

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 S5 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 genomosp.*, *Peptostreptococcus 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 suntoryeus* and *Lactobacillus vaginalis* showed a potential protective role against CIN3 development in women with persistent hr-HPV infection. We confirmed S5 scores are increasing with cervical disease severity. Increasing *Sneathia amnii* abundance was directly proportional to S5 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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**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 heterodimers (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.

**Abstract 2022-RA-1198-ESGO Table 1**

	Patients, N	Responders, n	ORR, % (95% exact CI)
Cohort A1	143	65	45.5 (37.1–54.0)
MLH1/PMS2 loss	94	46	48.9 (38.5–59.5)
MSH2/MSH6 loss	16	9	56.2 (29.9–80.2)
Other <sup>a</sup>	33	10	30.3 (15.6–48.7)
Patients with mutation data	101	—	—
MLH1 loss	78	31	39.7 (28.8–51.5)
MLH1 loss and mutation in MMR gene	12	5	41.7 (15.2–72.3)
MLH1 loss and no mutation in MMR gene	66	26	39.4 (27.6–52.2)

<sup>a</sup>Other includes any other pattern of absence of expression of 1 or greater MMR proteins. MMR, mismatch repair; ORR, objective response rate.

**Conclusion** Patients with dMMR advanced/recurrent EC benefited 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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**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