2022-RA-1314-ESGO  EVALUATION OF THE CONCENTRATION OF THE SOLUBLE FORM OF PROGRAMMED CELL DEATH-LIGAND 2 IN PATIENTS WITH ENDOMETRIAL CANCER

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Introduction/Background Endometrial cancer (EC) is the most common gynecological cancer and the second most common female malignancy in the developed world. Circulating soluble programmed death-2 ligand (sPD-L2) plays a crucial role within the tumor microenvironment for tumorigenesis. Not much is known about the functional consequence of cell surface-expressed PD-L2 or sPD-L2 in oncologic diseases, but understanding the molecular alterations involved in endometrial cancer provides personalized treatments through the incorporation of targeted therapies.

Methodology Our study aimed to investigate the percentage of peripheral blood (PB) monocytes (MO) with PD-L2 expression, and the prevalence of the sPD-L2 in the plasma of patients with endometrial cancer in comparison to healthy blood donors.

The percentage of PD-L2 positive MO was evaluated by flow cytometry. Soluble PD-L2 levels in the plasma of the EC patients (n=45) and the plasma of the healthy blood donors (n=20) were investigated via an immunoassay kit ELISA (sPD-L2 as specified by the manufacturer Invitrogen, USA). Plate absorbance was read on an ELX-800 plate reader (BioTek Instruments, Inc, USA) and analyzed by Gen5_ (BioTek 218 Instruments, Inc). The concentrations of sPD-L2 (pg/mL) were calculated via interpolation from a standard curve.

Results The concentrations of sPD-L2 in the plasma of the EC patients were: median 134.720, range 47.696–321.12 pg/mL. The concentrations of sPD-L2 in the plasma of the control group were: median 9446.710, range 7767.216–11551.89 pg/mL. The sPD-L2 levels in the plasma of patients with endometrial cancer were significantly lower than in the control group (p<0.0001). The percentage of PD-L2 positive MO was significantly lower in the PB of patients with EC than in the control group (3.32% vs. 71.48% p<0.0001).

Conclusion There are significant differences in both, the percentage of PD-L2 positive MO, and sPD-L2 levels in patients with endometrial cancer and healthy women.

2022-RA-1315-ESGO  ANTI-LSR MONOCLONAL ANTIBODY EXERTS AN ANTITUMOR ACTIVITY ASSOCIATED WITH APOPTOSIS IN ENDOMETRIAL CANCER

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Introduction/Background Advanced endometrial cancer (EC) remains a disease with a poor prognosis. Since the efficacy of current chemotherapy is limited, new therapeutic agents are needed to be investigated. We focused on lipopolysaccharide-stimulated lipoprotein receptor (LSR), a membrane protein highly expressed in EC cells, and developed a novel chimeric chicken-mouse anti-LSR monoclonal antibody (mAb). The aim of this study was to investigate the function of LSR and the antitumor activity of anti-LSR mAb in EC.

Methodology The relationship between LSR expression level and clinical outcomes was investigated using immunohistochemistry in 230 clinical samples of EC. To clarify the function of LSR, we conducted in vitro assays using LSR-knockdown EC cell lines (HEC1 and HEC116) generated by transfected with siRNA. We investigated the antitumor activity of anti-LSR mAb in EC cell xenograft mouse model.

Results Patients were divided into two groups based on LSR expression level; High-LSR (n=153) and Low-LSR (n=75) groups. The 5-year overall survival rate in High-LSR group was significantly lower than that in Low-LSR group (hazard ratio: 3.53, 95% confidence interval: 1.35–9.24, p=0.01). In addition, High-LSR expression was associated with deep myometrial invasion and distant metastasis in EC (p < 0.05, respectively). In vitro analysis demonstrated that LSR-knockdown suppressed the activation of MEK/ERK signaling and subsequent matrix metalloproteinases (MT1-MMP and MMP2), which downregulated cell proliferation, invasion, and migration. Our anti-LSR mAb significantly inhibited the tumor growth in EC cell xenograft mouse model (p = 0.019). Anti-LSR mAb suppressed the activation of ERK1/2 and increased the expression of cleaved caspase-3 in vivo. Moreover, anti-LSR mAb also suppressed the activation of MEK/ERK signaling in vitro.

