methylation were 67.2% and 89.6% in all CIN3+ subjects compared with HPV16/18 (68% and 66.4%) and LBC (≥ASCUS; 93.6% and 23.6%). The specificity of HPV 16/18 and CisCer methylation combined screening method were 96.1% in CIN3+. The CIN2, CIN3, and cancer immediate risk with combined screening method were 79.2%, 61.46%, and 26.04%, respectively.

Conclusion The preliminary results indicated that the CisCer testing is promised for cervical cancer detection with high sensitivity and specificity for hrHPV. It can be used as a new non-invasive diagnosis method and its utility as a second triage step after hrHPV testing in women with cervical lesions to improve the accuracy of referral colposcopy.

2022-RA-911-ESGO ¹⁸F-FDG-PET/CT IN ORTHOTOPIC MOUSE MODELS OF ENDOMETRIAL CANCER: MULTIPARAMETRIC CHARACTERIZATION AND EVALUATION OF TREATMENT RESPONSE

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Introduction/Background Using clinically relevant imaging modalities in relevant animal models is crucial for strengthening the translational value of preclinical discoveries in endometrial cancer (EC). Imaging by ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) is commonly used in diagnostic work-up in EC. ^{18}F-FDG PET/CT in orthotopic mouse models of EC have been shown to be feasible, but standardized guidelines for image acquisition and interpretation is missing. Utilizing a large imaging database of orthotopic EC models, we aimed to characterize primary tumour ^{18}F-FDG PET parameters and assess treatment response in a subset of mice.

Methodology The database consists of 91 ^{18}F-FDG-PET-CT scans in 66 mice orthotopically implanted with patient-derived xenografts (n=30) or organoid-based patient-derived xenografts (n=36). A subset of mice was used for evaluation of treatment response (n=25). The mice were fasted for 12–16 hours prior to imaging, intravenously injected with ^{18}F-FDG and scanned for one hour. The following tumour parameters were extracted; max, mean and peak standardized uptake value (SUV_{max}/SUV_{mean}/SUV_{peak}), metabolic tumour volume, total lesion glycolysis, the 10 hottest voxels and metabolic rate of FDG. Interreader reliability between two readers were evaluated using intraclass correlation coefficient (ICC) test (n=25).

Results We utilized a 50% of SUV_{max} -segmentation threshold for tumour delineation, which correlated well with anatomical tumour volume extracted from MRI for a subset of mice (r^2=0.74, n=25). There was a significant difference between treatment and control groups for the parameters SUV_{max}(p=0.020), SUV_{peak} (p=0.038) and the 10 hottest voxels (p=0.034) and the agreement between the readers were good (ICC; 0.89–0.97).

Conclusion ^{18}F-FDG PET/CT in EC mouse models is feasible and multiple metabolic tumour features can be extracted. Using a clinically relevant imaging modality strengthens the potential for preclinical to clinical translation and reproducibility. Our work provides a basis for future studies on orthotopic mouse models of EC.

2022-RA-915-ESGO STK11 ADNEXAL TUMORS: CHALLENGE OF A NEW TUMOR ENTITY

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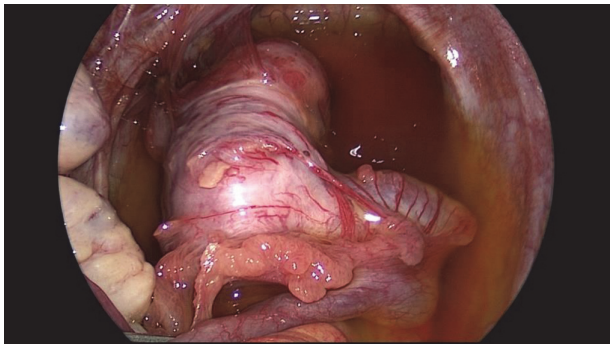
Introduction/Background STK11 adnexal tumors represent a recently novel entity of rare tumors harboring a serine/threonine kinase 11 (STK11) gene mutation. Most STK11 tumors arise from the paratubal soft tissue and frequently metastasize in the pelvis and omentum. Here, we discuss the challenging diagnosis and treatment with a case of a young woman.

Methodology A 31-year-old female was admitted to the hospital with a left adnexal mass and ascites. A transvaginal ultrasound showed a paraovarian solid tumor IOTA M1 M2; serum CA125 was 52.8kU/l. Her MRI abdomen confirmed a mass, probably originating from the Fallopian tube of 6.5x3 cm size. During laparoscopy, a solid tumor directly adjacent to the fallopian fimbriae was seen with 300 ml of serous ascites and three peritoneal nodules in the pouch of Douglas. A laparoscopic resection of all lesions including a left salpingectomy and flush cytology was performed. Histology was suspicious for a sex cord-stromal tumor with peritoneal metastases. Immunohistochemistry showed a homogenous WT1- and PAX8- positivity and a highly variable staining pattern for other markers, not leading to a conclusive diagnosis. Next-generation sequencing (ngs) showed an STK11 mutation (c.734+1G>A 86.3%), which is specific for this entity.

Results Currently, only 22 cases of these tumors are described in the literature. Characteristically, they show different growth patterns, a highly variable immunohistochemical profile and their histologic origin remains uncertain to date. In approximately 50%, there is a hereditary predisposition and association with Peutz-Jeghers syndrome (PJS). The clinical outcome is variable and depends on the completeness of the surgical resection.



Abstract 2022-RA-915-ESGO Figure 1

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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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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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