Result(s)* Results show no statistical significance in difference between age of patients in the moment of surgical treatment ($p=0.126$). There was statistical significant difference in positive peritoneal cytology between group with endometrioid compared with nonendometrioid endometrial carcinoma ($p=0.000$) group. Also there was, statistical significant difference between group with endometrial cancer confined to uterus compare with patients with carcinoma beyond the uterus ($p=0.000$) and statistically significant was confirmed with high tumor grade ($p=0.000$).

Conclusion* The positive peritoneal cytology was found statistically significance in the group of the patients with non endometrioid type of the tumor, highest tumor grade and higher FIGO classification. For these group of patients have to consider to still recommend using peritoneal washings cytology analyses during surgery.

996 EPIGENETIC METHYLATION IN ENDOMETRIAL CANCER (EC): AN UMBRELLA REVIEW OF PUBLISHED EVIDENCE

¹K Rallis*, ²M Sideris, ¹YA Wang, ¹C Hillyar, ¹S Makker, ²E Emin, ²T Mould. ¹Barts and the London School of Medicine and Surgery, London, UK; ²University College London Hospital, London, UK; ³Kingston University, Kingston, UK

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Introduction/Background* EC is the commonest gynaecological malignancy in developed countries accounting for 97,000 deaths annually worldwide. Methylation of DNA, histones, and micro-RNA (miRNA) are important epigenetic events which predominantly repress gene expression, reversibly, thus altering the tumour-cellular phenotype. We performed an umbrella review of relevant narrative (NR) and systematic reviews (SR) to identify prognostic and/or predictive methylation biomarkers for clinical decision-making.

Methodology We followed the PRISMA guidelines and prospectively registered our protocol with PROSPERO (CRD42021225841). We searched MEDLINE from inception to December 4th, 2020, for NRs and SRs, published in English, discussing the association between methylation of DNA, histones or miRNA and early detection, prognosis or treatment response in EC. Three reviewers extracted and assessed the quality of the evidence for qualitative synthesis.

Result(s)* Our search yielded 86 publications. We included 19 articles: 2 SRs with meta-analysis and 17 NRs. Type I and II EC exhibit distinct methylation profiles of gene silencing. Type I EC contains near-diploid cells (vs. aneuploid in type II) and its progression is more strongly associated with epigenetic changes. Global hyper- or hypomethylation and CIMP are described. Gene promoter hypermethylation predominates especially in hormone receptor, MLH1, MGMT, CDKN2A/P16, WNT/b-catenin/E-cadherin, PIK3CA/MAPK/RAS, and FGF pathway components. Ribosomal DNA hypomethylation, DNA aneuploidy, and lack of *CDH13* hypermethylation predict poor prognosis. Dysregulated miRNA expression and processing differentially promotes oncogenesis. Histone methyltransferases (EZH2) and demethylases (LSD1, KDM4A/B) are overexpressed correlating with aggressiveness. Meta-analyses report significant associations with *RASSF1A* promoter methylation and *CDKN2A/p16* hypermethylation which occur early in carcinogenesis potentially aiding non-invasive detection.

Conclusion* As type I EC primarily affects younger women, some of whom have yet to complete their family, prognostication via (epigenetic) biomarkers is important for treatment

stratification. Predicting response to conservative (progestone) treatment via methylation biomarkers could help identify eligible women for 'watch and wait' until they complete their family. Artificial intelligence (AI) could facilitate such efforts.

1006 MOLECULAR SUBTYPE DIAGNOSIS OF ENDOMETRIAL CARCINOMA USING AN NGS PANEL

^{1,2}J Huvila*, ^{1,2}K Orte, ^{1,2}P Vainio, ³T Mettälä, ³T Joutsiniemi, ³S Hietanen. ¹Turku University Hospital, Department of Pathology, Finland; ²University of Turku, Department of Biomedicine, Finland; ³Turku University Hospital, Department of Obstetrics and Gynecology, Finland

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Introduction/Background* The molecular classification of endometrial carcinoma (EC) is integrated in the new ESMO-ESGO-ESTRO treatment guidelines and is needed for appropriate treatment planning. An NGS panel can be used for molecular classification, assessing *POLE* mutation status, microsatellite instability (MSI) and *TP53* mutation status. We describe the process of molecular classification on 60 EC cases based on

Abstract 1006 Figure 1

an NGS panel, identifying challenges in case classification and possible solutions.

Methodology We performed the FoundationOne CDx NGS panel on 60 EC and assigned molecular subtype: *POLE* mutated (*POLEmut*), mismatch repair deficient (MMRd), p53 abnormal (p53abn) or no specific molecular subtype (NSMP).

Result(s)* In 55 patients the molecular classification was successful. A pathogenic *POLE* mutation was detected in 9 cases (*POLEmut*). 20 were MMRd (12 MSI-high, 8 MSI-indeterminate based on the NGS panel MSI classifier) and a known or likely MMR gene mutation was found in 7 of these. Of the remaining 26 cases, 17 carried a *TP53* mutation (p53abn) and the remaining 9 were considered to be NSMP. The tumor mutation burden (TMB) was significantly different ($p < 0.001$) in the molecular subtypes (A) and high TMB (> 55 mut/MB) was 100% specific for *POLEmut* EC ($p < 0.001$). High TMB was specific for known pathogenic *POLE* mutations and was not elevated in cases with solely non-pathogenic *POLE* mutations (B).

In non-*POLEmut* cases, TMB was higher in MSI-high and MSI-indeterminate than microsatellite stable (MSS) cases (C), and a TMB of > 7 mut/MB was 100% specific for MMRd EC. There was one MSS EC with a TMB of 18 mut/MB but it showed loss of MLH1 and PMS2 proteins on immunostaining and was classified as MMRd.

