

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.

2022-RA-1574-ESGO APPLICATION OF *EX-VIVO* TUMOUR EXPLANT CULTURES TO PREDICT PLATINUM RESPONSES IN HIGH GRADE SEROUS OVARIAN CANCERS WITHIN A CLINICALLY RELEVANT TIMELINE

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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.

2022-RA-1582-ESGO INHIBITION OF THE WNT/ β -CATENIN PATHWAY WITH DKK3 PROTEIN – A NEW VIRAL THERAPY FOR TREATMENT OF OVARIAN CANCER?

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Introduction/Background Wnt/ β -Catenin signalling pathway plays an important role in many cellular processes, including cell proliferation. Abnormal functioning of the pathway has been demonstrated in ovarian cancer and therefore could be the focus for novel treatments, including viral therapies. In this study, we examined the effects of Wnt/ β -Catenin pathway inhibition in ovarian cancer by infecting ovarian cancer cells with modified adenovirus 5 (Ad5) expressing Dickkopf-3 (DKK3) protein, a known Wnt/ β -Catenin pathway inhibitor. **Methodology** DKK3 expression in the virus was confirmed by quantitative PCR test against DKK3 and other Wnt target genes and Western Blot. Once confirmed, 10k epithelial ovarian cancer cells (SKOV3 cell line) were infected with the modified virus at 1k, 2.5k, 5k and 10k virus particles per cell for CellTiter Glo (CTG) assay with results analysed at 24, 48 and 72hrs post infection. In Colony Forming Assay, 300 SKOV3 cells were infected at the same virus particles per cell ratios and analysed after 14 days. The same assays were performed with doxorubicin and Ad5RAD as positive and negative controls respectively.

Results CTG assay showed reduced cell viability and proliferation of cancer cells for the first 48hrs post infection. In the colony forming assay, ovarian cancer cells were able to form multiple colonies of more than 50 cells 2 weeks after viral suppression of the Wnt/ β -Catenin pathway, indicating the inhibition may not have long standing effects on cancer cells' ability to grow and multiply.

Conclusion Our results indicate infecting cancer cells with Ad5 expressing DKK3 successfully inhibits the Wnt/ β -Catenin pathway and leads to short-term reduction in cell proliferation. Further studies are needed to establish any long-term effects and potential translation into clinical practice.

2022-RA-1608-ESGO CLINICAL IMPLICATIONS OF GENOMIC INTRATUMOURAL HETEROGENEITY IN HIGH GRADE SEROUS OVARIAN CANCER

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Introduction/Background High-grade serous ovarian cancer (HGSOC) is typified by extensive genomic instability and intra-tumoural heterogeneity (ITH). Most patients relapse and eventually acquire resistance to platinum- or PARP inhibitor-based therapy. Diverse mechanisms leading to therapy resistance and a lack of predictive biomarkers means that matching the best treatment options to patients is difficult. This study aims to describe the extent of spatial and temporal ITH in advanced stage HGSOC at presentation and relapse and its implications for patient management.