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 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.

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 OVCA4 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 X², 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.
BRCA1/2 mutations). Interestingly, Chechen BRCA1 c.3629_3630delAG allele was not observed among patients of Ingush ethnicity, despite these nations are believed to have common Nakh (Vainakh) roots. In Ingush patients, there were two recurrent alleles in the BRCA2 gene (c.5351dupA: 5 out 13 BRCA1/2 mutations; L1686X: 3 out 13 mutations). BRCA2 Q3299X mutation was repeatedly observed across several ethnic groups. OC patients from Kabardino-Balkaria had unusually high frequency of germ-line ATM truncating alleles (3/49, 6%); all 3 ATM mutations were represented by distinct ATM pathogenic variants.

Conclusion Genetic analysis of non-selected ovarian cancer patients is highly revealing in explaining ethnicity-specific BRCA1/2 mutations. Contribution of BRCA1/2 pathogenic alleles in OC and BC morbidity is high across various ethnic groups. Founder BRCA1/2 alleles are characteristic for some but not all North Caucasian nations.