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 similarity with in vivo tumour. We aimed to characterise inter- and intrapatient heterogeneity in PDOs from multiple sites in chemonaive 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 chemotherapy 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/intrapatent 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.

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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 HRHd (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. MRD 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.
(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.

**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 the real-world benefits of first-line niraparib in non-BRCAm HRD 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 time from 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 neo-adjuvant 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 neo-adjuvant 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.

**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 death characterized by gasdermin-mediated inflammatory cell death is recognized to play a critical role in various diseases. Gasdermin D (GSDMD) is a key effector protein involved in the death of all cells. High GSDMD expression is associated with poor prognosis for a variety of malignancies. Omental adipocytes are highly expressed in advanced ovarian cancer compared to adjacent areas, which may contribute to the progression of the disease. The aim of this study was to examine the expression of GSDMD in omental adipocytes and its association with the clinical characteristics of patients with advanced ovarian cancer.

**Methods** This was a retrospective cohort study involving patients with advanced ovarian cancer who underwent surgical resection at our institution between January 2018 and December 2020. Omental adipocytes were isolated from resection specimens and GSDMD expression was assessed by immunohistochemistry. The association between GSDMD expression and clinical characteristics was analyzed using logistic regression analysis.

**Results** A total of 50 patients were included in the study. The median age of the patients was 55 years (range 30–80). The majority of the patients (78%) had stage III disease. GSDMD expression was significantly higher in patients with advanced ovarian cancer compared to those with stage I disease (p=0.03). Patients with high GSDMD expression had a shorter median overall survival compared to those with low expression (p=0.02). In multivariate analysis, high GSDMD expression was an independent predictor of poor survival (HR=2.4, 95% CI 1.2–4.7, p=0.02).

**Conclusion** High GSDMD expression in omental adipocytes is associated with poor prognosis for patients with advanced ovarian cancer. This finding may provide new insights into the pathogenesis of ovarian cancer and potential therapeutic targets.