EP241/#516 PATIENT DERIVED ORGANOIDS AS EX-VIVO MODELS FOR HIGH GRADE SEROUS OVARIAN CANCER RESEARCH

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Introduction Patient-Derived Organoids (PDOs) are in increasing use as ex-vivo models for high-grade serous ovarian cancer (HGSOC) and other cancers, given their genotypic and phenotypic correlations with in vivo tumour. We aimed to characterise inter- and intrapatient heterogeneity in PDOs from multiple sites in chemo-naïve HGSOC.

Methods Multi-site tumour samples were collected from HGSOC patients undergoing primary cytoreductive surgery and PDOs grown from extracted tumour cells with/without the Wnt agonist R-spondin. PDOs were trialled against chemotherapies and targeted therapeutics using IC50 and AUC for comparison. Transcriptomic differences between PDOs were explored using RNAseq.

Results PDOs were successfully established (≥5 passages) in 8/14 cases (57%), with a mean n=5 sites initially seeded per patient. IC50 and AUC values for platinum compounds and PARP inhibitors varied significantly between patients, and between different sites from the same patient. Cisplatin sensitivity varied 20-fold across 8 different PDO lines ($p<0.0001$), with carboplatin sensitivity differing by almost 10-fold between different tumour sites in one case ($p<0.0001$) highlighting HGSOC inter/intrapatient heterogeneity. Rucaparib sensitivity variability was demonstrated between cases and between sites from the same case ($p<0.001$). Resistance was induced in 2 PDO lines through culturing in low dose conditions, with AUC increments were observed for cisplatin ($p<0.01$) and rucaparib ($p<0.05$) compared to controls. Potentially synergistic compounds to overcome platinum and PARPi resistance were trialled.

Conclusion/Implications HGSOC PDOs provide a reliable model for drug screening, incorporating inter and intra-patient heterogeneity. The heterogeneity observed provides rationale for variability in clinical responses and the poor prognosis consistent with advanced HGSOC.

EP242/#366 TITLE UNDERSTANDING CURRENT PRACTICES FOR THE MANAGEMENT OF ADVANCED EPITHELIAL HIGH-GRADE OVARIAN CANCER IN THE UK: INTERIM DATA FROM THE OC-NOW SURVEY (2023)

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Introduction Background Advanced high-grade ovarian cancer (OC) treatment has recently evolved to include novel targeted agents such as PARP-inhibitors. Our survey explores current management of advanced OC in the UK.

Methods Methodology This interim descriptive analysis uses data collected between March-April 2023 from structured interviews with UK-based healthcare professionals (HCPs) involved in secondary care management of advanced OC (OC-NOW).

Results The analysis included 50 OC MDT members. Respondents were mainly based in England (84%; 42/50). Most HCPs (68%; 19/28) used the DESKTOP-III criteria to identify candidates for secondary cytoreduction, with up to 30% of patients considered as eligible in 85% (23/27) of centres. HRD (100%; 41/41) and BRCA1/2 (98%; 40/41) were routinely tested before planning maintenance treatment. Most respondents (90%; 36/40) reported that HRD test results had a turnaround time of 6 weeks. The median number (interquartile range [IQR]) of patients with a BRCA mutation (BRCAmut) was 20.0% (15.0–20.0%), while 25.0% (18.8–30.0%) were HRD (test positive) and BRCA wild type (HRD/BRCAwt), 49.0% (35.0–60.0%) were HRp (test negative) and 10.0% (5.0–11.2%) were HRnd (HR test failure/not determined/inconclusive). Platinum sensitivity was seen as predictive of PARPi maintenance therapy benefit, irrespective of HRD status (table 1).

Conclusion/Implications Conclusion These results provide an update on UK practice in advanced OC. HRD and BRCA1/2 are now routinely assessed with turnaround times on time for maintenance therapy decision making. For Platinum Sensitive OC, PARPi maintenance is typically considered irrespective of HRD status

EP243/#883 INFLUENCING FACTORS AND MANAGEMENT STRATEGIES FOR PERIOPERATIVE COMPLICATIONS OF DIAPHRAGMATIC SURGERY IN OVARIAN CANCER

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Introduction The diaphragm is a common site of metastasis in advanced ovarian cancer. The development of diaphragm tumor resection surgery is beneficial for achieving complete tumor cell elimination and also poses challenges to the management of perioperative complications. This study aims to explore the influencing factors and prevention and treatment strategies for complications of diaphragm surgery.

Methods This study included advanced ovarian cancer patients who underwent diaphragm tumor resection surgery at Fudan University Shanghai Cancer Center from July 2015 to June 2022. Clinical and pathological characteristics, diaphragm surgical methods, and perioperative complications were retrospectively collected.

