

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 mono-specific 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.

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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 [99mTc] 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%