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1. Myomscore: Neuer diagnostischer Standard in der Uteruschirurgie?
Prüfung der klinischen Relevanz eines Myomscores in der präoperativen Uterusbeurteilung

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Das Fehlen adäquater präoperativer Diagnostik birgt die Gefahr einer unbewussten Tumorzellausbreitung im Bauch-raum während einer standardisierten minimalinvasiven Uterusoperation. Das Risiko liegt zwischen in den Literaturangaben zwischen 0,3 und 0,7 %. Seit der FDA Warnung vor Morcellement droht die jahrzehntelange Entwicklung der MIC Standards und deren gesundheitliche und ökonomische Vorteile, wieder von der traditionellen abdominellen Chirurgie abgelöst zu werden. Auf der Suche nach einerseits Bewahrung der MIC Vorteile und gleichzeitiger Steigerung der onkologischen Sicherheit, entwickelten wir ein präoperatives Untersuchungssystem zu Voraussage der Dignität der zu operierenden uterinen Neubildungen.

Die Anwendung des MHH Myomscore bietet eine klinische Möglichkeit zu Präzisierung des Malignitätsrisikos im Hinblick auf die Entwicklung eines sog. mesenchymalen Uterustumors oder seiner Entwicklungsvorstufen. Mit seiner Hilfe lässt sich eine Risikopopulation definieren, bei welcher weitere Diagnostik bzw. operative Vorkehrungen getroffen werden können, um eine unvorhergesehene Tumorzellausbreitung im Bauchraum zu vermeiden. Die Inzidenz kann von 0,525 im Gesamtkollektiv, auf 12,5% in der Risikopopulation gesteigert werden. Es erlaubt darüber hinaus eine risikoadapierte, personalisierte Aufklärung. Ein zielgerichteter Einsatz der operativer MIC Verfahren kann damit patientinnen- und befundorientiert erfolgen.

Tab. 1 Myomscore und Handlungsempfehlung

Alter	< 49	1	> 49	2
Blutunganamnese	regelh. o. verstärkt	1	irregulär	2
Wachstumsanamnese	„statisch"	1	„schnell" u./o. unter Therapie wachsend	2
Myomgröße	< 5 cm	1	> 5 cm	2
Echogenität	geordnet	1	bizarr	2
Begrenzung	scharf	1	unscharf	2
Elastosonographie	hart	1	weich	2
Doppler Power Mode	zirkuläre Durchblutungsmuster	1	diffuse, ungeordnete Durchblutung	2
Resistent Index	RI > 0,4	1	RI < 0,4	2
LDH 1,2 x Referenzwert	niedriger	1	höher	2
Score	bis 12 Punkten:		ab 13 Punkten: OP ohne Uterusserosaverletzung, event. Morcellement sollte nur im sog. „zellsicherem" Verfahren erfolgen. Risikoaufklärung!	

2. Leiomyosarcoma of the Broad Ligament : A Case Report

Khalfaoui I. , Minoungou N. , Alami A. , Bouchbika Z. , El mansouri F. , Benchekroun N. , Jouhadi H. , Tawfiq N. , Sahraoui S. , Benider A.

Leiomyosarcoma of the broad ligament is extremely rare, rapidly progressive and highly malignant gynecological tumor. Most of the time they are diagnosed in postmenopausal women.
We Herein report a rare case of locally advanced leiomyosarcoma of the broad ligament in a 40-years-old woman. Clinical presentation and histological diagnosis is discussed. The patient has been operated in emergency, we found a necrobiosis mass para-fallopian tubal. Complete surgical resection was performed and patient received chemotherapy.
Primary leiomyosarcoma of the broad ligament remains unusual and the management is difficult, it requires surgery (hysterectomy with bilateral salpingoophorectomy) for all cases. Adjuvant chemotherapy or radiotherapy is used in seleted cases.

Key words: Broad ligament, Leiomyosaroma, Uterus

3. Attitudes towards HPV vaccines in rural area in Poland

Joanna Kacperczyk-Bartnik[1], Patryk Rudziński[2], Paweł Bartnik[1], Agata Go-lik[2], Aleksandra Szczęsna[2], Agnieszka Dobrowolska-Redo[1], Ewa Romejko-Wolniewicz[1]
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Background: Despite documented effectiveness and safety of Human papilloma virus (HPV) vaccines, HPV vaccination rates in Poland remain relatively low. The aim of the study was to determine what types of beliefs and concerns are associated with HPV vaccines among population living in rural areas and searching for possibilities of increasing HPV vaccine coverage.

Method: It was a cross-sectional survey study performed by means of paper questionnaires distributed to mothers and teachers during parents' gathering in a primary school in a rural area in Holy Cross Province. Altogether 170 surveys were collected.

Results: Mean age of surveyed women was 38 (between 19-63 years old). 10% of respondents had a history abnormal Pap smear result, 2.3% were vaccinated against HPV, 7% were recommended by a physician to get vaccinated. 5% of surveyed women vaccinated their children against HPV. 10% were recommended by a physician to vaccinate their child. 83% of respondents believed that vaccination is an effective protection against HPV caused diseases. 43% answered that HPV vaccine leads to sexual promiscuousness among adolescents. 96% stated that HPV vaccine should be fully funded by state and that in such condition – 86% would have vaccinated their daughter and 87% would have vaccinated their son. Most common reasons for not vaccinating were: no physician's recommendation (58%), unawareness of such possibility (44%), and price (26%).

Conclusions: Main barriers associated with low vaccination rate were unawareness of such possibility and high price. Increase in HPV vaccine coverage could be achieved by educating parents and organizing funding sources.

4. Secondary cervical cancer prevention in routine prenatal care – coverage, results and lessons for future

Introduction: For most women, pregnancy is a period of increased medical supervision, which makes it a good opportunity for increasing secondary cervical cancer prevention coverage. According to the Ordinance of the Polish Minister of Health (2018) Pap smear should be performed in every pregnant woman till the end of the 10th gestational week. The aim of the study was to assess the prevalence of Pap smear performance in pregnant women and to determine possible factors affecting it.

Methods: Self-composed questionnaire was distributed among 638 women managed in a tertiary obstetric referral centre. The survey included 33 questions regarding performance of Pap smear, its frequency and results, vaccination against HPV, performance of colposcopy or histopathological examination. Statistical analysis was performed with the use of Statistica 13.3.

Results: The average age of surveyed women was 26±5. 96.9% of respondents had undergone Pap smear and 80.6% had it performed during pregnancy. 47.4% declared to undergo the test once a year, 22.7% every 2 years, 7.8% every 3 years, and 7.9% less often. For 11.5% women Pap smear in pregnancy was the first in a lifetime. The most common reasons for lack of Pap smear performance were: no subjective need to perform it (40.9%) and no doctor's suggestion (28.6%).8.8% of surveyed women had positive family history of cervical cancer but 67.9% of them indicated no impact of this fact on Pap smear performance.

Conclusion: Although the prevalence of Pap smear performance among surveyed patients was relatively high, there is a group of women who perform their first test during pregnancy. Therefore, secondary cervical cancer prevention as part of perinatal care is a useful prophylactic strategy in underscreened populations.

Keywords: Cervical cancer, Pap Smear, Perinatal Care, Pregnancy, Secondary Prevention

5. New serum tumor markers S100, TFF-3 and AIF-1 and their possible use in oncogynecology

Authors: Maderka M., Pilka R., Neubert D., Hambalek J., Marek R., Jancekova V.

Objective: In our paper we were studied literature about possible new tumor markers, S100 proteins, trefoil factor 3 and AIF-1, and their possible use in oncogynecolic patients.

Design: Review.

Setting: Department of Obstetrics and Gynecology, Faculty of Medicine, Palacky University and University Hospital in Olomouc.

Methods: Review of articles in PubMed database published till January 2019.

Results: The association of S100A2, S100A4, S100A6, S100A7, S100A8, S100A9 and S100A11 with breast carcinoma has been demonstrated in the literature. The association of S100A2, S100A4, S100A6, S100A7A, S100A10, S100A14, S100A16, S100B, S100P (up-regulation associated with a lower survival) and S100A1, S100A13, S100A5, S100A13 and S100G proteins (up-regulation associated with a better survival) have been demonstrated in ovarian cancer patients. Cervical carcinoma has been shown to be associated with the S100A9 protein. TFF3 association with endometrial cancer, breast cancer (worse prognosis) and ovarian cancer (better prognosis) has been demonstrated. AIF-1 has been shown to increase expression in cervical cancer.

Conclusion: Tumor markers can be a very useful tool for patient management when used appropriately. Further research in this area and the search for new tumor markers, including S100, TFF-3 and AIF-1, are needed. In future studies, scientists should focus not only on one time point, but assess the trend of the tumor markers for a specific time axis.

Keywords: oncogynecology, tumor markers, S100, TFF-3, AIF-1.

6. Does anal HPV infection coexist with vaginal HPV infection in the long-term period after hysterectomy, a preliminary study

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Aim: Anal HPV infection with high risk types that is major risk factor for anal cancer can coexist with cervical-vaginal HPV infection. In this study we aimed to screen for anal HPV infection to explore its coexistence with vaginal HPV infection in the long-term period after hysterectomy.

Material and Methods: Patients that had at least one positive cervical high risk HPV test and further had a hysterectomy operation for benign reasons were retrospectively screened. Anal HPV testing was offered and the specimen for HPV testing was collected by a swap through the anal canal in patients willing to participate. All cases had undergone hysterectomy more than 1 year ago at the time of testing. Previous HPV test and/or vaginal pap-smear results (if performed) in the last year were also retrieved.

Results: Preliminarily, 25 women were analyzed. Mean age of the patients was 51.8 (SD:8.6) years. Among 25 anal swaps, 10 (40%) specimens were found to be positive with high risk HPV types (one type 16, 9 other high risk types). There were only two samples that were inadequate for analysis. Of these 10 women with positive anal HPV test, only 5 had a previous positive vaginal HPV test in the last year. The HPV type 16 were found in the same case at both cervical and anal samples.

Conclusion: In hysterectomized patients with a history of high risk cervical HPV test, anal HPV infection can be found even in the cases after negative vaginal HPV re-test. Clinical significance and prognosis of this is needed to be investigated. Such information is required to design the long-term follow-up schema of patients with a history of high risk HPV infection even after hysterectomy is performed.

7. Assessing referral and follow-up of women screened in breast and cervical cancer screening programs in Kenitra Province, Morocco, 2015

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Background: Organized screening programs for breast and cervical cancer were implemented in Morocco in 2010. Screening is only effective in reducing cancer incidence if women who screen positive have access to diagnostic and treatment services to prevent progression to invasive cancer. Follow–up of women screened in the cancer screening programs in Kenitra Province is yet to be evaluated.

Methods: We conducted a retrospective study to assess follow-up of women screened in breast and cervical cancer screening programs in Kenitra from January 1–December30, 2015. All women screened during this period were included. We abstracted patient medical records from: i)31 primary care centers; ii)the singlediagnostic centerin Kenitra, and iii) the national oncology center. Medical records were matched based on name, national ID and address. We examined the proportion of women lost-to-follow-up and associated social factors (chi-square tests) in Epi Info v7.

Results: A total of 1225 women were included in the study; 865 were referred for breast abnormalities and 360 for cervical lesions detected. The proportion of women lost tofollow-up for cervical cancer at the primary health care level (26.7%) was significantly higher (p=0.004) than for breast cancer (19.3%). At diagnosticand treatment levels, loss-to-follow-up for breast cancer (25.1% and31.0%, respectively) was greater than that from cervical cancer (4.2% and 7.1%%, respectively) (p<0.001). Characteristic-sassociated with loss-to-follow-up for both cancers were older age (p=0.001), being single (p=0.03), distance to centers(p <0.001) and not having medical insurance(p=0.001).

Conclusion: Approximately 20% of women who screen positive for breast cancer and over 25% of those who screen positive for cervical cancer in Kenitra Province are lost-to-follow-up and don't receive diagnosis or treatment.Possible strategies to ensure continuity of patient care between different levels include: improving counselling done after a positive screening test, usinga unique identifier in data systems, and ensuring the availability of diagnostic and treatment appointments at referral centers.

Key words: Screening program, breast cancer, cervical cancer, loss-to follow up, referral.

