cervix was good [AUC (95% CI): 0,784 (0,715 – 0,842)]. Sensitivity and specificity with corresponding 95% CI was 65 (52 – 76) and 85 (77 – 91), respectively. Cut off value was  $\leq 56$  kU/L.

Our results suggest that PON1 arylesterase activity is reduced in patients with premalignant lesions of the cervix. Furthermore results of diagnostic accuracy in discriminating between healthy subjects and individuals with premalignant lesions of the cervix indicated that PON1 arylesterase activity could be considered as a potentially valuable biomarker for premalignant lesions of the cervix.

**MOLECULAR TARGETED THERAPIES IN OVARIAN CANCER IDENTIFYING POTENTIAL BIOMARKERS AND OVERCOMING MECHANISMS OF RESISTANCE FOR OVARIAN CANCER. A NEW MODEL OF COMBINING TRANSLATIONAL SCIENCE WITH CLINICAL SERVICES IN FRONTLINE ACUTE ONCOLOGY SERVICES**

H. Cooper, R. Woolas, A. Diaper, S. Rahimi, S. Glaysher, C.C. Yeoh  
*Queen Alexandra Hospital, Cosham, Portsmouth - United Kingdom*

**Background:** The evolution of Acute Oncology in the United Kingdom has given rise to a frontline service of emergency medicine for all oncology patients directed by oncologists. This service deals directly with oncology patients presenting with complications of their cancer treatment as well as symptoms from their cancer, supporting a more direct contact between the patient and their oncologist. Logistic and special means of walk in centers for emergency services such as drainage of malignant effusions and ascites are done as day cases, planned one stop at Acute Oncology. We now collect all malignant ascites (where consent is given) for use in translational molecular studies, as set up by our study MTOC. With knowledge of cancer growth pathways and resistance mechanisms, analyses of novel targeted drug combinations for their potential use in ovarian cancer are assessed. These sensitivity data are directly compared with potential molecular biomarkers for possible future use in patient stratified treatment selection.

**Method:** We have a steady stream of 2-4 patients per week presenting to our walk-in bay in Acute Oncology for draining of ascites. At presentation of their ovarian cancer, they will be asked to consent for the use of excess ascites fluid within our translational study (REC approved: 14/NI/0050). These patients can generate between 4-6 litres ascites fluid, providing a valuable source of assay ready cancer cells. Clinical study data are collected by the clinician data managers, in a clean format as indicated below. Follow up on future treatment and prognosis is carried out per standard in our institution. Samples are collected in sterile containers containing a cell supportive media and either taken immediately to the laboratory or kept refrigerated at 4°C until it can be collected by the laboratory. Where cell concentration and viability is sufficient, cellular and molecular assays are performed. Targeted therapy combinations of interest being tested in our cellular assays are listed below.

**Results:** To date the recruitment has been consistent at 2 per week. Patients have a close relationship with their Oncologist and during these acute events of ascites drain, they are happy and trust their regular clinician oncologist with enrolment into trials. Previous to Acute Oncology, these acute admissions would likely occur in Accident and Emergency department where patients are not known to the emergency team. In these circumstances would not really be suitable for the discussion of enrolment on to clinical trials. We have had some success identifying two potential pathway targets that seem to be important in ovarian cancer. Within the next year we aim to recruit 60 patients for this trial. This is nearly 95% of all stage 3c/4 ovarian disease with ascites (the most common stage for presentation of ovarian cancer within the United Kingdom).

**Conclusion:** This study will potentially generate data useful in future stratified medicine trials, for us as researchers and for the patients. Future commercial trials with eligibility criteria requiring patients whose tumour harbour specific mutations can be identified quickly; as patients already enrolled in this study will have the prior knowledge of their tumours molecular profile.

**CLINICAL AND PRACTICAL STUDY OF TENDENCY LOCAL PRODUCTION OF LEVEL CYTOKINES IL-6, IL-8 AND ANGIOGENETIC POTENTIAL OF IT IN THE PERITONEAL FLUID IN PATIENTS WITH BENIGN TUMORS OF THE UTERUS**

V.V. Yevdokymova

*Odessa by the National Medical University, Department of Obstetrics and Gynecology, N° 1 Academician, Zaporozhan VM - Ukraine*

A sentence stating the study's purpose is detect of pathogenic role and tendency of production of inflammatory cytokines (IL-6, IL-8) in peritoneal fluid (PF) in patients with benign tumors of the uterus (BTU).

A brief description of methods. Determination of levels of IL-6, IL-8 was performed in PF in 32 patients suffering on benign tumors of the uterus with different size of BTU. The diagnosis of BTU in all patients was verified during laparoscopic intervention and according to the ultrasound result. The concentration of cytokines in PF was assessed by ELISA methods, using test-kits for the determination of IL-6, IL-8.

A summary of the results obtained. We had found in PF an increasing levels of IL-8 and IL-6 in patients with BTU than in the control group. Established that the presence of elevated levels of IL-8 and IL-6 in women, patients with BTU increases the proliferative and angiogenic potential, as evidenced by an increase in the content of IL-8 in women with much larger size of BTU compared to less pronounced their size and the control group.

A statement of conclusions reached. In findings suggest that the progressive increase in production of inflammatory cytokines with increasing disease severity (size of BTU) is a measure of amplification of the inflammatory reaction in the abdomen and also in peritoneal fluid. Therefore, increasing the indicators of IL-6 and IL-8 in the PF and it is a typical for the proliferative activity in patients with benign tumors of the uterus, what is increase a vascularization of this formations.

## **GERMLINE GENES – A GOLDMINE FOR OVARIAN CANCER BIOMARKERS?**

J. Sammut<sup>1</sup>, J. Feichtinger<sup>2</sup>, R. McFarlane<sup>3</sup>

<sup>1</sup>*School of Medical Sciences, Bangor University, Wales, UK;* <sup>2</sup>*Institute of Knowledge Discovery, Graz University of Technology, Austria;* <sup>3</sup>*School of Biological Sciences, Bangor University, Wales, UK*

The search for cancer specific biomarkers is a hugely important area of translational clinical research. Cancer/testis antigens (CTAs) are antigens that are normally present in the tissues of the testis, but are also aberrantly produced by cancers. Meiosis occurs in the foetal ovary but is confined in adults to the testis; germline genes are specifically associated with this process. There is increasing evidence to suggest that a soma-to-germline transition may be of fundamental importance in cancer pathogenesis. The aim of the current study was to identify if meiosis-specific genes are activated in cancer.

**Methods:** First, we identified the human orthologues of a cohort of mouse genes specifically associated with meiosis. An in silico pipeline was then set up from expressed sequence tag (EST) data sets; genes were excluded if found to be expressed in normal tissue other than central nervous system or testis. The candidate genes expression profile was then validated in a range of normal and cancerous tissues by utilising polymerase chain reaction (RT-PCR). Finally, the possible clinical relevance of the validated genes was explored by meta-analysing patient-derived cancer microarray data sets.

**Results:** Of the 400 genes that were initially identified, just over half were excluded at the EST filtering stage. Of this cohort, eighty five were validated by RT-PCR as predominantly testis expressed (i.e. seen in a maximum of two other normal tissues). When the results were meta-analysed using clinically derived microarray data sets, ovarian cancer stood out as the predominant cancer type displaying statistically significant upregulations in gene expression. 31 genes displayed a significant up-regulation in any cancer type and in twenty nine of these cases there was an upregulation in ovarian cancer (alone or in combination with another cancer type). Similarly, when a broader approach was used incorporating all known germline genes, ovarian cancer again stood out as the most common cancer associated with meta-upregulations, although not to such a striking degree as for the meiosis-specific cohort.

**Conclusions:** A novel subcategory of CTA genes, specifically associated with meiosis, has been identified. These germline genes, which we term meiCT genes, are associated with statistically significant upregulations in gene expression predominantly in ovarian cancer. This may be due to conserved germline/meiotic functions, which are silenced in the adult ovary. In any case they provide a large cohort of cancer-specific biomarkers that may not only be useful in diagnosis or risk stratification but also targets for powerful novel immunotherapeutic strategies, as the antigens produced should not be recognised as 'self' by the immune system. Furthermore, important insights in cancer pathogenesis may become apparent, as the same genes that govern the complex chromosome dynamics that occur in meiosis may be driving the oncogenic process.

### **CD157: A NEW PROGNOSTIC MARKER IN OVARIAN CANCER**

G. Borghese<sup>1</sup>, G. Lanzo<sup>1</sup>, R. Benvenuto<sup>1</sup>, R. Arisio<sup>1</sup>, D. Katsaros<sup>1</sup>, M. Volante<sup>2</sup>, I. Rapa<sup>2</sup>, E. Ortolan<sup>3</sup>, C. Benedetto<sup>1</sup>, A. Funaro<sup>3</sup>

<sup>1</sup>*Gynecology and Obstetrics I, Department of Surgical Sciences, University of Turin, Sant'Anna Hospital, Città della Salute e della Scienza, Turin;* <sup>2</sup>*Pathology Unit, Department of Clinical and Biological Sciences, University of Turin, San Luigi Hospital, Orbassano, Turin;* <sup>3</sup>*Laboratory of Immunogenetics, Department of Medical Science, University of Turin, Turin - Italy*

**Introduction:** CD157 was found to be expressed in most Epithelial Ovarian Cancer (EOC) and its high expression level proven to be an independent prognostic factor of rapid tumor recurrence and poor prognosis in patients, hinting to promising clinical application for CD157 in EOC (Ortolan E. et al. J Natl Cancer Inst. 2010). The aim of the present study was to compare CD157 expression in primary tumors (P) and synchronous disseminated lesions (D) from advanced ovarian carcinoma, and to assess whether this parameter has a predictive or prognostic relevance.

**Methods:** 45 cases of EOC with synchronous metastasis collected between 2001 and 2007 at the Sant'Anna Gynecological Hospital (Torino, Italy) were included in this study and subjected to immunohistochemical analysis. The expression of CD157 was quantified through histological score (H score).

**Results:** CD157 was expressed in 34 (75.56%) primary tumors and 35 (77.78%) metastasis. The CD157 H-score was higher in lymph node metastasis ( $p < 0.005$  ANOVA) than in other intra- and extra-pelvic sites. The CD157 H-score was compared in P and the corresponding D: in 24 cases (53.3%) the expression of CD157 was higher in D than in P ( $P < D$ ), while in 21 cases (46.6%) the CD157 H-score in D was equivalent to or lower than in P ( $P \geq D$ ). The patients were divided into two groups based on the trend of the expression of CD157 in D versus P ( $P < D$  vs  $P \geq D$ ) and the trend in H-score was correlated with the clinical-pathological features of the tumors. The increase in H-score of CD157 in D ( $P < D$ ) group was proven to be associated with tumor stage and overall survival at follow-up. Univariate analysis of survival according to the Kaplan-Meier method in 40 patients (5 patients were lost at follow up) highlighted that patients with  $P \geq D$  had a significantly higher overall survival (OS) than patients with  $P < D$  [ $P \geq D$  n=18 median OS not reached;  $P < D$  n=22, median OS (95% CI)=27(28,68-51,13)months; HR(95% CI)=3.439(1.493-7.922)](log-rank test  $p=0.002$ ). The multivariate analysis according to Cox method showed that the increase in the expression of CD157 in D ( $P < D$ ) is an independent factor of poor prognosis [HR (95% CI)=2.837(1.177-6.840)  $p=0.020$ ].

**Conclusions:** The results of this study demonstrate that the increase in the expression of CD157 in D compared to P was associated with tumor stage and overall survival and proved to be an independent factor of poor prognosis. In conjunction with conventional diagnostic markers CD157 may indicate a highly aggressive tumor requiring specific treatment, and it may help to classify ovarian cancers into molecular subtypes with different outcome.

## **TUMOUR MOLECULAR PROFILE-DIRECTED TREATMENT IS ASSOCIATED WITH IMPROVED SURVIVAL IN RECURRENT EPITHELIAL OVARIAN CANCER**

H. Gabra<sup>1</sup>, K.E. Oliver<sup>2</sup>, N. Xiao<sup>3</sup>, D. Spetzler<sup>3</sup>, N.T. Phippen<sup>2</sup>, R.T. Oleszewski<sup>2</sup>,  
W.P. McGuire III<sup>2</sup>

<sup>1</sup>*OCA Research Centre, Imperial College London – United Kingdom;* <sup>2</sup>*Walter Reed National Military Medical Center, Bethesda, MD - USA;* <sup>3</sup>*Caris Life Sciences, Phoenix, AZ - USA*

**Background.** We sought to determine whether tumour molecular profile-directed treatment of recurrent ovarian, primary peritoneal and fallopian tube carcinomas influenced survival.

**Methods.** With IRB approval, Caris Life Sciences maintains the Caris Registry, a database of clinicopathologic and outcome variables from consenting patients whose tumours underwent molecular profiling. Molecular profiling was performed using a multiplatform approach to stratify agents by degree of potential therapeutic benefit. The Caris Registry was queried for all patients with a diagnosis of ovarian, primary peritoneal and fallopian tube carcinomas enrolled between 2010 and 2014. Patients were stratified based on chemotherapeutic agents employed during their disease course: the Benefit cohort received at least one agent designated to be of potential benefit and no agents with potential lack of benefit while the Lack Of Benefit cohort received at least one agent with potential lack of benefit. Survival was calculated from the date of profiling and from the date of diagnosis to the date of death/censoring using the Kaplan-Meier method.

**Results.** Of 450 patients identified in the registry, 102 were excluded due to non-invasive pathology, non-epithelial histology, and missing or ambiguous treatment information. Of the remaining 348 eligible and evaluable patients, 170 formed the Benefit cohort and the remaining 178 were assigned to the Lack Of Benefit cohort. There were no significant differences in baseline clinicopathologic characteristics between the two groups. Patients in the Benefit cohort experienced significantly longer post-profiling survival when compared with patients in the Lack Of Benefit cohort, HR 0.54 (CI 0.37 – 0.80, p = 0.0018).

**Conclusions.** Tumour molecular profile-directed treatment significantly improves post-profiling survival in patients with recurrent ovarian, primary peritoneal and fallopian tube carcinomas. Despite immature outcome data, trends toward improved overall survival were also demonstrated.

## **INTEGRIN BETA6 SIRNA INHIBIT INVASIVENESS OF HUMAN OVARIAN CANCER CELLS IN VITRO AND IN VIVO**

Du Xue-lian

*Department of Gynecologic Oncology, Shandong Cancer Hospital, Jinan - P. R. China*

**Objective:** The aim of this study is to investigate the inhibitory action of beta6 siRNA on invasiveness of human ovarian cancer cells HO-8910PM.

**Methods:** Using liposome as a vector, integrin beta6 siRNA and non-oligonucleotide were transfected into HO-8910PM cells, which were then randomized to siRNA group, neo group and control group. The proliferation, anoikis, adhesion, migration and invasion were measured by MTT, adhesion and transwell ventricle, respectively. Then cells were inoculated subcutaneously into the left flank of nude mice. The expressions of integrin beta6 in transplanted tumors of mice were detected by immunohistochemical method as well.

**Results:** Compared with control group, the migration and invasiveness of HO-8910PM cells transfected by integrin beta6 siRNA was obviously decreased ( $P=0.013$  and  $P=0.003$ , respectively). The cell adhesion, laminin, and fibronectin were also enhanced ( $P=0.007$ ,  $0.039$ , and  $0.014$ , respectively). Furthermore, cells transfected with beta6 siRNA formed smaller tumor and fewer metastases in transplanted tumors of mice than control ( $P=0.006$  and  $P=0.006$ , respectively).

**Conclusion:** Integrin beta6 siRNA can inhibit migration, invasiveness, tumorigenicity and metastasis of human ovarian cancer cells in vitro and in vivo, and might be of great benefit for finding rational approach in ovarian cancer therapy.

## **IMMATURE TERATOMA IN 21 YEAR OLD PATIENT: CASE REPORT AND BRIEF LITERATURE REVIEW**

S.Stavros, E. Domali, D. Haidopoulos, D. Vlachos, P. Drakakis, P. Katafygiotis, I. Papaspirou, K. Syrios, S. Mesogitis

*University of Athens, Alexandra Hospital, 1st Gynaecology Department, Athens - Greece*

A 21 year-old female patient attended our hospital, complaining for sustained episodes of diarrhea and feeling of gradually increasing abdominal bloating since 48 hours. Clinical evaluation proved increased abdominal size and revealed a palpable mass on the right lower abdomen.

Ultrasonography showed a mass of 91x101x100 mm dimensions originated from the right ovary; based on IOTA criteria, mass has been described as a multilocular-solid lesion, containing >5 loci. The solid part of 75x59x77 mm was completely irregular. More than 5 irregular papillations were calculated, while 3 of them presented internal flow. Vascularization pattern was estimated as color score IV. Ascites was clearly obvious and the suggestion of “floated uterus” was included in the report. Enlarged left kidney was identified; the last was attributed to the pressure induced by ascites. Swollen left iliac lymph nodes were recognized but without clinical significance. Based on the above reported ultrasonographic data and regarding IOTA simple rules, the ovarian lesion was characterized as a “certainly rare malignant tumor”. Histological diagnosis of grade III immature teratoma, confirmed the preoperative ultrasonic suggestion.

Ovarian teratomas are the most common germ cell tumors. They divided into 3 subcategories; mature, immature and monodermal teratomas. Immature teratomas consist of immature neuroepithelial tissue; they are categorized in 3 grades depending on the amount of neuroepithelial tissue forming rosettes and tubules. Grade III has the worst prognosis. Immature teratomas and monodermal teratomas represent hazardous lesions with various clinical symptoms. Their diagnosis is mainly based on imaging methods and secondly on hematological examinations. Ultrasound plays a pivotal role supplemented with MRI and CT scan. Surgery alone or in combination with chemotherapy is the proposed treatment of immature teratoma.

## **POST-OPERATIVE MRI FINDINGS IN PATIENTS WITH FERTILITY-SPARING SURGERY FOR EARLY CERVICAL CANCER**

C. Bourgioti<sup>1</sup>, K. Chatoupis<sup>1</sup>, A. Rodolakis<sup>2</sup>, N. Thomakos<sup>2</sup>, M-E. Nikolaidou<sup>3</sup>,  
L.A. Mouloupoulos<sup>1</sup>

<sup>1</sup>University of Athens, 1st Radiology Dpt, Athens - Greece; <sup>2</sup>University of Athens, 1st Gynecologic and Obstetrics Dpt, Gynecologic Oncology Unit, Athens - Greece; <sup>3</sup>Rea Maternity Hospital, Athens - Greece

**Aim:** To report normal and abnormal post-operative MRI appearances in young women with early-stage cervical cancer treated with abdominal radical trachelectomy (ART).

**Material and method:** During a 5-year period, 21 patients with biopsy-confirmed cervical carcinoma, FIGO stage  $\leq$ IB1 were treated with ART. All patients were evaluated with dedicated pelvic MRI prior to surgery. Follow-up MRI was performed in 17/21 trachelectomy patients, 6 months after surgery and every 6 months thereafter, for a total of 6-48 months (mean 24 months). Two radiologists, expert in female imaging, reviewed normal post-ART MRI findings and post-operative complications.

**Results:** Baseline follow-up MRI clearly demonstrated the cervicovaginal anastomosis, vaginal neofornix and the presence of a cerclage suture in all 17 patients. Magnetic susceptibility artefacts caused by cerclage suture were noted on gradient echo sequences only, partially degrading image quality. In 12/17 post-ART patients, MRI showed diffuse vaginal wall oedema/haematoma, which gradually resolved on serial follow-up studies. Asymptomatic lymphocysts occurred in 3/17 post-ART patients. Hydrosalpinx formation, an unknown complication, was evident in 3/17 patients at follow-up MRI; in 2/3 ART patients, the dilated tubes were discovered incidentally 6 months after ART. One patient who complained of prolonged and painful menstruation a year after surgery, MRI showed severe isthmic stenosis and unilateral hydrosalpinx. Follow-up MRI detected local tumor recurrence in one and lymph node metastases in another of 17 patients, within 48 months after ART.

**Conclusion:** MRI is a reliable tool in monitoring post-ART patients. Hydrosalpinges is an unusual complication, which should be noted since it may influence patients' fertility potential.

