Gemcitabin + Carboplatin chemotherapy may show slightly better results than other chemotherapies, so additional research on this seems necessary.

PR062/#686 FIRST-IN-HUMAN PHASE 1 STUDY OF TORL-1–23, A NOVEL CLAUDIN 6 (CLDN6) TARGETED ANTIBODY DRUG CONJUGATE (ADC) IN PATIENTS WITH OVARIAN CANCER

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Introduction CLDN6 is highly expressed in multiple cancers with little to no expression in normal tissues, thus is an ideal target to explore a novel therapeutic. TORL-1–23 is first-in-class ADC targeting the tumor-specific antigen CLDN6.
Methods A first in human, 2-part study (TORL123–001 [NCT05103683]) is characterizing the safety, tolerability, pharmacokinetics (PK), maximum tolerated dose (MTD), and anti-tumor activity of TORL-1–23 monotherapy in participants with ovarian and other advanced solid tumors. Dose escalation (Part 1) implemented an accelerated titration design with up to 6 participants per dose level cohort. Dose expansion (Part 2) will assess participant cohorts with CLDN6-expressing tumors including gynecologic cancers using a CLDN6 IHC companion diagnostic.
Results 19 patients with platinum-resistant/refractory ovarian cancer were evaluated across 8 dose levels (0.2 to 2.4 mg/kg IV every 3 weeks, 21 day cycles) (data cutoff 01APR2023). Most pts had $\geq$ 3 prior treatment lines in the metastatic setting. The most common treatment-related adverse events were Gr1 peripheral neuropathy (n=3), Gr1/2 fatigue (n=2), and Gr1 nausea (n=2). Dose-limiting toxicities have not been observed. PK data show sustained exposure over the dosing interval. Partial responses (PR) were reported in 6/18 efficacy evaluable participants with CLDN6+ ovarian cancer across all dose levels. 3 of 4 participants with ovarian cancer responded at the 2.4 mg/kg dose level.
Conclusion/Implications In participants with heavily-pretreated CLDN6-expressing ovarian cancer, the novel TORL-1–23 ADC shows a favorable safety/tolerability profile and encouraging antitumor activity. Dose finding is ongoing to identify optimal doses for subsequent development.

PR063/#79 SEROUS TUBAL INTRAEPITHELIAL CARCINOMA (STIC) OUTCOMES IN AN AVERAGE RISK POPULATION

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Introduction Serous tubal intraepithelial carcinoma (STIC) are precursors for high grade serous carcinomas (HGSC) of tubo-ovarian origin. It is most commonly encountered during risk-reducing surgery for patients with a BRCA germline pathogenic variant (PV). An isolated STIC at risk-reducing surgery is associated with a 27.5% risk of primary peritoneal HGSC at 10 years. There is little known about the risk of subsequent HGSC in an average risk patient found to have an isolated STIC. The objective of this study is to explore the outcomes of STIC diagnosed in a population of patients without a known hereditary mutation at the time of surgery.
Methods Retrospective population based cohort study from British Columbia, Canada. Chart review of patients with an isolated STIC from January 2012 to May 2022. The estimated population prevalence of STIC, and outcomes including subsequent HGSC and BRCA mutations are described.
Results Twenty nine patients were identified, including 20 patients with no known BRCA PV ('average risk') undergoing primary surgery for non-risk reducing indications. The estimated prevalence of STIC in this population was 0.1%. Patients were followed for a median of 63 (9–127) months. Five of these 20 average risk patients (25%) developed HGSC at 18, 29, 70, 80, 106 months, and only 1 (5%) of these was subsequently found to have a BRCA PV.
Conclusion/Implications STIC identified in average risk population patients with negative genetic testing are still at risk of subsequent HGSC. Recommendations for STIC management should be applied to all patients regardless of BRCA status.

PR064/#206 MULTICENTER REAL-WORLD EXPERIENCES OF PARPI RECHALLENGE IN PATIENTS WITH OVARIAN CANCER IN CHINA

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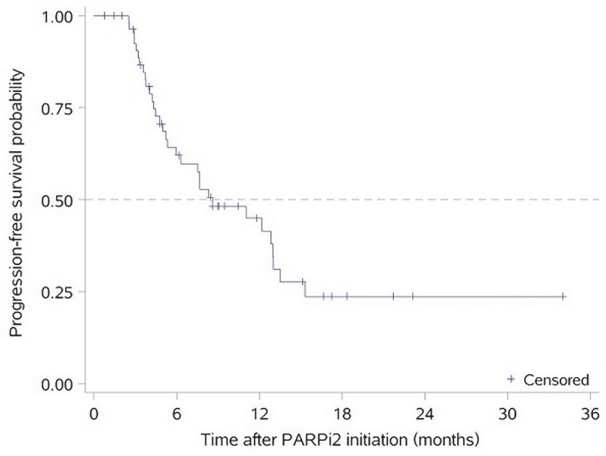
Introduction The OReO/ENGOT Ov-38 trial showed maintenance olaparib rechallenge improved progression-free survival (PFS) compared with placebo. However, subpopulation benefit more from Poly (ADP-ribose) polymerase inhibitors (PARPi) rechallenge was unclear. The objective of this real-world study is to evaluate the effectiveness, safety and explore benefit population of PARPi rechallenge in China.
Methods This multi-center, non-interventional study included patients with PARPi-treated recurrent ovarian cancer who rechallenged PARPi as maintenance therapy or salvage treatment at 12 institutions between June 2019 and March 2023. Patients' demographics and outcomes were analyzed.