8. Validation of a QuantiGene-HPV cervical disease-screening test using RT-qPCR

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Background: In Germany 38,1% of woman between 20 and 25 years are screened positive for HPV. Woman older than 20 years are invited for cytology-based screening. As of 2020 primary HPV-based screening with cytology co-testing in a 3-year interval in women older than 35 years will be implemented. While cytology has a low sensitivity (50%) and a high specificity (>90%), molecular HPV-testing has a very high sensitivity (>95%) but a low specificity (<40%). Thus, additional tests like colposcopy, biopsy, p16/Ki67 immunohistochemistry, and testing of other biomarkers have to be performed. A triage method with high specificity, sensitivity, and positive predictive value is needed.

Methods: A multiplexed mRNA quantifying assay that combines detection of HPV genotype-specific oncogene expression with cellular biomarkers routinely used for diagnosis and markers for cancer stem cells and tumor markers was designed. The Luminex bead-based QuantiGene 2.0 technology platform (Thermo Fisher Scientific) is used to detect mRNA expression of all markers simultaneously from a crude lysate of a cervical smear sample.
In order to validate the data using the gold standard for mRNA quantification, we performed RT-qPCR analysis for the subset of biomarkers: HPV16-E7, HPV18-E7, STMN1, BIRC5, MCM2, Ki67, ALDH1A1, CDKN2A, UBC, and ACTB.

Results: 46 markers were validated in a clinical retrospective (300 samples) and a prospective trial (1400 consecutively collected samples) and were proven to distinguish the different clinical dysplasia stages: normal, low grade (CIN I, CIN II), high-grade (CIN III), and invasive cancer, with high accuracy (e.g. 90% for CIN III). Comparing RT-qPCR with QuantiGene data from every clinical dysplastic stage, good correlation coefficients between 0.55 and 0.9 were demonstrated.

Conclusion: mRNA quantification by QuantiGene Plex is reliable and reproducible by RT-qPCR and both assays could be alternative methods for mRNA expression profiling for dysplasia diagnosis.

9. High risk Human Papillomavirus (HR-HPV)–prevalence and clinical findings among women with Human Immunodeficiency Virus (HIV) treated at Charité – Universitätsmedizin Berlin: preliminary results

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Objective: HIV-infected patients are more susceptible for HR-HPV-persistent infections, at higher risk for progression to cervical cancer, and screening is suboptimal. We investigated the prevalence of HR-HPV infections in HIV-infected women and correlated them to clinical findings.

Methods: Following informed consent, prospective data on gynecological examination, cytology, HR-HPV (MPG-Luminex-PCR), and colposcopy results was collected. Analysis was performed using SPSS. A two-tailed p-value ≤ 0.05 was considered statistically significant.

Results: For this preliminary analysis, 50 patients (median age 41.7) were enrolled.

Origin: 27 (54%) Sub-Saharan Africa, 20 (40%) Western Europe, 1 (2%) Eastern Europe, 1 (2%) Middle East. 96% were receiving antiretroviral therapy (ART). 39 (81.3%) had a viral load (VL) <50 cop/ml, 9 (18%) VL $\geq$50 cop/ml. CD4 counts of 41 patients (82%) had a median of 500/μl: 58.5% >500/μl, 19.5% 350-500/μl, 19.5% 200-350/μl and 2.5% <200/μl.

24 (48%) were HR-HPV positive (In decreasing order HR-HPV: 16,51,52,56,53,66,59,31,35,45,18,33,73,82). 15 (62.5%) had multiple HR-HPV infections. 47 (94%) patients had a Pap smear result (42% Pap I, 40% Pap IIa, 2% Pap IIp, 6% Pap IIID1, and 4% Pap IIID2).

Colposcopy: 21 (42%) non-evaluable (T3 zone). **22 (44%) normal.** 6 (12%) minor changes, 1 (2%) major changes. HR-HPV infection and cytology was significantly associated (p=0.03). The number of HR-HPV types showed no significant association with cytology (p=0.056). Patients with an HIV VL $\geq$50 cop/ml were significantly likelier to have HR-HPV infection than patients with a VL <50 cop/ml (p=0.04). VL and cytology (p=0.89) or colposcopic findings (p=0.463) was not significantly associated. Neither was CD4 count and findings in colposcopy (p=0.981), HR-HPV infection and colposcopy (p=0.182), and the amount of HR-HPV types and colposcopy (p=0.830). There was a significant correlation between colposcopy and cytology (p=0.02).

Conclusion: HR-HPV prevalence in HIV infected women is high, with high genotype variety, and a large number of patients with multiple infections. Additional markers to determine clinically relevant HR-HPV infections in women with HIV are needed.

Keywords: HIV-infected women; HPV; Pap smear; cervical cancer screening.

10. Factors associated with HPV persistence after excisional procedures in patients with high grade cervical lesions

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Aim: Almost all cervical cancers are associated with high risk HPV infections. Therefore, patients with HPV persistence after excisional procedures carry on the cancer risk. We aimed to analyze the status and related factors for HPV persistence after excisional procedures in patients with high grade cervical lesions.

Methods: Patients in whom excisional procedures were performed due to high grade cervical lesions were retrospectively analyzed. Follow-up data and patient characteristics were recruited from patient files.

Results: Overall 81 files were recruited with complete follow-up data. All underwent excisional procedures. Hysterectomy for benign reasons were performed in 23 of them during the following years. Mean age, gravida, and age at first sexual intercourse of the patients were 44.7 (± 9.3) years, 2,9 (± 1.5), and 20.5 (± 3.8) years retrospectively. In 30 patients (37%), HPV infection persisted after conization. Initial HPV type16/18 at the time of first admission, gravida, age at first intercourse, presence of multiple sexual partner and smoking status but age were found to be similar among HPV persistent and non-persistent cases (Table 1). HPV persistent cases were significantly older (48.8 years) than non-persistent cases (42.2 years).

Conclusion: HPV persistence after conization for high grade cervical lesions is not rare. Known risk factors of cervical cancer are not associated with this condition. Only age seems to be significantly associated with persistence. Surgical technique and results of the initial procedure should be investigated in larger populations.

Table 1. Comparison of HPV persistent and non-persistent cases

	HPV non-persistent N=51(63%)	HPV persistent N=30(37%)	p
Age (years)	42.2	48.8	.001*
Gravida	3.0	2.7	.37
Age at first intercourse (years)	20.2	21.1	.28
Multiple partner	11 (21.6%)	5 (16.7%)	.40
Smoking status	14 (27.5%)	7 (23.3%)	.45
Başvuruda HPV 16 ve/veya 18	35 (68.6%)	16 (53.3%)	.23

11. Surgical Staging Of Locally Advanced Cervical Squamous Cell Carcinoma

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Objective: To explore the necessity of surgical staging of locally advanced cervical cancer and the retention of reproductive endocrine function in young women.

Methods: A retrospective analysis of the surgical staging of Beijing Obstetrics and Gynecology Hospital Capital Medical University from May 2016 to March 2018 Case data of patients with locally advanced cervical cancer.

Results: The sensitivity of CT/MRI for lymphatic metastasis in patients with locally advanced cervical cancer was 66.6%, specificity was 75%, average surgical time was 134±33 minutes, and intraoperative bleeding was 240±73 ml. The hospital stay was 8±3 days, and the postoperative radiotherapy time was 9.2±2.3d. One patient underwent ovarian transplantation after treatment, the hormone level was stable, and the symptoms of menopause were completely relieved.

Conclusion: Laparoscopic surgery for locally advanced cervical cancer has small trauma and rapid recovery. It is an important means to evaluate lymph node metastasis. Ovarian cryopreservation has become a new choice to solve the problem of preservation and restoration of reproductive endocrine function in young cervical cancer patients.

Key words: Locally advanced cervical cancer, Surgical staging, Ovarian cryopreservation

12. Killing of cervical cancer cells by specific chimeric antigen receptor-modified T cells*

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Our objective was to investigate the in vivo and in vitro killing effect of mesothelin chimeric antigen receptor T cells (MESO-CAR-T) in cervical squamous cell carcinoma. In vitro verification of the killing effect of MESO-CAR-T cells was performed in the presence of SiHa cells (Shanghai Cenechem Company) by the lactate dehydrogenase release assay and cytokine release assay. In vivo experiments were performed in immuno-deficient NCG mice. After successful tumor formation with the subcutaneous implantation of SiHa cervical cancer cells, injections of MESO-CAR-T cells into the tumors at different doses were performed. Subsequently, the growth rate of the tumors in NCG mice (Nanjing Institute of biomedicine) were observed. The result of marker detection in the prepared MESO-CAR-T cells showed that CD3+ T lymphocytes accounted for 97.0% of all cells, indicating successful preparation of MESO-CAR-T cells. Expression of the membrane protein MESO was detected in 12.8% of SiHa cells. When the ratio of MESO-CAR-T cells to SiHa cells was 20:1, the lysis of target cells was most significant and was observed in 22% of the cells. In the presence of SiHa cells, the secretion of IL-2, IL-4, IL-5, IL-10, TNF-α, and IFN-γ in MESO-CAR-T cells was higher than that in the control group. The effect of two consecutive intratumoral injections of MESO-CAR-T cells was more obvious than that of one injection. The pharmacological effect of the injection was observed within 1 week. Our finding identified the certain in vivo and in vitro killing activity of MESO-CAR-T cells to SiHa cells.

13. Breast cancer prevention in rural area in Poland

Joanna Kacperczyk-Bartnik[1], Aleksandra Szczęsna[2], Paweł Bartnik[1], Agata Golik[2], Patryk Rudziński[2], Agnieszka Dobrowolska-Redo[1], Ewa Romejko-Wolniewicz[1]
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Background: According to Globocan the incidence of breast cancer in Poland in 2018 was 59 per 100 000 and breast neoplasms constituted for 11.6% of new cancer cases worldwide. Since 2018 according to the Polish Society of Gynecologists and Obstetricians screening breast ultrasound is recommended in every pregnant woman. The aim of the study was to examine breast cancer prophylaxis coverage in rural area in Poland.

Methods: It was a cross-sectional survey study performed by means of paper questionnaires distributed to mothers and teachers during parents' gathering in a primary school in a rural area in Holy Cross Province. Altogether 170 surveys were collected.

Results: Mean age of surveyed women was 38 (between 19-63 years old). 12% of respondents had a positive family history of breast cancer. 3% had breast biopsy and 2.3% underwent treatment for breast cancer.
49% of surveyed women had palpation breast examination performed by a physician, 22% underwent breast ultrasound and 1.7% had a mammography. During pregnancy – 49% had a palpation examination by physician and 14% had breast ultrasound.
90% of respondents believed that breast ultrasound is an effective way of breast cancer prevention. 65% were recommended by a physician to undergo this examination – 62% by a gynecologist and 6% by a general physician.
77% of women performed breast self-exam, however only 30% did it regularly once a month.

Conclusions: Percentage of women living in rural areas who undergo prophylactic breast examinations is not satisfactory. Routine screening in pregnancy as well as referral by a general physicians could be beneficial for increasing coverage of screening for breast cancer.

14. Human Papillomavirus in Ovarian Cancer: A Meta-Analysis

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Objective: The role of human papillomavirus (HPV) in ovarian cancer is still controversial. We performed a meta-analysis to estimate the published prevalence of HPV in ovarian cancer.
Material and methods: A systematic literature search was performed to identify all eligible articles. Observational studies published from 1989 until 2017 were identified in PubMed and Embase. We followed the PRISMA guidelines and included 27 studies. The pooled prevalence of HPV in ovarian cancer and 95% confidence interval (CI) were calculated by using the Mantel-Haenszel method and Laird method. The heterogeneity was measured by the Cochran Q test. The rate of inconsistency was estimated by the I^2 in studies that could not be interpreted by chance. A cumulative meta-analysis was used to investigate the association between HPV and ovarian cancer. The statistical analyses were performed by using the Comprehensive Meta-analysis software, version 2.
Results: Twenty-seven studies were included in this meta-analysis. Studies from 16 countries contained data on HPV in ovarian cancer, including 1909 subjects. Overall, the HPV prevalence in ovarian cancer patients was 13.7%, (95% CI 8.9-20.4%). The highest prevalence of HPV was reported by studies from the Middle East (Prevalence: 25.2%, 95% CI: 21.8%-28.8%), and the lowest prevalence was reported in Western Europe (Prevalence : 0.22%, 95% CI : 0.01%-1.27%). The most frequently detected HPV genotype was HPV16. The statistical heterogeneity was moderate (I^2 = 48%, p<0.0001).
Conclusion: Our meta-analysis suggests a great difference in the prevalence of HPV detected in ovarian cancer which is not seen in strongly HPV-associated cancers such as cervical cancer. However, further studies are needed using more precise assays that identify active infection by testing for HPV oncoprotein expression to prove causality of HPV detection with cellular transformation. In addition, other covariates such as ethnicity, age, and lifestyle have to be considered.

