Conclusion Ngs can help classify rare deseases if the classical pathological diagnostics do not give a satisfying diagnosis. There are currently no clear treatment recommendations for STK11 adnexal tumors yet. International registries and solid clinical follow-up data are urgently needed to enhance our knowledge on these potentially aggressive tumors.

2022-RA-945-ESGO ANTITUMOUR ACTIVITY OF DOSTARLIMAB BY PD-L1 AND TUMOUR MUTATION BURDEN IN PATIENTS WITH MISMATCH REPAIR DEFICIENT AND PROFICIENT TUMOURS IN THE GARNET TRIAL

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10.1136/ijgc-2022-ESGO.878

Introduction/Background Dostarlimab is a programmed death 1 (PD-1) inhibitor approved as monotherapy in patients with mismatch repair deficient (dMMR) recurrent/advanced endometrial cancer (EC) that has progressed on or after platinum-based chemotherapy or solid tumours that have progressed on or after prior treatment, with no satisfactory alternative treatment options. We report a post hoc analysis of antitumour activity by PDL1 expression and tumour mutational burden (TMB) in patients with dMMR and MMR proficient (MMRp) solid tumours in the GARNET trial.

Abstract 2022-RA-945-ESGO Table 1

	A1 (dMMR EC) N=103	F (dMMR non-EC) N=106	**A1+F (dMMR combined) N=209**	A2 (MMRp EC) N=142	**A1+A2+F (Total) N=351**
Biomarker distribution, n (%)					
TMB					
High	85 (82.5)	79 (74.5)	**164 (78.5)**	9 (6.3)	**173 (49.3)**
Low	13 (12.6)	9 (8.5)	**22 (10.5)**	129 (90.8)	**151 (43.0)**
Unknown	5 (4.9)	18 (17.0)	**23 (11.0)**	4 (2.8)	**27 (7.7)**
PDL1					
High	56 (54.4)	52 (49.1)	**108 (51.7)**	56 (39.4)	**164 (46.7)**
Low	23 (22.3)	17 (16.0)	**40 (19.1)**	45 (31.7)	**85 (24.2)**
Unknown	24 (23.3)	37 (34.9)	**61 (29.2)**	41 (28.9)	**102 (29.1)**
ORR by BICR per RECIST v1.1, n/N (%, 95% CI)[a]					
Overall	46/103 (44.7, 34.9–54.8)	41/106 (38.7, 29.4–48.6)	**87/209 (41.6, 34.9–48.6)**	19/142 (13.4, 8.3–20.1)	–
TMB-L/PDL1-L (L/L)	1/5 (20.0, 0.5–71.6)	1/3 (33.3, 0.8–90.6)	**2/8 (25.0, 3.2–65.1)**	2/43 (4.7, 0.6–15.8)	**4/51 (7.8, 2.2–18.9)**
TMB-L/PDL1-H (L/H)	2/5 (40.0, 5.3–85.3)	1/2 (50.0, 1.3–98.7)	**3/7 (42.9, 9.9–81.6)**	7/50 (14.0, 5.8–26.7)	**10/57 (17.5, 8.7–29.9)**
TMB-H/PDL1-L (H/L)	5/17 (29.4, 10.3–56.0)	3/14 (21.4, 4.7–50.8)	**8/31 (25.8, 11.9–44.6)**	0/1 (0, 0–97.5)	**8/32 (25.0, 11.5–43.4)**
TMB-H/PDL1-H (H/H)	29/50 (58.0, 43.2–71.8)	22/43 (51.2, 35.5–66.7)	**51/93 (54.8, 44.2–65.2)**	4/6 (66.7, 22.3–95.7)	**55/99 (55.6, 45.2–65.5)**

[a]Only those patients with both known TMB status and known CPS were included in ORR calculations.
BICR, blinded independent central review; CPS, combined positive score; dMMR, mismatch repair deficient; EC, endometrial cancer; H, high; L, low; MMRp, mismatch repair proficient; ORR, objective response rate; PDL1, programmed death ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TMB, tumour mutational burden.

Methodology GARNET (NCT02715284) is a phase 1, multicentre, open-label, single-arm study of dostarlimab in patients with advanced/recurrent solid tumours. Three expansion cohorts enrolled patients based on MMR status: dMMR (A1) and MMRp (A2) advanced/recurrent EC, and dMMR non-EC solid tumours (F). Patients received dostarlimab 500 mg IV Q3W for 4 cycles, then 1000 mg IV Q6W until progression or discontinuation. TMB and PDL1 were exploratory biomarkers. TMB status was determined by FoundationOne test; TMB-high (TMB-H) was defined as ≥10 mutations/Mb. PDL1 expression was determined by combined positive score (CPS) by Ventana assay; PDL1-high (PDL1-H) was defined as CPS ≥1. The study was not powered to assess antitumour activity within subgroups.

Results TMB-H and PDL1-H were common in dMMR solid tumours; PDL1-H was observed in 39.4% of MMRp EC tumours (table 1). Objective response rate (ORR) was higher in patients with TMB-H/PDL1-H tumours (55.6% for all cohorts, combined; Table). Safety for each cohort was previously reported.[1]

Conclusion PDL1-H and TMB-H were frequently observed in the dMMR EC and non-EC cohorts, regardless of tumour type; PDL1-H was also prevalent in MMRp EC tumours. Although not a powered analysis, ORR by BICR per RECIST v1.1 was higher in patients with TMB-H and PDL1-H solid tumours. Across cohorts, dMMR status was predictive of response.

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2022-RA-968-ESGO IMMUNOTHERAPY RESPONSE MONITORING USING PERSONALIZED CIRCULATING TUMOR DNA ANALYSIS IN PATIENTS WITH RELAPSED GYNECOLOGIC MALIGNANCIES

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10.1136/ijgc-2022-ESGO.879

Introduction/Background Immunotherapy has transformed cancer care. Unfortunately, responses within gynecologic malignancies have been modest when compared to other disease sites. Biomarkers for early determination of treatment benefit are urgently needed to spare unnecessary toxicity and cost. We evaluated if circulating tumor DNA (ctDNA) dynamics enable early detection of progressive disease (PD) and treatment response in patients with recurrent, gynecologic malignancies receiving immunotherapy.

Methodology Longitudinal plasma samples (n=138) were collected from 25 patients with recurrent cervical (N=6), endometrial (N=12), or ovarian (N=7) cancers who received immunotherapy. A personalized, tumor-informed multiplex PCR assay (Signatera™ bespoke mPCR NGS assay) was used for the detection of ctDNA in plasma samples.

Results Pre-treatment samples were available for 9 patients (78% ctDNA detection rate) and all 25 patients had on-treatment samples (68% ctDNA detection rate). Serially ctDNA negative patients (3/15 with imaging) had no evidence of disease on-treatment. ctDNA clearance was observed in 3 (cervical, N=2; endometrial, N=1) of the remaining 12 patients and correlated with clinical benefit. ctDNA decreased in additional 2 patients, both with objective response, while all 7 patients with increased ctDNA had PD. Increased ctDNA