Abstract PR064/#206 Table 1

Patients' Characteristic	Total (N = 70) N (%)
Age, years	
Median (Q1-Q3)	58 (53-63.75)
***BRCA* mutation status, *n* (%)**	
Wild-type or unknown	43 (61.4)
BRCA1/2 mutated	27 (38.6)
Histology, *n* (%)	
High-grade serous carcinoma	68 (97.1)
Endometrioid	1 (1.4)
Others	1 (1.4)
Name of PARPi1	
Olaparib	50 (71.4)
Niraparib	20 (28.6)
Treatment phase of PARPi1	
Neoadjuvant	1 (1.4)
Maintenance therapy	67 (95.7)
Salvage treatment	2 (2.9)
PARPi1 treatment outcomes	
Disease progression	61 (87.2)
Adverse events	5 (7.1)
Others	4 (5.7)
Switch to other PARPi or not after PARPi1	
Switch	48 (68.6)
No switch	22 (31.4)
Treatment phase of PARPi2	
Maintenance therapy	57 (81.4)
Salvage treatment	13 (18.6)
Lines of PARPi2	
1	1 (1.4)
2	18 (25.7)
3	30 (42.9)
≥4	21 (30.0)
Treatment pattern of PARPi rechallenge	
Maintenance after maintenance	56 (80.0)
Treatment after maintenance	11 (15.7)
Treatment after treatment	2 (2.9)
Maintenance after neoadjuvant	1 (1.4)
Name of PARPi2	
Olaparib	23 (32.8)
Niraparib	42 (60.0)
Fuzoloparib	3 (4.3)
Pamiparib	2 (2.9)
PARPi2 treatment outcomes	
Still on treatment	24 (34.3)
Disease progression	43 (61.4)
Adverse events	3 (4.3)



Abstract PR064/#206 Figure 1 Kaplan-Meier plot of progression-free survival of patients receiving PARPi2 as maintenance therapy after PARPi1 maintenance therapy (N=56)

Results Seventy patients were included, and the median follow-up time was 13.0 months. Fifty-six (80%, 56/70) patients received PARPi as maintenance after maintenance therapy (table 1). The median PFS (mPFS) was 10.6 months (95% confidence interval [CI], 7.1–12.0) with first PARPi (PARPi1) and 8.6 months (95% CI, 5.3–13.0) with PARPi retreatment (PARPi2) (figure 1). 32.1%(18/56) patients were BRCA1/2 mutated, the PFS were not significantly different from BRCA wild-type or unknown patients (BRCAm vs. BRCAwt or unknown, HR=0.997 [95%CI: 0.480–2.072], P=0.9935). 87.5% (39/56) of patients switched to other PARPi when rechallenging. Patients switched to other PARPi rechallenging had numerically longer mPFS compared with those didn't switch (mPFS: 8.6 vs. 7.7 months; HR=0.820 [95%CI: 0.394–1.707], P=0.5958). Overall, 4.3% (3/70) discontinued PARPi2 due to adverse events, most commonly due to hematologic adverse events.

Conclusion/Implications Our study is the first multicenter real-world study to evaluate the rechallenge of PARPi in ovarian cancer patients in China. There is a pressing need to identify the biomarkers except BRCA to select appropriate patients for PARPi rechallenge.

PR065/#611 METASTATIC PATTERN OF OVARIAN CANCER DELINEATED BY TRACING THE EVOLUTION OF MITOCHONDRIAL DNA MUTATIONS

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Introduction Ovarian cancer (OC) is the most lethal gynecologic tumor and is characterized by a high rate of metastasis. Challenges in accurately delineating the metastatic pattern have greatly restricted the improvement of treatment in OC patients.

Methods We applied multiregional sampling and high-depth mitochondrial DNA (mtDNA) sequencing to determine the metastatic patterns in advanced-stage OC patients. Somatic mtDNA mutations were profiled from a total of 195 primary and 200 metastatic tumor tissue samples from 35 OC patients.

Results Our results revealed remarkable sample-level and patient-level heterogeneity. In addition, distinct mtDNA mutational patterns were observed between primary and metastatic OC tissues. Further analysis identified the different mutational spectra between shared and private mutations among primary and metastatic OC tissues. Analysis of the clonality index calculated based on mtDNA mutations supported a monoclonal tumor origin in 14 of 16 patients with bilateral ovarian cancers. Notably, mtDNA-based spatial phylogenetic analysis revealed distinct patterns of OC metastasis, in which a linear metastatic pattern exhibited a low degree of mtDNA mutation heterogeneity and a short evolutionary distance, whereas a parallel metastatic pattern showed the opposite trend. Moreover, a mtDNA-based tumor evolutionary score (MTEs) related to different metastatic patterns was defined. Our data showed that patients with different MTESs responded differently to combined debulking surgery and chemotherapy. Finally, we observed that tumor-derived mtDNA mutations were more likely to be detected in ascitic fluid than in plasma samples.

Conclusion/Implications Our study presents an explicit view of the OC metastatic pattern.