Introduction/Background Biomarkers are used to classify endometrial cancer (EC) into molecular subtypes such as TCGA and/or a surrogate classification (POLc mutated [mut], mismatch repair/microsatellite instability [MMR/MSI], TP53mut, and no specific mutation profile [NSMP]) or by estrogen receptor (ER) status. Here, we report on a post hoc analysis of objective response rate (ORR) by a surrogate classification of ER status. Here, we report on a post hoc analysis of objective response rate (ORR) by a surrogate classification of ER status.

Methodology GARNET is a multicentre, open-label, single-arm phase 1 study. Patients were assigned to cohort A1 (MMR deficient/MSI-high [dMMR/MSI-H EC]) or A2 (MMR proficient/microsatellite stable [MMRp/MSI-EC]) based on local assessment. Patients received 500 mg of dostarlimab IV Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal. The primary endpoints were ORR and duration of response by blinded independent central review. Molecular subtype was determined by POLc and TP53 mutation status by Foundation Medicine, and MMR/MSI status was determined by local immunohistochemistry or next-generation sequencing; all others were assigned as NSMP. The hierarchy for classification was POLcmut → MMR/MSI → TP53 status → NSMP. ER status was determined by local immunohistochemistry testing. Only patients with samples available for additional biomarker testing were included in the biomarker analysis.

Results 143 patients with dMMR/MSI-H EC and 156 patients with MMRp/MSI were included in the efficacy-evaluable population. ORRs were determined for molecular subtypes and ER expression (table 1). Safety has been previously reported.
Additionally, 30 hr-HPV+ women, who developed CIN3 at the first follow-up, then were surgically treated for the disease and testing hr-HPV- after, were also included. Exfoliated cervical specimens were used for whole genomic and bacterial DNA extraction. Vaginal microbiota composition was determined by 16S rRNA gene fragments sequencing. The SS methylation classifier assays were performed as previously described (Brentnall et al, 2015).

**Results** We identified unique microbial biomarkers associated with CIN3 development and recovery after surgical treatment. Hr-HPV+ women with CIN3 showed a significant overrepresentation of following microbial species: *Sneathia amnii*, *Megasphaera genomops*, *Pepstoportiococcus anaerobius* and *Achromobacter spanius*. *Sneathia amnii* was the only bacteria consistently associated with CIN3 in all group comparisons performed (p<0.01). Conversely, after successful treatment women were hr-HPV- and exhibited an increased representation of *Lactobacillus* species, especially *Lactobacillus gasseri* (p<0.01). Higher proportions of *Lactobacillus helveticus*, *Lactobacillus sputorynemus* and *Lactobacillus vaginalis* showed a potential protective role against CIN3 development in women with persistent hr-HPV infection. We confirmed SS scores are increasing with cervical disease severity. Increasing *Sneathia amnii* abundance was directly proportional to SS score increase during cervical disease development.

**Conclusion** Our results might indicate *Sneathia amnii* possible role in modifying the epigenetic landscape of the cervicovaginal space. Further investigations are required to establish a link between the identified potential vaginal microbiome biomarkers and their influence on epigenetic mechanisms.

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**Abstract 2022-RA-1198-ESGO**

**POST HOC ANALYSIS OF OBJECTIVE RESPONSE RATE BY MISMATCH REPAIR PROTEIN DIMER LOSS/MUTATION STATUS IN PATIENTS WITH MISMATCH REPAIR DEFICIENT ENDOMETRIAL CANCER TREATED WITH DOSTARLIMAB**

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**Introduction/Background** Mismatch repair (MMR) deficiency is caused by loss of expression of MMR proteins, MLH1, PMS2, MSH2, and/or MSH6, that function as homodimers (MLH1/PMS2 and MSH2/MSH6) to mediate DNA repair. Loss of function caused by mutation or epigenetic methylation leads to defective MMR and genomic instability. MMR deficient (dMMR) tumours can respond to anti-programmed death 1 (anti-PD-1) therapy. We report a post hoc analysis of objective response rate (ORR) with loss of MMR dimers and mutation status of MMR genes in patients with dMMR endometrial cancer (EC) treated with dostarlimab.

**Methodology** GARNET is a multicentre, open-label, single-arm phase 1 study. Cohort A1 enrolled patients with dMMR advanced/recurrent EC. Patients received 500 mg of dostarlimab intravenously Q3W for 4 cycles, then 1000 mg Q6W until disease progression, discontinuation, or withdrawal. MMR protein status (presence or loss) was determined by local immunohistochemistry. MMR gene mutation was determined by FoundationOne. MLH1 loss without MMR gene mutation was a surrogate indicator for epigenetic methylation.

**Results** Cohort A1 included 143 patients; MMR gene mutation data were available for 101 patients (table 1). Cohort A1 ORR was 45.5%, 66% of patients had loss of MLH1/PMS2; ORR was 48.9%. 11.2% of patients had loss of MSH2/MSH6; ORR was 56.2%. ORR was 41.7% for MLH1 loss with MMR gene mutation and 39.4% for MLH1 loss without MMR gene mutation.

**Conclusion** Patients with dMMR advanced/recurrent EC benefitted from dostarlimab, with no noticeable difference by dimer-pair loss or MMR gene methylation/mutation status. These data suggest the route to MMR deficiency does not influence response to dostarlimab.

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**Abstract 2022-RA-1218-ESGO**

**PHYSIOLOGICALLY RELEVANT TREATMENT MODELS TO INVESTIGATE EPIGENETIC MECHANISMS DRIVING PLATINUM RESISTANCE IN OVARIAN HIGH GRADE SEROUS CARCINOMA**

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**Introduction/Background** The prognosis for patients with platinum-resistant ovarian High Grade Serous Carcinoma (HGSC) remains poor. Data from the BriTROC-1 study...