indicate that genomic alterations alone cannot explain acquired platinum resistance in many cases, and emerging evidence suggests epigenetic alterations may be critical. We wish to investigate epigenetic changes that may drive platinum resistance in HGSC by treating established HGSC cell lines and patient-derived cells with pulses of carboplatin and investigating the nature, kinetics and plasticity of platinum-induced epigenetic changes.

Methodology We will mimic, using in an *in vitro* two-dimensional model, multiple cycles of platinum-based chemotherapy as used clinically. We will generate preliminary results from established cell lines and primary cultures. The primary cell cultures are collected from the ascites of patients with HGSC treated at Imperial College NHS Trust, London. Following validation (p53, PAX8 immunocytochemistry), carboplatin sensitivity is assessed (sulforhodamine B assay). Cells are then pulsed with four cycles of carboplatin (50μM for 6 hours) with a week of recovery between each cycle. Chemosensitivity of surviving cells is measured after each cycle. The cells are then harvested for downstream methylation (Illumina 850k array), transcriptomic (RNA sequencing) and chromatin accessibility (ATAC sequencing) assays. Cells are also imaged using STORM (Stochastic Optical Reconstruction Microscopy). Preliminary STORM data already indicate differences in chromatin structure and the distribution of specific histone modifications between paired sensitive and resistant HGSC cell lines.

Results We will receive the raw data within 8–12 weeks from now for the bioinformatic analysis. Differential gene expression analysis will uncover differently enriched pathways under the selective pressure of platinum-based chemotherapy.

Conclusion Understanding the epigenetic landscape of HGSC in real time using physiologically relevant models will allow us to identify possible therapeutic targets that could eventually prevent platinum resistance.

2022-RA-1251-ESGO P-CADHERIN: A PROMISING PROGNOSTIC BIOMARKER FOR HOMOLOGOUS REPAIR PROFICIENT HIGH GRADE SEROUS OVARIAN CARCINOMA

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Introduction/Background Homologous repair (HR) proficient tumours constitute 2/3 of high grade serous ovarian carcinoma (HGSOC), being associated with worse prognosis. Therefore, the identification of clinically relevant biomarkers is an urgent unmet clinical need. Once classic cadherins are transmembrane glycoproteins involved in cell-cell adhesion that are frequently deregulated in cancer, we aimed to: 1) characterize the expression pattern of E-cadherin (*CDH1)*, N-cadherin (*CDH2)* and P-cadherin (*CDH3*); 2) evaluate their prognostic impact in terms of overall survival (OS), according to HR status.

Methodology Retrospective study using a convenience sample of archive human tissue (Fallopian tube epithelium (FTE), serous precursor lesions and chemo-naïf HGSOC) from a Portuguese cancer centre. *In vitro* and *in silico* validation performed using HGSOC cell lines (BG1 and OVCAR4 cell lines) and CCLE database, respectively. Protein expression evaluated using immunohistochemistry (H-scoring system) and western blot. Comparisons between groups were made using T-test and X^2, where appropriate. Survival analyses were estimated using Kaplan-Meier analysis and Log-rank test.

Results We included 321 samples (130 FTE, 53 precursor lesions and 138 HGSOC; 41.2% *BRCA1/2* or *RAD51D* mutated) from 221 patients. All HGSOC co-expressed the 3 cadherins (28% with high co-expression scores). Expression pattern did not differ according to HR status. P-cadherin was significantly upregulated both in precursor lesions and HGSOC, when compared with FTE. *CDH3* expression was positively correlated with *CDH1*, *EpCAM* and *GRHL2* and inversely correlated with *VIM*, both *in silico* and *in vitro*. HGSOC with high cadherin co-expression and high P-cadherin expression were significantly associated with shorter OS in the HR proficient subgroup.

Conclusion Our results suggest that P-cadherin upregulation may be an early event in the serous carcinogenesis and a poor prognosis biomarker in HR proficient HGSOC. Functional assays are currently ongoing to unravel the biological mechanisms underlying P-cadherin role in this subgroup.

2022-RA-1342-ESGO ETHNICITY-SPECIFIC SPECTRUM OF *BRCA1, BRCA2* AND *ATM* PATHOGENIC VARIANTS IN OVARIAN AND BREAST CANCER PATIENTS FROM NORTH CAUCASUS

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Introduction/Background North Caucasus hosts several large ethnic groups, which preserved their national identity through the course of history. These populations are likely to have a unique pattern of disease-predisposing alleles reflecting the genetic background of their ancestors.

Methodology This study involved ovarian cancer (OC) and breast cancer (BC) patients from Chechnya (n = 147), Kabardino-Balkaria (n = 139), North Ossetia (n = 83), Ingushetia (n = 88) and Dagestan (n = 137). The entire coding sequences of BRCA1, BRCA2 and ATM genes were analyzed by next-generation sequencing (NGS) in 180 OCs and 414 BCs.

Results Consecutive OC series were characterized by high frequency of BRCA1/2 mutations across all analyzed ethnic groups, ranging from 18% to 33%. BC patients, which were enriched by early-onset, family history-positive and receptor triple-negative disease, showed mutation rate varying from 4% to 14%. There were founder pathogenic alleles in Chechens (BRCA1 c.3629_3630delAG; 10 out of 20 BRCA1/2 mutations) and North Ossetians (BRCA2 c.6341delC; 6 out 10