

OP021/#475

## SEPARATING THE BRCA1 AND BRCA2 PHENOTYPE, A PATHWAY ANALYSIS

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**Objectives** To identify gene expression profiles and interacting pathways in BRCA1- and BRCA2- associated high grade serous ovarian cancer (HGSOC) as compared to one another and to BRCA wild type, homologous recombination proficient (HRP) tumors.

**Methods** of 657 total HGSOC samples, 15 BRCA2 mutated (2.3%), 16 (2.4%) BRCA1 mutated, and 375 (57.1%) HRP samples were analyzed. Gene expression data was collected from Tempus and unpaired t-tests were used to identify differentially expressed genes (DEG) with unadjusted p-value <0.05 and fold change of 1.5. Meta and pathway analyses were performed among BRCA1, BRCA2 and HRP groups using Venn diagram and Advaita Bio's iPathwayGuide. BRCA mutated and wild type (wt) ID8 mouse cell lines were used for protein expression and seahorse assay for metabolism analysis.

**Results** From 18,284 genes with measured expression, 843 (4.6%) DEG were found between BRCA2 vs BRCA1, 748 (4.1%) between BRCA2 vs HRP and 1,858 (10.2%) between BRCA1 and HRP. On meta-analysis of the three comparisons, pathway analysis revealed significant involvement of Wnt signaling pathway and oxidative phosphorylation unique to BRCA2 group compared to fibroblast growth factor signaling and PI3K-Akt signaling for BRCA1. Western blot analysis confirmed higher expression of oxidative phosphorylation complex proteins in BRCA1/BRCA2 mutated lines and differential expression of  $\beta$  catenin between BRCA mutated versus wt cell lines. Seahorse assay showed higher oxidative consumption rate in BRCA mutated versus wt cells.

**Conclusions** Our study identified differential pathway regulation for BRCA2 versus BRCA1 associated HGSOC, suggesting each should be considered a separate phenotype with unique opportunities for targeted therapy.

OP022/#597

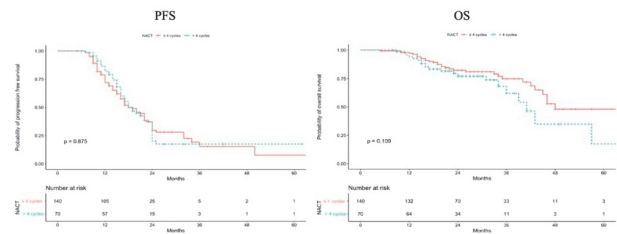
## OPTIMIZING THE NUMBER OF CYCLES OF NEOADJUVANT CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CARCINOMA: A PROPENSITY-SCORE MATCHING ANALYSIS

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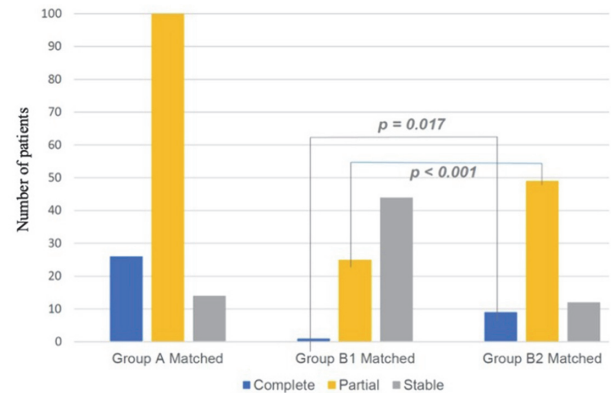
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**Objectives** Neoadjuvant chemotherapy and interval debulking surgery are widely offered in advanced ovarian cancer patients; the number of NACT cycles to be given is still an issue. Our aim was to compare survival outcomes of patients with advanced ovarian cancer treated with <4 or more NACT cycles.

**Methods** A cohort of patients with stage III-IV epithelial OC undergoing NACT followed by IDS was identified. Patients were classified in group A ( $\leq 4$  cycles) and group B (>4



**Abstract OP022/#597 Figure 1** Overall survival and disease free survival in group A and group B



**Abstract OP022/#597 Figure 2** Treatment response between groups. Group A (3–4 cycles); Group B (at least 6 cycles); B1 response assessment after 3–4 cycles; B2 response assessment after at least 6 cycles

cycles). Selection bias was avoided using propensity score matching (2:1 ratio).

**Results** 140 (group A) and 70 (group B) patients were included. After the propensity score matching, there were no imbalances in baseline characteristics. BRCA status was associated to improved OS (HR=0.41; 95%CI 0.18-0.92, p=0.032) and residual tumor to decreased OS (HR=1.93; 95%CI 1.08–3.46, p=0.026). Statistically significant differences were not observed in OS (2-year OS 82.4% for group A versus 77.1% for group B, p=0.109) and PFS (2-year PFS 29.7% for group A versus 20.0% for group B, p=0.875) (figure 1). In group B, the administration of >4 cycles was related to an additional chance of achieving complete (12.9%) and partial (34.3%) responses compared to responses after 3–4 cycles (figure 2).

**Conclusions** Receiving more than 4 cycles of NACT is no detrimental in terms of OS and PFS in advanced ovarian cancer. Response rates can increase following further cycles administration.

OP023/#658

## CORRELATION OF HRD STATUS WITH CLINICAL AND SURVIVAL OUTCOMES IN PATIENTS WITH ADVANCED-STAGE OVARIAN CANCER UNDERGOING FRONTLINE AND MAINTENANCE THERAPY

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**Objectives** We aimed to compare clinical and survival outcomes in high grade ovarian cancer (HGOC) stratified by homologous recombination deficiency (HRD) status undergoing frontline and/or maintenance therapy.

