

dissemination patterns. Tumour biopsies were collected (range 4–15, median 9), placed in short-term cultures, treated with cisplatin (25 μ M overnight) and apoptosis/viability assayed. When relapsed, patients also had paired biopsies collected for genomic and phenotypic analysis. DNA was extracted from tumours (5 per patient, n=49 patients plus relapse samples) and Illumina Human OmniExpress genotyping performed. Allele-specific copy number (CN) was quantified using ASCAT. Genomic heterogeneity was quantified as the estimated number of CN aberration events distinct between each pair of tumour deposits. Clonal diversity within a patient's deposits was calculated using the difference between within-patient and between-patient heterogeneity.

Results Broad heterogeneity was detected in response to platinum treatment across cases at the phenotypic level in vitro (n=49), with higher variances in apoptosis induction observed in patients with platinum resistant disease. Genomic analysis revealed widespread variations in patterns of evolution for different patients' tumours, including the relationship between primary tumours and relapsed disease. Extensive variations in CCNE1, MYC and PTEN CN were observed across multiple tumours in the same patients, and overall higher CCNE1 CN associated with poorer patient outcome (p=0.038).

Conclusion Vast intra-tumoural heterogeneity is observed at the phenotypic and genomic level in HGSOE patients. Extensive copy number variations in genes such as CCNE1, MYC and PTEN across multiple disseminated samples within patients, indicates that sampling of a single tumour site does not accurately represent overall disseminated HGSOE biology and has implications for overinterpretation of studies relating to outcome and platinum-resistance.

Disclosures CF: advisory boards and honoraria from Roche, Tesaro, Sequana, Olympus, Astra Zeneca. Other authors have no disclosures to declare.

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NOVEL 3D MODEL SYSTEMS TO ASSESS HETEROGENEITY IN RESPONSE TO PLATINUM THERAPY IN HIGH GRADE SEROUS OVARIAN CANCER

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10.1136/ijgc-2020-ESGO.172

Introduction/Background High-grade serous ovarian cancer (HGSOE) is the most common subtype of ovarian cancer, characterised by vast genomic instability and heterogeneity and acquired resistance to platinum-based chemotherapy. However, matching the most beneficial treatment options to patients is difficult to predict due to different platinum resistance mechanisms and limited effective predictive biomarkers. A study characterising intra-tumoural heterogeneity in HGSOE has identified variations in phenotypic responses to platinum treatment between different metastatic sites. In this study, we aim to develop novel clinically-relevant 3D ex-vivo models of HGSOE to investigate the effect of the local microenvironment on metastatic tumour cells' response to treatment, and potential use as a screening tool to predict drug responses.

Methodology Three different ex-vivo models were developed: organotypic, organoid and tumour slice. For organotypic and organoid models, tumour cells were extracted

from metastatic deposits obtained from defined anatomical regions during upfront radical debulking surgery of advanced stage HGSOE patients. Organotypic models were assembled using normal omental stromal cells embedded in Collagen-1 and tumour cells were added. Organoid models were propagated from tumour cells and embedded in basement membrane extract. For slice culture models, tumours were sliced into 350 μ m sections using a vibratome and cultured on cell culture inserts. All models were treated with cisplatin and assessed for apoptosis and viability read-outs.

Results Organotypic models showed that tumour cells cultured in 3D showed heterogeneity in response to cisplatin treatment, data showed a trend towards reduced response to treatment within 3D models compared to 2D (n=8). Changes in patterns of response to treatment between samples from 2D to 3D within the same patient was also demonstrated (n=5). Organoid models were successfully propagated from different metastatic sites and maintained long term growth (>15 passages). Histological read-outs for slice culture models demonstrated slices from different metastatic sites maintained viability in culture for up to 5 days.

Conclusion We have established growth, drug treatment conditions and assay read-outs for 3 different ex-vivo models of metastatic HGSOE. We have established that organoid culture must be generated within 24 hours of tumour cell extraction. Furthermore, both fresh and viably frozen tumours can be used to generate organotypic and organoid models. The broader implication of establishing clinically-relevant complex tumour models as routine methodologies for screening novel therapeutics and capturing the complex heterogeneity of individual patients, may lead to better development of therapeutic strategies including tumour/microenvironment combination strategies and also better personalisation of therapy for patients with HGSOE.

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Trophoblastic diseases

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A CLINICAL AUDIT OF MOLAR PREGNANCIES AND GESTATIONAL TROPHOBLASTIC NEOPLASIA CASES OVER 1YR IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA WITH RESPECT TO THE INCIDENCE OF DISEASE, FACTORS RELATED TO ETIOPATHOGENESIS, DIAGNOSIS AND MANAGEMENT

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10.1136/ijgc-2020-ESGO.173

Introduction/Background A Clinical Audit of molar pregnancies and gestational trophoblastic neoplasia cases over 1yr was conducted at Kolkata Medical College & Hospital, a tertiary care hospital of Eastern India with respect to the incidence of disease, factors related to etiopathogenesis, diagnosis and management and effects on maternal morbidity and mortality.

Methodology A total of 10000 patients attended this institution during 2017 June to 2018 June for pregnancy or its complication in department of gynaecology & obstetrics. 85 molar