## **PREOPERATIVE EVALUATION OF BORDERLINE OVARIAN TUMORS BY RISK OF MALIGNANCY INDEX, CA125 AND ULTRASOUND**

C. Dane, N. Bilgili

*Haseki Training and Research Hospital, Department of Gynecology and Obstetrics, Istanbul, Turkey*

**Objective:** To assess the ability of the risk of malignancy index (RMI) based on a serum CA125 level, ultrasound findings and menopausal status, to discriminate borderline serous from borderline mucinous.

**Materials and Methods:** The study consisted of 38 patients with BOT diagnosed and treated between 2003-2013 in the retrospective study. The sensitivity, specificity, positive predictive values, negative predictive values and diagnostic accuracy of preoperative serum levels of the CA125, ultrasound findings and menopausal status, and RMI were calculated for prediction of discrimination between borderline serous and borderline mucinous tumors and the results were compared.

**Results:** The mean age  $45.1 \pm 14.3$  (range 19-83) was detected in study group. From a total number of 38 women, 20 women had borderline serous tumors; 18 women, borderline mucinous tumors. The best RMI cut-off was found to be 162 for discrimination of borderline mucinous and borderline serous tumors. Using a cut-off level of 162 to discriminate, the RMI showed a sensitivity of 72.2 %, a specificity of 65 %, a PPV of 65 %, a NPV of 72 % and positive likelihood ratio 2.06. The areas under curve of RMI to discriminate borderline serous from borderline mucinous were found to be  $0.646 \pm 0.09$  (0.474-0.794).

**Conclusion:** RMI is a simple, easily applicable method in the primary evaluation of patients with adnexal masses resulting in timely referral to gynecological oncology centers. Our optimal cut-off point for the RMI was 162 giving a sensitivity of 72.2 %, and NPV of 72 % in discriminating serous and mucinous borderline ovarian tumors.

## **FOLLOW UP OF ENDOMETRIAL AND OVARIAN CARCINOMA PATIENTS**

S Budithi<sup>1</sup>, A. Nassar<sup>2</sup>, S. Leeson<sup>3</sup>

<sup>1</sup>*Ysbyty Gwynedd, Department of Gynaecological Oncology, Bangor, United Kingdom;* <sup>2</sup>*University hospital of wales, Department of Obstetrics and Gynaecology, Cardiff, United Kingdom;* <sup>3</sup>*Ysbyty Gwynedd, Department of Gynaecological Oncology, Bangor, United Kingdom*

**Background:** Follow up of endometrial and ovarian carcinomas may allow earlier detection of recurrences and earlier treatment of such recurrences may result in improved outcome. The aim of this study was to evaluate the differences in outcomes for patient reported recurrences as opposed to asymptomatic recurrences detected on routine clinical examination.

**Methods:** This was a retrospective review of endometrial and ovarian carcinomas from 2002-2006 in North Wales. Data was collected using case notes, MDT records and death records.

**Results:** A total of 224 endometrial carcinoma and 214 ovarian carcinoma cases were included. Recurrence rates were 16% and 47% for endometrial and ovarian carcinomas respectively. In the endometrial carcinoma group, there was equal occurrence of clinically detected and patient reported recurrences. In the ovarian carcinoma group, recurrences were more frequently detected by clinicians (61%) compared to patient reported recurrences (39%). The 5-year survival rates were 68.3% and 19.0% for endometrial and ovarian carcinomas respectively. The 5 year survival rates for recurrences were 34% and 14%. Time to recurrence from initial diagnosis was significantly shorter for clinically detected cases compared to patient reported recurrence in endometrial carcinoma (20.23 vs 32.15 months,  $p=0.03$ ). There is no significant difference in time to death from recurrence (2.5 vs 2.0 years,  $p=0.61$ ). In ovarian carcinoma group, the time to recurrence was not significantly different between groups (21.22 vs 16.97 months,  $p=0.22$ ). However, the time to death from recurrence was significantly longer for clinically detected group compared to patient reported group (1.60 vs 1.03 years,  $p=0.046$ ). The drawback of this study was unknown recurrence status for 61 cases.

**Conclusion:** Longer survival is expected if patients with ovarian carcinoma have recurrences which were clinically detected compared to patient reported group. We recommend follow up with CA 125 or imaging if there is suspicion of recurrence

## **QUALITY OF LIFE AND RETURN TO WORK FOR BREAST CANCER SURVIVORS**

L. Bouzgarrou<sup>1</sup>, H. Laajili<sup>2</sup>, A. Slama<sup>2</sup>, A. Kraiem<sup>1</sup>, C. Amri<sup>3</sup>, T. Khalfallah<sup>1</sup>, M. Sakkouhi<sup>2</sup>

<sup>1</sup>*Occupational Department of Medicine, university hospital of Mahdia;* <sup>2</sup>*Obstetrics and gynecology department of medicine university hospital of Monastir;* <sup>3</sup>*occupational Department of Medicine, university hospital of Monastir - Tunisia*

**Background:** In Tunisia, the incidence of breast cancer, the first cancer of woman, is estimated to 2000 new cases per year, with an age of attente significantly younger compared to international literature. Multiple international surveys have reported that serious consequences of this disease on the quality of life of patients: family relationships, psychologically, socially, and sexually; on their ability to work and their professional future.

**Aims:** The purpose of this survey was to evaluate the quality of life among young actives patients with breast cancer on different scales (physical, emotional, social, sexual ) and also their professional future especially return to work.

**Methods:** This survey have concerned patients initially active and followed in the Maternity Center of Monastir during at least two years after the breast cancer diagnosis. It was performed with through two validated questionnaires EORTC QLQ-C30 and QLQ-BR23. The survey featured two parts "Medical part" and a part "Quality of life and professional future".

**Results:** The average age was  $48 \pm 11$  years. Our patients were singles in 9% of cases. They have worked in public sector in 87% of cases. The tumor's average size at diagnosis was  $4 \pm 1$  cm. Among our patients, 97% were operated and 80% received chemotherapy. Radiotherapy was performed in all cases. The average score for physical functioning was  $53.7 \pm 19.8$ . For emotional functioning the average score was  $31.7 \pm 12$ . Global health score was below the average in 74% of cases. 2/3 of married women have been separated after their cancer diagnosis. Colleague discrimination was noted by 49% of our patients. Workplace management was performed in 28% of cases. At the time of the survey, 28% of our patients have no longer job.

**Conclusion:** Our study has highlighted the need for a multidisciplinary management of patients with breast cancer. Such management shall integrate the various aspects of quality of life and return to work

## **LESS FREQUENT FOLLOW-UP AFTER PRIMARY CERVICAL CANCER TREATMENT, BETTER PATIENT CARE?**

J. Hellendoorn-van Vreeswijk<sup>1</sup>, K. Gaarenstroom<sup>2</sup>, Y. Smit<sup>1</sup>, D. Stemkens<sup>1</sup>

<sup>1</sup>*Comprehensive Cancer Centre, Utrecht, the Netherlands;* <sup>2</sup>*Leiden University Medical Centre - The Netherlands*

**Purpose.** The Dutch guideline ‘Cancer Survivorship Care’ (Comprehensive Cancer Centre The Netherlands, 2011) questions the effectiveness of existing long-term routine follow-up after treated primary cancer. Although early detection of recurrent disease is assumed to provide higher survival rates and/or a better quality of life even after many years for a number of tumours, in other cases, the evidence is lacking. In such cases, early detection provides patients with a false sense of security about the status of their disease and requires regular check-ups which are emotionally challenging and possibly damaging, but ultimately unnecessary. It also results in irrational medicalization of the patient. The aim of this project was to evaluate the effectiveness of routine early detection of new manifestations of treated primary cervical cancer in terms of survival and/or quality of life.

**Methods.** The project was carried out in collaboration with the Dutch guideline committee on cervical cancer. Literature was reviewed in order to assess the scientific evidence for follow up. The research questions of the guideline ‘Cancer survivorship care’ were the starting point:

- When does recurrent disease (local or regional recurrences, distant metastases or second primary tumours) occur after primary treatment of cervical cancer?
- Is there effective treatment for this recurrent disease?
- Does treatment efficacy increase with earlier detection of recurrent disease?
- Which diagnostic detection methods are most suitable for accurate diagnosis of treatable recurrent disease at an early stage?

**Results.** The Dutch guideline committee on cervical cancer decided to decrease the recommended period of routinely follow-up from five to two years. This decision was based on the following conclusions and considerations, the aim being to improve patients’ quality of life and sparing them routine follow-up visits that are not proven useful and possibly harmful:

- 62-89% of recurrent disease appear to occur in the first two years after primary diagnosis
- recurrence rates for early stage disease range from 8% to 26% of patients
- 85% of the patients are symptomatic when diagnosed with recurrent disease, only 15% are asymptomatic
- only patients with locoregional recurrence (14-57%) can be treated with curative intent
- direct evidence that earlier detection of recurrent disease is worthwhile in terms of quality of life and/or prognosis is lacking
- 29-71% of recurrent disease can be diagnosed by physical examination.

**Conclusions.** In the Netherlands, recommendations on early detection of recurrent disease have been adjusted downwards from five to two years in the clinical practice guideline on cervical cancer. A similar evaluation of the impact of routine follow-up on survival and quality of life, which guards patients for unnecessary and emotionally challenging check-ups, is likely to be useful for other tumour types.

## **CHORIOCARCINOMA: A 23-YEAR REVIEW OF CLINICAL EXPERIENCE AT INSTITUTE OF ONCOLOGY IN WARSAW, POLAND**

B. Osuch<sup>1</sup>, K. Gawrychowski<sup>2</sup>, M. Kowalska<sup>1</sup>, B. Śpiewankiewicz<sup>1</sup>

<sup>1</sup>*The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology Warsaw;*

<sup>2</sup>*Medicaver Hospital Warsaw - Poland*

**Objective:** Choriocarcinoma belongs to rare medical condition and mostly responds very well to chemotherapy(excluding placenta side tumor).

**Study Design:** The therapy of patients diagnosed with choriocarcinoma over 23 years period has been analysed.

**Results:** Choriocarcinoma belongs to the multifaceted group of gestational trophoblastic diseases.239 cases of GTD and 30 cases of choriocarcinoma among them were diagnosed during 23 years period of time.It makes up to 12,6 % choriocarcinoma cases of all diagnosed GTD.Patients were between 17 and 53 years old ( average 32,2 ).The level of beta hCG before treatment was between 3,7 and 699,000 IU/L.Distant metastases were diagnosed in 11 cases (36,7 %).In 4 cases were found in both lungs, in further 4 cases in lungs and vagina,in 1in liver,in 1 in vagina,in 1case in ribs and right lung.Multidrug chemotherapy has been administrated in 11 cases. The rest of the patients were treated with monotherapy.In all cases the complete responce has been achived.

**Conclusions:** It would be recommended that only highly specialised centres should provide treatment for GTD patients.Failures are mostly caused by late diagnosis,late introducing of treatment or cytostatic resistance.

## **CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR MANAGEMENT OF RECURRENT/RELAPSED OVARIAN GRANULOSA CELL TUMOR: A SINGLE-CENTER EXPERIENCE**

I.A. Al-Badawi<sup>1</sup>, A. Abu-Zaid<sup>1,2</sup>, A. Azzam<sup>3,4</sup>, O. AlOmar<sup>1</sup>, H. AlHusaini<sup>3</sup>, T. Amin<sup>3</sup>

<sup>1</sup>*Department of Obstetrics and Gynecology, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia*

<sup>2</sup>*College of Medicine, Alfaisal University, Riyadh, Saudi Arabia*

<sup>3</sup>*Oncology Center, King Faisal Specialist Hospital and Research Center, Riyadh*

<sup>4</sup>*Faculty of Medicine, Alexandria University, Alexandria, Egypt*

**Aim:** To retrospectively report our experience (efficacy/morbidity) with cytoreductive surgery+hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) for the management of recurrent/relapsed ovarian granulosa cell tumors (OGCTs).

**Materials and Methods:** from 2010—2013, six patients underwent CRS+HIPEC. CRS was performed with standard peritonectomy procedures and visceral resections directed towards complete elimination of tumors from abdominopelvic cavity. HIPEC was performed with cisplatin (50 mg/m<sup>2</sup>) and doxorubicin (15 mg/m<sup>2</sup>) and allowed to circulate in abdominopelvic cavity for 90 minutes at 41.0–42.2 °C.

**Results:** complete cytoreduction completeness (CC-0) was achieved in all except one patient (CC-1). Five patients had OGCT recurrences in abdomen+pelvis and one patient in abdomen only. No grade V morbidity (Clavien-Dindo classification) occurred. Two patients developed lung atelectasis which was managed by mere chest physiotherapy (grade I). One patient developed urinary tract infection (grade II) and another 1 patient developed pneumonia (grade II) — both of which were managed by antibiotics. One patient developed splenic bed and anterior abdominal wall collections requiring ultrasound-guided aspiration without general anesthesia (grade III). One patient developed pulmonary embolism requiring intensive care unit management (grade IV). Four chemo-naïve patients received adjuvant chemotherapy whereas the remaining 2 previously chemo-exposed patients received no adjuvant therapy. All patients were alive and disease-free without proof of recurrence/relapse at 40, 32, 27, 24, 20 and 16 months. The average interval of follow-up after CRS+HIPEC was roughly 27 months (range: 16-40 months).

**Conclusion:** CRS+HIPEC appear to be an efficacious and morbidly well-tolerated therapeutic modality for recurrent/relapsed OGCTs. Long-term follow-up data and further research are needed.

## **RESULTS OF TWO YEAR FOLLOW UP AFTER HIPEC IN PATIENTS WITH OVARIAN CANCER**

B. Spiewankiewicz, B. Osuch, A. Mazdziarz, G. Gerulewicz

*Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Oncological Gynecology, Warsaw - Poland*

Results of 2 years follow up after HIPEC In patients with ovarian cancer. HIPEC is a novel therapeutic modality implemented in selected cases of genital malignancies with patients with intraperitoneal cancer dissemination. 97 HIPEC procedures were performed at the Department of Oncological Gynecology of Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology In Warsaw since 2012 to June 2014.

**The aim of the study** was to present results of 2 years follow up after HIPEC procedure In patients with ovarian cancer. The study included 20 patients with ovarian cancer with intraperitoneal dissemination of a malignant tumor, treated since May thru December 2012 by cytoreductive surgery combined with HIPEC. In this group 19 patients were affected by ovarian cancer and 1 patient by malignant peritoneal mesothelioma.

Selection criteria for HIPEC procedure included presence of intraperitoneal spread of malignant tumors, lack of metastasis in lymph nodes and absence of distant metastases. In all cases, HIPEC was preceded by cytoreductive surgery and systemic treatment. 2 patients were prior treated by neoadjuvant chemotherapy, 18 patients were treated because of recurrences. Mean number of chemotherapy lines were 2.8 per patient (from 1 to 7 lines). Surgery was performed under general anesthesia with expanded hemodynamic monitoring using the transpulmonary thermodilution technique. Chemotherapeutics used included platin related medicines.

**Results.** In our material 8 patients remains without recurrence (40%). Recurrence occurred in 9 patients. In 5 after 10 to 12 months, in 4 after 6-9 months. 3 patients died (1 after 3 months and 2 after 11 months).

**Conclusions.** Two-year observation showed that HIPEC is a promising method for the treatment of ovarian cancer, allowing for prolonged remission

## **ROLE OF TIBETAN MEDICINE AS ADJUVANT THERAPY IN LATE STAGE OVARIAN CANCERS: AN INDIAN EXPERIENCE**

M. Sharma<sup>1</sup>, A. Sharma<sup>2</sup>, P. Yangchen<sup>3</sup>

<sup>1</sup>Maulana Azad Medical College New Delhi; <sup>2</sup>All India Institute of Medical Sciences New Delhi;

<sup>3</sup>MenTsee Khang, New Delhi - India

**Purpose of the Study:** To know the role of alternative medicine in providing better quality of life and prolongation of life in late stage ovarian cancers in Indian poor socio economic settings. Stage III ovarian cancers have a poor prognosis with upfront chemo regimen. The loco regional ( abdominal) and distant recurrences are the rule. Survivals do not exceed more than 30-35 months in most sub optimal surgical series. With this idea an adjuvant therapy the Tibetan Medicine from the Schools of His Holiness Dalai Lama (Men Tsee Khang) was started in the trial group while as usual the control group was only followed up as their affordability of higher molecules such as Avastin etc was nil.

**Material and Methods:** Only stage IIIC cases were selected for this study who have been operated with doubtful /suboptimal debulking and have completed their chemotherapy with six cycles of Platinum -Taxane combination. Patients were subjected to end of therapy CT, CA 125 estimations as austerity measures. CA 125 estimations were repeated every third monthly during follow up. No immunological parameters were estimated due to lack of funds. The control group (50 so far recruited) was observed only while the study group (60 recruited) received Tibetan Medicine as per the evaluation methods of Tibetan "Senior Doctors" who have been ordained in this ancient expertise. The fundamental of Tibetan medicine is to correct three systems of body viz the Kaph (Breath / cardio- respiratory Systems) Pitt (Bile and digestive system ) and Vaat (the Neurohumoral system) This is believed to strengthen the immune system of the body hence it helps growth restrain of cancer cells.

**Summary of the results:** The patients who received Tibetan medicine have improvement with regards to QOL parameters during immediate post chemotherapy period while the controls deteriorated due to Platinum and Taxane cumulative dose toxicity in post six course period. At first year 50 % of the patients in control group showed slow rising titres of CA 125 while 80 % of study group maintained the Ca 125 equilibrium within normal limit. At second year 66 % of the control cases showed symptoms of recurrence while only 16 % showed symptoms of recurrence in study group ( Ascitis, image evidence of abdomino pelvic mass.) At third year end 80 % of the control group had florid progressive disease where same or alternative chemoregimen was started according to affordability while only 20% of the study group had recurrence with stable disease. At fourth year 60 % of the control case were dead with progressive disease while in study group 20 % had died. At fifth year, there were 26% survivor while the 70 % patients were still alive out of which 26.2 % had reappearance of disease.

**Conclusions:** Tibetan medicine has shown remarkable improvement in stage IIIC ovarian cancers with sub-optical surgical clearance where survivals with available modes of treatment is dismal in Indian settings.

**MAY PELVIC PET NODAL STATUS IMPACT ON INDICATION OF SURGICAL PARA-AORTIC NODE STAGING IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER?**

L. Rousseau<sup>1</sup>, S. Roemers<sup>2</sup>, C. Beckers<sup>3</sup>, K. Delbecque<sup>4</sup>, M. De Cuypere<sup>2</sup>, E. Leblanc<sup>5</sup>, F. Kridelka<sup>2</sup>, A. Kakkos<sup>2</sup>

<sup>1</sup>Faculty of Medicine (student), University of Liege, Liege, Belgium. <sup>2</sup>Obstetrics & Gynaecology, University of Liege - CHU Liège, Liege, Belgium. <sup>3</sup>Nuclear Medicine and Oncology Imaging, University of Liege - CHU Liège, Liege, Belgium. <sup>4</sup>Anatomopathology, University of Liege – CHR Citadelle, Liege, Belgium. <sup>5</sup>Obstetrics & Gynaecology, Centre Oscar Lambret, Paris, France.

**Aims.** Locally Advanced Cervical Cancer (LACC) is treated by concurrent chemoradiotherapy (CCRT). Prior to initiation of treatment, para-aortic (PA) nodal status is evaluated to adapt EB-planning. PET-CT or para-aortic node dissection can be proposed. We report our experience with Transperitoneal Para-Aortic Node Staging (TPPANS) and confront it to the metabolic nodal status.

**Methods.** Between 2006 and 2013, 39 patients treated for FIGO≥1B2 cervical cancer by CCRT at the University of Liege underwent a PET-CT followed by TPPANS. Para-aortic PET data were compared to the definitive histological status. Sensibility, specificity, positive and negative predictive value were generated. Finally the accuracy of PA PET was evaluated at the light of the pelvic nodal PET status.