Conclusion LSR is associated with tumor growth, invasion, metastasis, and poor prognosis through MAPK signaling in EC. Anti-LSR mAb is a potential therapeutic agent which induces apoptosis and shows a significant antitumor effect in EC.

2022-RA-1321-ESGO  ROBOT ASSISTED VAGINAL NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC HYSTEROECTION FOR PATIENTS WITH STAGE III A ENDOMETRIAL CANCER-FARGHALY’S TECHNIQUE

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Introduction/Background Natural orifice transluminal endoscopy (NOTES) minimally invasive surgery improves cosmetic outcomes and reduces surgical injury. This in turn decreases the inflammatory and neuroendocrine responses resulting in less postoperative pain and quicker recovery.

Methodology Patients with stage I/IIA endometrial cancer are selected for this procedure.

The HominisTM Surgical System is used. The System consists of sterile components: the Hominis ArmsTM and the GYNTracor Kit, and non-sterile capital equipment: the ControlConsole and the Motor Units. The Arms are inserted transvaginally through the posterior fornix to the pelvic cavity, retroflexed towards the point of entry. This enables
performing the procedure with a clear view and reaching various structures in the pelvic cavity. Each Arm corresponds to the respective hand of the surgeon as controlled by the right and left Joysticks. The surgeon controls the Hominis Arms through two Hominis motor units, the motor units house a motorized prismatic joint that enables controlled linear motion to insert and extract the Arms from the pelvic cavity. Blunt dissection is performed with vaginal total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, approximation, and electrosurgery, using monopolar and bipolar energy systems. The vaginal cuff is closed with Vicryl sutures.

**Results**

The procedure is successfully performed. No conversion to standard multi-incision laparoscopy or laparotomy is necessary. Mean vaginal time is 19 minutes, mean docking time is 18 minutes, and mean console time is 35 minutes. The mean drop in hemoglobin level is 1.3 g/dl. Most patients score a low postoperative pain score (range 3–6).

**Conclusion**

Robot-assisted natural orifice vaginal hysterectomy for early-stage endometrial cancer – Farghaly’s Technique is associated with minimal blood loss, short operative time and length of hospital stay, lower pain score, and low use of analgesics. Thus, it may be considered a reasonable alternative to the robot-assisted abdominal approach in medically compromised women.

**Abstracts**

**2022-RA-1322-ESGO**

**A FEASIBILITY STUDY OF ENDOMETRIAL CAVITY CYTOLOGICAL SAMPLING FOR PRECISION TREATMENT IN ENDOMETRIAL CANCER**

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**Introduction/Background**

Understanding biological characteristics of endometrial cancer (EC) has opened possibilities of treatment individualisation. Enabling non-invasive methods of evaluation in patients with EC can therefore aid decision making in the office setting. Herein, we present the feasibility study evaluating endometrial cytological sampling and mutational analysis of catenin beta-1 (*CTNNB1*) gene to aid integrated molecular classification of tumours prior to treatment.

**Methodology**

Women were recruited at the University Medical Centre Maribor between November 2020 to May 2022. Prior to surgical treatment for benign disease or EC, endometrial cytological sample was obtained using Endobrush (Lab CCD, Paris, France) and stored in DNA/RNA Shield™. Tumour biopsies were stored following routine pathologic examination. DNA was extracted from tumours and cytological samples using QIAamp DNA Mini Kit and Quick-DNA/RNA MinPrep Plus Kit, respectively. Sanger sequencing was used to detect mutations in the exon 3 of *CTNNB1*. Cytological samples were compared to tumour tissue. Continuous variables were expressed as median, and proportions indicated as percentages. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for *CTNNB1* mutational status determination.