15. Establishment of diagnostic value of endometrial thickness in breast cancer patients taking tamoxifen after operation

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Purpose: To investigate the endometrial changes after receiving tamoxifen and the ultrasonic diagnostic threshold of abnormal endometrial hyperplasia in breast cancer.

Methods: This was a single-center, retrospective, cohort study. Breast cancer patients who received tamoxifen after operation were examined by ultrasonography. Hysteroscopic curettage was performed to obtain endometrial pathology because of vaginal bleeding, endometrial thickening, and abnormal intrauterine echo.

Results: There were no significant differences between abnormal endometrial and benign endometrial hyperplasia in pregnancy, parity, age, tamoxifen receiving time, menopause, chronic disease, family history of tumor, and vaginal bleeding (P > 0.05). The incidence of abnormal endometrial hyperplasia was 22.1% (13/59) after hysteroscopic surgery. The highest incidence of endometrial polyps was 39.0% (23/59) in patients pre- and postmenopause. The endometrial thickness of tamoxifen-treated postmenopausal women was higher than the recent standard (0.5 cm). With increased endometrial thickness premenopause, the incidence of abnormal endometrial hyperplasia was greater (P = 0.035); there was no significant difference in endometrial thickness between postmenopausal abnormal endometrial and benign endometrial hyperplasia. Ultrasound diagnosis of endometrial dysplasia in tamoxifen-treated premenopausal breast cancer patients is used to build the characteristics of the curve; endometrial thickness at 1.55 cm can be used as a diagnostic threshold for ultrasound diagnosis of abnormal endometrial thickening.

Conclusion: The endometrial thickness in tamoxifen-treated premenopausal breast cancer patients is 1.55 cm (proliferative phase), a diagnostic threshold for abnormal endometrial hyperplasia and a further indication for hysteroscopic surgery. Attention should be paid to endometrial thickness > 0.5 cm in postmenopausal women, especially when there is vaginal bleeding.

Keywords: Breast cancer; Tamoxifen; Endometrium thickness; Ultrasound

16. Expression of 3 microRNAs asa prognostic biomarkers for breast, ovarian and cervical cancers among Moroccan women

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Breast and gynecologic cancers (cervical cancer, ovarian cancer) represent a real public health problem in Morocco. In 2011 these cancers accounted for 60% of all cancers among women and 50% of cancer among women treated at the National Institute of Oncology. In spite of significant advances in research on these cancers, with the new tools of molecular biology, viral etiology of these cancers is often associated and reported to oncogenic DNA and RNA viruses mainly HPV (Human Papillomavirus), EBV, MMTV, HBV, and the most affected virus is often the HPV. Therefore their diagnosis is frequently performed late to the metastatic stage.

Currently, more research is directed towards the molecular signatures of different cancers including research on newly discovered biomarkers and highlighted called miRNAsthat allow early diagnosis of these cancers. Among these, the identification of MicroRNAs (miRNAs), which are epigenetic biomarker able to regulate promoters of genes of cancer cells and which are released early in the general circulation, thus providing potential targets for diagnosis.

The aim of this study is to determinate the expression profile of microRNAs and establish the relation between viral etiology of these cancers and MicroRNAs.

It is in this context that our research project established the link between cervical cancer and HPV using specific primers, and detected once extracted and purified 3MiRNAs associated to breast and gynecologic cancers among 70 Moroccan patients in approximately 80% of fresh biopsies, and 2 miRNAs levels were significantly higher in cancer tissues than in control tissues. collected from Obstetrics gynecology service of CHU Ibn Rochd of Casablanca using real time PCR. These Mirnas have been demonstrated as early biomarkers of these cancersin previous studies.

These newly discovered molecular signature of cancer could contribute to an early and selective cancer diagnosis if the molecular profile is well establish and can provide a new tool of prevention to ensure a better prognosis and improving therapeutic monitoring for patients in Morocco for breast and gynecologic cancer or another type of cancers.

Keywords: Biomarkers, Breast Cancer,Gynecologic cancers (cervical and ovarian), MiRNAs, real time PCR,Viral etiology.

17. Study of the PRR11 critical role in progression and metastasis of Breast cancer

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Breast cancer (BC) is the most common cancer among women with high incidence and mortality, mainly due to late detection and bad prognosis. Thus, the identification and functional analysis of potential new BC genes is essential to develop diagnostic, preventive and therapeutic strategies for early cancer management. Recent studies have revealed that proline-rich protein 11 (PRR11) is dysregulated in different cancers and participates in their initiation and progression. However, the involvement of PRR11 in the breast cancer is not yet clear. The present study consists of isolating and identifying the PRR11 associated with BC in Moroccan women, as well as characterizing the related cell signaling pathways. The expression of PRR11 in BC tissues and cells will be evaluated by immunohistochemical staining, reverse transcription polymerase chain reaction (RT-PCR) and Western blot. Then, an analysis of the correlation between PRR11 expression and clinicopathological data of the patients will be carried out. However, in order to specify the PRR11 role in the biological malignant behavior of BC, in vitro, a positive and negative regulation of PRR11 expression through an overexpression vector of PRR11 and a small interfering RNA (SiRNA) specific to PRR11, respectively, will be performed.
The expected results of this study concern the detection of the PRR11 overexpression in BC and the involvement of PRR11 in the deregulation of critical signaling pathways and genes implicated in cell cycle, tumorigenesis and metastasis.
The demonstration that the PRR11 gene is involved in BC and plays a critical role in cell cycle progression and tumorigenesis may serve as a potential new target for the diagnosis and/or treatment of BC in women.

Keywords: PRR11, Breast Cancer, Cell Progression, Cell Signaling Pathway.

18. The usefulness of HE4 in the differential diagnosis of malignant and benign adnexal masses in women.

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Objective: Human epididymis protein 4 (HE4) is a novel bio-marker for ovarian cancers. The aim of this study is to assess the usefulness and efficacy of HE4, in comparison with CA125 in the differential diagnosis of malignant and benign gyneco-logical diseases in women with adnexal masses.

Methods: 85 patients diagnosed with adnexial mass and with-out renal failure who were scheduled for operation were in-cluded in the study. Demographic data, physical examination, results of the laboratory tests, imaging, and pathology were recorded. Blood samples were collected before surgery for the evaluation of HE4 and CA 125 levels. Patients were divid-ed into 4 groups according to their histopathologic diagnosis: benign (n:58), malignant (n:17), borderline (n:5) and meta-static (n:5). Serum Ca 125 and HE 4 levels were compared.

Results: Using 35 U/mL as the cut-off value, CA-125 had a sensitivity of 82.4 %, spesificity of 67.2%, a negative predic-tive value of 92.9%, and a positive predictive value of %42.4%. For the same sensitivity level, specificity was 87.9%, negative predictive value was 94.4%, and the positive predictive value was 66.7% for HE4. Receiver operator characteristic (ROC) area under the curve was higher in both the premenopausal and postmenopausal group for the HE 4 curve. Accordingly, sensitivity at set specificity of 90% was 82.4%, and 70.6 % for 95% of specificity and 41.1% for 98%. Same sensitivity values for CA 125 were 47.1 %, 35.3% and 23.5%, respectively. HE4 were more discriminative for endometrioma and metastatic malign ovarian tumours from primer malign ovarian tumours compared with CA-125 . Also HE4 values were higher in all stage I malign ovarian tumours but CA-125 values were not.

Conclusion: In our study, HE4 showed higher sensitivity and specificity than CA-125. These findings favourite the use of HE 4 as a biomarker for the diagnosis of women with an ad-nexial mass.

Key Words: Adnexial mass, ovarian cancer, CA-125, HE4.

19. Title: The external validation of International Ovarian Tumor Analysis (IOTA) ADNEX model in differential diagnosis of ovarian tumors.

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Introduction: The aim of the study was the external validation of the International Ovarian Tumor Analysis (IOTA) ADNEX model for differential diagnosis of adnexal tumors.

Material and methods: A total of 342 patients with adnexal masses (231 benign and 111 malignant) treated at the Division of Gynecologic Surgery, Poznan University of Medical Sciences, Poland were enrolled into the study. Prior to the surgery, clinical data and CA125 levels were obtained and the ultrasonography was performed by an experienced sonographer according to IOTA guidelines. We have evaluated the multiclass diagnostic performance of the ADNEX model with the incorporation of relative risk for the analyzed tumor type.

Results: The model achieved very high Area under ROC curve, which was equal to 0.921 (95%CI 0.881 - 0.951). The highest accuracy of the model was found at 30% threshold. At this threshold, the sensitivity, specificity, positive and negative predictive values were as follows: 90%, 84.2%, 73% and 94.8% respectively. In the multiclass analysis, sensitivity and specificity for the diagnosis of benign, borderline, stage I ovarian malignances, stage II-IV ovarian malignancies and metastatic tumors were as follows: 76% and 94%, 55% and 88%, 30% and 90%, 59% and 89%, 25% and 94% respectively.

Conclusions: The ADNEX model achieved very high accuracy in differentiating between malignant and benign adnexal tumors. The ADNEX model is characterized by very high specificity in multiclass differentiation of ovarian tumors.

20. Expression of MUC16 in OVCAR-3 cells under normothermic, hyperthermic conditions and cisplatin

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Background: MUC16 gene promotes cancer cell proliferation and inhibits anti-cancer immune responses. MUC16 is overexpressed in the majority of epithelial ovarian cancers (EOC). Hyperthermic intraperitoneal chemotherapy (HIPEC) has been considered a promising treatment method for EOC. However, little is known about the changes of MUC16 expression under HIPEC. The purpose of this study was to investigate the expression of MUC16 in OVCAR-3 cells in vitro exposed to hyperthermia and cisplatin. MUC16 mRNA levels were measured by RT-PCR. This research was funded by the Research Council of Lithuania (No. SEN – 01/2015).

Results: MUC16 mRNA levels in OVCAR-3 cells are high under normothermic conditions (37°C). Cisplatin IC50 forced the increase of MUC16 expression by 0,88 – fold in normothermia (37°C). The temperature rise from 37°C to 43°C boosted MUC16 expression by 1,30 – fold. However, an exposition of the cells to concomitant cisplatin IC50 and hyperthermia (43°C) treatment increased MUC16 expression by 3,78 - fold when compared to control.

Conclusions: Hyperthermia and cisplatin increase MUC16 expression in OVCAR-3 cells. Potential impact of the modulation of MUC16 in HIPEC must be proven in further investigations.

21. Delayed interval debulking surgery in advanced ovarian cancer patients; a root cause analysis of a small case series

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Objectives: Adherence to cancer guidelines is attractive as a quality process measure. According to the British Gynaecological Cancer Society (BGCS) guidelines, neoadjuvant chemotherapy (NACT) with interval debulking surgery (IDS) after three cycles of platinum-based chemotherapy is noninferior to primary debulking surgery (PDS) and adjuvant platinum-based chemotherapy. The role of delayed IDS following six chemotherapy cycles has not been thoroughly evaluated. We audited the prevalence pertaining to the total cohort of our serous advanced (stage 3c-4) ovarian cancer (sAOC) patients and performed a simple root cause analysis to identify reasons for the deviation from the BGCS guidelines as a quality measure of our treatment of sAOC.

Methods: The Trust Patient Pathways Manager (PPM) was queried for sAOC between 2007 and 2016 and delayed IDS cases were identified. All the cases were discussed at the Central Gynaecological Multidisciplinary Team (MDT) Meeting. Treatment type, reasons for surgical treatment after six chemotherapy cycles and clinicopathologic factors were collected. Descriptive statistics were performed.

Results: Seven out of 675 sAOC patients (1%) underwent delayed IDS. They all presented with stage 3C disease with a mean age 69 ± 7 years. In all but one cases, EBL was <500 ml. Complete cytoreduction (R0) and R<1 cytoreduction were achieved in three and four cases respectively. There were neither Clavien-Dindo 3-5 complications nor hospital readmissions. The median survival time for this group was 61 months (9-96 months), largely attributable to one patient. In three of seven patients, persistent disease warranted delayed surgery to facilitate additional chemotherapy response and/or symptomatic relief.

Summary: Only 1% of sAOC patients received delayed IDS, which appears reassuringly low. Review of the reasons for nonadherence to guidelines revealed appropriate clinical reasons being made in an MDT setting.

22. Giant mucinous ovarian borderline tumor

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Objective: Cases of giant mucinous ovarian tumors are rarely described in the literature. Clinical manifestation can appear differently. Compressive symptoms or visible abdominal mass are the most frequent observations with elevated surgical risks and life-threatening complications.