**Results.** FIGO stage varied from 1B2 to 4A. The performance of para-aortic PET-CT was as follows.

	Para-AO Histo+	Para-AO Histo-	
Para-AO PET+	2	1	PPV : $2/(2+1) = 0,667$
Para-AO PET-	3	33	NPV : $33/(3+33) = 0,916$
	Sensibility : $2/(2+3) = 0,4$	Specificity : $33/(33+1) = 0,97$	

If pelvic PET-value is taken into consideration, patients with pelvic PET - status and para-aortic PET -status have a risk of PA PET false negativity of 5.5%. Patients with pelvic PET + status and para-aortic PET- status have a corresponding risk of 11%.

## **EARLY EFFICACY OF BEVACIZUMAB IN ADVANCED OVARIAN CANCER**

A.Maździarz, M.Kowalska, B.Śpiewankiewicz

*The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology*

**Introduction:** Ovarian cancer is the most lethal gynecological cancer, mainly because of the delay in diagnosis. . Recently, much effort has been put into investigating and introducing novel targeted agents into clinical practice, with the aim of improving prognosis and quality of life. Angiogenesis is a possible target. Therapeutic strategies include monoclonal antibodies. One of them, Bevacizumab was investigated in several Phase III studies, with interesting results. Today, there is strong evidence for introducing bevacizumab in the treatment of patients with advanced ovarian cancer.

**Objective:** To determine the efficacy of combination of paclitaxel, carboplatin, and bevacizumab as first-line treatment of advanced cancer of the ovary, peritoneum or fallopian tube after initial debulking surgery.**METHODS:** Eligible patients (stage IIIa-IV) with diagnosis of ovarian cancer, fallopian tube cancer or peritoneum cancer were treated with 6cycles of carboplatin (AUC 6), paclitaxel (175mg/m<sup>2</sup>), and bevacizumab (7,5mg/kg) every 3weeks, followed by single-agent bevacizumab 7,5mg/kg every 3weeks to complete 18 cycles of therapy.

**Results:** Between Jan 2012 and Dec. 2013 29 patients with measurable disease at baseline was enrolled, and 23 received study treatment. At diagnosis, 91% of patients had stage IIIc disease and 9% had stage IIIb. All of them were suboptimally cytoreduced. No fatal adverse events were observed. Overall confirmed response rate (complete response+partial response [measurable disease subgroup]) was 56,5%. Due to progression of the disease, 26% of patients have interrupted the therapy.

**Conclusions:** This treatment regimen may provide a promising therapeutic approach for women with ovarian, primary peritoneal, or fallopian tube carcinoma. No unanticipated safety concerns were identified.

## **CLINICAL SIGNIFICANCE OF THE RESISTANCE PROTEINS LRP, PGP, MRP1, MRP3, AND MRP5 IN EPITHELIAL OVARIAN CANCER**

J. Tošner<sup>1</sup>, I. Sedláková<sup>1</sup>, J. Laco<sup>2</sup>, K. Caltová<sup>3</sup>, M. Červinka<sup>3</sup>, A. Řezáč<sup>1</sup>, J. Špaček<sup>1</sup>

<sup>1</sup>*Department of Gynecology and Obstetrics, University Hospital Hradec Králové and Medical Faculty;* <sup>2</sup>*The Fingerland Department of Pathology, University Hospital Hradec Králové;*

<sup>3</sup>*Department of Medical Biology and Genetics, Medical Faculty Hradec Králové - Czech Republic*

**Objective:** To evaluate the correlation between the expression of Lung Resistance Protein (LRP), P-glycoprotein (Pgp), Multidrug Related Protein (MRP)-1, MRP3, and MRP5 and histopathological parameters and clinical outcome, and to determine the predictive and prognostic value of these transport proteins in ovarian cancer patients.

**Methods:** Clinical samples from 111 chemo-naïve patients with epithelial ovarian cancer who underwent primary surgery from 2006 to 2010 were immunohistochemically stained for LRP, Pgp, MRP1, MRP3, and MRP5 expression.

**Results:** MRP1 expression was greater among patients with late disease than among patients with early stage ovarian cancer (FIGO I+II: 71.6% (CI: 60-100); FIGO III+IV: 83.6% (CI: 100-100); P=0.03). The histological subtype correlated with the expression of LRP, Pgp, MRP1, and MRP3. Relapse of disease during the next 24 months occurred more often among patients with higher Pgp and MRP1 than among patients with lower Pgp and MRP1 expression. FIGO stage, histological type, debulking efficiency, strong Pgp expression, and strong MRP1 expression correlated significantly with shorter progression-free survival (log-rank test, P=0.001, P=0.004, P=0.001, P=0.051, and P=0.046, respectively). FIGO stage, histological type, debulking efficiency, and strong MRP1 expression correlated with poor patient survival (log-rank test, P=0.001, P=0.042, P=0.005, and P=0.018, respectively).

**Conclusions:** Pgp and MRP1 expression were clinically significant in ovarian cancer patients. Pgp and MRP1 may be reliable independent predictive and prognostic factors regarding the clinical outcome of ovarian cancer. MRP3 is less important as a predictive and prognostic factor than MRP1 expression. MRP5 and LRP expression were not applicable prognostic parameters regarding ovarian cancer.

**LIPOPHILIC STATINS AS ANTICANCER AGENTS: MOLECULAR TARGETED ACTIONS AND PROPOSAL IN ADVANCED GYNAECOLOGICAL MALIGNANCIES**

S. Gizzo, M. Noventa, E. Ancona, P. Litta, G.B. Nardelli

*University of Padua, Department of Woman and Child Health - Italy*

Despite the adequate surgery, women affected by advanced-stage gynecological cancers (ovarian/endometrial malignancies) show very poor prognosis and a better oncological prognosis could largely depend from the improvement in adjuvant treatment.

Recent data showed that, in patients affected by endometrial/ovarian cancers, statin-users demonstrating less cancer-related mortality than non-users, suggesting trials to define the statins anticancer-properties.

In-vitro/in-vivo evidences found that pleiotropic effects of statins could have a chemo-preventive potential through cancer-cells apoptosis induction and cancer-cells growth, proliferation, invasion, and metastasis inhibition.

The potential oncological impact of this discovery lead us to investigate all the possible molecular targeted anticancer activities of statins in order to detect a rationale in proposing their administration in association to standard chemotherapy/radiotherapy protocols after adequate surgical-treatment for advanced-stages gynecological malignancies.

## EVALUATION OF PROTEIN SIGNALING ACTIVATION MAPPING IN EPITHELIAL OVARIAN CANCER AND IMPACT ON PERSONALIZED THERAPIES

A. Ravaggi<sup>1</sup>, M.I. Sereni<sup>2,3</sup>, E. Baldelli<sup>2,3</sup>, G. Gambara<sup>2</sup>, L. Zanotti<sup>1</sup>, E. Bandiera<sup>1</sup>, E. Bignotti<sup>1</sup>, C. Romani<sup>1</sup>, R.A. Tassi<sup>1</sup>, P. Todeschini<sup>1</sup>, L. Tassone<sup>1</sup>, S. Ficarelli<sup>5</sup>, M. Ragnoli<sup>5</sup>, G. Tognon<sup>5</sup>, A. Gambino<sup>5</sup>, F.E. Odicino<sup>5</sup>, M. Memo<sup>3</sup>, E. Sartori<sup>5</sup>, L.A. Liotta<sup>2</sup>, S. Pecorelli<sup>2,5</sup>, E. Petricoin III<sup>2</sup>, M. Pierobon<sup>2</sup>

<sup>1</sup>"A.Nocivelli" Institute of Molecular Medicine, Division of Gynecologic Oncology, University of Brescia, Brescia - Italy; <sup>2</sup>Center for Applied Proteomics and Molecular Medicine, George Mason University., Manassas, VA-USA; <sup>3</sup>Department of Molecular and Translational Medicine, University of Brescia, Brescia-Italy; <sup>4</sup>Medical Oncology Division, S. Maria della Misericordia Hospital, Perugia-Italy; <sup>5</sup>Department of Obstetrics and Gynecology, University of Brescia, Brescia-Italy

**Background:** Epithelial ovarian cancer (EOC) is the leading cause of death from gynecological cancers, being characterized by early widespread metastasis and high-grade malignancy at diagnosis. The purpose of the study was to perform broad-scale protein signaling activation mapping and phosphoprotein analysis of kinase-driven drug targets and downstream substrates of EOCs in order to evaluate the impact of tumor histology on the activated signaling network, and to identify new druggable targets for personalized therapy.

**Methods:** Laser Capture Microdissection (LCM) was used to isolate tumor cells from 72 snap-frozen EOCs, representative of the main histological types: 38 serous, 13 endometrioid, 8 mixed, 7 clear cells, 3 mucinous, 3 undifferentiated. LCM tumor cells were lysed and subjected to reverse phase protein microarray to measure the expression/activation level of 117 protein drug targets and downstream substrates. Unsupervised hierarchical clustering analysis was utilized to explore the overall signaling network. One-way ANOVA was used to detect significant differences across the histological groups ( $p < 0.05$ ).

**Results:** Regardless of histology, the unsupervised clustering analysis revealed significant heterogeneity in the signaling network activation architecture and in particular five main signaling activation clusters were identified, including glucose metabolism (AMPK/mTOR pathway), AKT-MAPK activation, HSP90 targets (Estrogen Receptor  $\alpha$ , IGF-Receptor, Survivin) and protein involved in cell cycle control, as well as a number of RTK-driven signaling events (HER and PDGF pathways). One-way ANOVA confirmed the statistical significance only for 11 out of 117 endpoints analyzed. In particular, only clear cell histotype showed a distinct signaling network that included enhanced activation of EGFR Y1068, Syk Y525/526, HER2/ErbB2 Y1248 and SHP2 Y580 compared to the other histotypes ( $p < 0.05$ ).

**Conclusions:** Our results indicated that, although ovarian tumors appear to be heterogeneous at the individual level, a number of subgroups were identified based on the canonical activation of specific signaling pathways comprised of the activation of the drug targets themselves. These subgroups were only partially histotypes-driven, suggesting that targeted therapy for EOC should be established based on the molecular characteristics of the patients malignant lesion, rather than empirically assigned based on histology.

## **CT-GUIDED AFTERLOADING BRACHYTHERAPY FOR ADVANCED CERVICAL CANCER**

D. Xue-lian, X-G. Sheng, T. Jiang, C. Wang

*Department of Gynecologic Oncology, Shandong Cancer Hospital, Jinan - P. R. China*

**Objective:** To assess the efficacy and toxicity of Computed tomography (CT)-guided high-dose-rate integrated afterloading brachytherapy (HDR-IABT) for patients with advanced cervical cancer.

**Patients and methods:** 144 consecutive patients with stage I B2-III B cervical cancer were included in this prospective study. CT-guided integrated afterloading brachytherapy (CT-BT group) and conventional brachytherapy (c-BT group) were randomly performed in 71 and 73 patients, respectively. High-dose-rate source iridium-192 was used with standard afterloading 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 CT localization, 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 29 months (range, 4-41 months). CT-BT plans yielded better dose conformity to the target and better sparing of the rectum and bladder than c-BT group ( $P=0.023$ , and  $P=0.041$ , respectively). The CT-BT patients experienced comparable short-term effects with c-BT group (CR: 93.0% vs. 86.3%,  $P=0.134$ ; PR: 4.9% vs. 6.9%,  $P=0.175$ ; CR+PR: 97.9% vs. 93.2%,  $P=0.287$ ). Obviously higher 1- and 2- year local failure free survival (LFF) was observed in CT-BT group (1-year: 92.5% vs. 81.0%,  $P=0.041$ ; 2-year: 88.4% vs. 71.6%,  $P=0.016$ ). However, no significant differences were found between treatment groups for 1- and 2-year overall survival (OS, 1-yr: 95.6% vs. 93.0%,  $P=0.408$ ; 2-yr: 89.7% vs. 84.5%,  $P=0.274$ ) and 1- and 2- year distant metastasis free survival (1-yr: 94.1% vs. 89.5%,  $P=0.277$ ; 2-yr: 95.0% vs. 85.0%,  $P=0.164$ ). Moreover, significant lower incidence of acute and chronic toxicities was observed in CT-BT group.

**Conclusion:** CT-guided afterloading brachytherapy can be performed safely and accurately in the treatment of cervical cancer. This approach makes promising treatment outcomes, excellent dose distribution and lower toxicities.

## THE OUTCOME AND CAUSES OF TREATMENT FAILURE IN PATIENTS WITH GYNECOLOGICAL SARCOMAS

M. Cieślak-Steć, E. Telka

*Gliwice Cancer Center Institut , Clinic of Gynecological Oncology*

**Aim:** The aim of study is identify causes of failure, the analysis of prognostic factors in patients with uterine sarcoma treated with radiation and evaluation after surgery overall survival and asymptomatic, depending on the degree of clinical advancement of the histological forms of cancer.

**Materials and methods:** Conducted a statistical analysis of clinical material includes 77 patients with uterine sarcoma treated at the Oncology Institute in Gliwice from 2005 to 2010. In the study group were in 37 patients were diagnosed with LSM, 10 patients diagnosed with low grade ESS 16 patients diagnosed with high-grade ESS, 7 patients were diagnosed with TMMM, 5 patients were diagnosed with CSM and 2 diagnosed with FSM. Age of patients was in the range from 31 to 75 years (mean 60.5). In 30 patients diagnosed with sarcoma of the uterus and degree of malignancy and according to FIGO, at 8 in the second degree, in 25 patients in grade III au 14 patients in level IV. The radical surgery was performed in 22 patients, non radical surgery (without lymph node or cyto-reduction) in 52 patients, 3 patients were not operated due to advanced tumor. Postoperative radiotherapy used in 20 patients, adjuvant chemotherapy in 30 patients, combination therapy with chemotherapy with subsequent radiotherapy in 17 patients, in 3 patients received BT , in 1 patient used hormonal - progestins, 4 remained in observation after previously have had surgery, and 2 patients remained without treatment. All patients were observed for at least 5 years if death had not occurred sick. To assess the impact of various factors on the tumor and the patient used parametric tests (Weibull regression model) and nonparametric (Cox proportional hazards model).

**Results:** In 24 patients were relapse (in 22 patients in the pelvis in 2 patients in the pelvic nodes and para aorta). Median time to recurrence ranged from 2 to 23 month. In 20 patients had been spread tumor. The most common place to spread were the lungs, bones, CNS and soft tissues. Multivariate analysis showed that independent prognostic factors in the test group were the degree of clinical stage, histological type of tumor, radical surgery.

In the group of patients with sarcomas low-use complementary radiotherapy reduced the risk of relapse by 50% but has proved ineffective in patients for advanced sarcomas, where the use of combination sequential chemotherapy and radiotherapy reduced the risk of recurrence and death by 40%. The primary cause of treatment failure in patients on LSM was tumor spread, the group of patients, or ESS non treatment regional recurrence of sarcoma.

**Conclusion:** The obtained results allow to formulate the following conclusions:

- 1) in patients with uterine sarcoma and second degrees of sophistication according to FIGO use postoperative radiotherapy reduces by half the risk of disease recurrence but is not sufficient to completely cure patients with locally advanced
- 2) for patients in the third degree of sophistication most optimal method of treatment seems to be combined sequential chemotherapy and radiotherapy, which reduces the risk of dying by one-third
- 3) the most relevant prognostic factors for survival are the primary advanced disease, tumor histological type and radical surgery. Not shown the effects of age and nuclear atyp on survival of patients
- 4) the most frequent cause of treatment failure for LSM is the spread of cancer or no healable local or regional recurrence locomotives for ESS

## **THE ASSESSMENT OF THE EFFECT AND THE TOLERANCE OF RADIATION THERAPY IN PATIENTS SUFFERING FROM CERVICAL CANCER AND ENDOMETRIAL CARCINOMA RADIATED WITH ITV-IMRT TECHNIQUES**

E. Telka

*Gliwice Cancer Center Institute, Department of Radiotherapy - Poland*

The purpose of the research is to assess the effects and postradiation reaction in patients suffering from cervical cancer and endometrial carcinoma irradiated with IMRT and ITV-IMRT techniques followed by brachytherapy HDR 3x5Gy of the apex of vagina.

**Methods and materials.** The object of the analysis constituted a group of 86 patients diagnosed with endometrial carcinoma and cervical cancer (stages I b to II a, i.e. clinically visible lesion >4.0 cm in greatest dimension, invasion of lymph glands and parametrium), in a very good and good general condition (Zubrod 0-2), and treated from March until April 2012 at the Radiotherapy Department of Cancer Center and Institute of Oncology in Gliwice, Poland. The patients were between 49 and 73 years of age (60 years median). The initial surgical treatment included radical abdominal or vaginal hysterectomy, and the lymph nodes removal in the case of cervical cancer (Wertheim-Meigs surgery). Whereas 43 patients were radiated with ITV-IMRT technique, the remaining 43 were radiated with the conformal technique of modulated intensity of beams. The radiotherapy 54 Gy in the 28 fractions included the lymph nodes of pelvis minor and the vaginal stump followed by brachytherapy HDR 3x5Gy of the vaginal apex. In the assessment of the radiation therapy were taken into account: the spot of the recurrence and the period of time until it happens, early and late post-radiation reactions from the critical organs (urinary bladder, rectum, intestines, femoral bone head) according to the EORTC/RTOG criteria, and the general and hematological toxicity according to WHO criteria. The comparison of the two radiation techniques was performed on the basis of X2 and Mann-Whitney analysis.

**Results.** None of the patients suffered local and regional recurrence during the minimal six months long observation. The patients radiated with ITV-IMRT and IMRT techniques developed similarly frequent post-radiation reactions in the rectum, the intensity of which did not exceed the second degree (43 versus 43 patients), in the case of ITV-IMRT the first degree, and in the case of IMRT the second degree. Equal incidence of early post-radiation reactions were also observed in the urinary bladder (11 versus 11 patients), intensity of which also did not exceed the 2nd degree (in the case of ITV-IMRT the 1st degree, in IMRT the second degree. No early reactions of 3rd and 4th degree were noted both in the rectum and the urinary bladder. The X2 and Mann-Whitney analysis did not demonstrate statistic differences between the two groups of patients.

**Conclusions.** 1. The planning of IMRT radiotherapy based on the fusion of CT with the full and empty bladder in patients diagnosed with cervical cancer and endometrial carcinoma does not significantly influence the the risk of post-radiation reactions, in comparison with the classic planning of IMRT (based on CT scans). 2. Radiation therapy with the modulated intensity of beams enables the elimination of early and late post-radiation reactions of 3rd and 4th degree.

## **GENITAL ATROPHY BEFORE AND AFTER PELVIC RADIOTHERAPY IN WOMEN WITH CERVICAL CANCER**

L.F. Baccaro, A.F. Vaz, R. Grion, F. Vianna Casellato, L. Costa Paiva, A. Mendes Pinto Neto  
*Department of Gynecology, Faculty of Medical Sciences, State University of Campinas – UNICAMP, Brazil*

**Purpose:** Cancer of the cervix is the second most common gynecological tumor and pelvic radiation therapy is one of the most used forms of treatment. It is known that it causes local side effects, but the factors associated with a higher intensity of genital atrophy are still poorly understood. Our objectives were to evaluate vaginal hormonal cytology and its associated factors in women with cervical cancer prior to and after radiotherapy. We aimed also to identify factors associated with worsening of genital atrophy after the completion of radiotherapy.

**Methods:** A prospective cohort study was conducted with 58 women with cervical cancer, aged 18-75 years, referred for radiotherapy at the Women's Hospital of the State University of Campinas – Brazil, from January 2013 to March 2014. The outcome variable was genital atrophy, measured by maturation index of the vaginal cells (Meisels Index). The independent variables were sociodemographic data, health related habits and the characteristics of the neoplasm. Statistical analysis was carried out using the Student's t-test, Mann-Whitney test and linear regression analysis using the stepwise selection criteria.

**Results:** The mean age of the women was 48.5 ( $\pm$  14.4) years. Twenty-six (44.8%) were postmenopausal, 55.2% were white and 58.6% had clinical stage IIIB. Some of the clinical and sociodemographic data are shown in table 1. The average maturation index before radiotherapy was 53.9 ( $\pm$  26.6) and after radiotherapy was 36.6 ( $\pm$  24.6). Being postmenopausal ( $p < 0.01$ ) was associated with a worse maturation index prior to radiotherapy. After the completion of radiotherapy, being older than 50 years ( $p = 0.01$ ) and do not experience sexual pleasure ( $p = 0.04$ ) were associated with a worse maturation index. Being employed ( $p < 0.01$ ) and not having undergone chemotherapy ( $p < 0.01$ ) were associated with a better maturation index. When comparing the maturation index before and after radiotherapy it was observed that 67.3% of the women had worsening of the maturation index, 26.5% had improvement of the maturation index and 6.1% maintained the same values. Being employed ( $p < 0.01$ ) was associated with improvement or maintenance of the maturation index. Not having undergone surgery with preservation of the ovaries ( $p < 0.01$ ) was associated with worsening of genital atrophy.

