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### EUROPEAN MULTI-DISCIPLINARY TUMOUR BOARDS SUPPORT CROSS-BORDER NETWORKING AND INCREASE TREATMENT OPTIONS FOR PATIENTS WITH RARE TUMOURS

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**Introduction/Background\*** EURACAN is the European reference network for rare adult solid tumours coordinated by the French Comprehensive Cancer Centre Léon Bérard in Lyon, France. It consists of 10 domains, of which rare gynaecological tumours make up domain 2 (G2). Within the G2 domain, virtual multidisciplinary tumour boards (MDTs) were created to get support in clinical management of rare tumours. The aim of this report is to evaluate the outcomes in terms of participation, adherence to recommendations and access to novel patient treatment strategies.

**Methodology** EURACAN G2 cross-border MDTs were initiated in November 2017 and organized by Karolinska University Hospital, Stockholm, Sweden. The MDTs were held monthly at pre-set dates and G2 health care providers (HCP) were invited to present patient cases. A standardized form was used for patient data collection and summaries of cases to be

#### Abstract 602 Table 1 Background data

##### EURACAN MDT 2017-2020

n=91 patients

Age median (IQR)	37 (27-52)
Diagnosis n (%)	19 (21)
• GTD	19 (21)
• MOGCT	13 (14)
• SCST	25 (27)
• Rare ovarian	9 (10)
• Rare uterine	2 (2)
• Rare cervical	4 (4)
• Other	
Previous lines of treatment median (IQR)	1 (0-2)
Indication for discussion* n(%)	59 (54)
• Primary treatment	7 (6)
• Disease progression	42 (39)
• Relapse	1 (1)
• Other	

\*n=109 individual case discussions

Abbreviations: GTD=gestational trophoblastic disease; MOGCT=malignant ovarian germ cell tumour; SCST=sex cord stromal tumour

#### Abstract 602 Table 2 Follow-up data

EURACAN MDT 2017-2020

n=64 patients

##### Adherence to treatment recommendations\* n(%)

• Yes	79 (99)
• No	1 (1)

##### Treatment not otherwise available n(%)

• Off-label treatment	11 (17)
• Clinical trial abroad	1 (2)

##### One-year follow-up n(%)

• Alive without disease	28 (44)
• Alive with disease	16 (25)
• Dead of disease	5 (8)
• One year not reached	15 (23)

\*n=80 individual case discussions s

discussed was distributed to all HCPs before each MDT. A video- and telephone conference system was used for the first two years, and thereafter Webex meetings. After each MDT, a meeting summary with treatment recommendations was sent to all HCPs and the project manager at the coordinating centre. MDT format and outcomes were discussed at G2 domain meetings. Data regarding clinical characteristics of discussed cases and treatment recommendations were registered in a prospective database. Follow up data were retrieved until May 15, 2021.

**Result(s)\*** Between November 2017 and December 2020, 31 MDTs were held with participants from 10 countries and 20 HCPs. 91 individual patients were discussed between one and six times for a total of 109 case discussions. Background data is presented in table 1. Follow-up data was retrieved from 64 patients and 80 case discussions (table 2). Adherence to treatment recommendations was 99%. As a result of MDT recommendations, 11 patients got access to off-label treatment and one patient was enrolled in a clinical trial in another European country. 14/91 patients were recommended surveillance only.

**Conclusion\*** Cross-border MDTs enable networking and clinical collaboration between health care professionals in different countries. Surveillance strategies, off-label drug use and participation in clinical trials in other countries are possible benefits to patients with rare gynecological tumours.

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### PELVIC EXENTERATION FOR LOCALLY ADVANCED AND RELAPSED GYNECOLOGIC CANCER: MORBIDITY AND LONG-TERM SURVIVAL

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**Introduction/Background\*** Pelvic exenteration (PE) can be described as the most radical surgery performed in patients with recurrence or persistence of gynecologic cancer. The aim of this study was to evaluate morbidity and survival after PE. Furthermore we analyzed the impact of type of PE and age on survival.

**Methodology** This is a retrospective observational study including patients with histological diagnosis of gynecologic malignant pelvic tumor (cervix, ovary, endometrium, vulva, vagina,

and sarcoma), who underwent PE with curative intention at our institution between 1999 and 2021.

Overall survival (OS) was assessed with Kaplan-Meier analysis. Differences in survival according to type of PE (anterior, posterior or total) were assessed using log-rank tests. Multivariate analysis using Cox-proportional hazard models was performed to determine the impact of age on survival outcomes. Results were considered statistically significant when  $p < 0,05$ .

**Result(s)\*** In total, 56 patients were included in the study. Average age at the time of surgery was 58,3 (SD 14,4) years. Distribution of tumor site was: ovary (n=32), cervix (n=10), endometrium (n=8), vulva/vagina (n=6). PE was anterior (n=6), posterior (n=31) or total (n=19).

One case of intraoperative complication was observed, with a vascular lesion that was sutured with no further aggravation. Overall, morbidity occurred in 46,4% of patients; 18 (32,1%) developed early complications and 8 (14,3%) developed at least one late complication, including 7 gastrointestinal, 3 urinary, 4 incision hernias and 11 infectious complications. Fourteen cases required reintervention due to complications. Only one case of early postoperative death was recorded.