Case report: A 50-year-old woman was admitted to our department with massively distended abdomen. She complained of dyspnea and abdominal pain for approximately 4 weeks. She stated that her abdominal circumference has continuously been increasing for about 10 years. None the less she avoided medical treatment. The last gynecological check-up took place 21 years ago. Transabdominal sonography and computed tomography revealed a cystic mass that filled the entire abdomen. A cystadenoma of the adnexa was assumed. Subsequent longitudinal laparotomy showed a giant cystic tumor of the left adnexa. After placing a purse-string suture and wrapping the tumor with alcohol-impregnated wipes, it was punctured. 55.1 liters of liquid content were aspirated. After closing the purse-string suture, adnexectomy was performed on the left side. The tumor still had a residual weight of 3.5 kilograms. Neither hemodynamic nor cardiac intraoperative complications were observed. The intraoperative fresh frozen section showed the preliminary result of a mucinous cystadenoma. The definitive histopathological examination showed a mucinous borderline tumor (pT1a). Following the recommendation of the interdisciplinary tumor conference, a second surgery was indicated. Hysterectomy, right adnexectomy, representative peritonectomy and omentectomy were performed as part of the re-laparotomy. The appendix had already been removed in the past. No further tumor seeding could be detected. The hospitalization with interim stay at the intensive care unit took 2 weeks. So far, the 1-year follow-up showed no sign of recurrent disease.

Summary: The current case shows an extreme example of an apparently slow-growing borderline tumor of the adnexa. Even more, the case illustrates that extreme findings with minimal symptoms can escape the diagnosis for a long time.

23. Mature cystic teratoma – a case report

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Introduction: Dermoid cyst is the most common ovarian neoplasms in reproductive age women with an overall incidence of benign ovarian masses of 5-25%. Mature cystic teratomas are usually unilateral and mostly benign but in rare cases (approximately 0.1-0.2%), they may undergo malignant transformation. Dermoid cyst shows different clinical manifestations such as lower abdominal pain, distension, tumor torsion, rupture or it may be asymptomatic. According to the results of a few reports, the rate of post-surgical recurrence of dermoid cyst appears to be approximately 3-4%. The risk factors of post-surgical recurrence are poorly known but the risk of post-surgical recurrence of dermoid cyst was higher in young patients with laparoscopically management for bilateral, multiple or large cyst. The standart management of dermoid cyst is laparoscopic or laparotomic surgical excision or oopherectomy for removing ovarian mature cystic teratoma. We presented the laparoscopic management of an unusual case with the history of 4 dermoid cyst.

Case: A 35-year-old woman (G1A1) was referred to our clinic because of reccurent dermoid cyst. She had previous history of 3 right dermoid cyst in the lef ovary that were managed surgically at the age of 16, 24 and 27 years-old. She presented with a history of intermittent lower abdominal pain. Transvaginal ultrasound scan showed the bilateral, complex and partially solid ovarian cyst of approximately 5.6 × 3.6 cm in right ovary and 2.4x2.4 cm in left ovary; her CA 125 level was normal (24 U/mL). MR initially suggested bilateral ovarian dermoids. She has already undergone embrio freezing for fertility preservation before surgery. Due to the presence of bilateral adnexal lesions, we performed a laparoscopically assisted pelvic adhesiolysis and ovarian cystectomy for left ovary and oopherectomy for right ovary, and the subsequent pathologic analysis revealed a mature cystic teratoma.

24. The clinical heterogeneity associated with BRCA mutations in advanced ovarian cancer

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Introduction: Ovarian cancer continues to be a highly heterogeneous disease where few significant changes in the survival outcome have been noted across decades. Occurrence of platinum resistant disease is a frequent clinical occurrence, with survival rates rarely exceeding 12 months. The presence of DNA damage repair pathway mutations, with BRCA1/2 as the most prevalent confers a different clinical outcome for this patients in approximatively 20% of cases.

Methods: We have longitudinally investigated a cohort of high grade serous ovarian cancer patients with a known BRCA1/2 mutation in comparison with cases with absent BRCA1/2 mutation, with respect to their clinical outcome.

Results: Sixty-one patients were included, with more than half of patients undergoing primary debulking surgery. BRCA mutant cases were associated with a significantly higher frequency for platinum sensitive relapse and pathologic response. Longer overall survival was noted for BRCA mutated patients treated with neoadjuvant chemotherapy.

Conclusion: Knowledge of BRCA status before the start of treatment could be useful for future treatment related decisions.

25. Predictors of short-term morbidity following cytoreductive surgery for advanced high grade serous ovarian cancer, a preliminary report.

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Objectives: The treatment of ovarian cancer patients frequently requires extensive surgical procedures. Their substantial morbidity risk provides an opportunity for surgical episode-of-care evaluation. Length of stay (LOS) reflects care efficiency and relates to the extent of surgery and postoperative complications such as severe surgical site infections (SSI). We aimed to identify predictive parameters for LOS and SSI to improve efficiency of treatment.

Methods: A cohort of patients with a diagnosis of advanced stage (FIGO II/IV) high grade serous ovarian cancer (HGSOC) who received surgical treatment as part of their management between January 2016 and December 2017 were identified by the local ovarian cancer database. Pre- and intra-operative parameters analysed were age, BMI, performance status (PS), Hb, Alb, CA125, surgical complexity score (SCS), operation time (OT) and estimated blood loss (EBL). Multiple regression analysis was performed to identify predictive parameters for SSI and LOS.

Results: Fifty-one patients were identified and analysed. Their mean age and BMI were 64 ± 10.4 and 27 ± 5.1 respectively. The median SCS was 2 but higher with delayed cytoreduction. The mean OT was > 150 min and the average EBL less than 500 ml. Two cases of SSI were identified and managed conservatively. The median LOS was 5d (4-7). Pre- and immediate post-operative Alb levels were negatively associated with LOS (p=0.002 and 0.003, respectively). There was a trend towards prolonged LOS with higher SCS and OT. Alb levels predicted SSI (p=0.05) in addition to EBL (p=0.03), and PS (p=0.05).

Summary: This analysis shows that low albumin levels are related to longer LOS and SSI. SSI was also related to blood loss and PS. This analysis indicates that nutritional support and patient optimization prior to surgery may reduce the need for a long hospital stay. Further studies that may address this are on-going.

26. Upfront surgical cytoreduction and radicality of surgery may have a positive impact on progression free survival in patients with an advanced stage of epithelial ovarian cancer.

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Objectives: Our goal in ovarian cancer surgery is to deliver optimal treatment aiming at maximal survival benefits. Quantifying radicality and timing of surgery may help to individualise their surgical treatment. We assessed the impact of these parameters on progression free survival (PFS).

Methods: A cohort of patients with a diagnosis of advanced stage (FIGO IIIC/IV) high grade serous ovarian cancer (HGSOC), undergoing surgical cytoreduction, from Jan 2015 to Dec 2017 was selected from the ovarian database. We evaluated age, timing of surgery (upfront vs delayed cytoreduction), surgical complexity score (SCS), and residual disease (RD). SCS was assigned based on the Aletti classification as low, intermediate and high. Descriptive and Kaplan Meier statistics were used to analyse PFS.

Results: Eighty patients were identified. Mean age and BMI were 63.5 ± 11 yrs. and 26.6 ± 4.8 respectively. The mean SCS was 3 ± 1 (1-8). Complete and optimal cytoreduction was achieved in 48/80 (58.7%) and 66/80 (82.6%) patients. Median PFS and OS were 17 and 44 months respectively.
The presence of RD had a negative impact on PFS: 20, 16, and 12 months for nil macroscopic residual, < 1 cm, and > 1 cm, respectively. Although not significant, upfront surgical cytoreduction vs delayed surgical cytoreduction resulted in a better PFS (NS). Patients with a higher surgical complexity score (≥ 3) showed a favourable trend in PFS compared to those with a low surgical complexity score (< 3): 25 vs. 16 months, p=0.19. Younger patients (< 75 yrs) may have a better PFS than those > 75 yrs (p=0.21).

Summary: We observed trends towards favourable prognosis in patients with upfront surgical cytoreduction, more radical surgery, and younger age. The cohort of patients in our database needs to be expanded to reach significance. Further studies are on-going.

27. Heat shock protein HSP27 is a progression-regulated factor in ovarian cancer cells and could potentially be used as a secreted, non-invasive biomarker

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Background: The heat shock protein HSP27 is an essential stress-induced survival factor in tumor cells. HSP27's protein expression often correlates with tumor progression and especially with resistance to therapy. In ovarian cancer (OC) cells, HSP27 seems to have a corresponding functionality, but molecular investigations are still insufficient.

Materials and Methods: An OC in vitro model (OVCAR-3 and SK-OV-3 cells) was used to characterize the intracellular induction and expression of HSP27 (western blotting). Secreted HSP27 was detected in the cell culture supernatant (ELISA) and the secretion pathway was investigated molecularly.

Results: After thermic induction or genetic overexpression, HSP27 is released into the extracellular space depending on concentration. A blockade of the endoplasmic reticulum secretion pathway with Brefeldin A did not affect HSP27 secretion. Similarly, the phosphorylation status of HSP27, which controls the polymerization status of the protein, did not affect the secretion of the protein. Analysis of prepared exosomes showed that HSP27 is released by exosomal particles.

Conclusion: In OC cells, the resistance factor HSP27 is induced by stress, including radio- and chemotherapy, and is secreted depending on the intracellular concentration. This release occurs via exosomes. The function of extracellular HSP27 is almost unexplored. First evidence suggests a modulation of the local immune response. Stress- and progression-dependent release of HSP27 in exosomal particles suggests that HSP27 may be a non-invasive biomarker for OC progression and therapy response.

28. Surgical anatomy of the Karez technique for vesico-uterine ligament during laparoscopic radical hysterectomy

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Introduction and hypothesis: The clinical effects of laparoscopic radical hysterectomy (LRH) were disputed recently. Our aim was to recommend a practical technique (Karez technique) for dissection of vesico-uterine ligament (VUL) during LRH, so as to perform the LRH safely and effectively.
Methods: One hundred and thirty-three patients (FIGO2009 stage: IB1: 85, IB2: 24, IIA: 21, IIB: 3) underwent LRH from August 2014 to December 2017. Data of operative duration, time of ureteral tunnel dissection, blood loss, ureteral injury and bladder injury were detailedly recorded.

Results: Based on the potential ureteral space, we proposed a new operative procedure called Karez technique. After separating the uterine artery and superficial uterine vein from the ureter, we could exposure the axillary space. Several Karez wells (potential space between cervicovesical vessels) were developed above the ureteral space. The cervicovesical vessels in the anterior leaf of VUL would be managed with the ultrasonic knife. Similarly, the posterior leaf of VUL with vascular bundles would be transected integrally by ligasure after the Karez wells (paravesical space and paravaginal space) were developed beneath the ureteral space.
The median operative duration was 171.5 ± 26.9 min, and the time of ureteral tunnel dissection was 27.0 ± 8.2 min. Blood loss during the separation of the VUL was 21.5 ± 6.4 ml (N=133) and after LRH was 143.6 ± 50.9 ml (N=133). In the regression analysis, operating time was steeply decreased with Karez technique for separation of ureter from VUL (Pearson correlation coefficient = -0.4447; $p < 0.001$).

Conclusions: The Karez technique is a safe and feasible surgical procedure for separation of ureter from VUL, and it is helpful to perform standard LRH and avoid the ureteral injury and bladder injury.

29. The value of HE4 as predictor recurrences in epithelial ovarian cancer.

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Ovarian cancer is one of the main causes of death from gynecological cancer in industrialized countries. Most are diagnosed in advanced stages, where the overall survival is limited. It has been studied the usefulness of tumor markers, even if most studies evaluate HE4 role in early diagnosis, it seems promising for detecting recurrences.

OBJECTIVE: To assess the utility of HE4 as an early biomarker of recurrence in epithelial ovarian cancer.

METHODS: Retrospective descriptive study, including all patients diagnosed with ovarian and primary peritoneal cancer from January 2015 to January 2018 at Hospital del Mar (Barcelona). We included patients with recurrent disease after being treated with surgery and/or chemotherapy.

Collected data: Histology, stage, surgery and serum values of HE4, CA 125 and creatinine at diagnosis, post-treatment, and follow-up until the detection of recurrence.

