EP241/#516 PATIENT DERIVED ORGANOIDS AS EX-VIVO MODELS FOR HIGH GRADE SEROUS OVARIAN CANCER RESEARCH
James Clark, Christina Fotopoulou*, Jennifer Plski, Cationa Dickie, Lydia Kondylisou, Jonathan Kliei, Paula Cumine, Imperial College London, Surgery and Cancer, London, UK
10.1136/ijgc-2023-IGCS.315

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 intra-tumor 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/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 drug 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 PARP 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.

1Stephen McCormack, 2Christina Fotopoulou*, 3Rowan Miller, 4Rebecca Bowen, 5Agnieszka Michael, 6Anthony Wesselbaum, 7Allan Ullmann, 8Sanjit Manchanda, 9GSK Medical, London, UK; 10Imperial College London, Surgery and Cancer, London, UK; 11University College Hospital, Gynaecology and Early Phase Clinical Trials, London, UK; 12Royal United Hospitals Bath NHS Foundation trust, Breast and Gynaecological Cancer, Bath, UK; 13Royal Surrey Hospital NHS Foundation Trust, Oncology Ovarian Cancer and Renal Cancer, Guildford, UK; 5Barts Health NHS Trust, Gynaecological Oncology, London, UK
10.1136/ijgc-2023-IGCS.316

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 HRd (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
Xinyu Ha*, Zheng Feng, Ziqi Liu, Hao Wen, Xingzhou Ju, Xiaohua Wu, Fudan University Shanghai Cancer Center, Department of Gynecologic Oncology, Shanghai, China
10.1136/ijgc-2023-IGCS.317

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

1Nicola Hannaway*, 2Stefania Kassaris, 3Janine Davies, 4Alannah Smrke, 5Anna Tinker, 6Yvette Drew. 1BC Cancer – Vancouver, Medical Onocology, Vancouver, Canada; 2University of British Columbia, Faculty of Medicine, Vancouver, Canada

Introduction Maintenance PARP inhibitor therapy after response to first-line chemotherapy is standard of care in advanced high grade serous ovarian cancer (HGSOC). Progession 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.