

blocks interaction with the PD-1 ligands, PD-L1 and -L2. GARNET is a phase 1 study assessing antitumour activity and safety of dostarlimab monotherapy in patients with advanced solid tumours.

Methodology This multicentre, open-label, single-arm study is being conducted in 2 parts, dose escalation and expansion. Here we report on 2 independent expansion cohorts of patients with recurrent or advanced endometrial cancer (EC) that progressed on or after a platinum-based chemotherapy regimen. Assignment to cohort A1 (mismatch mutation repair deficient [dMMR] EC) or cohort A2 (mismatch mutation repair proficient [MMRp] EC) was determined by immunohistochemistry (IHC) testing. Patients received 500 mg dostarlimab intravenously once every 3 weeks for 4 cycles, then 1000 mg once every 6 weeks until disease progression, discontinuation or withdrawal. The primary endpoints are objective response rate (ORR) and duration of response (DOR) by blinded independent central review using RECIST version 1.1.

Results In total, 126 dMMR and 145 MMRp pts identified by IHC were enrolled and dosed. Of these, 103 dMMR and 142 MMRp pts had measurable disease as baseline and sufficient follow-up time (6 months) for efficacy analyses, respectively. Patients that progressed prior to 6 months were included in the evaluable population. ORR for dMMR EC was 44.7%; ORR for MMRp EC was 13.4% (table 1). Median DOR and OS were not reached in either cohort. Overall, 15 pts (5.5%) discontinued treatment due a TRAE (5 dMMR, 10 MMRp). Safety by cohort and overall are shown in table 2. There were no deaths attributed to dostarlimab.

Conclusion Dostarlimab demonstrated durable antitumour activity in both dMMR and MMRp advanced/recurrent EC. dMMR status by IHC was associated with a higher response rate. Dostarlimab demonstrated a notable disease control rate (35.2%; 2.1% complete response, 11.3% partial response, 21.8% stable disease) in patients with MMRp EC, which comprised a higher percentage of patients with Type II EC and is historically associated with a worse prognosis. No new safety signals were detected. These cohorts are the largest prospective evaluation of a PD-(L)1 therapy in EC to date.

Disclosures Clinical trial registration: NCT02715284

This study was sponsored by GlaxoSmithKline, Waltham, MA, USA.

Dr. Oaknin reports consulting and honoraria from AstraZeneca, Tesaro, Clovis, PharmaMar, and Roche.

Dr. Gilbert reports honoraria from Meck, AstraZeneca, and Pfizer.

Dr. Tinker reports grants and personal fees from AstraZeneca.

Dr. Sabatier reports grants from EISAI and AstraZeneca; personal fees from Roche, Pfizer, Tesaro, Novartis and AstraZeneca; and non-financial support from Roche, Pfizer, AstraZeneca, and Amgen.

Dr. O'Malley reports personal fees from Immunogen, Eisai, Agenus, GSK : Consultant/Advisory Board for Clovis, Ambray, Abbvie, Janssen/J&J, Regeneron, Novacure, Myraid Genetics, Tarveda, Amgen, VentiRx, Array Biopharma, EMD Serono, Ergomed; Steering committee for Genentech/Roche and Merck; Institutional funding from Ajinomoto Inc, Ludwig Cancer Research, Stemcentrx, Inc, CERULEAN PHARMA, GOG Foundation, BMS, Serono Inc, TRACON Pharmaceuticals, Yale University, New Mexico Cancer Care Alliance, INC Research, Inc., Inventiv Health Clinical, Iovance Biotherapeutics, Inc, and PRA International.

Dr. Ghamande reports consulting fees from Seattle Genetics; speakers' bureau fees from GSK; and institutional grants from GSK, Merck, Roche, Genentech, Takeda, Seattle Genetics, Advaxis, BMS, Clovis, Abbvie, and Tesaro.

Dr. Pothuri reports grants, personal fees and non-financial support from GSK; Advisory Board fees from AstraZeneca and Clovis Oncology.

Dr. Boni has nothing to disclose.

Drs. Guo and Im are employees of GlaxoSmithKline.