RESULTS: 52 patients of 95 primary treated, recurred. Finally, 28 patients were included for analysis. 93% were high grade carcinomas, 75% of them were serous, 10% primary peritoneal and the rest were endometrioid or poorly differentiated. 18 patients were diagnosed in stage IIIC, 8 in stage IV, one in IC and 1 in IIIA. All patients with high-grade serous ovarian cancer showed high levels of HE4 and CA125 at diagnosis; and decrease post-treatment. In recurrence, 93% patients showed increase of both tumor markers, only HE4 rised in 7% patients, and none showed an increase of CA125 isolated.
The median of the elevation from post-treatment to recurrent levels was 56 in HE4 and 48 in CA125. The recurrence levels were raised by an average of 74% in HE4 with respect to post-treatment levels, and 226% in CA125.

SUMMARY: Although the differences were not statistically significant, it has been showed that in high-grade serous ovarian cancer, HE4 could be an early marker in recurrences, with marked increase in some cases.

30. The role of toll-like receptors in advanced stage ovarian cancer

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Introduction: Complex tumor-host interactions in ovarian cancer have been recently recognized as an important element of tumor progression. Toll-like receptors (TLRs) are protein bound receptors that play a major role in the innate immune system. Activation of various transcription factors, can lead to an adaptive immune response, but activation of TLRs on cancer cells can lead to an opposite response that favors tumor progression.

We have evaluated the expression of four different toll like receptors (4,5,7 and 9) in advanced stage ovarian cancer in association with clinical data and evaluated their prognostic significance.

Methods: Sixty-seven cases diagnosed as advanced high grade serous ovarian cancer were included the present analysis. A semi quantitatively IHC scored was developed to assess TLR expression, while CD68 and CD163 macrophage expression was used to infer on their density.

Results: Above median values for TLR4 were associated with clinical features such as peritoneal carcinomatosis or ascites. Patients with a platinum-free interval over one year had a higher CD68 density score and a lower CD163 density score. TLR7 positivity was associated with a lower overall survival ($p<0.05$).

Conclusion: In our preliminary analysis, TLRs and CD68/163 seem to have a prognostic role and research is needed to clarify the immune function in ovarian cancer.

31. Disulfiram synergistically increases cisplatin sensitivity in ALDH positive stem-like cells in breast cancer cell lines

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Background: Cisplatin is used as first-line chemotherapy in breast cancer. However, tumor cells that are irresponsive to cisplatin treatment will eventually lead to multiple recurrences. Recurrences and resistance have been linked to cancer stem cells (CSC) with high aldehyde dehydrogenase (ALDH) activity. Investigation of the mechanisms and development of sensitizing agents to overcome cisplatin resistance of cells will potentially improve the therapeutic outcomes of patients.

Methods: The cytotoxic effects of disulfiram (DSF), cisplatin alone, or in combination on breast cancer cell lines was investigated by MTT assay. Description of synergy of the DSF/cisplatin combined treatment was based on the combination index (CI). To explore the mechanism of DSF, cell cycle distribution and intracellular reactive oxygen species (ROS) measurement was performed by multiparameter flow cytometry (FACS). ALDH+ and ALDH- cells isolated by FACS-sorting were treated by cisplatin and/or DSF and were analyzed by MTT assay and flow cytometry assay.

Results: We provide evidence that DSF sensitizes cancer cells and CSC to cisplatin treatment. Cell viability dropped by 50% in cell lines MCF-7, and 20%-30% in MDA-MB-435S and SKB-R3 cells in cisplatin/DSF-treated cells compared to cisplatin-treated cells (P<0.05). DSF overcame cisplatin resistance of ALDH+ cells and yielded a synergistic effect combined with cisplatin (CI<1). The mechanisms of enhanced cytotoxicity by the combination treatment, was due to cisplatin contributing more to the cell cycle blockade while DSF caused a short-term killing and a delayed cytotoxicity to cancer cells by accumulation of ROS. Importantly, DSF induced a greater increase of ROS generation in ALDH+ CSC.

32. Vascular endothelial growth factor receptor 2 (VEGFR2) correlates with long-term survival in patients with advanced high-grade serous ovarian cancer (HGSOC). A study from the Tumor bank Ovarian Cancer (TOC) Consortium

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Objective: The impact of angiogenesis on long-term survival of high-grade serous ovarian cancer (HGSOC) patients remains unclear. This study investigated whether angiogenic markers correlated with 5-year progression-free survival (PFS) in a large cohort of matched advanced HGSOC tissue samples. **Methods:** Tumor samples from 124 primary HGSOC patients were retrospectively collected within the Tumor Bank Ovarian Cancer (www.toc-network.de). All patients were in advanced stages (FIGO stage III-IV). No patient had received anti-angiogenesis therapy. The cohort contains 62 long-term survivors and 62 controls matched by age and post-surgical tumor residuals. Long-term survivors were defined as patients with no relapse within 5 years after the end of first-line chemotherapy. Controls were patients who suffered from first relapse within 6 to 36 months after primary treatment. Samples were assessed for immunohistochemical expression of vascular endothelial growth factor (VEGF) A and VEGF receptor 2 (VEGFR2). Expression profiles of VEGFA and VEGFR2 were compared between the two groups. **Results:** Significant correlation between VEGFA and VEGFR2 expression was observed (p<0.0001, Spearman coefficient 0.347). VEGFR2 high expression (VEGFR2^{high}) was found more frequently in long-term survivors (77.4%, 48/62) than in controls (51.6%, 30/62, p=0.001), independent of FIGO stage and VEGFA expression in multivariate analysis (p=0.005). Also, VEGFR2^{high} was found the most frequently in women with PFS ≥ 10 years (p=0.001) among all 124 patients. However, no significant association was detected between VEGFA expression and 5-year PFS (p=0.075). **Conclusions:** VEGFR2 overexpression significantly correlated with long-term PFS in HGSOC patients, independent of age, FIGO stage, tumor residual and VEGFA expression.

33. Long Noncoding RNA HOTAIR is overexpressed in ovarian cancer and interacts with tumor suppressor P53

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Ovarian cancer is one of the three most prevalent gynecological cancers with the highest mortality rate. Despite the advancements in surgical, chemotherapy and radiotherapy, the prognosis of ovarian cancer is poor, with an overall 5-year survival rate of around 30%. This is due to the no specificity of early ovarian cancer symptoms and the absence of effective early detection strategies. Thus, our objective is to understand the molecular mechanism underlying this pathology to establish better strategies to prevent it. In the present work, we are interested in studying the involvement of the long noncoding RNAs in the downstream interactions leading to ovarian cancer development.

Therefore, we first performed qPCR in order to measure the expression of long noncRNA HOTAIR in ovarian cancer tissues in comparison to controls. Then, we adopted a computational methodology based on Protein to Nucleic Acid Docking and Virtual Matching to study the interaction between HOTAIR and key oncoproteins along with tumor suppressors.

The qPCR results showed a significant overexpression of HOTAIR in ovarian cancer samples. Furthermore, the structural modeling of 200 nt of the 3'region in HOTAIR showed its direct interaction to proteins. These interactions differ according to the 3D nature of the protein. Particularly, HOTAIR showed strong binding to P53, indicating a putative inhibitory interaction between these molecules.

In conclusion, our results suggest a role of HOTAIR in ovarian cancer, which can partly be explained by its direct binding to tumor suppressor gene P53. In addition, the differential expression of HOTAIR provides new approach of detection as a putative biomarker.

Keywords: HOTAIR; NcRNA; Oncogenes; Ovarian cancer; P53

34. Disulfiram reverses resistance in acquired cisplatin resistant cells

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Background: Resistance of tumor cells to chemotherapeutic drugs is one major cause of recurrence after adjuvant therapy. Identification of drugs that overcome such resistance, like for cisplatin, and enhancement of cytotoxicity of e.g. cisplatin is needed to improve outcomes of cancer treatment. Objective: To explore the characteristics of cisplatin resistant cells and to evaluate the effect of disulfiram to overcome this resistance.

Methods: Cisplatin-resistant cell lines from SKB-R3 and A2780 were generated by progressive selection in a step-wise concentration increasing procedure. MTT assay, clonogenicity assay, and flow cytometry-based apoptosis assay were performed. Results: Cisplatin resistant cell line variants are more quiescent with significantly longer population doubling time (SKB-R3 vs. SKB-R3-cis-re: 24.8 vs. 40 h, $P < 0.05$) (A2780 vs. A2780-cis-re: 20.95 vs. 29.36 h, $P < 0.05$) and higher IC_{50}. Cisplatin resistant cells have increased colony-forming ability, and are more resistant to cisplatin-induced cell cycle arrest. Disulfiram (DSF), an anti-alcoholism drug, enhances cisplatin cytotoxicity and reverses cisplatin resistance. Significantly more cellular apoptosis and necrosis is induced by DSF/cisplatin combination treatment in cisplatin resistant cells than in their parental cell lines (SKB-R3 vs. SKB-R3-cis-re: 38.8% vs. 55.8%, $P < 0.05$) (A2780 vs. A2780-cis-re: 50.1% vs. 81.5%, $P < 0.05$). Conclusion: DSF may be repurposed and be investigated as a novel adjuvant chemotherapeutic sensitizing agent combined with cisplatin to reverse acquired cisplatin resistance in cancer adjuvant treatment.

Keywords: cisplatin resistance; adjuvant chemotherapy; novel chemotherapeutic agent, Antabuse

35. Use of mesothelin as a tumor-associated antigen in cervical squamous cell carcinoma

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Aim: To explore the feasibility of using mesothelin (MESO) as a tumor-associated antigen (TAA) in cervical squamous cell carcinoma and its function in the development of cervical cancer.

Methods: We collected eight cervical tissue samples of squamous cell carcinoma as the test group and eight samples of cervicitis as the control group from patients who underwent a hysterectomy because of a diagnosis of myoma. Then we used western blotting to screen for a potential TAA in cervical squamous cell carcinoma samples. In addition, Lentivirus-mediated RNAi was used to downregulate the expression of the MESO gene (MSLN) in SiHa cells. Fluorescence-activated cell sorting (FACS), 3-(4,5)-dimethylthiahiazo (-z-y1)-3,5-di- phenytetrazoliumromide (MTT), and wound healing were used to examine cell apoptosis, cell proliferation, and cell migration respectively. Results: Results of the western blotting showed that the MESO protein expressed highly in the cervical squamous cell carcinoma and paracancerous tissues in contrast to the cervicitis tissue (p=0.242). We used quantitative PCR to verify that the expression of MSLN was 21.6% in the cells undergoing knockdown compared to that in the control cells, and thus, decided to continue with further experiments. We confirmed by FACS that the apoptosis rate in the SiHa cell group undergoing MSLN knockdown (KD group) was significantly higher than that in negative control (NC) group of SiHa cells (p=0.014). The proliferation of cells was examined by MTT and the difference between the KD and NC groups was found to be statistically significant (p=0.0084). However, since the difference was less than 20% we did not consider it to be clinically significant. Cell migration ability was verified by wound healing test and found to be 43% in the KD group and 38% in the NC group after 48 h, but the difference was not statistically significant (p>0.05).
Conclusions: MESO can be used as a TAA for diagnosing cervical squamous cell carcinoma. When MSLN was knocked down in SiHa cells, cell apoptosis increased, but no significant effects were observed on cell proliferation and migration. Thus, our study shows that MSLN plays a role in the apoptosis of cervical squamous cell carcinoma cells, and since this might affect tumor progression, further research is warranted to understand how MSLN plays this role.
Keywords: cervical cancer, mesothelin, tumor-associated antigen, chimeric antigen receptor.

36. The analysis of the accuracy of selected ovarian tumor predictive models according to the degree of uncertainty in subjective assessment.

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Introduction: The idea behind the development of predictive models for differential diagnosis of ovarian tumors is to facilitate the diagnosis by inexperienced sonographer. In this context, the physician who is less experienced in gynecologic ultrasound, may differentiate malignant from benign ovarian tumors with the use of predictive model. Therefore, the experience determines the need for predictive model application. In our study we wanted to assess how diagnostic tests behave depending on the degree of uncertainty judged in the subjective assessment.

Material and methods: The analyzed group consisted of 177 (59%) patients with benign and 121 (41%) patients with malignant ovarian tumors treated in the Division of Gynecologic Surgery, Poznan University of Medical Sciences. Prior to the surgery, ultrasonography was performed by an experienced sonographer and CA125 levels were assessed. In subjective assessment tumors were divided for six groups: certainly benign (CB), probably benign (PB), uncertain but benign (UB), uncertain but malignant (UM), probably malignant (PM) and certainly malignant (CM). We have analyzed the Area under the ROC Curve (AUC) of risk of malignancy index (RMI), International Ovarian Tumor Analysis (IOTA) ADNEX model, IOTA logistic regression model 2 (LR2) and CA125 in the group of tumors as follows: CB+CM (group 1) vs. PB+PM (group 2) vs. UB+UM (group 3).