**Conclusions:** Genital atrophy causes uncomfortable symptoms and worsening of quality of life. Most women undergoing radiotherapy had worsening of vaginal atrophy. Women who were employed or who had undergone surgical treatment for cervical cancer with ovarian preservation had fewer adverse effects of radiation therapy on the vaginal tissue. Knowing the factors associated with genital atrophy after radiotherapy is important to identify women requiring more attention to vaginal health.

*Acknowledgments: Funding by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) number 2012/09215-7*

## Clinical and sociodemographic data (n=58)

Characteristics	%
<b>Color</b>	
White	55.2
Non-white	44.8
<b>Menopausal status</b>	
Premenopausal	55.2
Postmenopausal	44.8
<b>Marital status</b>	
With partner	51.7
Without partner	48.3
<b>Smoking</b>	
Yes	18.2
No	81.8
<b>Schooling</b>	
≤ 8 years	62.1
> 8 years	37.9

## **CHEMORADIATION FOR SQUAMOUS CELL CARCINOMA OF CERVIX: SINGLE CENTRE EXPERIENCE**

M.S. Iqbal<sup>1</sup>, A. Hughes<sup>2</sup>, G. Shaikh<sup>1</sup>, W. Taylor<sup>1</sup>

<sup>1</sup>Northern Centre for Cancer Care, Freeman Hospital, Newcastle upon Tyne; <sup>2</sup>Newcastle University, Newcastle upon Tyne - UK

**Purpose:** Definitive treatment with concurrent cisplatin and radiotherapy is the standard of care in locally advanced carcinoma of cervix. We conducted a retrospective study looking at our clinical practice of management of these patients. The objective was to review our findings against the published evidence.

**Methods:** Patients diagnosed with locally advanced cervical cancer who underwent (chemo)radiation between January 2007 to December 2009 (3-year period) were identified from the local database. The following data were collected retrospectively;

- Patient's demographics
- Their disease characteristics
- Treatment regimes
- Acute and late toxicities
- Disease recurrence and survival

**Results:** A total of 94 patients were identified. The median age was 65 years (range: 28 - 94). Majority of the patients had a WHO performance status of 0 or 1 (86%). The most common FIGO stage was IIB (36%) followed by IB (23%), IIIB (17%), IIA (11%) and IVA (8%). Various dose fractionation regimes were used; 50 Gy in 25 fractions of external beam radiotherapy (EBRT) followed by high dose rate (HDR) brachytherapy 14 Gy in 2 fractions being the most common (59%). Two third of the patients (66%) received concurrent chemotherapy with cisplatin (40mg/m<sup>2</sup> on a weekly basis during EBRT) and the remaining patients (34%) were deemed unfit for chemotherapy mainly due to renal dysfunction. Majority of the patients developed up to grade 2 acute toxicities but no grade 4 toxicity. The incidence of grade 3/4 late toxicity is 15%, mainly bowel and bladder dysfunction. In total, 33% of patients had recurrent disease with 12% having local only and distant metastases were also confirmed in 21% of the patients. At the point of writing 54% of the patients are alive. Three year overall survival was 55% with a median overall survival of 40 months (range 2 – 83 months).

**Conclusions:** Definitive chemoradiation remains gold standard treatment option for locally advanced carcinoma of cervix. One third of our patients could not receive concurrent chemotherapy in view of their comorbidities. The survival rate is comparable to that of published literature though our study revealed higher incidence of late toxicities. This has lead our centre to gradually move from conventional radiotherapy to implementation of intensity modulated radiotherapy (IMRT) in treating cervix cancer.

## **GUIDANCE ON LONG TERM CONSEQUENCES OF TREATMENT FOR GYNAECOLOGICAL CANCER ; PELVIC RADIOTHERAPY**

T. Miles, L. Holmes

*National Forum Gynaecology Oncology Nurses United Kingdom*

**Study Purpose:** Approximately 19,500 women a year are diagnosed in the UK with gynaecological cancer. It is estimated that 19 % will receive pelvic radiotherapy. An estimated 67% of women survive more than 5 years following gynaecological cancer. The literature indicates that over 50% may experience some sort of long term problem<sup>4</sup>.

The National Forum of Gynaecological Oncology Nurses (NFGON), The Society and College of Radiographers (SCoR) and Macmillan Cancer Support identified a need to provide accessible guidance which signposts professionals to (a) ways of supporting women to self-manage and (b) key advice and source documents for clinical management.

**Methods:** This guidance was developed through the compilation of published guidance sourced via literature searches, hand searches of journals, conference proceedings, personal communications and consensus opinion on best practice agreed an expert multiprofessional group. The publication is endorsed by patient charity groups.

**Results:** The pelvic radiotherapy guidance covers good practice recommendations:

Prior to pelvic Radiotherapy;

= Information to facilitate informed consent

= Fertility issues

= Menopause

= Prevention of consequences of treatment.

= Smoking Cessation

Support for psychosocial issues

Monitoring during and after radiotherapy - Pathways to identify issues/problems

Management of symptoms due to long term consequences of pelvic radiotherapy

= Identified levels of intervention ( dependent on expertise of practitioner)

= Management plans for levels of intervention

= Referral pathways for specialist level of intervention

Symptoms covered;

= Bowel toxicity

= Bladder toxicity

= Bone pain

= Hormonal symptoms

= Sexual difficulties

= Lymphoedema

**Conclusion:** The guidance was launched in the keynote survivorship session at the British Gynaecology Cancer Society (BGCS) annual congress this year. It has also been endorsed by UKONS, affiliated with the European Oncology Nursing Society (EONS). Parts 2 and 3 (chemotherapy and surgery) are planned for publication 2015.

## **RETROSPECTIVE ANALYSIS OF THE CLINICAL OUTCOMES IN BORDERLINE OVARIAN TUMOR**

C. Dane, N. Bilgili

*Haseki Training and Research Hospital, Department of Gynecology and Obstetrics, Istanbul - Turkey*

**Objective:** The aim of study was to evaluate the patients' clinical and pathological characteristics and treatment results in women with borderline ovarian tumors

**Methods:** A clinical study was made on 38 cases of borderline ovarian tumors that were treated at the training and Research hospital in Istanbul between 2003 and 2013. Clinical and pathological characteristics, treatment results, follow-up data for 38 women with borderline ovarian tumors were collected retrospectively from medical records.

**Results:** The mean age and SD was detected  $45.1 \pm 14.3$  in retrospective study. Majority (66 %) of the patients were found to be premenopausal. Of these, 169 (66 %) were premenopausal and 27 (34 %) postmenopausal; average cyst diameter was  $15.7 \pm 8.1$  cm. The histologic subtypes were serous (48 %), and mucinous (52 %). Abdominal pain was the most common symptom, seen in 39 % of the patients. Disease stage was IA in 26 patients (86.8 %) and stage III in the other 3 patients (13.1 %). The mean values of CA 125 were  $139.5 \pm 153.8$  U/ml. Patients with elevated CA 125 ( $>35$ ) were 55.2 %. The five year disease free survival rate was 99 %. Fertility preserving surgery was performed 26.3 % in study group. Eight patients (24.2 %) in stage I and three patients (60 %) in stage III developed recurrence in follow-up period.

**Conclusion:** Borderline ovarian tumors usually has good prognosis. Patients performed by cystectomy as the initial surgery had disease recurrence frequently in our series. Fertility preserving surgery whenever feasible remains the standard of care.

## **SUCCESSFUL NEAR TERM PREGNANCY AFTER PARTIAL HYSTERECTOMY TO TREAT CHEMOREFRACTORY PERSISTENT MOLAR PREGNANCY: A CASE REPORT**

F. Farzaneh<sup>1</sup>, S. Fatehi<sup>1</sup>, H.R. Rezvani<sup>2</sup>, F. Mohsenifar<sup>3</sup>

<sup>1</sup>*Prevention Gynecology Research Center (PGRC), Obstetrics and Gynecology Department, Imam Hossein HP, Shahid Beheshti University of Medical Sciences, Tehran, Iran;* <sup>2</sup>*Medical Oncology Department, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran;* <sup>3</sup>*Pathology Department, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

**Study's purpose:** The preferred treatment for patients with the gestational trophoblastic disease (GTD) who wish to preserve their fertility is surgical evacuation of the uterus, and in cases of persistent disease, chemotherapy is very curative. For persistent localized uterine lesions, partial uterine resection and reconstruction is an alternative modality of treatment before hysterectomy. In this report we present the case of a patient with persistent GTD treated with uterine partial resection and reconstruction followed by a successful pregnancy.

**Method:** A 26 year old woman gravid 1, with history of spontaneous abortion (last month), presented with continuous vaginal bleeding. Transvaginal sonography (TVS) revealed enlarged uterus with 74\*55 mm heterogeneous mass containing cystic area (suggesting hydatiform mole). Her  $\beta$ HCG level was equal to 390430 u/ml and was therefore a candidate for uterine curettage. She received simultaneously methotrexate (50 mg every other day for 5 doses) and locoverin (every other day for 4 doses). For the three weeks after the treatment,  $\beta$ HCG level was 112230 u/ml, 16300 and 17100 respectively. TVS showed a 50\*55 mm heterogeneous mass with cystic areas and low resistance in color Doppler, suggesting invasive mole. She received single agent chemotherapy with dactinomycin, then due to the same scenario the 3 cycle course EMACO regimen. The  $\beta$ HCG titer before beginning EMACO regimen was 4155 unit/ml and after first and second course was 1906, 1640 respectively. In weekly follow ups after completion of treatment, the size of the uterine lesion had decreased to 42\*35mm in the right posterior part of the fundus and  $\beta$ HCG remained high around=7000 U/ml. At this stage uterine wedge resection was performed and 1/3 of the uterus (containing the lesion) was removed.

**Results:** Permanent and frozen pathology report showed invasive mole with free margin. Post operation period was excellent, after two weeks  $\beta$  HCG level fell to normal and remained normal during 1 year follow up. TVS in 2 weeks after surgery showed normal uterine size with no lesion. One month after surgery, the patient received the last course (4th) of EMACO. After 4 years of contraception, she conceived spontaneously. She had a normal pregnancy with no problems in the first two trimesters. At 33w of gestational age, the patient was admitted in hospital due to abdominal pain for close observation. A Cesarean Section was performed at age of 35w due to active labor and healthy female infant, weighing 2500gr, was born. Six weeks after delivery  $\beta$  HCG was negative.

**Conclusion:** This case study along with other few reports in literature suggest that uterine resection, and reconstruction could be a suitable treatment for selected patients with GTD (focal uterine lesion persistent to curettage and chemotherapy) who desire to preserve fertility.

**EFFICACY AND SAFETY OF ENOXAPARIN VERSUS UNFRACTIONATED HEPARIN FOR PREVENTION OF VENOUS THROMBOEMBOLISM IN ELECTIVE GYNE CANCER SURGERY: A RANDOMIZED CONTROLLED, OPEN LABEL STUDY**

F. Al Safi, N. Al Mutairi, A. Gasmalseed, N. Sheblaq

*Department of Oncology, King Abdulaziz Medical City for National Guard Health Affairs, Riyadh - Saudi Arabia*

**Background:** Surgery of gyne malignancy carries a high risk of thromboembolic disease. The aim of this study was to evaluate the prophylactic effect of a low molecular weight heparin enoxaparin versus unfractionated heparin.

**Methods:** Patients included were all women who was diagnosed or suspected malignancy, undergo for the planned of elective curative surgery for cancer in KAMC Riyadh, Oncology Department. The study was designed as a randomized controlled open label study. Primary outcome was venous thromboembolism as detected by clinical and imaging study with follow-up of 3 months.

**Results:** A total of 120 patients were randomized into two study groups, 65/120 patients had proven tissue gynecologic cancer post-operatively. Five/65 cancer patients developed pulmonary embolism within a median time duration of 3 days (2-7) from the day of surgery.

Three of them were on heparin, multivariate analysis, risk of pulmonary embolism in those treated with heparin versus enoxaparin was higher but not statistically significant (HR 1.526, 95% CI (0.246-9.478) P-value 0.649). Bruises and vomiting was more in heparin group with no statistical difference (HR 1.909, 95% CI (0.811-4.493) P-value 0.7294) respectively. None of the two study groups developed major bleeding or DVT.

**Conclusion:** The study revealed no significant difference between the two group in developing PE and side effect.

**FROZEN SECTIONS HISTOLOGICAL ANALYSIS ACCURATELY PREDICTS PATIENTS WITH HIGH RISK ENDOMETRIAL CANCER WHO BENEFIT FROM COMPLETE SURGICAL STAGING.**

P. Sala<sup>1</sup>, M. Morotti<sup>1</sup>, N. Bizzarri<sup>1</sup>, L. Parodi<sup>1</sup>, V.G. Vellone<sup>2</sup>, S. Costantini<sup>1</sup>, M. Valenzano Menada<sup>1</sup>

<sup>1</sup>*University of Genoa, Gynaecology Dpt and IRCCS AOU San Martino Hospital, Ist, Genoa;*

<sup>2</sup>*University of Genoa, Pathology Dpt and IRCCS AOU San Martino Hospital; Ist, Genoa – Italy*

**Purpose.** To assess the accuracy of the Mayo Clinic algorithm using frozen sections to select patients with high risk endometrial cancer even in another institution.

**Methods.** We reviewed women with type I endometrial cancer treated from January 2011 through January 2013 at the Gynaecology Department of the University of Genoa, Italy. Intraoperative frozen sections were analyzed to select patients at high risk for metastases, according to Mayo Clinic algorithm. All patients underwent hysterectomy with bilateral adnexectomy. High risk patients underwent complete surgical staging. We assessed the accuracy of frozen sections in selecting patients affected by high risk endometrial cancer, using permanent sections histology as positive control. Chi-squared test, Landis and Koch kappa statistics (k), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were determined for the Mayo Clinic algorithm.

**Results.** 139 women were included. Applying the Mayo Clinic algorithm for frozen sections, only three out of 139 analyzed patients (2.2%) showed clinically significant discordant risk predictions. In these three cases, the risk of lymphatic spread was underestimated, so they didn't undergo lymphnode excision even if later indicated by permanent sections histological results. Analysis of frozen sections never overestimated metastasis risk, so no unnecessary surgical staging was performed. 136 patients (97.8%) underwent appropriate surgical treatment. Frozen sections demonstrated 97.3% sensitivity, 100% specificity, 100% PPV, 90.0% NPV, 97.8% accuracy and an optimal kappa statistics (k=0.934, p<0.001).

**Conclusions.** We proved the utility of the Mayo Clinic algorithm even in our institution.

## **PROGNOSTIC SIGNIFICANCE OF LYMPH NODE DISSECTION IN TERMS OF OVERALL SURVIVAL OF INVASIVE CERVICAL CANCER**

E. Ismail, Y. Kornovski

*MHAT "St. Anna" Varna, Gynecological clinic - Bulgaria*

**Objective:** To establish the role of the lymph node dissection ( LND ) and the overall survival of patients with invasive cervical cancer depending on their lymph node status.

**Material and methods:** The follow-up period includes the date of registration until September 2011 or exitus letalis. ( from 2 to 96 months, average 45 months ).

**Results:** We presented the relationships between presense of lymph node metastases ( LNM ), number of LNM, localization of LNM, micro- and macro- LNM and the overall survival of patients staged IB1 – IIB.

**Conclusion:** Patients with microscopic LNM reveal similar overall survival ( 81% ) to patients without LNM ( 86% ). In these patients LND demonstrates therapeutic effect.

Key words : lymph node dissection, lymph node metastases, overall survival, cervical cancer

## **EARLY STAGE CERVICAL CANCER - 5 YEARS FOLLOW UP - OUR CLINICAL EXPERIENCES**

K. Mastilovic, D. Zikic, J. Rajovic, M. Popovic, M. Zivaljevic, A. Mandic, D. Nincic, B. Gutic  
*Institute of Oncology Vojvodina - Serbia*

**Introduction:** Cervical cancer still takes a significant place in morbidity and mortality of female population. Despite applied therapy and a very selective choice of patients for surgical treatment, with certain number of patients the disease will relapse, and it is unavoidable despite regular check-ups.

**Material and work method:** This work included 212 patients who, due to cervical cancer stage Ib1, Ib2, IIa and IIb, went through radical hysterectomy with pelvic lymphadenectomy. These patients were operated between 2007 and 2009 with monitoring period of 5 years. We evaluated the occurrence of relapse in relation to the stage of the disease, lymphonodal status, relapse localization and the time of coming to the doctor. In relation to all stages, 46 (21,7%) patients had a relapse. In stage Ib1, out of 137 patients 20 (14,5%) patients had a relapse of the disease. In stage Ib2 out of 27 patients, 8 (29,6%) had a relapse. In stage IIa out of 6 patients 2 (33%) had a relapse while in stage IIb out of 30 patients 12 (40%) got a relapse.

**Conclusion:** Follow up patients with cervical cancer demands three-dimensional structure: monitoring in relation to the stage of the disease, risk factors and lymphonodal status. It is necessary to identify high-risk patients for the relapse, and determine monitoring intervals which would establish the relapse as early as possible and thus contribute to better efficiency of further treatment and better quality of life.

## **BILATERAL SALPINGECTOMY IN YOUNG PATIENTS WITH OVARIAN CANCER AND DESIRE FOR FERTILITY PRESERVATION**

G.M. Makris, N. Evangelinakis, V. Bolkas, P. Panagopoulos, C. Siristatidis, C. Chrelias  
*3rd Department of Obstetrics and Gynecology, Attikon Hospital, University of Athens - Greece*

**Aim:** The ovarian cancer is a rare malignancy in young women, nevertheless it is detected in women below their 30s. The mean age of childbearing in the advanced world has increased therefore the number of women that have not yet completed their family planning and wish to preserve their fertility and have been diagnosed with ovarian cancer is rising. There is an increased need to detect the optimal treatment and surveillance strategy of these patients. The theory is that is currently popular is the genesis of cancer cells in the distal part of the fallopian tubes. The aim of the study is to investigate the value of bilateral salpingectomy in patients with ovarian cancer and desire for fertility preservation.

**Methods and Material:** We searched the guidelines of international gynecological societies in particular the NCCN, AGO and NICE of the respective gynecological societies of the USA, Germany and the UK. In addition to that we searched the randomized trials in the world wide web search engines of medical publications; Cochrane Central Register of Controlled Trials in the Cochrane Library, EMBASE and MEDLINE. The research criteria were prospective studies of the evaluation of the need for bilateral salpingectomy to women affected with ovarian cancer in their reproductive age and with the desire for fertility preservation. The research took place in June 2014.

**Results:** There are no randomized prospective trials that compare the safety of maintaining the contralateral salping in patients affected with ovarian cancer desire for fertility preservation. In the current revised guidelines of the international gynecological societies there is no specific guideline concerning the bilateral salpingectomy for the staging of the ovarian cancer.

**Conclusions:** The decision for fertility preservation in women affected by ovarian cancer is oncologically unsafe. Ideal candidates for fertility preservation are women affected with ovarian cancer Grade 1 non clearcell histologically and under certain conditions Grade 2. There are no specific guidelines regarding the genetical background of the patient, BRCA carrier or not. Alternatively patients of stage Ic could be included as far as both ovaries are not affected. The proposed operation is the removal of the affected ovary, the surgical staging of the patient with laparotomy, multiple peritoneal biopsies, cytologic sampling of the peritoneal cavity and the preservation of the uterus and the contralateral ovary. Further studies should be carried out so as to demonstrate the point of deterioration of the disease, the prognosis of those who wish to preserve their fertility, the optimal surgical treatment with or without the preservation of the contralateral ovary and the safety of IVF in patients affected by ovarian cancer.

