Result(s)* Since the beginning of the project we recruited more than 440 patients. Discovery proteomics and discovery metabolomics phase have been concluded. Targeted proteomics and targeted metabolomics analysis are currently in progress and we are awaiting the results.
Conclusion* Within the project we expect to find different metabolic and protein profiles in patients with early stages of EC as compared to controls and in patients with poor prognosis and high risk of disease progression and recurrence as compared to those with favorable prognosis.

Great effort was put into informing the lay and expert public about the importance of the translational studies in EC. We have established an official website (https://bioendocar.eu/), Twitter profile and Facebook page (https://www.facebook.com/bioendocar) where we post all news concerning the project.

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Nothing to disclose.

416 VALIDATION OF THE PORTEC NOMOGRAMS IN PATIENTS WITH EARLY ENDOMETRIAL CANCER – A RETROSPECTIVE ANALYSIS

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Introduction/Background* Treatment for endometrial cancer consists of surgery followed by appropriate risk adapted adjuvant treatment. Pooled analysis from the PORTEC-1 and -2 trials was used in development of nomograms that incorporated mode of adjuvant treatment in predicting risk of recurrence. In the present study, we have validated performance of the PORTEC nomograms in patients with early endometrial cancer treated at a single tertiary cancer centre in India.
Methodology A retrospective analysis of patients of endometrial cancer treated with Observation (Obs), Vaginal Brachytherapy (VBT), or External beam Radiotherapy (EBRT) as adjuvant post-surgery was carried out. All patients were with endometrioid histology and had Stage I (FIGO 2009) disease. Patients who received chemotherapy were excluded. Three-hundred and eighteen patients treated between 2009-18 were included. Nomogram validation was performed by calculation of Concordance Index using Harrell's estimator.
Result(s)* Median age at diagnosis was 57 years (IQR 52-63 yrs). 201 (63.2%) patients had Stage IA disease, while 117 (36.8%) patients had Stage IB disease at presentation. According to the ESMO-ESGO-ESTRO 2016 risk stratification 168 (52.8%) patients were low risk, 76 (23.9%) patients were intermediate, 42 (13.2%) were high-intermediate and 32 (10.1%) patients were high risk. Lymphovascular space invasion was seen in 22 (7%) patients. The adjuvant therapy offered was Observation in 136 (42.8%) patients, VBT in 109 (34.2%) patients and EBRT in 73 (23%) patients. With a median follow-up of 40 months the loco-regional control, distant-relapse free survival, disease-free and over-all survival at 3-yrs were 97%, 97.3%, 94.8% and 97.8% respectively. Concordance index for Overall Survival (OS) was 0.72 (95% C.I: 0.45-0.99), for Disease-free survival (DFS) was 0.74 (95% C.I.0.66-0.83) and for Distant Relapse was 0.65 (95% C.I. 0.54-0.77). Concordance index for loco-regional recurrence could not be reliably derived.
Conclusion* The PORTEC nomograms for DFS and OS were validated in patients with stage I endometrial cancer in an Indian cohort and could be used for shared decision making regarding adjuvant treatment in patients with early endometrial cancer.

419 HYSTEROSCOPIC DIAGNOSIS OF ENDOMETRIAL CANCER IN PREMENOPAUSAL WOMEN: A DESCRIPTIVE RETROSPECTIVE STUDY

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Introduction/Background* The aim of the present study was to determine the epidemiological, clinical and diagnostic features of endometrial cancers (EC) in premenopausal women diagnosed with hysteroscope.
Methodology We conducted a descriptive retrospective study in a university hospital. We involved 2367 patients who underwent office-based hysteroscopy from 1st January 2017 to 31st December 2019. Our research identified 47 patients with histological diagnosis of EC. Of these, 6 were premenopausal women.
Result(s)* Out of the 2367 office-based hysteroscopies performed, 47 cases (1,98%) of EC diagnosed by hysteroscopic exam and endometrial sampling. 6 records (12,76%) were premenopausal. These patients were referred to our gynaecological service complaining about abnormal uterine bleeding. 5 patients (83,3%), with heavy menstrual bleeding (HMB) and one case of inter-menstrual bleeding (IMB). Premenopausal patients aged 34-52 years (mean age 42,83 years).

Risk factors of endometrial cancer to highlight in our premenopausal cohort were the following. Obesity was the strongest risk factor; 4 patients (66,6%) showed a body mass index (BMI) $\geq$30kg/m^2. The average BMI was 35kg/m^2. On the other hand, two patients had normal BMI. Additionally, we found two nulliparous women (33,3%), and two patients (33,3%) carrying Mirena IUD. We did not get any interest family history.

At the ultrasound examination, endometrial pathology was identified in 5 patients (83,3%). The most frequent ultrasonographic pathological finding was endometrial polyp in 4 cases (66,6%), two of which showed myoma too. Also, one result of submucosal myoma without other lesion.

If we focus on hysteroscopic lesions, atypical polyps were found in all cases. The final histological examination showed endometrioid endometrial adenocarcinoma. There were 3 results (50%) in situ and the other three were stage IA G1.
Conclusion* This review supports that obesity is a significant modifiable risk factor for EC during premenopause. The overall rate of BMI $\geq$ 30kg/m^2 in this study was 66%.