Results: The AUC for RMI, LR2, ADNEX and CA125 in the group 1 were as follows: 0.981, 0.997, 1.00 and 0.928. The respective AUC in the group 2 were: 0.898, 0.725, 0.893 and 0.833, while in the group 3 were as follows: 0.781, 0.595, 0.710 and 0.796.

Conclusion: We have observed progressive decrease of diagnostic performance of ovarian tumor prognostic models and CA125 according to the increase of sonographer uncertainty. This implicates the need of prospective trials evaluating the clinical utility of predictive models in daily practice.

37. Vitamin D receptor polymorphisms and biomarkers of breast cancer

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Breast cancer is a multifactorial chronic disease that is a major concern worldwide. Several scientific studies are designed to confirm the preventive effect of vitamin D on this cancer whose action in the maintenance of the body's immune system is demonstrated in several epidemiological studies.(Briot et al, 2010).

Indeed, vitamin D affects more than 200 genes that influence particularly the proliferation and differentiation of cancer cells (Ebert et al, 2006). Likewise, it slows the growth of certain cancer cells in culture.

It is in this context that we intend to investigate the vitamin D receptor polymorphism (s) associated with breast cancer and to establish a relationship between these polymorphisms and the development of gynecologic breast cancer.

Therefore, we will first proceed to the molecular detection of VDRs by realtime RT-PCR using specific primers and probes to each studied polymorphism in biopsies collected in University Hospital Centers. (CHU) of Morocco. Subsequently we will carry out an overall analysis of the results obtained in order to establish the possible relationship between breast cancer and the dominant polymorphism(s).

The expected results of this research are to identify the VDR polymorphism (s) associated with breast cancer and to determine the relationship between them.

The study of this relationship will enable us to establish the primordial role of these receptors in modulating the immune response with respect to these cancerous cells as well as to identify the vitamin D receptor polymorphisms as the most correlative biomarkers with breast cancer.

Key words: Breast cancer, Vitamin D, VDR polymorphisms, Biomarker.

38. Olaparib in German routine clinical practice – C-PATROL interim results

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Background: Olaparib (50mg hard capsules (HC)) is approved in the EU as monotherapy for maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (BRCAm) ovarian cancer (PSR-OC) who are in response to platinum-based chemotherapy. So far, only limited data on real-world olaparib treatment are available.

Methods: The German prospective non-interventional study C-PATROL (NCT02503436) collects routine clinical and patient-reported outcome data in BRCAm PSR-OC patients treated with olaparib HC or film-coated tablets (FC) according to label (recommended total daily dose of 800mg and 600mg, respectively). Descriptive data on safety and dosing are provided in this 2nd interim analysis (cut-off: 01FEB2018) for patients treated with olaparib HC (FPI: OCT2015). Subgroup analyses were performed according to age and comorbidities.

Results: 165 BRCAm PSR-OC patients treated with olaparib (HC) and ≥3 months follow-up were analyzed (median age: 61 yrs; ECOG ≤1: 92.7%; ≥2 relapses: 40.0%; ≥3 prior platinum chemotherapies: 40.0%). 22.4% of patients were ≥70 yrs of age and 48.5% had comorbidities at baseline.
Most patients (83.6%) were initiated with a daily dose of 800mg olaparib (HC). 40.0% had ≥1 dose reduction and 33.9% had ≥1 therapy interruption (median duration: 13 days). 47.9% discontinued treatment, mainly due to progression; 7.3% discontinued due to AEs.
89.7% of patients had AEs (any grade). Nausea (44.2%), fatigue (34.6%), anemia (28.5%) and vomiting (17.0%) occurred most frequently, with anemia and vomiting being less frequent in patients ≥70 yrs and without comorbidities. First occurrence of these four AEs was mainly within the first 3 months of treatment.

Conclusions: This 2nd interim analysis indicates that treatment with olaparib (HC) is well tolerated under routine conditions, with a manageable toxicity profile also in patients of higher age and with comorbidities. The toxicity profile observed so far is in line with results of the clinical trial program for olaparib in PSR-OC.

39. SCORE: Identification of parameters to calculate a score and predict the non-compliance of patients with relapsed ovarian cancer treated with treosulfan

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RATIONALE AND OBJECTIVE: Crucial for the efficacy of a drug, especially when administered orally in patient responsibility, is the patient compliance with the therapy. Chemotherapy related side effects often cause an early ending of treatment. If patients, who are most likely discontinue treatment, can be identified before the therapy will start, they can be supported and motivated more specific.

The primary objective of this non interventional study is to identify parameters related to non-compliance in Treosulfan therapy (p.o. or i.v.) under real life conditions and to calculate a predictive score for non-compliance based on this parameter.

In contrast to other clinical trials, this non-interventional study includes patients of all ages and with all co-morbidities.

The collected data is based on the clinical examinations done in the daily practice of the center and additional questionnaires.

CURRENT STATUS OF RECRUITMENT: On March 4th 2019, 106 Patients have been registered. The age of the patients at registration ranges from 31 to 85 years, the number of previous therapy lines ranges from 1 to 5 .The administration of at least one cycle of treosulfan has already been reported for 86 Patients. 70 patients received treosulfan iv. while 17 Patients were treated with the oral formulation.

40. Comparison of QoL between Trabectedin / PLD and standard platinum-based therapy in patients with platinum sensitive recurrent ovarian, fallopian tube and peritoneal cancer - Intergroup-Study of NOGGO and BNGO (COMPASS)

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Background: The COMPASS-study is a multicenter, randomized, controlled, open-label study (phase IV) including patients with recurrent, platinum-sensitive, ovarian, peritoneal or fallopian tube cancer.

The main scope of the trial is to evaluate Quality of life (QoL) during and after chemotherapy comparing trabectedin/PLD with other standard platinum-based chemotherapy in platinum-sensitive disease.

Ovarian cancer remains the second-most lethal gynecologic malignancy after cervical cancer, with approximately 125,000 deaths annually worldwide. Because most women with recurrent ovarian cancer ultimately die of their cancer, QoL and regimen convenience are objectives that are as important as efficacy. In palliative cancer therapy, the QoL is one of the most important objectives; besides the prolongation of overall survival. Platinum-based combination chemotherapy is known to be intense and toxic and can therefore, be associated with impaired QoL. Therefore, there is a strong rational to compare the platinum-free combination trabectedin/PLD with other standard platinum-based combinations in terms of their impact on QoL.

Procedures used in this study (such as the chemotherapy, the blood tests and the radiology investigations) are in line with those usually used in the treatment of patients with recurrent ovarian, peritoneal or fallopian tube cancer in routine clinical practice. In terms of the chemotherapy, carboplatin/PLD, carboplatin/gemcitabine, carboplatin/paclitaxel are recommended chemotherapy regimens by the S3 German Guideline (highest-level national guidelines in Germany) for platinum-sensitive relapse, as just mentioned above. Taken together, the risks emerging from participation in this clinical trial are acceptable and the results of the study may have an impact on future treatment of patients in the given indication.

Methods: Patients with recurrent, platinum-sensitive, ovarian, fallopian tube and peritoneal cancer will be stratified according to surgery for relapse (tumor free vs. not tumor free resection) vs. no surgery in the same setting and age (<75 years vs. ≥75 years), and randomized 1:1 to receive either trabectedin/PLD (Arm A) or one of 3 platinum-based standard therapies without bevacizumab (Arm B, "other standard therapy"). In case of randomization to "other standard therapy", the investigator has the choice between carboplatin/PLD, carboplatin/gemcitabine and carboplatin/paclitaxel. Patients in both treatment arms will receive chemotherapy up for 6 cycles or until disease progression (PD), unacceptable toxicities or patient's wish to stop therapy whichever occurs first.

In both of the arms, tumor assessments (CT or MRI) are performed before randomization, week 12 (± 2 weeks), at end of

treatment (EOT) and then every 6 months thereafter until progression/relapse, death or end of follow-up (current standard of care in Germany). During treatment, clinical visits (blood cell counts, detection of toxicity) occur prior to every treatment dose. Safety will be monitored continuously by careful monitoring of all adverse events (AEs) and serious adverse events (SAEs).

The main inclusion criteria are: Histologically confirmed diagnosis of epithelial ovarian cancer, primary peritoneal carcinoma or fallopian tube cancer, patients must be eligible for platin-containing therapy; an ECOGperformance status of ≤ 2; adequate baseline organ function and an adequate cardiac function defined as left ventricular ehjection fraction (LVEF) ≥50% as determined by echocardiogram.

The main exclusion criteria are malignancies, which influence the prognosis; any unstable or serious concurrent condition (e.g. active infection requiring systemic therapy); chemotherapy or radiation therapy or tumor embolization within 2 weeks prior to the first dose of study drug or planned during study participation; patients who have refractory disease; hypersensitivity to the active substance or to any of the excipients of study drug; findings from ECG and/or assessment of LVEF which indicate an anthracycline-related cardiotoxic process which contradicts administration of liposomal doxorubicin in accordance with the requirements of the SmPC of PLD and biological therapy, immunotherapy, hormonal therapy or treatment with an investigational agent within 14 days (for bevacizumab, 30 days) prior to the first dose of study drug.

Since study start on December, 2017, 29 patients from planned 206 patients (Arm A, 103; Arm B, 103) could be enrolled (status: 08.02.2019). 20 German study sites are participating. The recruitment period lasts for 40 months.

The clinical trial registry number is: EudraCT 2016-005029-36 21SEP2017

41. Impact of HIPEC on disease relapse pattern in recurrent ovarian cancer patients.

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Background and objectives: Retrospective analysis of clinical data of recurrent epithelial ovarian cancer (EOC) patients treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) at National Cancer Institute of Lithuania and patients treated with CRS alone in order to estimate HIPEC impact to daily practice and future prospects.

Materials and Methods: Retrospective data was collected of patients with EOC who underwent optimal CRS followed by HIPEC in comparison with CRS alone between January 2013 and December 2016. All patients underwent systemic chemotherapy after CRS followed by HIPEC or CRS without HIPEC. The outcome measures were completeness of cytoreduction (CC score), morbidity, mortality rate, progression-free survival (PFS), overall survival.

Results: There were 27 patients included in the study: 18 patients were treated with CRS and 9 had CRS followed by HIPEC. Characteristics of the patients were homogeneous. The median PFS after CRS followed by HIPEC was 23 months versus 17 months after CRS alone. Different disease recurrence pattern was observed in two groups: patients who underwent CRS without HIPEC had peritoneal recurrence in 100 % of cases vs 22.2 % in group with CRS + HIPEC. No ascites was determined at the first relapse or later follow up in group of patients treated with CRS followed by HIPEC contrary to CRS alone group.

Conclusions: In selected patients with recurrent EOC complete CRS followed by HIPEC provide promising results in terms of outcome. CRS followed by HIPEC is associated with supreme local disease control and lower rate of relapse in peritoneal cavity, that can impact survival rate. This treatment method has to be analyzed in future prospective studies with lager cohort.

42. Survey on Probiotic intake in Patients with Gynecologic Malignancies

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Background: Gynecologic cancer patients are generally presented with symptoms of indigestion, bloating, sleep and psychological disturbances. Probiotics haven been commonly used to enhance well-being, improve digestion and metabolic functions. In this survey, we have attempted to assess the effect and influence of probiotic intake in gynecologic cancer patients for the first time.

Materials and Methods: We have developed a questionnaire that has been distributed to patients at the time of admission prior to their therapy. Gynecologic cancer patients who were admitted for pre-therapeutic diagnostics and supportive procedures (physiotherapy, nutritional and respiratory therapy) were asked to rate their overall wellbeing, digestion and sleep quality on a scale from 1 to 5 (1 pertaining to very good and 5 to very poor). Probiotics (Omnistress) have been administered orally during the hospital stay twice a day. We obtained each patient's BMI and BIA measurement for reference. Upon discharge, the patients answered the same questionnaire in addition to a fourth yes or no question which aimed to asses if the patients had noticed any type of psychological relief since their hospital stay and intake of probiotics.

Results: Between February 2018 and February 2019, 176 patients were enrolled in our study. The complete data was obtained from 55 patients. The median period of probiotics intake in this group was 4 days (range 3-20 days). Forty percent (40%) of patients noticed psychological relief after probiotics intake. 40%, 58% and 33% of patients rated their general wellbeing, digestion and sleep prior to Intake as good respectively. However, there was no significant change after intake.

