

Methodology Patients (n=49) undergoing maximal-effort upfront-debulking surgery for advanced HGSOC had a tumour mapping of their tumour dissemination. Tumour biopsies were collected (range 4–15) from patients, and also at time of relapse (n=10 patients). DNA was extracted from tumours (5 per patient, n=49 patients plus paired relapse samples) and Illumina Human OmniExpress genotyping performed. Allele-specific copy number (CN) was quantified using ASCAT. CN signature exposures were determined for all samples. Homologous recombination (HR) scores were estimated using a scarHRD algorithm, applying a cut-off >42 for HR-deficient.

Results Extensive genomic variations in CN signature exposures for different patients' tumours were observed, including between matched primary and relapse tumours. Increased CN signature exposure scores for Signatures 2 (p=0.00017), 4 (p=0.0029) and 6 (p=0.001) correlated with poor outcome in platinum-resistant/refractory patients, increased Signature 3 correlated with favourable outcome (p=0.00018) for platinum-sensitive and no-relapse patients. Variations in HR scores were observed across the cohort with one fifth of patients presenting with a mixed HR score profile across their tumour deposits, demonstrating both HR-deficient and HR-proficient tumours within patients.

Conclusion Extensive CN variations in CN signature scores and mixed HR-deficiency/proficiency scores indicates that a single tumour biopsy does not accurately depict disseminated HGSOC biology, and therefore should not be used as the basis to derive biomarker profiles for prediction of patient treatment responses or outcomes.

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EPITHELIAL OVARIAN CANCER IS INFILTRATED BY ACTIVATED EFFECTOR T CELLS COEXPRESSING MULTIPLE INHIBITORY RECEPTORS AND BY MYELOID CELLS EXPRESSING INHIBITORY RECEPTOR LIGANDS

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Introduction/Background Despite evidence suggesting a potential role for immunotherapy in Epithelial Ovarian Cancer (EOC), initial attempts had limited efficacy. A better characterization of tumor infiltrating lymphocytes' (TIL) immunophenotype appears crucial to deeply understand their role in anti-tumor immunity and to set the basis for their potential modulation to optimize adoptive cell therapies approaches. We extensively characterized the composition and phenotype of immune cells in EOC to identify pathways involved in limiting anti-tumor immunity.

Methodology Immune infiltrate was investigated for phenotype in 48 EOC specimens by immunohistochemistry (IHC) and flow cytometry (FC). Furthermore, the gene expression of

tumor samples was evaluated with a panel of 799 immune and cancer-related genes by the Nanostring platform. FC was also used to compare T cells isolated from tumor, ascites and peripheral blood of 19 patients for memory phenotype and for the expression of multiple inhibitory receptors (IRs) and of activation markers.

Results Both IHC and FC revealed a high infiltration by T lymphocytes and myeloid cells, while B cells were scanty. High-dimensional analysis of FC data identified 2 metaclusters of CD4⁺ and CD8⁺ T cells exclusively present in tumors, characterized by a CD137⁺CD39⁺PD-1⁺TIM-3⁺CD45RA⁻CD62L⁻CD95⁺ phenotype. Gene expression profile revealed a peculiar microenvironment in samples characterized by high TIL content, with increased expression of immunity- and myeloid-related genes. Accordingly, the ligands for IRs and co-stimulatory molecules were mainly provided by myeloid rather than neoplastic cells.

Conclusion Our data suggest that EOC is infiltrated by antigen-experienced T lymphocytes displaying features of both activation and partial exhaustion, possibly driven by IRs ligands expression by infiltrating myeloid cells.

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EVALUATION OF ADVANCED LUNG CANCER INFLAMMATION INDEX AS A PROGNOSTIC FACTOR IN PATIENTS WITH OVARIAN CANCER TREATED WITH PRIMARY DEBULKING SURGERY

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Introduction/Background Advanced Lung Cancer Inflammation Index (ALI) reflects systemic inflammation and has been shown to be a prognostic factor for lung cancer patients undergoing surgery. No previous study has assessed the prognostic significance of ALI in patients with ovarian cancer (OC). This study aimed to explore the relationship between ALI and prognosis of OC.

Methodology Electronic records of 83 patients with OC who underwent primary debulking surgery (PDS) at Tata Medical Center between 2017 and 2018 were reviewed. Patients treated with primary chemotherapy and those treated with palliative intent were excluded. The ALI score was calculated as body mass index x serum albumin/neutrophil to lymphocyte ratio. A web-based programme [Cutoff Finder (<http://molpath.charite.de/cutoff/>)] was used to deduce the appropriate cut-off value for ALI. The Kaplan-Meier method and Cox Proportional Hazards model were used to compare survival among prognostic groups.

Results The optimal cut-off value of ALI was determined as 12.5. Among the 83 patients, 10 had low ALI (<12.5), and 73 had high ALI (≥12.5). The low-ALI group had more complications of Clavien-Dindo grade 3 or higher after PDS (P=0.04). The patients with low ALI had higher chances of 30-day-mortality following PDS compared to the high-ALI group (P=.005). Median relapse-free survival (RFS) in the low-ALI group was 9 months compared to 32 months in the high-ALI group (hazard ratio [HR] for relapse, 0.16; P<0.001). Median overall survival (OS) in the low-ALI group was 20 months, and in the high-ALI group median OS was 56 months (HR 0.12, P<0.001).