### **Literature**

1. NCCN guidelines for ovarian cancer 2.2014 edition
2. NICE guidelines 2013. Scientific Impact Paper No35. Fertility Sparing Treatments in Gynaecological Cancers
3. AGO (Arbeitsgemeinschaft Gynaekologische Onkologie) German guidelines 4.2013
4. Morice P, Denschlag D, Rodolakis A, et al. Fertility task force of the European Society of Gynecological Oncology. Recommendations about the conservative management of ovarian malignant tumors. *Int J Gynecol Cancer* 2011;21:951-63
5. Tone AA, Salvador S, Finlayson SJ et al. The role of the fallopian tube in ovarian cancer. *Clin Adv Hematol Oncol* 2012 May;10(5):296-306
6. Crum CP, Drapkin R, Miron A et al. The distal fallopian tube: a new model for pelvic serous carcinogenesis. *Curr Opin Obstet Gynecol* 2007 Feb;19(1):3-9
7. Park JY et al. Outcomes of fertility sparing surgery for invasive epithelial ovarian cancer: oncologic safety and reproductive outcomes. *Gynecol Oncol* 2008 Sep;110(3): 345-53

## **A SYSTEMIC APPROACH TO THE SURGICAL TREATMENT OF PATIENTS WITH EXTENSIVE TUMORS OF THE SMALL PELVIS**

O.V. Lukyanchuk, V.V. Lysenko, V.G. Dubinina, M.A.Lysenko

*University clinic, Odessa - Ukraine*

**Introduction.** We often encounter the locally spread ovarian, uterus, cervical tumors in the clinical practice.

**Objective.** To assess the results of the “salvage surgery” of the patients with extensive tumors of the small pelvis and determine most optimal ways to reconstruct the urinary tracts during surgery.

**Materials and Methods.** Retrospectively we analyzed the medical history of 29 patients with extensive tumor diseases of the small pelvis those were operated in our clinic between 01/2010 and 01/2013.

**Results.** The small and large intestine was involved in the tumor process in 62% of cases. The isolated involvement of the ureter was revealed in 10.3% cases. The isolated tumor invasion into the bladder was detected in 41.2% of patients and 6.9% of patients had concomitant tumor invasion of the bladder and ureter. Only 13.8% of patients needed total pelvic exenteration. In other cases the natural urination was preserved. Cancer specific mortality was 6.9% in a mean follow-up of 18 months. Overall mortality was 10.3% within 26 months after surgery. There were no cases of intraoperative and early postoperative mortality. 86.2% of patients took adjuvant radiation or/and chemotherapy with satisfactory tolerance.

**Conclusion.** The intestinal loops are most frequently involved in the tumor process in primary tumors of the ovaries. The tumor process more often spread to the urinary tract in primary cervical, uterus cancer. The tumor invasion of the urinary tract is not a contraindication to surgical treatment in such patients. Modern methods of the urologic tract reconstruction have a good tolerance and functional outcome in the patients with extensive tumors of the small pelvis.

## **LAPAROSCOPY VS LAPAROTOMY FOR THE MANAGEMENT OF ADVANCED OVARIAN CANCER AFTER NEOADJUVANT CHEMOTHERAPY: RESULTS FROM A PROPENSITY-MATCHED ANALYSIS**

G. Siesto, F. Romano, G. Musicò, N. Palma Iedà, C. Bulletti, D. Vitobello

*Department of Gynecology, Cancer Center, IRCCS, Humanitas Clinical and Research Center, Rozzano, Milan - Italy*

**Aim:** To evaluate the surgical and survival outcomes of laparoscopic and open abdominal interval debulking surgery (IDS) of patients with advanced epithelial ovarian cancer (EOC) after neoadjuvant chemotherapy (NACT).

**Materials and Methods:** A prospectively entered oncologic database was queried to identify all patients who underwent IDS after NACT for advanced EOC since 2009, regardless the surgical approach. Cases managed through laparoscopy and laparotomy have been matched through a propensity score analysis. Propensity score was defined as the estimated probability of a woman having laparoscopy or laparotomy and was developed through a binary logistic regression model. It includes the following variables: age, BMI, ASA score, residual disease, histologic type (serous vs other), FIGO stage (III vs IV), Grade (1-2 vs 3), lymphovascular space invasion (present vs absent). Women who underwent laparoscopy were matched 1:1 to women who underwent open surgery. Calipers of width equal to 0.2 SD of the logit of the propensity score were used for matching.

The Kaplan–Meier method was used to estimate survival curves. Survival time was calculated in months from the date of surgery to either the date of recurrence (PFS) or death (OS), or to the date of last follow-up visit for surviving patients.

**Results:** The study group consisted of 30 propensity-matched women who underwent laparoscopic and abdominal IDS. The mean±SD propensity score was 0.56±0.16 and 0.56±0.16 for laparoscopic and abdominal group, respectively (p=0.96). No differences were found between patients in terms of baseline characteristics, particularly for age (61.0±12.1 vs 61.6±10.3 years; p=0.58), BMI (25.5±4.4 vs 25.3±4.1 kg/m<sup>2</sup>; p=0.62), ASA score (5 vs 5; p>0.99) respectively for patients submitted to laparoscopy and laparotomy. Similarly, no difference were recorded in terms of operative time (170.9±70.8 vs 172.40±45.1 min; p=0.23) and residual disease (2.5±3.1 vs 3.1±7.9 mm; p=0.23). A trend toward reduced blood loss (108.7±69.7 vs 276.7±184.1 mL; p=0.10) and hospital stay (3.1±0.8 vs 4.6±0.9; p=0.09) was observed in the laparoscopic group. No differences were recorded in terms of transfusions, intra- and post-operative complications rate.

After a median (range) follow-up of 18.0 (6.0-57.3) vs 17.3 (5.2 -58.0) months (p=0.38), 13 recurrences (5 vs 8; p=0.43) were recorded and 5 women (2 vs 3; p>0.99) died of disease. No differences were found between groups in terms of progression-free survival (p=0.34) and overall survival (p=0.27).

**Conclusions:** Because of the nonrandomized nature of the study, the propensity-matched analysis to obtain a less biased estimate of the effects. Our initial experience shows that in responders to platinum-based NACT for EOC, minimally invasive approach represents a viable option to achieve optimal IDS and comparable survival outcomes of those achieved by conventional open approach. Larger series are welcome to confirm our findings.

## **DOES PELVIC AND PARAORTIC LYMPHADENECTOMY AFFECT THE OVERALL SURVIVOR OF PATIENTS WITH ENDOMETRIAL CANCER?**

D. Vaidakis, C. Tatsi, C. Goudeli, G. Danilatos, J. Papapanagiotou, E. Terzakis

*Gynecological department Anticancer Hospital of Athens 'St. Savas' - Greece*

**Introduction:** Endometrial cancer is the commonest gynecological cancer in developed countries. The 5 year survival rates, for stages I is above 80%. In this stage it is still under debate whether pelvic and paraortic lymphadenectomy should included in standard surgical treatment.

**Material and Methods:** From 2004 to 2011, we retrospectively follow up 241 patients with endometroid adenocarcinoma cancer stage I, operated in our department. In all patients diagnosis was established with endometrial biopsy (pipelle or D&C). The patients divided in 2 groups: Group A consists from 117 patients which performed only total abdominal hysterectomy with bilateral oophorectomy and Group B consists from 124 patients which also pelvic and paraortic lymphadenectomy were performed. The demographic characteristics were similar in both groups.

**Results:** The mean age of the patients was 62 year old. Pre- or pere- menopausal were 87 patients. In 90% abnormal uterine bleeding was the initial symptom. Nuclear grade I had 189 patient, and II 52. Myometrial invention <50% had 126 while >50% 115 patients. The Overall survival was 77 months (84 months for stage Ia, 70 months for stage Ib). The 5year survival was 86% for both groups. In 2 patients positive nodes were found. All patients with stage Ia were under close observation while stage Ib patients receive adjuvant therapy.

**Conclusion:** The results from our study show that paraortic and pelvic lymphadenectomy doesn't affect the overall survivor or the 5year survival. But provide information for more accurate staging so in consequence better planning of adjuvant therapy. Due to increase morbidity of lymphadenectomy sentinel node biopsy is recommended for early stage endometrial cancer.

## **FOLLOW UP IN PATIENTS WITH UTERINE LEIOMYOSARCOMAS: OUR 20 YEARS EXPERIENCE**

D. Vaidakis, C. Goudeli, L. Pilatec, G. Danilatos, J. Papapanagiotou, E. Terzakis  
*Gynecological department, Anticancer Hospital, "Saint Savvas" - Greece*

**Introduction-Aim:** Uterine leiomyosarcomas are very aggressive neoplasms with poor prognosis and high recurrence rates, even when diagnosed in early stages. Aim of the present study is to correlate survival rates with clinicopathological characteristics in patients with uterine leiomyosarcomas in order to focus the follow up examinations.

**Material and method:** From 1993 till 2011, 2384 patients with uterine malignancies were retrospectively reviewed. Thirty one (1.3%), were diagnosed with uterine leiomyosarcoma. The mean follow up period was 11 years (20-3). For the first year we follow up the patients every 2 months and then for the next 2 years every 3 to 6 months according the findings. The Kaplan-Meier method was used to generate overall survival (OS) data. Factors predictive of outcome were compared using univariate analysis.

**Results:** The mean age of the patients were 55 years old, 7(22.5%) were premenopausal and 24(77.5%) were post menopausal. In all patients total abdominal hysterectomy with bilateral oophorectomy was performed, 4 patients (13%) receive adjuvant radiotherapy and 5 (16%) receive combination of radiotherapy and systemic chemotherapy. Fourteen (45.1%) had stage I, 6(19.3%) had stage II, 7(22.5%) stage III and 4(13%) had stage IV. The mean overall survivor was higher than 120 months for stage I, 54 months for stage II, 10 months for stage III and 13 months for stage IV. The corresponding mortality per stage was 14%,66%,80%,100%, for stage I,II,III,and IV respectively. Age, low BMI, lower grade, smaller tumor size, low number of mitosis and absent of necrosis were identified as variables with positive prognostic influence on survival rate.

**Conclusion:** Leiomyosarcomas are very aggressive malignancies, with poor prognosis, which are more common after menopause. Since its high recurrence rate close follow up it is recommended with primary goal to identify local recurrence. But since most of the positive prognostic factors affecting survival rate, are invariable, early diagnosis is the primary concern.

## **STANDARDS AND INNOVATIONS IN SURGICAL TREATMENT OF CHEMORESISTANT GESTATIONAL TROPHOBLASTIC NEOPLASMS**

N. Tsip<sup>1</sup>, L. Vorobyova<sup>1</sup>, N. Khranovskaya<sup>2</sup>, M. Krotevich<sup>3</sup>

<sup>1</sup>National Cancer Institute, Oncogynaecology Dpt, Kiev; ; <sup>2</sup>National Cancer Institute, Experimental Oncology Dpt, Kiev; <sup>3</sup>National Cancer Institute, Pathology Dpt - -Ukraine

Gestational trophoblastic neoplasia is primarily a disease of reproductive age women so treatment with preservation of fertility is definitely important for this group of patients. The aim of this study was to improve the effectiveness of treatment and quality of life of patients with chemoresistant gestational trophoblastic neoplasms (GTN)

23 patients aged of 17 to 32 years (average age 25.5±3.0) with morphologically verified chemoresistant GTN were divided to research group (11 women, who underwent uterine resection with uterine reconstruction) and control group (12 women, who underwent standard surgical treatment - type I hysterectomy). Stage I disease was diagnosed in 18 women (78.3%), III stage – in 5 (21.7%); in the research group stage III was diagnosed in 3 cases. In all patients, according to ultrasound (Doppler sonography) and MRI visualized tumor nodules in the myometrium 4-5 cm in diameter (average nodules size 4.75±0.68). Multiagent chemotherapy protocols carried EMA- EP, BEP, TP, TP-TE.

Uterus resection involves removal of the trophoblastic node with macroscopically intact surrounding myometrium, indented from the edge of the tumor - 0.5-1.0 cm. Reconstruction of the uterus was performed by three-row seams using absorbable suture. Angioarchitectonic of uterus (according to Doppler sonography) restored within 3 months after surgery. In the research group fertility preserved - 3 patient gave birth to healthy children. There is no differences in 3-year overall survival: 100% - in research group vs 91.7% - in control group, p>0,05.

Resection and reconstruction of the uterus - the method of choice and should be performed only in centers with experience in complex multimodal treatment of patients with chemoresistant GTN.

## USE OF FROZEN SECTION AND IMAGING TO AVOID LYMPHADENECTOMY IN ENDOMETRIAL CANCER, THE HOSPITAL TENGKU AMPUAN AFZAN CANCER UNIT EXPERIENCE

M. Awang<sup>1</sup>, AR. Zakaria<sup>2</sup>, N. Ong<sup>2</sup>, AL. Roslani<sup>2</sup>, N. Mat-Ali<sup>2</sup>, R. Ismail<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Kulliyah of Medicine, International Islamic

University Malaysia, Kuantan, Pahang; <sup>2</sup>Gynaecological Oncology Unit, Department of Obstetrics and Gynaecology, Hospital Tengku Ampuan Afzan, Kuantan, Pahang - Malaysia

**Objectives:** The purpose of this study was:

1. To evaluate the significance of nodal size on CT imaging in term of predicting nodal metastasis
2. To examine the correlation between the number of nodes harvested and the incidence of nodal metastasis
3. To compare the reliability of frozen section against magnetic resonance imaging (MRI) in predicting the depth of myometrial invasion

**Methods:** This is a retrospective observational study of all cases of endometrial carcinoma managed in Hospital Tengku Ampuan Afzan (HTAA), from January 2011 until December 2013

**Results:** There were 48 cases of endometrial carcinoma that underwent surgical intervention during this study period. The mean age at diagnosis was  $53 \pm 10.5$  years (range 30-79 years). Office endometrial biopsies were performed in 52.1% of cases as a primary investigative tool with a positive predictive value (PPV) of 76.0%. Pre-operative assessment of locoregional and distant metastasis were carried out in 85.4% of cases out of which the majority (63.4%) had CT scan. Only about a-third of cases (36.6%) had MRI as a method of locoregional assessment of disease spread. Based on both of these imaging techniques, we found that the PPV of nodal size of 1 cm or more is 75.0% and the negative predictive value (NPV) of lymph node less than 1cm is 84.2%. The difference observed is statistically significant with a p-value of 0.006. Besides that, we also found that removing at least 10 nodes or more was associated with higher probability of yielding positive nodes,  $p = 0.018$ . We also compared the PPV of MRI versus intra-operative frozen section in predicting the depth of myometrial invasion. We found that intra-operative frozen section had a higher PPV compared to MRI i.e. 80.0% versus 40.0% respectively with a p-value of 0.07 showing a trend towards statistical significance.

**Conclusion:** From this study, we strongly feel that in patients with low grade tumour i.e. grade 1 or 2 tumour with myometrial invasion of less than 50% on frozen section and with no significant nodal enlargement on either CT scan or MRI, pelvic and para-ortic lymphadenectomy can be safely omitted.

Clinical characteristics	No. of cases (%)
<u>Office endometrial sampling</u>	
Conclusive results	19 out of 25 cases (76)
Inconclusive results	6 out of 25 cases (24)
<u>Imaging modalities</u>	
CT scan	26 (54.2)
MRI	15 (31.2)
Chest x-ray only	7 (14.6)
<u>Accurate assessment of depth of myometrial invasion</u>	
MRI	2 out of 5 cases (40)
Frozen section	10 out of 12 cases (83.3)
<u>Nodal metastasis</u>	
Pelvic nodes	9 out of 39 cases (23.0)

Para-aortic nodes 1 out of 10 cases (10.0)

<u>Nodal metastasis versus nodes count</u>	
0-9 nodes	6 out of 35 cases (17.1)
10-19 nodes	2 out of 3 cases (66.7)
20-29 nodes	1 out of 1 case (100.0)
<b>p-value=0.018</b>	

Nodal metastasis versus nodal size on radiological imaging

Subcentimeter (<1cm) 6 out of 38 cases (15.8)

More than 1 cm 3 out of 4 cases (75.0)

**p-value= 0.006**

## **MICROINVASIVE CERVICAL CANCER AFTER PREGNANCY “VANISHED”**

D. Butorac<sup>1</sup>, D. Eljuga<sup>1</sup>, V. Gall<sup>1</sup>, T. Leniček<sup>2</sup>, L. Jokanovic<sup>1</sup>, A. Vuković<sup>1</sup>, M. Grdić Rajković<sup>3</sup>, K. Kuna<sup>1</sup>, Z. Kraljević<sup>1</sup>

<sup>1</sup>*Clinic of Gynecology and Obstetrics, Clinical Hospital Center Sestre milosrdnice, Zagreb;*

<sup>2</sup>*Section for Gynecologic and Perinatal Pathology, University Hospital Center Sestre milosrdnice Zagreb;*

<sup>3</sup>*Department of Medical biochemistry and Hematology, Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb - Croatia*

**Background:** Diagnosis of malignant and premalignant cervical lesions during pregnancy is complex due to increased risk for overlooking invasive cervical carcinoma and the need for minimally aggressive approach at the same time due to increased pregnancy related risk of procedure complications. (1,2). Immunological changes during or after pregnancy are partially responsible for altered response to premalignant cervical lesions and HPV infection which are considered to be precondition for micro invasive cervical cancer.(3). Colposcopy controlled targeted biopsy except physical removal of the lesion presumably has effects which encourage local or systemic immunological response to tissue damage.

**Case report:** Thirty-four year old women in 15 th week of pregnancy during cytological screening, high grade intraepithelial cervical lesion (CIN III) was diagnosed. Following the Rio de Janeiro (4) colposcopy classification, colposcopy showed possible invasive disease with characteristic description of atypical blood vessels. The patient refused proposed cervical biopsy and further regular cytology and colposcopy controls during pregnancy were performed. The patient was delivered at term pregnancy. Six weeks after delivery, colposcopy controlled targeted cervical biopsy was performed. Histology result showed micro invasive cervical cancer which reaches the edges. Conisation was performed and histology result did not find previously described lesion, only inflammatory- fibrous reaction on the place of previously performed biopsy. The results are multiple checked and both histology results are confirmed.

**Conclusion:** We confirmed the importance of colposcopy in diagnostics and therapy of premalignant and malignant cervical intraepithelial lesion. Immunologic changes after pregnancy and artificial damage of the tissue can be additional reason for unexpected vanishing of micro invasive cervical cancer.

**Key words:** colposcopy, micro invasive cervical cancer, pregnancy

### **References:**

1. Arbyn M, Anttila A, Jordan J, et al. European Guidelines for Quality Assurance in Cervical Cancer Screening. Second edition – summary document. *Ann Oncol*2010;21:448–58.
2. G. Grubisic et al.: Diagnostic Approach for Cervical Cancer, *Coll. Antropol.* 33 (2009) 4: 1431–1436
3. Joško Zekan, Maja Sirotković-Skerlev and Mihael Skerlev. Oncogenic Aspects of HPV Infections of the Female Genital Tract // DNA Replication-Current Advances / Herve Seligmann (ur.). New York : InTech, 2011. Str. 595-612
4. Bornstein J, Bentley J, Bösze P, Girardi F, Hefner H, Menton M, Perotta M, Prendiville W, Russell P, Sideri M, Strander B, Tatti S, Torne A, and Walker P. 2011 Colposcopic Terminology of the International Federation for Cervical Pathology and Colposcopy, *Obstet.Gynecol* 2012;120:166-72

## **MODERATELY - POORLY DIFFERENTIATED SQUAMOUS CELL CARCINOMA OF THE OESOPHAGUS, WITH LOCAL INVASION IN PREGNANCY: A CASE REPORT**

A. Alessandra, L. Ganzitti, E. Baruzzo, M. Della Martina, V. Capodicasa, G. Fabiani, D. Marchesoni

*Clinic of Obstetric and Gynecology Udine, University of Udine Medical School and University Hospital, Udine - Italy*

**Introduction:** Esophageal cancer in pregnancy is extremely rare. The symptoms could be misinterpreted as pregnancy related. Cancer stage is usually advanced at time of diagnosis and prognosis is poor.