Conclusion: To the authors' knowledge, this is the first attempt to asses probiotics influence during the pre-therapeutic period in gynecologic oncology patients. Despite the small number of patients and short intake period, our observations have shown a psychological relief and a need for further prospective trials.

43. Management of patients with gynecological sarcoma - a survey among gynecologists within the framework of the German Registry of Gynecological Sarcoma (REGSA)

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Background: Gynecological sarcomas are rare neoplasms that account for approximately 1% of all gynecological malignancies. So far, success in treatment is disappointing due to, among other things, low prevalence and difficult differential diagnosis.

REGSA is the largest gynecological register for Sarcoma in Germany which is performed with the aim to prospectively collect data of patients with gynecological sarcomas and to describe their course of disease, diagnostics and therapies. The goal is to pave the road for further, more extended studies and therefore to improve progression-free and overall survival for patients with gynecological sarcoma. Furthermore, the results might help to evaluate better standard of care.

All study sites that collect patient data are also asked about their experience and treatment standards for gynecological sarcoma.

Methods: An electronic case report was designed to register clinical data from patients with gynecological sarcomas such as disease, surgery, therapy and success of therapy (obtained after informed consent). Additionally, the information about clinical management as stated by the participating physicians will be also recorded. This information is completed once per study site.

Patient recruitment has started in September 2015 and is currently still ongoing. Up to date, 106 German study sites and one Austrian site are participating, whereas a total of 389 patients have been already enrolled (last status obtained on 25.01.2019)

The evaluation of the register data will be exploratory and descriptive. There will be a descriptive analysis of the forms of therapy according to the different types of gynecological sarcoma and their outcome. The REGSA study is registered on German Register of Clinical Trials (DRKS) with the number: DRKS00009240.

44. FraStROC —Frailty Stratification for ROC Development and prospective validation of a Frailty Score for chemotherapy associated toxicity in Relapsed Ovarian Cancer

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Introduction: Ovarian cancer (OC) is the fifth most common cancer in European women. Evidence about optimal treatment strategies in recurrent ovarian cancer (ROC) is limited. Particularly one of the critical issues in the treatment of ROC is how to manage an appropriate treatment of vulnerable, elderly or multimorbid patients.

Rationale and Objective: Treatment of ROC has to consider that especially older or highly pre-treated patients may suffer from a number of co-morbidities and persisting toxicities of previous therapies. However, chronologic age should not be the only factor used for treatment decisions. Organ function, cognitive factors and social behavior has influence on the patient's well-being and can be used as prognostic factors. Thus, it would be advantageous if predictions concerning of a premature termination based on special factors could be made. The aim in this trial is the development of a predictive score which can identify patients who interrupt or discontinue recurrent chemotherapy within 12 weeks of therapy start due to defined parameters. Different geriatric, psychological and functional assessments as well as mental, emotional and patient-reported disease-related aspects together with the evaluation of other potential variables will be used for the development of a predictive score.

45. Adenoid cystic carcinoma of cervix: A case report

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Adenoid cystic carcinoma (ACC) is a rare and aggressive tumor that rarely occurs in the cervix, it has a higher tendency to local and metastatic recurrence even if diagnosed at its earliest stages, and the lack of data and clinical research led to unavailable treatment guidelines. We will discuss the characteristics of this tumor through a case of adenoid cystic carcinoma in 62 years old women, who has been treated with curative intent. The patient underwent surgery and concurrent chemoradiotherapy with a satisfying outcome after 2 years follow up.

Keywords: Adenoid cystic carcinoma, cervix, cervical carcinoma

46. Molar Pregnancy: Retrospective Analysis

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Gestational trophoblastic diseases are a large title that originates from placental trophoblastic tissue, ranging from benign molar pregnancy to malignant choriocarcinoma. One of the most common among them is molar pregnancy, approximately one in 1000 pregnancies. Although its frequency is not low, epidemiology and risk factors are not clear.

Age, ethnicity, a history of molar pregnancy and ABO blood group interactions appear to be important risk factors for molar pregnancy. In most cases, molar pregnancy is discovered when a miscarriage occurs; if suspected before a miscarriage occurs, it can usually be detected by ultrasound. Epidemiological factors will be helpful in identifying and facilitating the diagnosis in cases without miscarriage.

The study is a retrospective study and the data were collected from the patient registry system of our hospital. In this study, some epidemiological features of patients with molar pregnancy were investigated and their relationships with pathological diagnoses were evaluated. In previous studies, it was found that molar pregnancy was more common in women with blood group A and AB, women younger than 20 years and women older than 35 years, and women who had previously had a miscarriage. In this study, the mean age of the patients was 30.06, and the blood group of the patients were predominantly A and O, and the number of women with abortion history was less than half of the study group. There were no patients with a history of molar pregnancy in the study. It should be emphasized that the present findings and molar pregnancy rates may vary according to the population, ethnic group, and this may mislead clinicians.

47. Atypical localization of lymphangiosarcoma (stewart-treves syndrome) in patient with breast cancer

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Introduction & Objectives: Lymphangiosarcoma (Stewart-Treves syndrome) is rare and aggressive tumour reported to occur following breast cancer surgery and post radiotherapy lymphoedema. Affecting the long term survivors of breast cancer,lymphangiosarcoma has a high mortality rate. Ussually affected the upper extremity years after lymphedema occurs. We are reporting a case of 79yr old female with breast cancer and chronic lymphedema of the arm. Sectoral resectionog the gland and axillary nodes dissection has been done 8 years ago, followed by irradiation of the breast as well as axillary and supraclaviculary area. In August 2018 appeared pink to blue colored patches on the remaining part of the breast. Subsequently the lesions developed into nodules which continued to spread rapidly. Biopsy was performed and lymphangiosarcoma was confirmed histologically and on immunohistochemistry.

Material & Methods: Patient : 79 yr old female operated 25/10/2010 for breast cancer of the right gland by sectoral resection of the gland and right axillary dissection of the lymph nodes.Radiotherapy of the rest of the right gland was performed as well as right axillary et supraclavicular area. Chemotherapy and Hormontherapy was performed.
08/2018 pink to blue patches appeared on the rest part of the right gland, which spreaded rapidly and developed into nodules. Biopsy 03/10/2018 was performed

Results: 25/10/2010 hystology from the right breast :invasive ductal breast carcinoma T1 G2-3 hystology from the right axillary lymph nodes :18 axillary lymph nodes have been detected - 2 of them affected metastasis from invasive ductal breast carcinoma (5mm), rest 16 lymph nodes with atrofic tissue 03/10/2018 skin lesion biopsy result: lymphangiosarcoma 14/01/2019 hystology from the rest of right breast approved lymphangiosarcoma

Conclusion: Surgery threatment in volume simple mastectomy was proposed to the patient

48. Melanoma of the uterine cervix – clinical case.

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After the discovery of melanocytes in the cervix by Cid in 1960, it was recognized that primary malignant melanoma of the cervix exists as a separate entity. It is a rare disease that chiefly occurs in postmenopausal women and has poor prognosis. Our aim was to present the case of a woman with a primary melanoma in the uterine cervix.

A 70-year-old woman with history of subtotal hysterectomy 10 years ago because of uterine myomatosis was admitted to the National Cancer Institute (Vilnius, Lithuania) with a chief complaint of vaginal bleeding. Clinical examination identified a 3x4 cm-diameter ulcerated, fragile tumor in the uterine cervix, spreading to the upper third of the vagina, with no indication of abnormality in the parametrium. CT did not detect any local or distant metastases.

Patient underwent radical hysterectomy, regional lymphadenectomy and removal of the upper vagina. A biopsy was taken and a histopathological diagnosis of cervical melanoma, pT2a2N0M0 (6 cm tumor with vaginal spread and without parametrial invasion, radical excision), was made.

Postoperatively, 2 months later, follow-up full body CT showed no clear metastasis, but suspect 5 mm-diameter tumor was detected in the vaginal stump. A biopsy was taken and the histopathology report showed melanoma. Following PET/CT revealed metabolic active spots in vagina, bilateral inguinal and retrocaval lymph nodes, also pulmonary nodules that suspected pulmonary metastasis. The patient received 5 courses of chemotherapy with dacarbazine. However, CT six months later showed multiple lung, aortocaval and iliac lymph nodes metastases with features of masses infiltrating surrounding tissues and structures. According to the findings, it was decided to administer second line chemotherapy with carboplatin/paclitaxel and imunotherapy. The patient received 3 cycles up to now and so far the response is stable disease.

49. Two Different Sex Cord Stromal Tumor at Same Ovary in 6 Months Period: A Case Report

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Introduction: Ovarian sex cord-stromal tumors(SCSTs) are rare, accounting for 7% of all ovarian malignancies. As a group, SCSTs constitute special clinical situations because of different hormanal secretions. The granulosa tumors account for the majority of SCST. Most granulosa tumors produce estrogen. Sertoli leydig cell tumors are rarely seen mostly in young womenwho usually become virilized.
We present a case of 24 year old female, detected granulosa cell tumor after an SLCT in a short time at same ovary

Case Report: A 24 year old female patient G0P0 was admitted to our clinic with hirsutism on her bac. No history of anorexia, weight loss, increased libido, or breast recession was noted. She had a past laparoscopic surgery of bening pure cyst extirpation from left ovary. In examination, We detected 106*80 mm solid tumor at right ovary with transvaginal ultrasonography . It was thought as a hormone-producing tumor when complaints of patient was considered. A blood examination revealed an elevated level of testosterone 2 ng/mL , and CA-125 level also increased to 93 U/ml. AFP level was also high;12,3 ng/ml. The patient was taken to operation; left ovary, uterus and other abdominal organs were seen normally. The peritoneal cytology did not include malignant cells. The final pathological report for ovarian cyst was reported as intermediate differentiation of SLCT. Post operative period was uneventful. Sixth months later she admitted to our clinic with bilateral lower quadrant pain and disparonia. When the patient was examined a 145*144 mm lobule cyctic lesion with 2 cm ascites around ovary was seen in ultrasonography. In laboratory examination testosterone level was normal, less than 0.1 ng/mL; but CA125 level was increased to 747 U/ml. The patient was taken to operation again. Right salpingo-oophorectomy was done and the specimen was examined in frozen sections, reported as a juvenile granulosa cell tumor. Fertility sparing surgery was done with addition of lymph node dissection and infracolic omentectomy the final patology report was same; there were no tumors in lymph nodes or omentum.

Conclusion: This rare case was showed us that the follow up of patients with ovarian tumors is very important . SLCTs and granulosa cell tumors are very rare ovarian tumors in the group of SCSTs. It is usually seen during reproductive ages. Prognosis of ovarian SLCTs is significantly correlated with degree of tumor differentiation and staging. The type of SCSTs is important for both treatment and long-term follow-up of patients.

50. A Case Report: Steroid Cell Tumour of the Ovary

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İntroduction: Steroid cell neoplasms are a heterologous group of tumors of the ovary. This tumors can not be characterized as stromal luteomas or Leydig cell tumors are uncommon sex- hormone secreting tumours characterized by a steroid cell proliferation. The steroid cell tumors of the ovary are accounted   only 0.1% of all ovarian tumors. They are androgenic tumors associated with hypercalcemia, eritrocytosis or ascites also.

We present a case of this rare tumor with it's clinical features.

Case Report: A 42-year-old patient G1P1 applied to our clinic with lower abdominal pain and seconder amenorrhea for 4 months. She had also secondary infertility for 5 years. She had not been treated for infertility before. She had well controlled hypothyroidism.

On physical examination the patient was obese with BMI 28. Frontal recession of hairline, temporal baldness, facial hair growth and breast atrophy was also seen. Transvaginal ultrasonography were applied to patient that solid lesion in right ovary measured 60*50 mm was seen. In laboratuary findings CA-125 was in the normal ranges accounted as 11,9 U/ml. She was taken to laparatomy and right ovarian cystectomy was done. The specimen was examined in frozen sections; reported as steroid cell tumor of ovary. Fertility sparing surgery was done. The operation was completed with right salpinghoooferectomy an unilateral pelvic lymph node dissection. Post operative period was uneventful.

Conclusion: Steroid cell tumors, are rare tumors which are associated with various virilizing symptoms and some other paraneoplastic manifestations . The primary treatment is surgery for these tumors. It is unknown if radiation therapy or chemotherapy is effective or not. %20 of these cases may spread to contiguous organs with hig mitotic activity. Therefore the follow up of these tumors is important after surgery.