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PATIENT-REPORTED OUTCOMES (PROS) IN THE GARNET TRIAL IN PATIENTS (PTS) WITH ADVANCED OR RECURRENT MISMATCH REPAIR DEFICIENT/ MICROSATELITE INSTABILITY-HIGH (dMMR/MSI-H) ENDOMETRIAL CANCER (EC) TREATED WITH DOSTARLIMAB

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10.1136/ijgc-2020-ESGO.72

Introduction/Background PROs enable direct measurement of the experiences of pts with cancer related to an intervention. Regulators increasingly use PROs to inform the risks and benefits of new drug candidates, focusing on 3 core concepts: physical functioning (PF), disease-related symptoms (DRS), and symptomatic adverse events (AEs).

Dostarlimab is an investigational anti-programmed death-1 monoclonal antibody that has shown activity in pts with advanced dMMR EC (objective response rate, 42%; disease control rate, 58%) and an acceptable safety profile. Here, we report on PROs in pts treated with dostarlimab in the single-arm GARNET trial.

Methodology Pts with recurrent or advanced dMMR/MSI-H EC that progressed on a platinum regimen received 500 mg Q3W*4 of dostarlimab, then 1000 mg Q6W until disease progression or discontinuation (DC). PRO assessment, an exploratory endpoint, was measured using the EORTC-QLQ-C30. PROs were collected at baseline (BL), each dose cycle, and after DC. For PF and DRS (pain and fatigue), we conducted multi-item descriptive analyses, including change from BL. For symptomatic AEs and tolerability (nausea, vomiting, constipation, diarrhoea, tiredness/fatigue), we conducted item-level analyses to understand response distribution and change in response categories from BL: improved, stable, and 1-, 2-, or 3-category worsening.

Results PRO data were available for 66/104 pts who received ≥ 1 dose of dostarlimab. Questionnaire compliance was consistent across domains, ranging from 100% at BL to 45% at cycle 7. Pain, fatigue, and PF were maintained above BL starting at cycles 1, 3, and 4, respectively. Symptomatic AEs were experienced by a minority of pts, with <25% and <6% of pts having 1- or ≥ 2 -category worsening, respectively. Improved scores were reported by 6% to 37% of pts.

Conclusions PROs from the GARNET trial showed that dostarlimab was generally well tolerated and disease-related symptoms were improved or maintained while on treatment. These data, along with the efficacy and safety profile of dostarlimab, support use of dostarlimab in pts with dMMR/MSI-H advanced EC.

Disclosures Clinical trial registration: NCT02715284

Funding: GlaxoSmithKline, Waltham, MA, USA

Encore statement: This data is presented on behalf of the original authors with their permission. Presented at European Society for Medical Oncology (ESMO) annual meeting, September 19–21, 2020, Virtual.

Dr. Kristeleit reports personal fees from Tesaro.

Dr. Mathews reports institutional grants from Tesaro.

Dr. Redondo reports institutional research funding from PharmaMar, Roche, and Eisai; and advisory roles at PharmaMar, AstraZeneca, Tesaro, Roche, and Eisai.

Dr. Brown reports honoraria from Olympus; consulting or advisory role at Caris, Tesaro, Clovis, AstraZeneca, and Genentech; and speakers' bureau at Clovis.

Drs. Huang, Eliason, and Im are employees of GlaxoSmithKline.

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CANCER CELL STEMNESS AND COLLAGEN REGULATORS OF STEMNESS IN UTERINE SEROUS CARCINOMA (USC) MIRROR OVARIAN SEROUS CANCER (OSC) CELL STEMNESS: EVIDENCE EMERGING FROM ARK1-USC

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10.1136/ijgc-2020-ESGO.73

Introduction/Background ARK1-USC, a highly annotated USC-derived cell line with a clinically relevant mutation spectrum,¹ is employed in vitro and in vivo for translational studies of novel USC therapies.² In ovarian cancer, stemness and malignancy-supporting collagen microenvironment coincide. Both promote resistance to therapy. Considering the shared histological and molecular characteristics of USC and OSC, we hypothesized that USC cells likewise display ovarian markers for stemness and collagen regulators of stemness. We tested this prediction in ARK1-USC.

Methodology Profiling of the time-dependent transcriptome, with flow cytometric analysis of select protein markers.