**Case Report:** This report describes the case of a 29-year-old woman at 23 weeks of gestation with rhinopharyngitis poor responder to antibiotic treatment and steroids. About 2 weeks after the first examination, patient was admitted to Otorhinolaryngology Unit for dyspnea, dysphagia, anemia and haemoptysis. Bronchoscopy revealed severe tracheal stenosis due to compression of posterior wall extended for about 5 cm. Biopsy had features suggestive for malignancy.

MR images showed a solid mass of 47x45 mm in axial section and 90 mm in sagittal section, from epiglottis down to medium and posterior mediastinum; trachea was displaced and infiltrated, and tracheal lumen was only 5x13 mm. Also oesophagus seemed to be infiltrated. Mass developed also to anterior mediastinum, in proximity of left common carotid artery and brachiocephalic trunk in absence of infiltration signs. There was also paratracheal lymph nodes involvement. Mass origin was not so clear: oesophagus, thyroid gland or lymph nodes. Upper gastrointestinal endoscopy revealed a tumor located in upper oesophagus, from cricopharynx to 28 cm from the incisor tooth, oesophagus' circumference was completely involved. Histopathological examination revealed moderately - poorly differentiated squamous cell carcinoma of the oesophagus, HPV16- related.

Thyroid fine-needle aspiration was performed and cytology yielded metastatic carcinoma.

Final diagnosis was made at 25 weeks and 3 days of gestation. Ethical dilemmas arose in managing this case. A multidisciplinary approach was adopted to find a good balance between preservation of foetal health and cancer treatment. A tracheostomy was placed. A second MR scan showed a locally advanced carcinoma with an enlargement of the mass.

Considering rapid progression of disease, patient's performance status and gestational age, caesarean section was performed at 28 weeks of gestation (female, birth weight 1,431 g). At the same time a percutaneous endoscopic gastrostomy was performed. After delivery, disease staging was completed: moderately - poorly differentiated squamous cell carcinoma of the oesophagus, with local invasion, T4bNxM0, G3, HPV-related. She went on to receive systemic chemotherapy (2 doses with cisplatin 100 mg and 5-fluorouracil 1000 mg and 2 doses with also cetuximab). Later a concurrent chemioirradiation was performed. At present the patient is being followed up in Cancer unit. Last TC scan revealed a significant reduction of the malignant mass. Tracheostomy and PEG are present to ensure good respiration and nutrition. Baby is 9 months old and is doing well.

**Conclusions:** Cancer management in pregnancy is extremely difficult and multidisciplinary approach must be adopted in order to make the best decision.

## **SUCCESSFUL PREGNANCY AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA**

D. Mocuta, C. Aur

*University of Oradea, Faculty of Medicine and Pharmacy, Obstetrics and Gynecology Department, Romania*

Pregnancy following hematopoietic stem cell treatment HSCT is considered to be a rare event. Female patients with acute lymphoblastic leukemia ALL and allogeneic hematopoietic stem cell treatment should be followed in a gynecology unit, because of the threat to fertility. The impact of the treatment on fertility cannot be prevented in many cases. Exposure of the ovaries to chemotherapy and high-dose radiation is significant risk factors for acute ovarian failure and premature menopause. The recovery of normal ovarian function and a viable pregnancy is a relatively rare possibility after the treatment for acute lymphoblastic leukemia received during childhood or adolescence. The uterine and ovarian damage, the changes of the uterine cavity and uterine tissue perfusion have a fundamental role for the pregnancy outcome. They can be responsible for the increased rate of spontaneous abortion, preterm labor and low birth weight babies. In our experience, we had a successful pregnancy and at term delivery in a 28 years patient at 10 years after acute lymphoblastic leukemia treatment and allogeneic hematopoietic stem cell transplant, complicated with chronic graft-versus-host-disease. The pregnancy had an uncomplicated evolution, finalized with a cesarean section for a 3000 gr. healthy baby girl.

## DIAGNOSTIC ACCURACY OF CT OR MRI IN THE STAGING OF ENDOMETRIAL CANCER

G, Eloundou<sup>1</sup>, H. Chong<sup>2</sup>, R. Athavale<sup>1</sup>

<sup>1</sup>University Hospital of Coventry and Warwickshire, Gynaecology Oncology Department; <sup>2</sup>Division of Reproductive Health, Warwick Medical School - UK

**Objective:** The purpose of this study was to compare preoperative radiological staging with definitive postoperative histopathology staging for patients with endometrial cancer at the University Hospital of Coventry and Warwickshire over a 12 month period. At present, preoperative radiological imaging either by CT or MRI is used selectively. This is due to the variable availability, cost of such investigations and differing surgical practices with respect to lymphadenectomy. FIGO recommends lymphadenectomy in high-risk cases, therefore accurate preoperative staging will influence the type of surgery performed

**Material and Methods:** This was a retrospective study involving patients diagnosed with endometrial cancers between January and December 2012. Patients were identified using the pathology register, and the electronic reporting system was used to assess the diagnostic accuracy of CT or MRI in identifying disease beyond FIGO stage 1a. Imaging findings were correlated with the histological staging. Data were extracted to generate two-by-two tables in order to calculate sensitivity, specificity and positive (PPV) and negative predictive values (NPV).

**Results:** Of 111 patients diagnosed with endometrial cancer during the study period, imaging and histology data were complete for 58 patients (52.3%). Of these, 53 (91.4%) had pre-operative staging MRI or CT. The sensitivity, specificity, PPV and NPV of MRI or CT for diagnosing disease equivalent to stage 1B or beyond was 57.1%, 100%, 100% and 57.6%, respectively. Pelvic lymphadenectomy was performed in 23 patients (39.7%). The sensitivity, specificity, PPV and NPV of CT or MRI for predicting pelvic nodal disease was 42.9%, 86.4%, 50% and 82.6% respectively. Para-aortic lymphadenectomy was performed in one patient (1.7%), therefore we did not analyse this data further.

**Conclusions:** Collectively, our data suggests a high specificity of MRI or CT in diagnosing disease less than stage 1b. However, this is less than that reported in a national audit published by the UK Royal College of Radiologists. This could be due to the small sample size in our cohort for which MRI and histology results were complete. The practice of pelvic lymphadenectomy parallels that of published data. Given that the sensitivity and PPV of MRI in predicting pelvic nodal disease is low, caution should be exercised in performing pelvic lymphadenectomy given the high morbidity associated with this procedure.

## **THE BAYES THEOREM FOR THE EVIDENCE BASED OVARIAN CANCER DIAGNOSIS**

G. Cardillo, I. Di Biase, U. Biscotti

*MeriGen Research S.r.l and Laboratorio C. Pandolfi & C. S.a.s. Napoli – Italia*

We setup a responsive web-app, Dibayco (<http://dibayco.altervista.org/>), reachable using modern web browsers on PC and mobile devices, to assess the risk of ovarian cancer on the basis of the evidences usually collected by physicians, using the Bayes Theorem.

The starting point (the “a-priori” risk) is the prevalence of this cancer stratified by age and regional residence: it is more frequent in post-menopausal than pre-menopausal women and at Northern than Southern Italy (Epidemiol Prev. 2010;34(5-6 Suppl 2):112).

At the first step, the risk is modified by using medical records: the presence of a first degree relative with ovarian cancer (risk factor - Ann Oncol. 2013;24(10):2651-6); use of oral contraceptives (protective factor - Lancet 2008;371(9609):303-14) and the Goff Index based on patient's symptoms (Gynecol Oncol 2010; 116(3):378).

At the second step the risk is modified by using Eco Color Doppler Trans Vaginal Ultrasound Scan. Several parameters like ovarian volume, Morphological Index (Obstet Gynecol. 1991;78(1):70-6), Pulsatility Index, Vessels location and Presence of intense echoes suggestive of adipose or fibrous tissue are combined into an Ovarian Tumor Index (Cancer 1999;86(11):2280-90).

At the third step, the risk is modified by using the serum markers CA125 and HE4. The cut-offs for these markers are differently set for pre and post menopausal women (Br J Cancer 2011;104(5):863-70). The web-app can also manage Osteopontin (J Obstet Gynaecol Res. 2013;39(11):1518-25) and Mesothelin (Arch Gynecol Obstet. 2014;289(6):1309-14).

Finally at fourth step the risk is modified by using Level II diagnostic imaging results from techniques like Magnetic Resonance, Computed Tomography and Positrons Emission Tomography (Eur J Radiol 2009; 71(1):164-74) or using the new molecular markers miRNAs (Cancer Res 2007;67(18):8699-8707).

Parameters of first three steps are routinely required for women with a suspicious ovarian mass and so they always are available. The sections are independent each other and the physician can decide, on the basis of collected informations, if further laboratory or diagnostic imaging tests are needed to be required, allowing a reduction of costs for useless tests. Moreover, the physician has an easy to use tool to retrieve a numeric and robust evaluation of the cancer risk on which to base the diagnosis.

## **THE DIFFICULTIES OF IMPLEMENTING A CERVICAL SCREENING PROGRAMME IN MALAYSIA – A ETHNOGRAPHIC REFLECTION**

M.J. Hussain

*University of Bristol, Central Manchester Foundation Trust, Wellbeing of Women Charity – United Kingdom*

**Introduction:** Cervical cancer is currently the 2nd most common female cancer in Malaysia and is responsible for significant number of cancer admissions and deaths in government hospitals. Nearly 80% of cervical cancer patients present with advanced stage disease. No national screening programme currently exists, instead screening is opportunistic.

The gynaecology department at the University of Malaya Medical Centre (UMMC) have been trying for the last 10 years to implement a cervical screening programme, however *'all the resources needed to implement and run a programme are available but the patients are not there'*. So where are the patients?

**Method:** Ethnographic research was conducted in the Obstetrics and Gynaecology department of UMMC and Likas Hospital, Peninsula and Borneo Malaysia, April-May 2013. Observations were conducted in a clinical setting with health professionals and patients. Interpretative phenomenological analysis was performed to explore the barriers and poor uptake of Cervical Screening amongst Malaysian Women.

**Results:** There was a general lack of awareness and information, which affected participation to screening. Inadequate knowledge of effectiveness and necessity of cervical screening and ignorance of perceived susceptibility to cervical cancer predicted cervical screening behaviours. Screening uptake was motivated by presentation of physical symptoms. Social and cultural factors excused examination or delayed screening. Lack of a systematic approach to opportunistic screening, poor health surveillance, commitment and follow-up by clinicians to opportunistic screening contributed to poor patient compliance, concordance and acceptance. Undervaluation of health status' and inequalities amongst rural populations, the socioeconomically deprived and immigrants predicted worse outcomes.

**Discussion:** Education of cervical screening and cancer is needed to challenge misconceptions, raise awareness, promote acceptance towards cervical screening. But barriers to screening still remain. Health professionals have a significant role in aiding compliance and concordance to screening. Home screening test offer new opportunities for wider participation of a cervical screening programme in Malaysia.

## **FOLLOW-UP IN PATIENTS WITH BRCA MUTATIONS; FOCUS ON OVARIAN CANCER RISK : A SINGLE-CENTER EXPERIENCE**

S. Giovannoni<sup>1</sup>, G.M. Campenni<sup>1</sup>, M. Palleschi<sup>1</sup>, M. Telesca<sup>2</sup>, E. Miglio<sup>2</sup>, V. Cipolla<sup>2</sup>, C. De Felice<sup>2</sup>, L. Ballesio<sup>2</sup>, F. Pediconi<sup>2</sup>, C. De Beranrdo<sup>3</sup>, P. Grammatico<sup>3</sup>, G. Naso<sup>1</sup>, L. De Marchis<sup>1</sup>

<sup>1</sup>*Oncology Unit B, Department of Radiology Oncology and Human Pathology, Sapienza University of Rome – Rome;* <sup>2</sup>*Department of Radiological Sciences, Department of Radiology Oncology and Human Pathology Sapienza University of Rome, Rome;* <sup>3</sup>*Division of Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome - Italy*

**Purpose:** to observe the outcome of BRCA carrier patients (pts) during surveillance program from 2007 to 2014.

**Methods:** We selected 114 women at high risk for HBOC (Hereditary Breast Ovarian cancer). 37 (32.5%) had previous history of Breast Cancer (BC) and 5 (4.4%) Ovarian Cancer (OC), of which 3 had previous history BC. 65 (57.1%) had no cancer history. All women were referred to oncogenetic counseling to schedule a surveillance and identify BRCA mutation carriers by direct sequencing and multiple ligation dependent probe amplification (MLPA). 53 (46.5%) of all screened women were positive for BRCA mutation: 30 (56.8%) were BRCA1 and 23 (37.8%) BRCA2 carriers. Of the 37 pts with previous BC, 24 (65%) were BRCA mutation carriers: 16 BRCA1 and 8 BRCA2. Out of the 5 OC patients, 4 were BRCA1 and only one BRCA2. For OC, Risk-Reduction Salpingo-Oophorectomy (RRSO) was advised to all pts, as recommended by guidelines [1]. 8 pts (7.1%) were not yet offered RRSO due to their young age. Pts refusing RRSO were included in a surveillance program with semiannual transvaginal ultrasonography (TU) along with CA-125 testing. The average follow-up of all pts was 45.5 months.

**Results:** Among the 5 pts with history of OC, one relapsed and is still under chemotherapy. 3 BRCA carriers were diagnosed during surveillance with advanced OC (FIGO stage IIIC). Median age at diagnosis was 45 yrs. The histology was poorly differentiated serous adenocarcinoma with peritoneal carcinomatosis in all cases. All 3 were relapses with average time to relapse of 9.6 months from adjuvant chemotherapy, and are still under treatment. 16 women (30.3% of the 53 showing mutations) accepted RRSO. The median age was 44 yrs. In two cases early stage ovarian cancer was detected, one case was a transitional cell carcinoma and the second one a serous adenocarcinoma. The remaining 43 BRCA carrier women are negative for OC as of the present day.

**Conclusions:** The identification of mutational status of BRCA1-2 in high risk women is essential to schedule a close surveillance to detect tumors in early stage of disease. For OC risk, no evidence shows reduction in cancer-related deaths with TU and CA-125 screening. However, these strategies continue to be recommended for BRCA carriers who have not yet had a RRSO. The effectiveness of such surveillance has been questioned by recent studies. [2-7]. Our results, despite coming from a small sample, reflect the recent criticism. The 3 cases of OC diagnosed after BRCA testing (during surveillance) were in advanced stage. All of them relapsed. All cases of OCs identified before BRCA detection were in advanced stage as well. Only the two pts who underwent RRSO had an early stage of disease. We believe that RRSO should be offered to all BRCA-positive pts, after being adequately informed by the oncologist/geneticist/surgeon team. Among our BRCA carriers, 30.3% accepted RRSO. It is, at the moment, the only effective treatment in OC reduction [8-11].

**References:**

1. NCCN Guidelines Version 1.2014 ; Genetic/Familial High-Risk ;Assessment breast and ovarian
2. Meeuwissen PAM et al. Outcome of surveillance and prophylactic salpingo-oophorectomy in asymptomatic women at high risk of ovarian cancer. *Gynecologic Oncology* 2005; 97(2): 476-82.
3. Oei AI et al. Surveillance of women at high risk of hereditary ovarian cancer is inefficient. *Br J Cancer* 2006; 27; 94(6): 814-9.
4. Woodward ER et al. Annual surveillance by CA125 and transvaginal ultrasound for ovarian cancer in both high-risk and population-risk women is ineffective. *BJOG*. 2007 Dec; 114(12):1500-9.
5. Stirling D et al. Screening for familial ovarian cancer: failure of current protocols to detect cancer at an early stage according to the International Federation of Gynecology and Obstetrics system. *JCO* 2005; 20; 23 (24):5588-96.
6. Van der Velde NM et al. Time to stop ovarian cancer screening in BRCA1/1 mutations carriers. *Int J Cancer* 2009; 124(4): 919-23
7. Hogg R and Friedlander M. Biology of ovarian cancer: implications for screening women at high genetic risk. *J Clin Oncol* 2004; 22:1315-27.
8. Rebbeck TR et al. Prophylactic oophorectomy in carriers of BRCA1 and BRCA2 mutations. *N Engl J Med*. 2002; 346: 1616-1622
9. Rebbeck TR et al. Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers. *J Natl Cancer Inst* 2009; 101:80-87
10. Eisen A et al. Breast cancer risk following bilateral oophorectomy in BRCA1 and BRCA2 mutation carriers : an international case-control study.

JCO 2005;23: 7491-7496

11. Rebbeck et al. Breast cancer risk after bilateral prophylactic oophorectomy in BRCA1 mutation carriers J Natl Cancer Inst. 1999; 91: 1475-1479

## **A REVIEW OF CASES UNDERGOING STRAIGHT WIRE EXCISION OF TRANSFORMATION ZONE (SWETZ) AT A TERTIARY CENTRE IN SCOTLAND**

F.M. Gaba, H. Ayaz, M. Cruickshank

*Department of Gynaecology, Aberdeen Royal Infirmary, United Kingdom*

**Background:** Needle excision of transformation zone was first described by Sadek in 1999 for conization of the cervix in women with histologically proven cervical intraepithelial neoplasia (CIN) as an outpatient procedure. However, there is limited literature regarding associated complications. With this in mind, the aim of our study was to determine complications and risk factors for complications with SWETZ.

**Methods:** Women undergoing SWETZ were identified using a computer-based system. 105 cases were identified between 2006-2013 and a retrospective case note review was undertaken.

**Results:** Of 105 cases, complete results were available for 73 due to insufficient record keeping. 45% (n=33) of SWETZ were performed for incomplete excision of high-grade cervical intraepithelial neoplasia (HGCIN), 40% (n=29) as primary treatment for HGCIN, 12% (n=9) for incomplete excision of cervical glandular intraepithelial neoplasia (CGIN) and 3% (n=2) for cervical cancer 1A/1B. Median age was 37.8 years (range 26-64). 31% (n=23) were nulliparous and 69% (n=50) parous. 67% (n=49) had previous LLETZ. Average depth of excision for women undergoing primary SWETZ was 18.7mm, and for SWETZ after previous LLETZ, 17.4mm. 64% (n=47) were performed under general anaesthetic, 36% (n=26) under local. Complication rate was 21% (n=15). A total of twelve cases were complicated by hemorrhage, in eight hemorrhage was primary and in four secondary (7-21 days post SWETZ). Mean blood loss was 350mls and 1960mls for primary and secondary hemorrhage respectively. Primary hemorrhage was treated with sutures and vaginal packs. All cases of secondary hemorrhage required an emergency examination under anesthesia/antibiotics/blood transfusion. In two of the four cases bleeding settled with diathermy and vaginal packs whilst two required an emergency hysterectomy. Ten out of twelve cases of hemorrhage occurred with excision depth of >20mm and two for depth of <20mm. There were three cases of cervical stenosis. Two presented as haematometras 6-12 months post SWETZ. The third was diagnosed during investigations for primary infertility 1-year post SWETZ. All three had cervical dilatation performed. Hysterectomy rate post SWETZ was 22% (n=16). Fourteen cases were for persistent HGCIN/CGIN and two were the emergency hysterectomies mentioned earlier.

**Conclusions:** SWETZ is associated with significant complications such as primary/secondary hemorrhage requiring blood transfusion and rarely hysterectomy. There also remains a small risk of cervical stenosis. Women need to be appropriately counseled regarding these risks prior to the procedure. In this case series it appears that an excision depth of >20mm increases risk of hemorrhage but reduces risk of hysterectomy. Conversely, <20mm excision depth increases risk of hysterectomy but reduces risk of hemorrhage. Further data is required to establish optimum excision depth with minimum risk of complications without compromising procedure efficacy.

## **FOLLOW UP AND PATIENT RETRIEVAL SYSTEMS FOR GYNECOLOGICAL CANCER PATIENTS : AN INDIAN SURVEY**

M. Sharma, A. Sharma

*Maulana Azad Medical College and AllIndia Institute of Medical Sciences, New Delhi - India*

**Introduction:** The foundation of evidence based medicine in oncological sciences is patient follow up . There are inherent problems faced in developing countries. The absence of follow up seems to affect the patient survival, intervention in case of predictive recurrence, fortifies authenticity of research and survival data. Paper outlines histrionics, evolved/recommended methodologies, nationwide survey with regards to awareness, practice of follow-up and obstacles faced in India institutions.

**Aims and Objective:** 1. To evaluate the effectiveness of follow up methodologies, 2. Compliance of institutions and oncologist with regards to follow-up of Gynec cancer patients.