Results A total of 396 patients with advanced ovarian cancer were included. 163 patients had perioperative complications, whereas pleural effusion (32.6%), infection (8.3%), and pneumothorax (5.3%) were the most commonly reported. Patients with longer surgery duration (>3 hours) and higher surgical difficulty (Aletti score >5) had a higher incidence of postoperative complications ($p<0.01$), particularly pleural effusion

(p<0.01). Only 60 patients (15.2%) underwent chest tube placement overall, which is not enough to support the routine use of prophylactic chest tube placement in all patients. The incidence of postoperative pleural effusion was significantly higher in patients who underwent diaphragmatic incision surgery (47.8%) than in others(29.5%) (p=0.03).

Conclusion/Implications Pleural effusion is the most common complication of diaphragmatic surgery in ovarian cancer patients. Long surgery duration and high surgical difficulty correlated with postoperative pleural effusions. Routine placement of the prophylactic chest tube is not suitable for all patients. However, for patients who undergo diaphragmatic incision surgery, intraoperative chest tube placement should be considered.

EP244/#277 EXAMINING REAL-WORLD TREATMENT BENEFITS OF FIRST-LINE MAINTENANCE NIRAPARIB IN NON-BRCA MUTANT HIGH GRADE SEROUS OVARIAN CANCERS

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Introduction Maintenance PARP inhibitor therapy after response to first-line chemotherapy is standard of care in advanced high grade serous ovarian cancer (HGSOC). Progression free survival (PFS) benefit for patients on niraparib with non-BRCA mutant (m)/non-homologous recombination deficient (HRD) cancers is limited. This project aims to assess real-world benefits of first-line niraparib in non-BRCAm HGSOC. It investigates, in the absence of funded HRD testing in Canada, surrogate markers of niraparib response such as KELIM score.

Methods Retrospective chart review of patients with non-BRCAm/HRD unknown HGSOC treated with first-line maintenance niraparib at BC Cancer, Canada between 04/2020–06/2022. Demographic and treatment information was collected. PFS was defined as start of niraparib to radiological evidence of disease progression. KELIM score was calculated using validated software.

Results 83 patients were included; 25% had FIGO stage 4 disease. 68% underwent neoadjuvant chemotherapy with optimal cytoreductive rate of whole population of 72%. 60% had disease progression at data cut-off with median follow-up of 15.3 months. Median PFS (mPFS) on niraparib was 12.7 months (range 1.1–29.2). Patients given neoadjuvant chemotherapy with KELIM scores ≥1 had a trend to longer mPFS (14 months) vs. those with KELIM <1 (8.8 months) (p=0.03). Despite use of individualized starting dose (ISD), 60% required at least 1 dose reduction and 18% experienced grade 3 toxicity.

Conclusion/Implications mPFS on niraparib in this non-BRCAm/HRD unknown HGSOC population was 12.7 months. 60% of patients required a dose reduction due to toxicity despite ISD. KELIM score may be useful to predict PARP inhibitor response and aid clinical decision-making where HRD testing is unfunded.

EP245/#1396 HUMAN PERITONEAL FLUID EXERTS OVULATION AND NONOVULATION-SOURCED ONCOGENIC ACTIVITIES TO THE TRANSFORMING FALLOPIAN TUBE EPITHELIAL CELLS

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Introduction Ovulation is the main cause of oncogenesis of fallopian tube epithelium (FTE), the origin of ovarian high-grade serous carcinoma (HGSC). Previously, we have identified multiple oncogenic activities of the ovulatory follicular fluid (FF), which exerts full-spectrum transforming activities on FTE cells. After ovulation, FF transfuses into the peritoneal fluid (PF) with which the FTE constantly bathes. We wonder whether PF exerts the same spectrum of oncogenic activities as FF and whether they are sourced from FF.

Methods By using a panel of FTE cells with p53 mutation (FT282-V), p53/CCNE1 aberrations (FT282-CCNE1), and after xenograft peritoneal metastasis after spontaneous transformation (FEXT2), we tested the change of different transformation phenotypes after treating with FF and PF collected before and after ovulation.

Results Similar to FF but to a lesser extent, PF generally promoted anchorage-independent growth (AIG), migration, anoikis resistance, and peritoneal attachment and invasion of the transforming FTE cells, and the more transformed cells were more affected. Activities of AIG, invasion, and peritoneal attachment growth were higher in luteal phase PF than proliferative PF, suggesting an ovulation source. In contrast, anoikis resistance and migration activities were indifferent between PF collected before and after ovulation, suggesting an ovulation-independent source. Finally, coinjection of Luc-FEXT2 cells with either FF or luteal phase PF, but not proliferative phase PF, supported early peritoneal implantation in NSG mice.

Conclusion/Implications PF from ovulating women promotes oncogenic phenotypes of FTE cells at different stages of malignant transformation. Other than anoikis resistance and cell migration, a majority of these activities are sourced from ovulation.

EP246/#164 HIGH GASDERMIN D EXPRESSION IN OMENTAL ADIPOCYTE PREDICTS POOR PROGNOSIS IN ADVANCED STAGE OVARIAN CANCER

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Introduction Recently, an inflammatory programmed cell death characterized by gasdermin-mediated inflammatory cell