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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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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.

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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

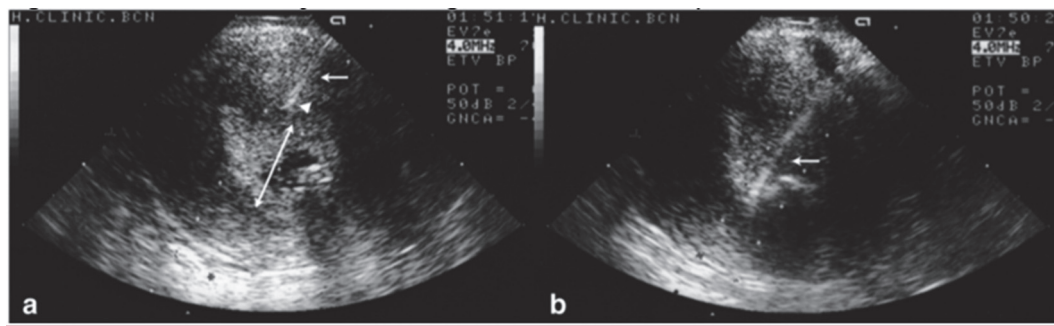
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Introduction/Background Sentinel lymph node (SLN) detection in patients with endometrial cancer (EC) is usually performed with a [99mTc] Tc-albumin nanocolloid radiotracer (RTs). The transvaginal ultrasound-guided myometrial injection of radiotracer, 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.

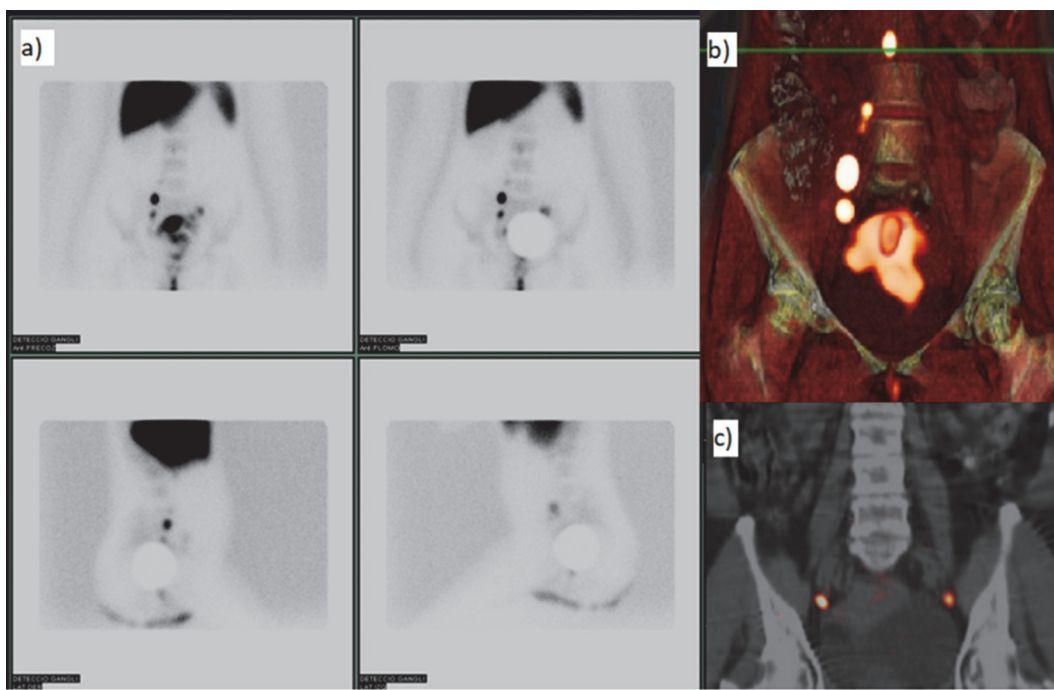
Methodology It is a retrospective study which has included patients with stage I/II CE, high/intermediate risk. Detection of SLN has been performed using the TUMIR technique (figure 1) with RT (8 ml with 6 mCi of RT) between 2006 and 2017 or hybrid tracer RT-ICG (4 ml with 6 mCi of RT 0.05 ml of ICG (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%



a) Injection into the anterior myometrial wall. b) Injection into the posterior myometrial wall. Arrow: needle; Triangle: Radiotracer cluster.

Abstract 443 Figure 1 Radiotracer injection using the TUMIR technique



Planar lymphoscintigraphy at 2h post injection of the radiotracer (a). Volumetric reconstruction of right hemipelvis SPECT / CT data showing pelvic and paraaortic drainage (b) Coronal section of fused SPECT/CT image demonstrating bilateral pelvic drainage (c)

Abstract 443 Figure 2 Planar lymphoscintigraphy and presurgical SPECT/CT

of the patients had positive SLN (1.5% exclusively para-aortic). The percentage of false negative (FN) was 12.5%.

The intraoperative SLN detection in the RT-ICG group was 68% (56% of pelvic drainage, 33% of paraaortic drainage, without cases with exclusively paraaortic drainage). A bilateral drainage was found in 56% of the cases. The 11.1% of the patients had a positive SLN without FN cases.

Conclusion Detection of the SLN with RT is slightly higher than with hybrid tracer. The hybrid tracer obtains a higher percentage of SLN with bilateral pelvic drainage than RT and reduces the number of contralateral pelvic lymphadenectomies. The TUMIR technique allows detection of para-aortic SNs in more than 30% of patients, much higher than that obtained with other techniques.

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SHOULD WE RE-STAGE AFTER POSITIVE SENTINEL NODE BIOPSY ON ENDOMETRIAL CANCER?

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Introduction/Background Approximately 10% of patients with intraoperative diagnosis of low risk Endometrial Cancer (EC) will suffer an upstage after the definitive histological evaluation of the piece of hysterectomy and bilateral adnexectomy. We aim to explore the results associated with the performance of pelvic and para-aortic lymphadenectomy as restaging these patients that will require a second surgery, and to compare