**Materials and Method:** The follow up methodology propagated; 1-6 address system (IARC 3 Address System), 2-Postcarding, 3-SMS /Telephony, 4-Door to door patient retrieval, 5-Family Physician referrals/ feedback, 6-Software Alert on follow up defaulters in the Hospital Based Cancer Registry etc. A stock taking was started 10 years back with repeated circulars on dates of “The National Cancer Calendar” ( one date every months) that were sent to some 10,000 email address of personnel/ institutions connected with oncological sciences. Over five years 150 postgraduate examinees were interviewed on their understanding of Follow-Up practices in Gynec cancers .As an inspector of a major medical accreditation institution 50 institutions were inspected and existence of their follow up methodologies were evaluated. 100 post graduate dissertations reviewed, were studied with regards to status of follow up in the study carried out or the existence of follow-up system in the institution. Undergraduate students and their text books were searched if they are educated about follow up and its significance in Medical science

**Observations and Results:** Response to circulars on follow up in cancer patients was cold shouldered, 95 percent of examinee PG students did not know how to follow up the cancer patients ,out which as many as 90 percent of their institutions did not have any follow up system in order.99 percent of dissertation did not show any effort from the side of candidate for patient retrieval system in order to fortify the research data. Only 20 percent institutions had infrastructure and significant effort ( including door to door retrieval) on following up the patients that are treated there. Non of the undergraduate text books had guidelines or teaching in follow up so were total blankness of concept of follow up with undergraduate students.

**Conclusion:** In order to improve the survival and timely therapeutic intervention ,follow up has to be strengthen at under graduate and post graduate medical teaching . This also applies for the authenticity of oncological research data that is produced in large numbers in developing countries This is especially significant in the large poor socio economic gynec cancer patient population with poor literacy levels and far off homes from cancer treatment centres.

## **CANCER FOLLOW-UP AIMING AT RECURRENCE DETECTION: A PATIENT CENTERED PERSPECTIVE**

J.A.A.M. van Dijck, A.L.M. Verbeek, S.M.E. Geurts

*Department for Health Evidence, Radboud University Medical Centre, Nijmegen - The Netherlands*

**Purpose.** Current guidelines for cancer follow-up are mainly consensus-based and includes a ‘one-size-fits-all’ advice on which test to perform and when. The optimal cancer-specific schedules of routine tests to ensure timely detection of recurrent cancer is unknown. It is also unknown how to design tailored and evidence-based cancer follow-up schedules.

**Materials and methods.** Patients should only undergo routine testing if the expected benefits exceed the potential harms. Routine testing may benefit a patient when the screening test is capable of detecting a recurrence in its preclinical phase, when the preclinical phase is significantly long and when treatment of recurrences in its preclinical phase improve patient outcomes. Tests and treatments are however costly to society and may cause physical and psychosocial harm to patients. We will discuss three ways for personalizing follow-up after curative-intent treatment for cancer, namely stratification according to risk of recurrence, recurrence growth rate and patient’s life expectancy.

**Results.** Stratifying follow-up according to the absolute risk of recurrence requires risk prediction by modelling patient, tumour and treatment characteristics. Theoretically, routine tests are not indicated when risk of recurrence is significantly low, i.e. where the risk of harm exceeds the potential benefit. Differentiating patients with a low risk from those with an intermediate or high risk may however be difficult because absolute risk differences between low and high risk groups are generally small. Heterogeneity of recurrence growth rate is a second factor to take into account. The faster the tumours’ growth rate, the shorter the preclinical phase. Consequently, patients prone to fast growing recurrences require a short test interval (intensive follow-up), whereas patients with slow growing recurrences require less frequent testing. Thirdly, follow-up tests should be offered only to those patients who are expected to live long enough to benefit and who are fit enough and willing to receive treatment if a recurrence were detected. Stratification of patients according to life expectancy requires determination of functional age, which may be estimated based on biological age and number and severity of co-morbidities.

**Conclusion.** While waiting for upcoming evidence on benefits and harms of routine testing, it is advisable to omit follow-up tests in patients for whom no recurrence treatment options are available, and also for those who are physically or mentally unable to undergo recurrence treatment or invasive follow-up tests. Patient’s voice should be heard in the decision to pursue or omit routine testing. A survivorship care plan may serve as a suitable tool for physicians and patients to discuss and weigh the benefits and harms of routine testing and provide patient-centred survivorship care.

## **IMMUNOLOGICAL PROFILE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER. DATA OF THE LOCAL RENO PROJECT AND THE FIS-PI13/02297 PROJECT**

J. Martínez-García<sup>1</sup>, M.V. Martínez Sánchez<sup>2</sup>, A. Torroba Caron<sup>3</sup>, B. Ferri<sup>3</sup>, E. Feliciangelli<sup>1</sup>, I. Legaz<sup>2</sup>, L. Gimeno<sup>2</sup>, B. Pisa<sup>2</sup>, N. Montes<sup>2</sup>, P. Cascales Campos<sup>4</sup>, J. Gil Martínez<sup>4</sup>, A. Nieto Díaz<sup>5</sup>, F. Barceló Valcarcel<sup>5</sup>, I. Martínez-Lacaci<sup>6</sup>, T. Escamez<sup>7</sup>, P. Sanchez-Henarejos<sup>1</sup>, A. Soto<sup>1</sup>, S. Montenegro Luis<sup>1</sup>, J.L. Alonso Romero<sup>1</sup>, A. Minguela Puras<sup>1</sup>

<sup>1</sup>Servicio de Oncología Médica, <sup>2</sup>Servicio de Inmunología Clínica, <sup>3</sup>Servicio de Anatomía Patológica, <sup>4</sup>Departamento de Cirugía General - Unidad de cirugía peritoneal, <sup>5</sup>Departamento de Ginecología y Obstetricia – Unidad de Ginecología Oncológica, <sup>6</sup>Servicio de Oncología Médica – Unidad de investigación traslacional, <sup>7</sup>BioBanco; Instituto Murciano de Investigación Biomédica University Clinical Hospital Virgen De La Arrixaca, Murcia - Spain

**Background.** The both innate and adaptive immune system plays an important role in tumor pathophysiology. Profile of NK cells at diagnosis of epithelial ovarian cancer (EOC) informs us of the immune status of the patient and may enable the discovery of new predictive and prognostic biomarkers. We present initial data from the local project RENO launched in 2014, which is a prospective observational study of comprehensive and multidisciplinary assessment of tumor resistance in patients with EOC. This project shares data with the FIS-PI13/02297 project that studies the anti-tumor response of NK cells and their relationship with various malignancies.

**Methods.** The presentation of receptors that regulate the function of NK cells (KIR) were evaluated and compared between a group of patients with EOC and a healthy control group. Expression of KIR2D molecules is analyzed in samples of mononuclear cells (separated by density gradient) by multiparametric flow cytometry (LSR-II, BD), and by analysis of CD3, CD4, CD8, CD16, CD56, CD158a (antigens KIR2DL1), CD158a / h (KIR2DL1/S1) CD158b2 (KIR2DL3) CD158b1b2j (KIR2DL2/L3/S2) and NKG2A, which allows determining the expression of these KIR2D molecules in T lymphocytes and NK cells.

**Results.** In the first four months were recruited 8 EOC patients and 8 patients in the control group. In EOC patients compared to the control group there were higher figures of post stress blood glucose, Ca 125 (1552 vs 12), and HE4 (599 vs 78), as well as lower figures of hemoglobin (13.0 vs 14.6 g / dL, p <0.05), albumin (3.9 vs 4.6) and platelet count (358 vs 254 x 10<sup>9</sup> / L, p <0.05). There were no differences in age, fibrinogen, LDH, and absolute numbers of leukocytes and lymphocytes. The numbers of CD3 + and CD3 + CD4 + lymphocytes is similar in both groups. No differences were seen in the total number of NK cells nor among different subpopulations of NK cells in the expression of different activating or inhibitor KIR receptors (KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1 and KIR2DS1).

**Conclusions.** Our initial data show no differences in the expression of receptors that regulate the function of NK cells (KIR) between EOC patients and the healthy control group.

## **MODELLING THE BENEFITS OF RISK-STRATIFIED FOLLOW-UP (RSF) OF EPITHELIAL OVARIAN CANCER (EOC) PATIENTS IN A SINGLE CENTRE INSTITUTION**

H.H. Wong, I. Gounaris, B. Hassan, K. Sayal, J. Brook, M. Noonan, J. Brenton, H. Earl, C. Parkinson

*Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital, Cambridge - UK*

**Background:** Oncology clinics around the UK are overwhelmed by the number of patients attending for routine follow-up appointments. At Addenbrooke's Hospital, Cambridge, oncology outpatient attendance is increasing by 4.3% per annum and the current model cannot be sustained given the predicted increase in cancer survivors. This has led to proposals for replacement of the 'one-size-fits-all' with 'risk-stratified' follow-up (RSF) pathways, tailored to a patient's circumstances (e.g. disease type, stage, treatment and benefit of continuing surveillance).

**Methods:** Local and international follow-up guidelines for EOC patients were reviewed. A new RSF pathway was designed and its benefits were assessed.

**Results:** Current international follow-up guidelines for EOC (ESMO, NCCN and SGO) recommend a schedule of 3-monthly clinic visits for the first 2 years, 3-6-monthly for year 3, and 6-monthly for years 4 and 5. This equates to at least 14 clinic appointments for each patient over a 5-year period. Risk of relapse is related to disease stage with much better disease free and overall survival for early stage patients. Patients with stage I EOC treated with adjuvant chemotherapy have 5-year recurrence free survival of 75%; additionally, there is no evidence that intensive surveillance improves outcomes. At Addenbrooke's Hospital, we have recently implemented a RSF pathway for ovarian cancer patients based on the disease stage (Figure 1). Under the new RSF, stage I EOC patients are seen 6 monthly for 2 years, then annually for the remaining 3 years before a patient is considered for discharge. At our centre, we saw 17 stage I EOC patients between 2012 and 2013. Based on the standard follow-up schedule, 48 clinic appointments would be needed over a 5-year period. With the new RSF, the number of clinic appointments could be reduced by half. Based on a predicted increase in new patients of 4.3% per year, 148 fewer appointments per year would be needed for stage I EOC patients (131 under the RSF compared with 280 under conventional follow up). Other important changes to the schedule include placing increased emphasis on patient self-management (with appropriate support and rapid re-assessment if needed) and the consideration of telephone follow-ups.

**Conclusion:** Not only could the risk-stratified follow-up approach reduce unnecessary follow-ups (which could lead to the reduction in hospital costs, decrease in clinic waiting times and pressure on healthcare workers), it could also encourage patients to take responsibility for their own health. Given the increasing pressure on the healthcare system and the mostly predictable nature of ovarian cancer, a risk-stratified follow-up approach is highly suitable and beneficial for this disease setting.

## **SYSTEMATIC USE OF HYSTEROSCOPY IN THE SURVEILLANCE OF PATIENTS WITH ENDOMETRIAL CANCER AND DESIRE FOR FERTILITY PRESERVATION**

G.M. Makris, V. Bolkas, N. Evangelinakis, C. Chrelias, C. Siristatidis

*3rd Department of Obstetrics and Gynecology, Attikon Hospital, University of Athens - Greece*

**Aim:** The endometrial cancer is the most common gynecological cancer in the developed world and its occurrence is rising. The prolongation of the mean age of childbearing in the developed world has led to the increase of the number of patients with endometrial cancers that have not yet completed their family planning. It is common that these patients express the desire for fertility preservation. The surveillance of these patients that initially are going to have conservative hormonal treatment is of great importance. The protocols of surveillance suggest frequent imaging, laboratory and histological control of the patients until the completion of family planning, followed by hysterectomy. The aim of the presentation is to validate the use of hysteroscopy in the surveillance of patients with endometrial cancer and desire for fertility preservation. Moreover we study the potential to replace the frequent endometrial biopsy.

**Methods and Material:** We searched the guidelines of international gynecological societies in particular the NCCN, AGO and NICE of the respective gynecological societies of the USA, Germany and the UK. In addition to that we searched the randomized trials in the world wide web search engines of medical publications; Cochrane Central Register of Controlled Trials in the Cochrane Library, EMBASE and MEDLINE. The research criteria were prospective studies of evaluation of the use of hysteroscopy (office and under local or general sedation) in affected women of reproductive age with endometrial cancer and desire for fertility preservation. The research took place in June 2014.

**Results:** The current treatment of endometrial cancer is surgery, mainly hysterectomy, bilateral salpingo-oophorectomy with or without pelvic and paraaortic lymphadenectomy or sampling. The candidates for fertility preservation and with endometrial cancer should fulfill some minimal criteria for oncological security. The malignancy should be glandular endometrioid cancer and Grade 1 as far as the histological type is concerned. The imaging methods such as transvaginal ultrasound, CT or MRI should indicate that the disease is limited in the endometrium without expansion in the myometrium. The patient should have no contradiction to receive hormonal treatment such as Megestrol Acetate and there should not be any other counter indication or limitation in her desire for childbearing. Relevant literature research has not indicated international guidelines for the systematic use of hysteroscopy as the sole and safe method without additional endometrial sampling or imaging for the surveillance of patients with endometrial cancer that are treated conservatively. No relevant randomized prospective studies have been found that study the sufficiency of hysteroscopy in the early detection of local recurrence in endometrial cancer in these women. There are observational studies of patients that have been treated conservatively with surveillance every three or six months with dilatation and curettage and hysteroscopy. Many of these patients had a successful obstetrical outcome and an alive child at home.

**Conclusion:** Prospective randomized studies should be carried out in order to answer the questions; is sole hysteroscopy efficient, is it efficient without histological confirmation, how often should be done, are additional imaging exams needed, does it increase the danger of further advancement of the disease. Currently all gynecological cancer societies agree to the conservative treatment within certain time limits under strict criteria. Due to the advantage of direct visualization of the uterine cavity and the accurate and targeted sampling, hysteroscopy is a useful tool in patient's surveillance. In any case hysterectomy follows the completion of the family planning or in the case of any advancement or persistence of the disease.

### **Literature**

*1. Shirali E et al. Pregnancy outcome in patients with stage 1a endometrial adenocarcinoma, who conservatively treated with megestrol acetate. Arch Gynecol Obstet 2012 March;285(3):791-5*

2. Gunderson CC et al, *Oncologic and reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 adenocarcinoma: a systematic review. Gynecol Oncol 2012;125:477-482*
3. Gracia CR, et al. *Lives in the balance : women with cancer and the right to fertility care. J Clin Oncol 2013;31:668-669*
4. Park JY, et al. *Pregnancy outcomes after fertility- sparing management in young women with early endometrial cancer. Obstet Gynecol 2013;121:136-142*
5. Mehasseb MK et al. *Controversies in the management of endometrial carcinoma: an update. Obstet Gynecol Int 2012;2012:676032*
6. *NCCN guidelines for uterine cancer 1.2014 edition*
7. Laurelli G et al. *Conservative treatment of early endometrial cancer: preliminary results of a pilot study. Gynecol Oncol 2011;120:43-6*
8. *NICE guidelines 2013. Scientific Impact Paper No35. Fertility Sparing Treatments in Gynaecological Cancers*
9. *AGO ( Arbeitsgemeinschaft Gynaekologische Onkologie ) German guidelines 4.2013*

## **THE CONSERVATIVE MANAGEMENT IN OVARIAN CANCER**

D. Mocuta, C. Aur

*University of Oradea, Faculty of Medicine and Pharmacy, Obstetrics and Gynecology Department, Romania*

The incidence of ovarian cancer, the leading cause of death among the gynecological malignancies, is now increasing significantly in young women, who still want to be pregnant. Women are conceiving at much more advanced ages and the incidence of cancer of the ovaries in those who still want to get pregnant is higher than before. Complete information on the impact of cancer treatment on fertility and fertility preservation options should be presented to all patients, when a cancer treatment is planned. Infertility risks are related to surgical oncologic treatment, chemotherapy or radiation therapy. The conservative management in ovarian cancer, which preserves fertility, could be an option for those patients who have not completed their childbearing. Well selected patients, with early phases of ovarian cancer may be candidates to a save-fertility preserving surgery. A careful selection of these patients, the treatment options, a careful staging and histological classification and the follow-up of the patients are essential to achieve success with this practice. Fertility sparing surgery is supported in stage I disease, in case of a normal appearance of the other ovary. It consists generally in unilateral adnexectomy, sometimes with biopsy of the contralateral ovary. The detection of recurrence must be done during the follow-up of these cases, by periodic physical examination, ultrasound exam, levels of tumor markers. Pregnancies after conservatory surgery achieved in a large proportion of these patients. Our gynecological oncology department can report such a successful management in a 28 years old women with a 20 cm left ovary tumor micropapillary serous carcinoma of the ovary, stage I, treated with conservative surgery.

## **IS LIQUID-BASED HYSTEROSCOPIC FALLOPIAN TUBE BRUSH CYTOLOGY THE FUTURE OF SCREENING OF OVARIAN AND FALLOPIAN TUBE CANCER IN HIGH-RISK WOMEN?**

J. Presl<sup>1</sup>, R. Slunecko<sup>1</sup>, P. Vlasak<sup>2</sup>, J. Bouda<sup>2</sup>, A. Bartakova<sup>2</sup>, Z. Novotny<sup>2</sup>

<sup>1</sup>University Hospital in Pilsen, Department of Pathology, Pilsen; <sup>2</sup>University Hospital in Pilsen, Department of Obstetrics and Gynecology, Pilsen - Czech Republic

**Aim:** Our pilot study was designed to answer the question whether it is possible to detect precursor lesions or initial stages of high-grade serous ovarian and Fallopian tube carcinoma using hysteroscopic Fallopian tube brush cytology. If feasible, this could start a cascade of preventive and therapeutic measures that would ultimately lead to a reduction in the incidence and mortality of advanced stages of those malignancies.

**Methods:** We report a pilot study performed at the Department of Obstetrics and Gynecology, University Hospital and Medical Faculty in Pilsen, Charles University in Prague. The cells for analysis were obtained with a sheathed brush, which was introduced into the Fallopian tubes via Versascope hysteroscopic system. The samples were transferred into a liquid media and processed using The ThinPrep system. The results of cytologic and immunohistochemical examination (p53, MIB1) were correlated with histological findings in the fallopian tubes.

**Results:** Eleven patients were enrolled at time of submission of this study for ESGO SoA. The study was commenced in October 2013 and is ongoing. The mean age of the patients was 46.5 years (range 40-74 years). One patient underwent a radical surgery for a borderline ovarian tumor, four patients had a radical surgery for ovarian cancer and the remaining six patients had a laparoscopically assisted vaginal hysterectomy with bilateral salpingo-oophorectomy for breast cancer. Purely hysteroscopic sampling was performed in the first four enrolled patients, in the following seven patients additional sampling was done from the ampullary and fimbrial part of the Fallopian tubes ex-vivo using a cytology brush. The primary aim of this modification (added ex-vivo brushing) was to verify the correlation of the cytologic and immunohistochemical findings with the histological examination of the fallopian tubes. The cellularity of the samples was always sufficient for the planned examinations. Interesting and partially expected results are summarized in Table 1.

**Conclusion:** Based on the current tubal hypothesis of ovarian cancer, Fallopian tubes can be considered a primary target for development of a screening test for high-grade ovarian and Fallopian tube cancer. A successful screening test could protect more than 50% of women, who would otherwise develop those lethal malignancies. To the best of our knowledge, only two studies dealing with in-vivo endoscopic brush cytology from Fallopian tubes had been published. It can be anticipated that, providing the results of future studies demonstrate that the method of in-vivo endoscopic brush cytology is capable for detection of initial tubal abnormality, office hysteroscopy could become an acceptable way of screening of high-risk patients. An example of this group could be BRCA positive patients.