Conclusion* An NGS panel can be used in the molecular classification of EC when there is sufficient tumor cellularity. TMB can be used as an adjunct in molecular subtype diagnosis for tumors that are difficult to classify. Additionally, TMB can potentially serve as a diagnostic adjunct in cases with *POLE* mutation of unknown significance.

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THE ROLE OF GENITAL TRACT MICROBIOTA CONTINUUM IN ENDOMETRIAL MALIGNANCY

^{1,2}A Semertzidou*, ¹D Macintyre, ¹J Marchesi, ^{1,2}P Bennett, ^{1,2,3}M Kyrgiou. ¹Imperial College London, Metabolism, Digestion and Reproduction, London, UK; ²Queen Charlotte's and Chelsea- Hammersmith Hospital, Imperial Healthcare NHS Trust, London, UK; ³Imperial college London, Metabolism, Digestion and Reproduction, London, UK

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Introduction/Background* Endometrial cancer has a dominant place among gynaecological cancers and is the fourth most common malignancy in women. Accumulating reports have associated gynaecological precancer and cancer with dysbiotic microenvironments. Our aim was to identify a microbial signature in endometrial cancer and explore its role in disease pathogenesis.

Methodology Eligibility criteria included patients undergoing total abdominal/laparoscopic hysterectomy for endometrial cancer or benign indications. Microbiome swabs were collected along the female genital tract (FGT) (vagina, external cervical os, endometrium, fallopian tubes and ovaries) and rectum. The V1-V2 hypervariable regions of 16S rRNA genes were sequenced (Illumina MiSeq platform), data were analysed with Mothur software package and OTU taxonomies were determined. Benign and malignant endometrial organoids were cultured and treated with increasing concentrations (10%, 20%, 30%) of *L. crispatus*- conditioned media. Proliferation was assessed by the CellTiter-Glo® 3D cell viability assay and cytokine/chemokine secretion (IL-1 β , IL-1ra, IL-2, IL-6, IL-8, IL-10, G-CSF, GM-CSF, IFN- γ , TNF- α , CCL4/MIP1beta,

CCL5/RANTES) by the Magnetic Multiplex Cytokine Array (R&D systems).

Result(s)* Sixty-one women were recruited; 37 had endometrial cancer and 24 were benign controls. We confirmed the presence of a genuine, low- abundance microbiome above background contamination in the endometrium, fallopian tubes and ovaries in a subset of benign and endometrial cancer patients, which was one- four orders of magnitude lower than the heavily colonised vagina, cervix and rectum. In 75% (12/16) of benign patients, we found that the most abundant species of the lower genital tract could also be recovered from the whole length of the upper genital tract, while the microbial continuum was less cohesive in endometrial malignancy. We also demonstrated that *Lactobacillus* depletion and high microbial diversity along the genital tract are characteristic in endometrial cancer patients with concurrent enrichment of *Porphyromonas*, *Prevotella*, *Peptoniphilus* and *Anaerococcus*. Different histotypes and grades of endometrial cancer were not marked by microbial differences. *L. crispatus*, a FGT commensal that is depleted in endometrial cancer, was shown to reduce viability of endometrial cancer organoids at high concentrations and impact on cytokine secretion by benign and malignant endometrial organoids.

Conclusion* Endometrial cancer displays a distinct microbial signature. *L. crispatus* may exert an anti- proliferative effect in endometrial cancer and interfere with inflammatory pathways.

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INTERIM ANALYSIS OF 10-YEAR DATA REGARDING TREATMENT AND PROGNOSIS OF UTERINE CARCINOSARCOMA CASES ACROSS THE THAMES VALLEY CANCER ALLIANCE NETWORK

¹SL Smyth*, ²A Gkorila, ³A Mcculloch, ⁴P Tupper, ²A Sattar, ²N Sadeghi, ²S Spencer, ²K Zarrindej, ²V Le Thanh, ²J Rencher, ²G Sharma, ²A Kashif, ²M Abdalla, ¹S Addley, ⁵S Siddiki, ²M Alazzam, ²H Soleymani Majid. ¹Churchill Hospital, Gynaecological Oncology, Oxford, UK; ²John Radcliffe Hospital, Oxford, UK; ³Royal Berkshire Hospital, UK; ⁴Stoke Mandeville Hospital, UK; ⁵Great Western Hospital, UK

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Introduction/Background* Uterine Carcinosarcoma (UCS) comprises $< 5\%$ of uterine malignancies, accounting for $> 15\%$ associated mortality. With no established guidelines, we present our experience to determine optimal treatment and prognosis of UCS.

Methodology We conducted a multicentre retrospective cohort study, including all surgically managed UCS cases between March 2010 and January 2020. Data was collected on FIGO staging and post-operative management, recurrence and survival outcomes.

Result(s)* 82 (9.7%) UCS cases were identified. Table 1 demonstrates case staging and management strategies. 23 patients underwent surgery alone due to poor performance status, comorbidities, age or treatment refusal. 15.8% had lymph nodes metastases, which was in keeping with the literature. Recurrence occurred in 47.8% and 77.8% of cases of early and late stage respectively; most frequently in the pelvis, but also commonly in the pelvic lymph nodes and chest. Both recurrence and subsequent death usually occurred within the first 1-2 years following treatment. This retrospective analysis explores for significance in overall and disease free survival between disease stage groups and treatment modalities using univariable and multivariable Cox regression models and Kaplan-Meier curves.