Results ARK1-USC expressed the repertoire of cancer stem cell (CSC) markers of ovarian malignancies, such as CD44, CD117, CD144, CD133, ROR1, and ALDH1A1. Relative to 12 h after plating, at 48 h expression was decreased (CD117 and ROR1 by half, FDR adjusted p-value [q] ≤ 0.003); increased (ALDH1A1 and CD144 2.5- and 2.1-fold (q=0.027 and q≤0.000, resp.); or unchanged (CD44 and CD133). ARK1-USC also expressed i) the stemness-maintaining COL18, shown in OSC³; and ii) the malignant microenvironment collagen types VI and XI, COL6A1/COL6A2/COL6A3 and COL11A1/COL11A2, shown in OSC to cause platinum resistance⁴ and poor prognosis.⁵ Using fluorophore-labelled monospecific antibodies, flow cytometry confirmed collagen type VI and XVIII production by ALDH1A1 expressing ARK1-USC. In contradistinction to ovarian cancer, ARK1-USC expressed the CSC marker nerve growth factor receptor (NGFR), increasing 3-fold by 48 h (q=0.039); nerve growth factor (NGF) was not expressed at any time. Nevertheless, multiple genes regulating neurogenesis, synaptic plasticity and excitation, axonal transport, and neuron epigenetic reprogramming were expressed, in addition to an inventory of neuronal receptors for neurotransmitters like acetylcholine (e.g. CHRNA3/

CHRNA4/CHRNA5), dopamine/epinephrine/norepinephrine (e.g. ADRA1B/ADRA2C/ADRB1/ADRB2/DDR2/DRD4), serotonin (e.g. HTR2B, HTR6) and the enzymes required for their synthesis (e.g. TPH2, TH).

Conclusion ARK1-USC classify as CSCs with neuronoid propensity. We propose that in reaction to therapies in vivo, a cancer cell subpopulation stabilized in its proper niche of malignant matrix can temporarily differentiate into neuron-like non-proliferative cells endowed with enhanced chemo- and radiation-resistance. This conceptual framework, which captures the current clinical experience with USC treatment, is worthy of further study as it envisions a previously unnoted cytological sanctuary that still holds promising novel mechanistic targets for interdicting cancer cell entry and persistence.

Disclosures The authors have nothing to disclose.

REFERENCES

1. Zhao, et al. (2013) *PNAS* **110**: 2916–2921.
2. Bonazzoli, et al. (2018) *Clin Cancer Res* **24**: 4845–4853.
3. Guenther, et al. (2001) *Brit J Cancer* **85**: 1540–1545.
4. Park, et al. (2013) *EMBO Mol Med* **5**:935–948.
5. Wu, et al. (2014) *Oncogene* **3**: 3432–3440.

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DETECTION OF THE SENTINEL LYMPH NODE BY ECOGUIDED MYOMETRIAL INJECTION (TUMIR) OF RADIOTRACER VERSUS HYBRID TRACER (RADIOTRACER-ICG) IN PATIENTS WITH INTERMEDIATE/HIGH RISK ENDOMETRIAL CANCER

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10.1136/ijgc-2020-ESGO.74

Introduction/Background Sentinel lymph node (SLN) detection in patients with endometrial cancer (EC) is usually performed with a [^{99m}Tc] Tc-albumin nanocolloid radiotracer (RTs). The transvaginal ultrasound-guided myometrial injection of radiotracer, unlike cervical injection, is more representative of tumor's drainage and obtains a higher percentage of SLN. Recently, the use of Indocyanine green (ICG) has gained relevance, although with this technique no pre-surgical lymphatic map is available. The hybrid tracer with RT-ICG could be an alternative to conserve the advantages of both components. The objective of this study is to see the performance of the detection of SLN with RT vs RT-CGI using the TUMIR technique in patients with EC at risk.

Methodology It is a retrospective study which has included patients with stage I/II CE, high/intermediate risk. Detection of SLN has been performed using the TUMIR technique (figure 1) with RT (8 ml with 6 mCi of RT) between 2006 and 2017 or hybrid tracer RT-ICG (4 ml with 6 mCi of RT 0.05 ml of ICG (25 mg/ 5 ml)) between 2014 and 2019. A planar and tomographic lymphoscintigraphy (SPECT/CT) has been performed preoperatively (figure 2). After detection and excision of the SLN, a systematic pelvic and paraortic lymphadenectomy has been performed. The histological study of the SLN has been performed by H&E and IHC.

Results A total of 155 patients have been included (102 with RT and 53 with ICG-RT). The intraoperative SLN detection in the RT group was 79.4% (92.6% of pelvic drainage, 45.7% of paraortic drainage and 7.4% exclusively paraortic). A bilateral drainage was found in 32% of the cases. A 19.6%