Results Using the HGSC-1LTR strategy we have identified a molecular signature (TKT, LAMC1 and FUCO) that combined with ready available clinical data (patients’ age, menopausal status, serum CA125 levels, and treatment approach) is able to predict patient response to first-line treatment with an AUC: 0.82 (95% CI 0.72 – 0.92).

Conclusion We have established a new strategy that combines molecular and clinical parameters to predict the response to first-line treatment in HGSC patients (HGSC-1LTR). This strategy can allow optimization of therapeutic decision making and individualize HGSC patients’ care.

Introduction/Background High grade serous ovarian cancer (HGSOC) management is based on maximal effort cytoreductive surgery and platinum chemotherapy. However, partly due to the high degree of heterogeneity in HGSOC, most patients will experience recurrent relapses and develop platinum resistance. In recent years, tumour models have been used to better understand HGSOC, particularly 3D patient-derived tumour models. Ex-vivo explant cultures preserve the tumour microenvironment and architecture, allowing more accurate study of tumour response to therapy. In this study, we develop a protocol for generating platinum sensitivity readouts of patient-derived ex-vivo explant culture within a clinically relevant period.

Methodology We generated ex-vivo explant cultures from tumours collected from chemo-naïve patients undergoing primary cytoreductive surgery for advanced disseminated HGSOC and treated with cisplatin for 48 hours. Immunohistochemistry was used to determine tumour content (PAX8, p53), and levels of proliferation (Ki67) and apoptosis (cleaved caspase-3). QuPath digital pathology software was used to quantify responses to cisplatin relative to untreated samples generated from the same tumour site.

Results Applying digital pathology to tumour explants allowed for reproducible and rapid quantification of proliferation and apoptosis markers to determine viability of explant cultures and apoptosis induction in response to drug treatments. We observed variations in responses to cisplatin treatments across patients (n=7) and multisite deposits within the same patient (n=3 patients, with 2-3 tumours each).

Conclusion Ex-vivo tumour explant cultures capture the heterogeneity of HGSOC and therefore are an ideal model for testing responses to platinum chemotherapeutics, targeted treatments or novel agents, and homologous recombination repair capacity. The use of multisite tumours confirms that intra-tumoural heterogeneity plays a role in responses to chemotherapy and emphasizes the value of multisite sampling for the study of HGSOC. From surgery to analysis, this method can be completed within 2-3 weeks, allowing it to be used to guide personalized chemotherapy regimens.