51. A case report from Mohammed VI Center: Locally advanced vaginal carcinoma treated with chemo radiotherapy

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Background: Primary vaginal cancer is rare. Although it's more seen in elder women, vaginal cancer is increasing in younger women due to HPV. The treatment is complex. We present a case of a patient with an advanced stage of vaginal squamous cell carcinoma treated with radiation and chemotherapy.

Results: Our patient, a 50 years old woman, had a history of high risk sexual behaviors and chronic tobacco use; she never had a pap smear. She noted on February 2018 the presence of a vaginal mass on the lower vagina, with increased pain.

Initial examination found an Irregular mass on the anterior wall of the lower third of the vagina measuring 4cm. Cervix examinations was normal.

The histopathology reports showed an invasive squamous cell carcinoma of vagina with HPV lesions.

MRI showed a tumor centered on the anterior wall of the lower third of the vagina with multiple pelvic and Para-aortic Lymph nodes.

We started two cycles of chemotherapy combining Carboplatin and Paclitaxel, because of radiotherapy delays in our hospital.

Clinical evaluation after chemotherapy showed progression of the tumor to the vulva with the apparition of a clitoral median mass measuring 8 cm. We started Radiation protocol with external beam pelvic therapy with Para-aortic nodal irradiation (46Gy) combined to weekly Cisplatin (40mg/m²/week)

The patient responded well to the chemo-radiotherapy protocol. The clinical examination showed the regression of the vulvar mass, with regular vaginal walls.

Pet-CT indicated FDG uptake to the primary tumor site but no evidence of FDG uptake to the lymph nodes. We decided to boost the initial tumor site. The patient was able to complete the prescribed course of radiotherapy till 60 Gy.

Physical examination One month after the treatment showed no evidence of recurrent tumor. She will undergo re-examination in our hospital every 3 months for the next two years.

Conclusion: In our patient the vaginal carcinoma might be related to HPV which explains the good response to radiation. There are few references about vaginal cancer optimal treatment. In our case a complete response was obtained with concurrent chemotherapy and radiotherapy.

52. Multimodal Prehabilitationfor Gynecologic Oncology patients in an ERAS program

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Objectives: Patients undergoing major surgery are predisposed to suffer functional capacity decrease as a response to surgical stress. Prehabilitation programs consist on patient's preparation between surgical indication and surgery, and describe a group of interventions aimed to enhance preoperative functional capacity and improve post-operative recovery. Multimodal prehabilitation may include exercise, nutritional optimisation, psychological support, and cessation of negative health behaviours, such as smoking and alcohol addiction. Currently, there are no standardized guidelines for prehabilitation and the existent studies are heterogeneous, however, multimodal approaches are likely to have a greater impact on functional outcomes than single management programs.

Methods: We reviewed the published literature on prehabilitation programs in general and gynecologic surgery to identify tools to establish an optimal prehabilitation program included in an ERAS (Enhanced recover afer surgery) protocol for gynecologic oncology patients.

Results: We suggest a safe, reproducible, functional, and easy-to-apply multimodal prehabilitation program for gynecologic oncology practice based on preoperative medical optimization, physical training, nutritional counseling, and psychological support. The program includes home-based exercise, protein supplementation and anxiety-reduction strategies. In patients with severe functional capacity, interventions are supervised by rehabilitation physicians, dieticians or psychologists. Perioperative care followed the guidelines of the ERAS program.

Summary: The analysis of the implementation of the Prehabilitation program in an ERAS protocol in our patients will be object of further studies. Further research is required in order to test the efficacy of the program on surgical outcome and recovery after surgery.

53. What women want: fertility-sparing surgery in Borderline ovarian tumors patients and pregnancy outcome

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Background: Borderline ovarian tumors (BOTs) are characterized by the presence of cellular proliferation and nuclear atypia without stromal invasion. Compared to malignant ovarian tumors, BOTs typically present in younger women and have better prognoses. The most important treatment of Borderline ovarian tumors (BOT) is surgery. Considering the good prognosis of BOT, fertility-sparing surgery can be considered for young women who desire to preserve fertility.

Objective: Our study evaluated the real pregnancy rate, the efficacy and risk of recurrence of women affected by BOTs who have undergone fertility-sparing surgery.

Methods: Patients characteristics have been restrospectively retrieved for diagnosis made from June 2000 to December 2017 from two institutions in Italy (San Raffaele Hospital, Vita e Salute University Milan and Policlinico Monserrato, University of Cagliari).
A series of 90 patients in reproductive age undergone fertility-sparing surgery for unilateral or bilateral BOTs. Patients characteristics including age at diagnosis, tumor pathological characteristics, surgical management at primary treatment and relapse, child wishing, type of conception, pregnancy rate, live birth rate, pregnancy outcome, follow up data were collected.

Results: Ninety patients were recruited for the study. Median age at diagnosis was 34 years (I.Q.R 29-38). Unilateral salpingo-oophorectomy was performed in 37 patients (41%), unilateral cystectomy in 41 (46%) and 12 underwent both procedures (13%). 40 women (45%) tried to conceive after surgery. We recorded 33 pregnancies, 8 miscarriages and 27 deliveries. The child wishing pregnancy rate was 72% and live birth rate was 67%.

Conclusion: Conservative surgical treatment seems to be a reasonable therapeutic option for women with BOTs who wish to preserve fertility. Our results suggest that the obstetric outcomes after fertility sparing surgery are promising. Maternal desire and the age of diagnosis are the most important factors to conceive after surgery.

54. Dosimetric comparison of conformationnal radiotherapy and VMAT® technique in patients with cervical cancer

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Introduction: Chemotherapy supplemented with brachytherapy is a standard in the treatment of locally advanced cervical cancer. Conformational radiotherapy (3D) does not allow a good intestinal sparing. Technological developments led to the emergence of Modulated Volumetric Arc Therapy (VMAT®), which showed a dosimetric value in pelvic irradiation compared to static beam IMR for intestinal sparing and homogeneity of projected target volume coverage. while decreasing treatment time.

The objective of the study is the dosimetric comparison of the conformational radiotherapy technique and VMAT® in cases of cervical cancer.

Material and Methods: This is a comparative retrospective study of 17 cases treated in our center for cervical cancer by pelvic radiotherapy without lumbar-aortic radiation. The cases that received a 3D irradiation were simulated in VMAT® and those who received a VMAT® irradiation were simulated in 3D. Data entry was done on Excel software and static analysis by SPSS software.

Results: 17 cases treated in our center with concomitant chemotherapy containing cisplatin 40 mg / m2 weekly in 16 patients and carboplatin-based AUC 5 in a single patient. The tumors were squamous cell carcinomas, classified according to FIGO, nine IIB, five IIIA, two IIIB and one IVA. The mean coverage of the Planning target volume was lower with VMAT® (p <0.001). This technique allowed better intestinal sparing (p <0.001) and fixed-beam IMRT, better bladder (p <0.001) and rectal sparing (p <0.001). MUs in VMAT® are much more important than in conformational radiotherapy (3D) (p <0.001) which influences the treatment time; 4 minutes for VMAT® and 3 minutes for 3D.

Conclusion: The technique of RCMI VMAT® is more interesting in matters of organ at risk sparing compared to the 3D technique, but with more UM and a relatively longer processing time.

Key words: Cervical cancer, conformal radiotherapy, Radiotherapy with volumetric intensity modulation

55. Individual management of cervical cancer in pregnancy-- five cases report

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Cervical cancer (CC) is one of the most three common pregnancy-associated cancer types and about 3% of cases of are diagnosed during pregnancy. Although different data suggest that diagnosis of CC in pregnancy does not affect survival rates negatively, its treatment is still a problem. As CC in pregnancy present patients and physicians with a dilemma because the negative treatment can seriously threaten the health of the mother, while positive treatment may carries the risk of losing the fetuses. The management for this situation mainly depend on the gestational age at the time of diagnosis, disease staging, size of the lesion and the patient's wish to maintain pregnancy and fertility. To provide a basis for treatment decisions, here, we present five reference cases diagnosed and treated with CC during pregnancy. Through the analysis of 5 cases of CC in pregnancy in our hospital, we found that vaginal bleeding is a prominent clinical manifestation of pregnancy with CC. CC progress often rapidly in pregnancy, and positive treatment has a great impact on the prognosis, regardless of whether the patient decides to continue pregnancy or not. Neglect of the patient's or doctor's subjective wishes or desire to continue treatment after childbirth is not recommended. Nowadays, the advantages of neoadjuvant chemotherapy in pregnancy complicated with cervical cancer to allow pregnancy to continue and control the development of disease have been widely recognized. Even if there is no standardized practices in the treatment of cervical cancer in pregnancy, the above five cases were analyzed, neoadjuvant chemotherapy can be a very useful strategy for patients and physicians facing the challenge. For the two cases reported in this article, both patients experienced a dramatic reduction in tumor volume, and there were no adverse fetal effects, and favorable neonatal outcomes were achieved.

56. High prevalence and concordance of anal and cervical HPV genotypes

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Background: The incidence of anal cancer is increasing by 2% each year in all genders. High-risk (HR) Human Papillomavirus (HPV) genotypes associated with cervical cancer can also cause anal cancer and its precursors (AIN). Women with history of CIN have a 10 fold increased risk of anal dysplasia. This study explores the correlation between cervical and anal HPV infection as well as the development of cervical and anal dysplasia.

Methods: Women with gynecological clinical indication (HPV/cytology/histology) were recruited. Initially, anal cells were collected using swabs for HPV testing and cytological examination, followed by a cervical smear to prevent contamination between the smears taken. All anal HR-HPV positive women were followed up and underwent high-resolution anoscopy (HRA). Anal and cervical smear tests were repeated after 12 months. Women becoming anal HR-neg. completed the study, anal HR-HPV positive but HRA inconspicuous women had a final examination after 48 months.

Results: So far, 69.7% (n=53) women had ≥1 anal HR-HPV type and HPV-positivity at the cervix (Visit1). From these, 84.9% (n=45) had ≥1 identical HPV type at cervical and anal sites. Cervical examination demonstrated 25 low-grade and 8 high-grade dysplasia's. The anal smear tests showed no clinical indication. 26 women underwent HRA with no clinical findings (no AIN n=25, non-valid result n=1). Until now, 20 women attended the 12-month follow up (V3). Anal HR-HPV and cervical HPV-positivity was detected in 60% (n=12), including 9 women with ≥1 identical HPV type cervical and anal. Five women had persistent co-infections (from V1-V3), whereas 7 women either had new co-infections or loss of HPV-genotypes.

Conclusion: HPV infection in the anus in women with cervical clinical indication and with HPV infection is common. The concordance between cervical and anal HPV is prominent (69.7%). Despite this very high anal infection rate, the rate of anal dysplasia is low as compared to cervical sites.

57. The role of adjuvant treatment in early stage endometrial cancer patients after radical surgery: a single center experience.

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Background: Endometrial cancer (EC) is the most common gynecological malignancy in developed countries. The standard treatment of EC is total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). The role of pelvic and para-aortic lymph node dissection is controversial in the surgical management of early stage EC. Adjuvant radiation therapy (RT)/chemotherapy (CT) for early stage EC is also controversial but is routinely recommended based on presence of adverse risk factors. Moreover the best RT options either external beam radiotherapy (EBRT) or vaginal cuff BRT is still controversial. We aimed to evaluate the outcomes of different adjuvant treatment options of early stage EC patients who undergone radical surgery with respect to disease control, and determine the risk factors.

Material method: Between June 2010-January 2019 382 early stage EC patients who underwent radical surgery ± adjuvant treatment in our university were retrospectively evaluated. The adjuvant treatment options were designed with respect to presence of adverse risk factors including higher stage, increased depth of myometrial invasion (MMI), higher grade, presence of lymphovascular space invasion (LVSI), increasing age, increasing tumor size, involvement of the uterine cervix and adverse histology. The survival times and disease control were analyzed regarding to different adjuvant treatment modalities; and the prognostic factors effecting the survival times and loco-regional control were determined.

Results: Of the 382 patients,172 Received adjuvant BRT, 62 received adjuvant EBRT, 103 received both CT and RT (either EBRT, or VBT, or both).162 patients did not receive any adjuvant treatment. Recurrence rate was %7.6 in early stage EC. There was no statistically significant relationship between the disease stage (1A, 1B, 2) and recurrence (p> 0.05). Mean survival time in patients with stage1A was 8.4 years , 6,7 years in stage 1B and 5,3 years in stage 2 .

Conclusion: Survival time in patients receiving External RT was significantly higher than in patients with BRT.

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