**Methods** We performed a retrospective analysis of HGOC from April 2013 to June 2019. Clinical outcomes were analyzed by (1) germline BRCA+ (2) germline BRCA - and somatic BRCA/HRD+, or (3) BRCA-/HRD-. Progression free (PFS) and overall survival (OS) were estimated using Kaplan-Meier methods and modeled via Cox proportional hazards regression.

**Results** 187 patients met inclusion criteria. 106 patients had germline BRCA mutation, 26 somatic BRCA/HRD+, and 55 BRCA/HRD-. Multivariate analysis for PFS revealed that age (HR 1.02, 95% CI 1.00–1.04),  $p=0.01$ ), stage (HR 5.7, 95% CI 1.39–23.4,  $p=0.02$ ), R0 resection at TRS (HR 0.41, 95% CI 0.21–0.83,  $p=0.01$ ), and BRCA/HRD- status (HR 1.63, 95% CI 1.07–2.48,  $p=0.02$ ) were significant factors impacting PFS. Multivariate analysis for OS revealed age (HR 1.07, 95% CI 1.03–1.10,  $p<0.001$ ) and R0 resection at TRS (HR 0.19, 95% CI 0.08–0.44,  $p<0.001$ ) were significant factors impacting OS. 17 of 187 patients received PARPi maintenance therapy. All harbored a germline or somatic mutation in BRCA1/BRCA2 (14) or had tumors characterized by HRD (3). Multivariate analysis for PFS revealed that PARPi maintenance therapy (HR 0.14 95% CI 0.04–0.57),  $p=0.006$ ) was a significant factor impacting PFS.

**Conclusions** Germline BRCA-mutant, somatic BRCA/HRD+ HGOC was associated with improved PFS and OS regardless of primary TRS or NACT. BRCA-/HRD- was a negative prognostic factor for survival in HGOC. PARPi maintenance therapy was associated with improved PFS in Germline BRCA-mutant, somatic BRCA/HRD+ HGOC

OP024/#182

#### FINDINGS AND OUTCOMES IN A POST-VACCINATION COHORT OF YOUNG WOMEN UNDER 25 YEARS ATTENDING A TERTIARY COLPOSCOPY SERVICE

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**Objectives** In 2007, human papillomavirus (HPV) vaccination was rolled out in Australia, with a high uptake of 73%, and a consequent reduction in high-grade dysplasia in young women. The aim was to provide descriptive data on post-vaccination women below 25 years between 2008 and 2017, prior to the change in cervical screening guidelines.

**Methods** A retrospective cohort analysis of women under 25 attending a tertiary colposcopy clinic.

**Results** 3128 women with a median age of 22 (range 14–24) years were identified. When comparing overall worst histology result, vaccinated women were less likely to have a high grade abnormality than unvaccinated women (RR 0.78, 95%CI 0.67–0.90,  $p=0.0006$ ). Amongst those with high grade abnormalities, there was no significant difference in rates of CIN2 or CIN3 between vaccinated and unvaccinated women (RR 0.81, 95%CI 0.62–1.05,  $p=0.1086$ ).

**Conclusions** This study provides baseline data on young women under the previous cervical screening program, following the introduction of the HPV vaccine.

OP025/#128

#### COMPREHENSIVE PERIOPERATIVE CARE PROGRAM TO IMPROVE SAME-DAY DISCHARGE AFTER MINIMALLY INVASIVE GYNECOLOGIC ONCOLOGY SURGERY

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**Objectives** Same-day discharge (SDD) after minimally invasive hysterectomy for gynecologic conditions has been shown to be safe and feasible. We designed and implemented a quality improvement perioperative program to improve SDD rate from 30% to 75% over a 12-month period.

**Methods** We included 102 consecutive patients undergoing minimally invasive hysterectomy at a single cancer centre during the 12-month implementation period. A pre-intervention cohort of 100 patients was identified for comparison of clinicodemographic variables and perioperative outcomes. We developed a comprehensive perioperative care program based on Early Recovery after Surgery (ERAS) principles and met bi-weekly for plan-do-study-act (PDSA) cycles. Patients were followed for 30 days after discharge. We used a run chart to monitor the effects of our interventions and conducted a multivariate analysis to determine patient factors or interventions associated with SDD.

**Results** SDD rate increased from 29% to 75% after implementation ( $p<0.001$ ). The post implementation cohort was significantly younger (59 vs. 65yrs;  $p=0.025$ ) and had shorter operative times (180 vs. 211 minutes;  $p<0.001$ ) but the two groups were similar in BMI, comorbidity, stage, and intraoperative complications. There was no difference in 30-day perioperative complications, readmissions, reoperations, emergency department visits, or mortality. The most common reason for overnight admission post intervention was nausea and vomiting (16%). Overall, 89% of patients rated their experience as 'very good' or 'excellent', and 87% felt that their post-operative length of stay was adequate.

**Conclusions** Following implementation of a perioperative quality improvement program, our interventions significantly improved SDD rates while maintaining low 30-day perioperative complications and excellent patient experience.

OP026/#45

#### MALNUTRITION AS A RISK FACTOR FOR POST-OPERATIVE MORBIDITY IN GYNECOLOGIC CANCER: ANALYSIS USING THE NATIONAL SURGICAL QUALITY IMPROVEMENT PROGRAM (NSQIP) DATABASE

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**Objectives** Malnutrition increases risk of post-surgical morbidity in gynecologic malignancies. We assessed whether different malnutrition definitions are suitable for predicting morbidity in each cancer type.