**Results**

Patient characteristics are presented in table 1. Among 24 women included in the study, 2 patients (8%) were identified having *CTNNB1*-mutated tumours. *CTNNB1* mutational status was not confirmed in cytological samples. The current approach to tissue sampling resulted in 50% sensitivity and 100% sampling specificity. The positive predictive value was 100% and the negative predictive value 94.7%. The test diagnostic accuracy is currently 92.3%. Cytology DNA isolation failure was present in one women with FIGO IA disease and in a control sample.

**Conclusion**

DNA isolation from endometrial cytology samples was successful in 91% of samples and isolation of *CTNNB1* mutations showed an appropriate level of specificity, but optimisation of sensitivity is needed for clinical use implementation.

**2022-RA-1323-ESGO**

**ENDOMETRIAL CANCER AGGRESSIVENESS MAY BE ASSOCIATED WITH EXPOSURE TO PHTHALATES**

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**Introduction/Background**

Phthalates are endocrine-disrupting chemicals (EDCs) widely used in consumer products. They can competitively bind to oestrogen and androgen receptors and impact signalling. In vitro studies have shown certain phthalates to cause considerable inflammatory reaction. Analysis of cellular lines exposure indicates butyl-benzyl phthalate (BBP) to influence transcription and miRNA expression. Certain phthalates, such as dibutyl phthalate (DBP) have also been directly associated with increased EC risk. Common phthalate esters (diethyl phthalate (DEP) and DBP) were evaluated in this study to examine the association of exposure to phthalates with EC risk profiles.

**Methodology**

A prospective, single-centre, cohort study including all women diagnosed with EC between December 2020 and February 2022. Patients were asked to provide a urine sample, peripheral venous blood sample as well as complete a lifestyle questionnaire before management. Gas chromatography-mass spectrometry (GC-MS) was used to detect phthalates. All results were adjusted for urinary dilution by measuring urinary creatinine levels.

**Results**

Thirty-nine women with a median age 60 (range 35–86) were included in this study, 29 women (74%) were diagnosed at FIGO I and II stage of the disease, while others were diagnosed at advanced stage. Women were stratified based on

**Abstract 2022-RA-1322-ESGO Table 1**

<table>
<thead>
<tr>
<th>Patient cohort characteristics</th>
<th>No. of patients</th>
<th>Parity</th>
<th>Menopausal status</th>
<th>Body Mass Index (BMI)</th>
<th>FIGO stage</th>
<th>Molecular subgroup classification*</th>
<th>Cytoplasmatic sampling</th>
<th>Cytological sampling</th>
<th>CENPB status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Time of Diagnosis</td>
<td></td>
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<tr>
<td>70.5 years (47.84 years)</td>
<td>20</td>
<td>1 (3)</td>
<td>Pre-menopausal</td>
<td>22 women (92%)</td>
<td>IA</td>
<td>POLE mutated</td>
<td>2 samples (3.83%)</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>60 years (51.10 years)</td>
<td>19</td>
<td>2 (5)</td>
<td>Post-menopausal</td>
<td>8 women (35.7%)</td>
<td>IB</td>
<td>6p11.2 mismatch repair deficient (MMRD)</td>
<td>2 samples (3.83%)</td>
<td>2 samples (3.83%)</td>
<td>0.51</td>
</tr>
<tr>
<td>50 years (49.84 years)</td>
<td>18</td>
<td>3 (6)</td>
<td></td>
<td>4 women (16.7%)</td>
<td>I</td>
<td>6p51 abnormal (6p51)</td>
<td>2 samples (3.83%)</td>
<td>2 samples (3.83%)</td>
<td>0.44</td>
</tr>
<tr>
<td>40 years (49.84 years)</td>
<td>17</td>
<td>4 (10)</td>
<td></td>
<td>4 women (16.7%)</td>
<td>II</td>
<td>DNA isolation failure</td>
<td>2 samples (3.83%)</td>
<td>2 samples (3.83%)</td>
<td>0.44</td>
</tr>
</tbody>
</table>