The 5-year OS in remaining cases was 31%. Median follow-up time was 22,5 months (range: 1-242). Mean overall survival tended to be longer for patients with anterior PE (150,6 months, SD 49,5) than for patients with posterior PE (51,0 months, SD 11,3) or total PE (41,2 months, SD 14,3), although this difference was not statistically significant ( $p=0,113$ ). The 5-year OS was 60%, 25% and 25%, respectively. Age had no impact on survival.

**Conclusion\*** PE is still the only curative option for selected patients, when chemoradiation and/or primary surgery failed in recurrent or persistent gynecological malignancies. When performed by expert gynecologic-oncology surgeons, this intervention has an acceptable survival and perioperative morbidity rate.

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#### LOCAL ANDROGEN SYNTHESIS AND METABOLISM IN ENDOMETRIAL AND OVARIAN CANCER

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**Introduction/Background\*** Endometrial (EC) and ovarian cancer (OC) are female pathologies that express androgen receptor (AR) to different extents, however, the role of the AR ligands, i.e., androgens and their 11-oxygenated metabolites in EC and OC onset and progression is poorly understood. Active androgens can form from the abundant precursor dehydroepiandrosterone sulfate (DHEA-S) from the adrenal cortex; however, local synthesis and metabolism in endometrial and ovarian cancer tissue may have important roles as well.

**Objective** To explore the local androgen synthesis and metabolism in EC and OC.

**Methodology** Gene expression of key enzymes involved in the androgen synthesis and metabolism was examined in model cell lines of type I and II EC, and high grade serous OC. The Cancer Genome Atlas (TCGA) database was searched for the expression of these genes in EC and OC tissues using the UCSC Xena platform.

**Result(s)\*** Our gene expression data indicate that model cell lines of EC and OC can potentially synthesize the potent

androgens testosterone (T) and 5 $\alpha$ -dihydrotestosterone (5 $\alpha$ -DHT) from DHEA-S, as well as the equally potent metabolites 11-keto-T and 11-keto-DHT from the adrenal precursor 11-OH-androstendione. Interestingly, the expression of *AKR1C3*, encoding an aldo-keto reductase family enzyme that catalyses the formation of T and 11-keto-T, and the expression of *SRD5A1*, encoding a steroid 5 $\alpha$ -reductase that catalyses the conversion of T to 5 $\alpha$ -DHT were higher in certain model cell lines of EC and OC comparing to the respective controls. According to the TCGA database, *SRD5A1* expression correlates with a worse overall survival in EC, whereas *HSD11B2* expression with a positive progression free survival in OC.

**Conclusion\*** Gene expression analysis indicate that active androgens and 11-oxyandrogens can form in EC and OC. Further metabolism studies are in progress. Assessment of the effect of androgens and their metabolites on EC and OC development and determination of their systemic levels may unravel novel therapeutic targets and new diagnostic and prognostic biomarkers.

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#### PROGNOSTIC FACTORS AND SURVIVAL OF PATIENTS WITH UTERINE SARCOMA – A GERMAN UNICENTRIC ANALYSIS

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**Introduction/Background\*** Uterine sarcoma (US) as a histologically heterogeneous group of tumours is rare and associated with a poor prognosis. This study aimed to describe the survival and identify prognostic variables in patients with US.

**Methodology** This unicentric, retrospective cohort study includes 57 patients with US over 18 years treated at the Department of Obstetrics and Gynaecology at University Hospital Freiburg, Germany between 1999 and 2017. Progression-free survival (PFS) and overall survival (OS) were calculated and visualised in Kaplan-Meier curves. Prognostic factors for total cohort and Leiomyosarcoma (LMS) patients were identified using log-rank test and Cox-regression.

**Result(s)\*** 44 LMS, seven low grade-endometrial stromal sarcoma (LG-ESS), four high grade-ESS and two undifferentiated US patients were identified. The median age at time of diagnosis was 51.0 years (range 18–83). The median follow-up time was 35 months. PFS for the total cohort was 14.0 months (95%-Confidence-Interval (CI) 9.7-18.3) and OS 36.0 months (95%-CI 22.1–49.9). Tumour pathology was prognostically significant for OS with LG-ESS being the most favourable (mean OS 150.3 months). In the multivariate analysis, patients over 52 years showed a four times higher risk for tumour recurrence (hazard ratio (HR) 4.4; 95%-CI 1.5-12.9). Progesterone receptor negativity was associated with a two times higher risk for death (HR 2.8; 95%-CI 1.0-7.5). For LMS patients in the univariate analysis young age ( $p=0.04$ ), clear surgical margins ( $p=0.008$ ), low FIGO stage ( $p=0.01$ ) and no application of chemotherapy ( $p=0.02$ ) were statistically significant positive factors for OS.

**Conclusion\*** In this analysis, tumour histology, age at time of diagnosis and progesterone receptor status were prognostic factors for US. Unfavourable OS in LMS patients was