tumours, 1 primary juvenile granulosa cell tumour and 1 primary Sertoli-Leydig cell tumour. Three samples were obtained from treatment-naïve GCT (2 immature teratomas and one dysgerminoma). For each phenotype of tumour cells, immune cells, endothelial cells and cancer-associated fibroblasts, we identified specific transcriptomic markers.

Results Based on differential expression analysis and expression of transcriptomic markers, we identified 27 clusters consisting of 9 tumour cell and 18 stromal cell clusters. The first results of subcluster analysis revealed nearly absence of B cells in all granulosa cell tumours. In addition, the immune cell subcluster mainly consists of T cells derived from the dysgerminoma (58%) and Sertoli-Leydig cell (20%) samples. Further characterisation and differentiation of distinct subclusters is currently ongoing and will be presented.

Conclusion With this analysis we aim to generate a publicly accessible comprehensive blueprint of the tumour micro-environment, aiding other researchers to gain high-resolution insights in the heterogeneity and complexity of these rare ovarian cancers.

2022-RA-1194-ESGO EFFICACY OF DOSTARLIMAB IN ENDOMETRIAL CANCER BY MOLECULAR SUBTYPE: A POST HOC ANALYSIS OF THE GARNET STUDY

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Introduction/Background Biomarkers are used to classify endometrial cancer (EC) into molecular subtypes such as TCGA and/or a surrogate classification (POLϵ 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 for EC in patients receiving dostarlimab monotherapy.

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/MSS] 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 POLϵ 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 POLϵmut → 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 assessment.

Results 143 patients with dMMR/MSI-H EC and 156 patients with MMRp/MSS were included in the efficacy-evaluable population. ORRs were determined for molecular subtypes and ER expression (table 1). Safety has been previously reported.

Abstract 2022-RA-1194-ESGO Table 1

	A1			A2		
Overall	65/143, 45.5% (37.1–54.0)			24/156, 15.4% (10.1–22.0)		
Molecular subtype	**N=101**			**N=153**		
POLεmut	2/3, 66.7% (9.4–99.2)			0/2, 0% (0.0–84.2)		
dMMR/MSI-H	43/98, 43.9% (33.9–54.3)					
	TP53mut 10/26, 38.5% (20.2–59.4)	TP53wt 33/72, 45.8% (34.0–58.0)				
	ERpos 19/44, 43.2% (28.3–59.0)	ERneg 1/2, 50.0% (1.3–98.7)	ERunk 23/52, 44.2% (28.3–59.0)			
TP53mut				17/94, 18.1% (10.9–27.4)		
				ERpos 4/28, 14.3% (4.0–32.7)	ERneg 7/19, 36.8% (16.3–61.6)	ERunk 6/47, 12.8% (4.8–25.7)
NSMP				7/57 12.3% (5.1–23.7)		
				ERpos 2/19, 10.5% (1.3–33.1)	ERneg 2/11, 18.2% (2.3–51.8)	ERunk 3/27, 11.1% (2.4–29.2)

Data are n/N, % (95% CI). Data cut: 1 November 2021.
dMMR, mismatch repair deficient; ERneg, ER negative; ERpos, ER positive; ERunk, ER unknown; MSI-H, microsatellite instability–high; mut, mutated; NSMP, no specific mutation profile; wt, wild-type.

Conclusion The observed ORRs in each molecular subgroup were consistent with the overall ORR in each cohort. Differences by ER expression status were not observed. These findings support the importance of testing patients with EC for MMR/MSI biomarker status as a predictor of response. Additionally, data suggest that TP53 mutation or ER expression should not modify treatment approach. The data are of interest for hypothesis generation.

2022-RA-1195-ESGO LONGITUDINAL STUDY OF VAGINAL MICROBIOME PRE- AND POST-TREATMENT IDENTIFIES BIOMARKERS FOR CERVICAL INTRAEPITHELIAL NEOPLASIA 3 (CIN3)

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Introduction/Background Increasing evidence suggests vaginal dysbiosis is associated with persistence of human papillomavirus (HPV) infection and cervical intraepithelial neoplasia (CIN1–3) development. In this pilot study we aimed to investigate the potential of vaginal microbiome biomarkers to predict CIN3 development in high risk HPV positive (hr-HPV+) women.

Methodology 59 women with normal cytology at initial screening and follow-up over six years were enrolled from ARTISTIC trial. The cohort included 14 hr-HPV negative (hr-HPV-) and 15 hr-HPV+ women through whole follow-up.

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.*, *Peptosterptoccocus 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.

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 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[a]	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)

[a]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 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.

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