**DO ASIAN WOMEN HAVE ENDOMETRIAL CANCER AT A YOUNGER AGE?**M. Awang<sup>1</sup>, AR. Zakaria<sup>2</sup>, N. Ong<sup>2</sup>, N. Mat-Ali<sup>2</sup>, AL. Roslani<sup>2</sup>, R. Ismail<sup>2</sup><sup>1</sup>*Department of Obstetrics and Gynaecology, Kulliyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang;* <sup>2</sup>*Gynaecological Oncology Unit, Department of Obstetrics and Gynaecology, Hospital Tengku Ampuan Afzan, Kuantan, Pahang - Malaysia***Objectives:** The purpose of this study is to examine the epidemiological and clinical characteristics of patients with endometrial adenocarcinoma.**Methods:** This is a retrospective observational study of all cases of endometrial adenocarcinoma managed in Hospital Tengku Ampuan Afzan, from January 2011 until December 2013.**Results:** During this study period there were 48 cases of endometrial adenocarcinoma. The mean age at diagnosis was  $53.5 \pm 10.5$  year-old (range 30-79). One-fifth of these patients were 45 years and younger. The mean parity was  $2.5 \pm 2.5$ . The majority (80%) were obese with a mean BMI of  $28.8 \pm 5.9$ . The prevalence of diabetes, hypertension and polycystic ovarian disease were only 30%, 25% and 15% respectively. A significant proportion of women (40%) were in their premenopausal period. The remaining (60%) were in their peri/postmenopausal period. All the patients presented with abnormal uterine bleeding with a mean endometrial thickness of  $22.7 \pm 13.9$ mm. Equal numbers of women had office endometrial sampling and hysteroscopy and dilatation and curettage as a primary endometrial assessment. In this study, we found that the positive predictive value (PPV) of office endometrial sampling is 76.0%. The majority of the endometrial carcinoma was of endometrioid type (81.3%) and the others were high-grade endometrial carcinoma (4.2%), clear cell adenocarcinoma (4.2%), papillary serous (2.1%) and others (8.3%). The PPV of histological grade obtained via office endometrial sampling for grade 1, grade 2 and grade 3 in comparison to the full histology was 81.8%, 58.8% and 60.0% respectively. However, the differences observed in the PPV for different histological grading did not reach statistical significance ( $p=0.185$ ). In this study, the majority of patients (66.7%) had stage 1 disease followed by stage 3 (23.0%) at diagnosis. Small percentages of women had stage 2 and stage 4 disease at diagnosis i.e. 6.3% and 4.2% respectively. The majority of patients, 58.3% required further adjuvant treatment while the remaining 41.7% did not need further treatment.**Conclusion:** The mean age of diagnosis of endometrial cancer in our studied population is about ten years younger compared to Western populations. The percentage of Asian women 45 years and younger diagnosed with endometrial carcinoma was alarmingly high i.e. 4 fold higher compared to Caucasian women. Thus we recommend a lower age threshold for proper evaluation of Asian women presenting with abnormal uterine bleeding i.e. 35 years instead of 45 years as recommended by most cancer centres in the west.

Epidemiological/ Clinical Characteristics	Mean $\pm$ SD/ Percentage
Age (years)	53.5 $\pm$ 10.5
Parity	2.5 $\pm$ 2.5
Body mass index (BMI)	28.8 $\pm$ 5.9
Duration of symptoms (weeks)	19.8 $\pm$ 23.7
Menopausal status (%)	
Premenopausal	39.6
Perimenopausal	6.3
Postmenopausal	54.2
Medical co-morbidities (%)	
Hypertensive disease	31.2
Diabetes mellitus	23.0
Polycystic ovarian syndrome	14.6

Histological subtypes (%)	
Endometrioids adenocarcinoma	81.3
Clear cell adenocarcinoma	4.2
High grade serous adenocarcinoma	4.2
Papillary serous adenocarcinoma	2.1
Others	8.3
FIGO stages (%)	
Stage 1a	37.5
Stage 1b	29.2
Stage 2	6.3
Stage 3b	4.2
Stage 3c1	16.7
Stage 3c2	2.1
Stage 4	4.2

## **RESULTS OF PHASE II TRIAL OF DENDRITIC CELL BASED VACCINE THERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER**

N. Tsip<sup>1</sup>, N. Khranovska<sup>2</sup>, L. Vorobyova<sup>1</sup>, O. Skachkova<sup>2</sup>, V. Svyntsytsky<sup>1</sup>, N. Svergun<sup>2</sup>, O. Gorbach<sup>2</sup>

<sup>1</sup>National Cancer Institute, Oncogynaecology Dpt., Kiev; <sup>2</sup>National Cancer Institute, Experimental Oncology Dpt., Kiev - Ukraine

Dendritic cells (DCs) are an essential target in efforts to generate therapeutic immunity against cancer. The aim of this study was to investigate clinical benefits of DC based vaccine therapy in patients with advanced epithelial ovarian cancer (AOC) as a primary endpoint and evaluate tumor cell-specific immune response as a secondary endpoint.

Eighty-one patients (average age 52.8±11.8) with AOC (stages III and IV) were enrolled into randomized clinical trial. All patients were randomly assigned to research group (41 women, who underwent primary cytoreductive surgery followed by adjuvant chemotherapy according CP regimen and DC-vaccine therapy) and control group (40 women, who underwent primary cytoreductive surgery followed by adjuvant chemotherapy according CP regimen). Autologous DC of monocytic origin obtained by culturing in the presence of GM-CSF and matured with LPS and IFN- $\gamma$  were used in the trial. Maturation state and functional activity of DCs were evaluated by the expression of cell surface markers CD83/86, HLA-DR and IL-12 p35/p40 mRNA levels. Novel DC-vaccine constructions have been used: DC loaded with lysate of tumor cells treated by exogenous cytotoxic lectins (DC/LTCCL) from *B.subtilis*. DC in amount  $4,62 \pm 0,37 \times 10^6$  per injection were injected intravenously to patients after basic treatment in 1-3 courses (6 months interval between courses). One course consisted of 5 injections with one-month interval. Clinical and immunological monitoring of DC-vaccine immunotherapy was performed.

DC-vaccine therapy was well tolerated without significant toxicity. Application of DC-vaccine therapy contributed to a significant increase in the 3-5-year overall (OS) and disease-free survival (DFS), prolong time to disease progression, contributed to an increase in median survival. Kaplan-Meier analysis revealed prolonged 3-year OS: 61 vs 34% in control group (F Cox test:  $P < 0,02$ ), HR 0.45; 95:CI=0.24-0.85 and 5-year OS: 58 vs 23% in control group (F Cox test:  $P < 0,01$ ), HR 0.42; 95:CI=0.23-0.77. 3- and 5-year DFS was 42 % and 35% in DC-vaccine group vs 19% and 5% in control group of patients (HR 0.59; 95:CI=0.34-1.04 and HR 0.54; 95:CI=0.31-0.92; F Cox test:  $p < 0,06$  and  $< 0,03$  respectively). The most pronounced changes in the immune system was defined only after fourth DC-vaccine administration. Th1-polarization of immune responses and increasing the number of CD8+IFN+CTL were obtained in 60% of patients.

Our study demonstrated that DC-vaccine therapy could be conducted without major toxicity and induced tumor cell-specific immunological and clinical responses in AOC patients. DC vaccine therapy is an approach that holds great promise for the future of cancer immunotherapy.

## **HIGH GRADE SEROUS OVARIAN EPITHELIAL CARCINOMA PRESENTING WITH SKIN AND BREAST METASTASIS: A CASE REPORT**

E. Baruzzo, Al. Arteni, L. Ganzitti, M. Della Martina, E. Vogrig, G. Fabiani, D. Marchesoni  
*Clinic of Obstetric and Gynecology Udine, University of Udine Medical School and University Hospital, Udine - Italy*

**Introduction:** Ovarian epithelial malignancies usually spread by direct extension, transperitoneal seeding or lymphatic spread. Extra-abdominal metastases are less frequent and breast metastases have scarcely been reported.

**Case Report:** This report describes the case of a 58-year-old woman that presented to our Clinic for a significant increase in Ca 125 and Ca15.3 levels, respectively 14,407 UI/ml and 399 UI/ml. Transvaginal ultrasound and TC scan showed a 5 cm heterogeneous solid mass involving the left ovary. Few days later, patient was admitted to our Unit for suspected intestinal obstruction and right hydronephrosis. Our patient presented also a thoracic skin lesion and a right breast nodule. A mammogram confirmed a 10 mm solid lesion in right breast. Skin biopsy and an ultrasound guided breast biopsy were performed. Histologically, the normal breast parenchyma was completely replaced by solid tumor with multiple areas showing papillary pattern. At immunohistochemical analysis, tumor cells were ER and CK 20 negative, CK 7 and WT-1 positive: these data were suggestive for high grade metastatic ovarian papillary serous carcinoma to the breast.

The patient underwent exploratory laparotomy. Ascitic fluid was sampled for cytological analyses. Pelvis was occupied by an extensive left ovarian mass which adhered to the rectum. It was biopsied, the extemporaneous histology during operation confirmed the diagnosis. Abdominal exploration showed multiple peritoneal nodules. Colon was dilatated and local perfusion was altered; for this reason a colostomy was performed. A thoracic drainage was placed in order to reduce pleural liquid; 10 days later patient underwent talc pleurodesis. Right percutaneous nephrostomy was also placed in order to reduce right hydronephrosis. After surgery, she went on to receive 6 doses first line systemic chemotherapy with Carboplatin AUC 5 and Paclitaxel 175 mg/mq q21. Progressively Ca 125 and Ca 15.3 decreased and also TC scan got better after chemotherapy. Therefore second-look laparotomy was performed: diffuse metastatic disease of diaphragmatic, abdominal and pelvic peritoneum was found; pelvis was completely occupied by tumor mass and therefore only bilateral salpingo-oophorectomy and appendectomy could be performed. TC scan revealed progression disease 2 months after of second-look surgery. Second line chemotherapy with liposomal doxorubicin 40 mg/mq q28 was started but the patient's clinical conditions rapidly deteriorated and therapy was stopped. She died for septic shock few days later.

**Conclusions:** A breast metastasis could be the first manifestation of a malignant tumor elsewhere. Histologically diagnosis is not easy to obtain.

## PROPOSAL FOR THE USE OF A TRIAGE MODEL FOR LYMPHEDEMA AFTER GYNAECOLOGICAL CANCER TREATMENT

R. Hoeben, H.J. Noordmans, E. van Dorst

*University Medical Centre Utrecht - The Netherlands*

A debilitating complication after cancer surgery is the occurrence of lymphedema. An estimated 6-40% of patients develop lymphedema after gynaecologic cancer treatment [Hareyama2012]. To effectively treat lymphedema, it is necessary to recognize and diagnose its occurrence quickly. The lack of a scientifically proven standard to diagnose and evaluate lymphedema hinders early intervention.

The aim of this study is to advise on the best method to measure lymphedema in the lower limbs and pelvic area. This advice is based on a literature review. Available measurement methods and their characteristics are summarized in Table 1. Besides an error margin due to measurement errors the volume and impedance also experience natural fluctuations (estimated to be maximum 100 ml (6%) in arms over a period of a month).

Lymphedema due to gynaecological cancer treatment occurs in the pelvic area and is often bilateral (both legs are affected). The ideal measurement method needs to be applicable in these areas and it has to be reliable (have good sensitivity, specificity, accuracy, and repeatability), be cost effective, and practical. Many studies have reviewed the measurement quality (reproducibility and reliability), but there is no consensus on the best measurement method. The question is if it is necessary (and possible) to have one optimal measurement method.

The need for lymphedema measurements is evident at four moments in the patients care cycle. We recommend using different measurement methods according to the aim of the care cycle step.

1) Screening (identifying the possibility/risk of lymphedema)

A general practitioner can monitor the patients general wellbeing post-surgery, and with the aid of dedicated questionnaires monitor occurrence of lymphedema. Bioimpedance measurements might be useful, as they can detect early changes in the balance between extra cellular and intracellular fluid.

2) Diagnosing lymphedema

A physician needs information on both volume and tissue consistency to accurately diagnose lymphedema. An MRI scan would meet both criteria.

3) Treating Lymphedema

A physiotherapist needs to monitor treatment efficacy, this can be monitored using concurrent volume measurements. Thermography can possibly be used to monitor the extent of inflammation.

4) Managing lymphedema

Patients find it challenging to adhere to certain diet and life style regulations to minimise the lymphedema. A bioimpedance measurement, thermography or volume measurements can offer feedback and thus mental support. Instead of searching for a single gold standard in lymphedema measurements we should focus on using a measurement that aids in early symptom recognition, diagnosis or intervention of lymphedema. This triage model is a first proposal to start improving early recognition of symptoms and diagnosis of lymphedema in gynaecological cancer survivors, thus preventing long term morbidity.

Table 1: Overview of measurement methods, their application and reliability

Measurement method	Parameter	Spot/Limb/Body	Uni-/bilateral	Diagnostic criteria*	Measurement error
Circumference measurement	Volume	Limb	Unilateral	+ 5-10%	100-150** ml
Water displacement	Volume	Limb, body	Unilateral	+ 5-12%	120 ml
Perometer	Volume	Limb	Unilateral	+ 10-15%	80 ml
Bioimpedance spectroscopy	Fluid content	Spot, limb	Bilateral	+ 3x standard	

				deviation	
Tonometer	Tissue tonicity	Spot	Unilateral		
Lymphoscintigraphy	Lymphatic function	Limb	Bilateral		
MRI/CT/DEXA	Volume and tissue consistency	Body	Bilateral		
Questionnaire	Symptoms	n.a.	n.a.		
Thermogram	Temperature	Spot	unknown		
(2D/3D) Photography	Volume (Appearance)	Limb, body	Bilateral		
<p>Where uni- and bilateral refers to the ability to detect lymphedema if both limbs are affected, and spot/limb/body refers to a spot measurement, only suitable for limbs or suitable for the whole body.            *Increase w.r.t. normal value, in the arms an increase in volume of 5% is in the order of magnitude of 80-125ml            ** Depending on usage of cylindrical or conical model respectively            *** BIS cut-off ratio 1.139 affected dominant arm, 1.066 affected non-dominant arm            Sources: [Spillane2008, Hayes2011, Czerniec2010, Sander2002, Taylor2006, Ward2006]</p>					

## **ABDOMINAL WALL METASTASIS FROM AN EARLY STAGE OVARIAN CARCINOMA: A CASE REPORT**

L. Ganzitti, E. Baruzzo, A. Arteni, C. D'Antonio, M. Della Martina, G. Fabiani, D. Marchesoni  
*Clinic of Obstetric and Gynecology Udine, University of Udine Medical School and University Hospital, Udine - Italy*

**Introduction:** Abdominal wall lesion from an ovarian carcinoma is an unusual manifestation of recurrent ovarian malignancy.

**Case Report:** This report describes the case of a 84-year-old woman that presented to our hospital for a large abdominal mass and 7 kg loss of weight in the previous 3 months. An abdominal computed tomography scan revealed a 13x10x16 cm heterogeneous mass of the right ovary with bladder involvement and possible involvement also of the anterior wall of the rectum. Blood tests showed a significant increase in Ca19.9, Ca 15.3 and Ca 125 levels. Cystoscopy and gastroscopy were negative. Rectal endoscopic ultrasound confirmed a lesion that imprinted the anterior wall of the rectum. Considering patient's age, comorbidities and performance status, she underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy and omental biopsy; no evidence of bladder and bowel involvement. There was no residual disease at the end of the surgery. Histology showed an endometrioid adenocarcinoma with focal squamous differentiation, 2nd grade according to Silverberg, high grade according to Malpica, involving only the right ovary (pT1a, FIGO IA stage). Because of the patient's will and her poor general conditions, adjuvant chemotherapy was not performed. She started a quarterly follow up. 9 months after surgery she suffered abdominal pain and a rapidly growing abdominal wall mass was diagnosed. The TC scan showed a mass of abdominal wall that extended also to symphysis and bladder; the scan detected also some small pleural nodules. The patient underwent a second radical surgery: a 15 cm mass was removed, abdominal wall was reconstructed by prosthesis. Histology confirmed that the abdominal wall mass was a metastasis of the endometrioid adenocarcinoma of the right ovary previously treated. One month later a new abdominal mass was diagnosed and patient's condition rapidly deteriorated. She died in a few days.

**Conclusions:** Usually, but not always, endometrioid histology and early stage ovarian carcinoma are associated with better survival compared with serous adenocarcinoma of the ovary and abdominal wall metastasis an unusual manifestations of recurrence.

## HOME CERVICAL CANCER SCREENING A NEW OPPORTUNITY FOR MALAYSIAN WOMEN - CAN SELF-TEST KITS REDUCE THE BURDEN OF CERVICAL CANER IN MALAYSIA?

M.J. Hussain

*University of Bristol, Central Manchester Foundation Trust, Wellbeing of Women Charity – United Kingdom*

**Introduction:** Cervical cancer is currently the 2nd most common female cancer in Malaysia and is responsible for significant number of cancer admissions and deaths in government hospitals. Nearly 80% of cervical cancer patients present with advanced stage disease. No national cervical screening programme currently exists, instead screening is opportunistic. Home self-testing offers a new opportunity to reduce the burden of cervical cancer in Malaysia.

**Methods:** Medline, Embase and PubMed databases were systematically searched from inception - June 2014 using key words ‘Self-test kits, cervical cancer, screening and Human papilloma virus (HPV)’ in English. Additional references from relevant papers were hand searched from pertinent publications.

**Results:** 88 articles were identified looking at effectiveness of self-samples vs. clinician obtained samples, HPV-DNA self-testing vs. Pap-smear testing, HPV-testing binary classification and value in a cervical screening programme. HPV-DNA testing can be used as primary screening in women >30years of age and as an adjunct to cytology, increasing sensitivity for detecting cervical neoplasia. Women are more receptive and compliant to home HPV-DNA self-testing compared to Pap-testing ( $p < 0.01$ ) with potential to increase participation and compliance with follow-up amongst non-attendees. Self-HPV testing is more sensitive (97.1%, 95%CI: 89.1-99.3%) and nearly equally specific (94.3%, 95%CI: 92.5-95.7%) as cytology for cervical intraepithelial neoplasia of grade 2 or worse. Furthermore, HPV self-sampling methods have shown concordant results (70-96%, Kappa 0.27-0.90,  $p < 0.05$ ) and similar binary classification (see table 1) with clinician obtained speculum cervical samples, irrespective of sampling method.

**Discussion:** Implementation of HPV-DNA self-testing as part of cervical screening in Malaysia can potentially increase participation and early detection of cervical neoplasia. However, HPV-testing is limited to those aged 30-65, due to high prevalence of transient HPV infections in those aged <30, which could lead to unnecessary evaluation and over treatment. Further study is warranted to test the efficacy and reception of home self-screening in Malaysia.

**Table 1 Binary classification of HPV self-sampling vs. Clinician obtained samples**

	Self-HPV testing (%)	Clinician sampling (%)
<b>Sensitivity</b>	82.5	87.5
<b>Specificity</b>	93.6	93.2
<b>Positive Predictive Value</b>	52.4	52.2
<b>Negative Predictive Value</b>	98.4	98.9

## **INCIDENCE RATE AND LOCALIZATION OF LYMPH NODE METASTASES IN PATIENTS WITH INVASIVE CERVICAL CANCER**

E. Ismail, Y. Kornovski

*MHAT "St. Anna" Varna, Gynecological clinic - Bulgaria*

**Objective:** To establish the incidence rate, localization and distribution of lymph node metastases FIGO stages I and II.

**Material and methods:** Between 2002 – 2011 294 patients FIGO stages ( IB1 – IIB ) had been operated on ( IB1 – 110; IB2 – 98; IIB – 86 ). The surgical management consisted in radical hysterectomy class III and pelvic lymphadenectomy. In cases with enlarged paraaortic lymph nodes – paraaortic lymphonodectomy was performed.

**Results:** Lymph nodes metastases ( LNM ) were detected in 82 patients ( 27,8% ). The number of LNM were 1 to 3 in 66 patients ( 22,4% ) and more than 3 – in 16 women ( 5,4% ). Pelvic LNM were found in 74 patients ( 25,17% ) and paraortic LNM – in 8 patients ( 0,34% ). LNM were evaluated as macrometastases in 45 women ( 15,31% ) and as micrometastases – in 37 women ( 12,59% ). The incidence rate of LNM in stage IB1, IB2 and IIB was 20,9% , 33,67% and 30,24% , respectively.

**Conclusion:** Bulky cervical lesions even tough in stage IB1 reveal higher aggressiveness and metastatic potential than small cervical lesions.

**Key words:** cervical cancer , lymph metastases