According to our findings, abnormal uterine bleeding is considered the guiding symptom for the diagnosis of this oncological pathology, being to one of the most frequent reasons to demand a gynecological evaluation.

Endometrial polyps are the main observed lesions in our cohort, in both ultrasound exam and hysteroscopy.

424 LSR PROMOTES TUMOR PROGRESSION BY REGULATING SIGNAL TRANSDUCTION OF APOPTOSIS AND FERROPTOSIS IN ENDOMETRIAL CANCER

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Introduction/Background* Since advanced endometrial cancer (EC) remains a disease with a poor prognosis, the development of novel therapeutic agents are warranted. Previously, we identified lipolysis-stimulated lipoprotein receptor (LSR) as a highly expressed molecule in ovarian cancer (OC) cells and developed an anti-LSR monoclonal antibody. The antibody significantly suppressed tumor growth in EC as well as OC, however the mechanism is largely unclear, and the function of LSR in cancer cells needs to be elucidated. In this study, we focused on apoptosis and ferroptosis in programmed cell deaths and investigated the function of LSR using in vitro and bioinformatic analysis.

Methodology We evaluated LSR expression by immunohistochemistry and analyzed overall survival (OS) and clinicopathological features in 228 EC patients. To investigate the mechanism by which LSR affects the prognosis of EC patients, the pathway enrichment analysis was conducted using published proteomic data of EC. In vitro analyses were performed using two human EC cell lines (HEC1 and HEC116) and the activity of signaling pathways were examined by western blotting.

Result(s)* Patients were divided into two groups based on LSR expression; High (strongly stained in ≥25% of the lesion, n=153) and Low (strongly stained in <25% of the lesion, n=75) groups. 5-year OS rate in High group was significantly lower than Low group (hazard ratio: 3.53, 95% confidence interval: 1.35 – 9.24, p=0.01). The pathway analysis demonstrated that proteins correlated with high LSR expression were enriched in MAPK signaling pathway, glutathione metabolism, and cysteine and methionine metabolism. In vitro and western blot analyses showed that LSR-knockdown suppressed EC cell proliferation and the phosphorylation of MEK/ERK signaling pathway including MEK1/2, ERK1/2, and p90RSK. ERK1/2-knockdown also suppressed cell proliferation, suggesting that LSR contributed to EC cell proliferation through the MEK/ERK pathway, which is one of the apoptotic signaling pathway. In addition, LSR-knockdown suppressed the expression of cystine/glutamate antiporter (xCT) and GPX4, which inhibit ferroptosis by regulating cystine/glutamine metabolism, as determined by western blot analysis.

Conclusion* LSR contributes to tumor progression and poor prognosis by regulating apoptotic and ferroptotic signaling pathways in endometrial cancer. LSR may be a novel therapeutic target molecule in EC.

428 COMPARING CHARACTERISTICS OF ENDOMETRIAL CANCER IN SOUTH ASIAN AND WHITE ETHNICITY WOMEN IN ENGLAND

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Introduction/Background* It is not known whether differences exist in the patient and endometrial cancer (EC) characteristics of South Asian patients currently living in England compared to women of White ethnicity.

Methodology A retrospective study of EC cases diagnosed at the University Hospitals of Leicester, UK between 2003-2018 was undertaken. Additional information on a subset of patients was available for patients recruited between January 2016 and January 2020.

Result(s)* A total of 1884 cases were included, 13% of South Asian ethnicity. South Asian women were diagnosed at a significantly younger age, mean age 60.3 years, compared to women of White ethnicity, 66.9 years, mean difference = 6.6 years (95% CI 5.1 to 8.1), p < 0.001. Rising BMI in the White ethnicity group significantly correlated with younger age at diagnosis (p < 0.001), however this association was not seen in South Asian patients. Logistic regression analysis was performed. After adjusting for the diabetes status and BMI, South Asian patients were almost three time more likely to be diagnosed with EC below the age of 55 years, as compared to White ethnicity patients, odds ratio = 2.85 (95% CI 2.01 to 4.04), p < 0.001. Analysis of a subset of 216 cases (40 South Asian and 176 White ethnicity) identified that the number of South Asian patients who were pre-menopausal at diagnosis was more than double that in the White ethnicity group, 8 of 40 cases (20%) compared to 16 of 176 cases (9.1%), (p=0.048). For the patients who were postmenopausal there was no difference in the age of menopause, median age 51 years for both groups (p=0.408).

Conclusion* There are significant differences in the demographic characteristics between co-located South Asian and White ethnicity patients diagnosed with EC, in particular age at diagnosis and greater proportion of premenopausal cases seen in the South Asian ethnicity group. Further investigation is needed to explain these differences, including dietary and activity differences, and to determine their impact on suspected cancer referral criteria.

434 CYTOREDUCTIVE SURGERY IN STAGE IV ENDOMETRIAL CANCER: A RETROSPECTIVE MULTICENTRE COHORT STUDY

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