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EFFICACY OF THE PORCUPINE INHIBITOR ETC-1922159 (ETC-159) PLUS PEMBROLIZUMAB IN MICROSATELITE STABLE (MSS) OR PROFICIENT MISMATCH REPAIR (PMMR) PLATINUM RESISTANT OVARIAN CARCINOMAS (PROC)

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Introduction
PD-(L1) inhibitors have limited efficacy in MSS/pMMR recurrent ovarian cancers. Upregulation of the Wnt pathway has been associated with immune exclusion in the tumour microenvironment. ETC-159 is a small molecule porcupine inhibitor that suppresses WNT secretion. Ph1B trial explored the combination of ETC-159 with PD-1 inhibition in PROC.

Methods
In a Phase 1B open label study patients ≥18 years, with adequate organ function and MSS/pMMR PROC were eligible. ETC-159 was dosed orally QOD in combination with 200 mg pembrolizumab IV every 21 days. Responses were evaluated via RECIST1.1 and iRECIST. PK, PD and tumour profiling were assessed at multiple time points throughout the trial.

Results
Six PROC patients were treated with the combination in dose escalation & expansion. The majority (66%) were high-grade serous ovarian carcinomas with a median 4 lines (2–7) of previous treatments. SAEs were pneumonitis and erythema with fever (8 mg, 1 patient). No fractures or other skeletal SAEs were observed. Of 6 evaluable patients, two patients had a PR. 1 harbouring a SUFU-1 mutation (on treatment for 27 weeks) and another with BRCA2 mutant who had progressed on PARPi and immunotherapy. Two others achieved SD as best response for 12 and 18 weeks, respectively, with 1 more currently ongoing. A disease control rate (SD/PR/CR ≥ 12 weeks) of 67% was observed.

Conclusion/Implications
Preliminary data suggest Wnt signaling inhibition with ETC-159 in combination with pembrolizumab is tolerable with no unexpected safety signals and may provide clinical benefit for platinum resistant MSS/pMMR ovarian cancer patients.

EP312/#540

INTRAPERITONEAL CHEMOTHERAPY WITHOUT BEVACIZUMAB VERSUS INTRAVENOUS CHEMOTHERAPY PLUS BEVACIZUMAB AS FRONTLINE THERAPY IN ADVANCED OVARIAN CANCER

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Introduction
To compare the clinical outcomes between intravenous carboplatin/paclitaxel chemotherapy plus bevacizumab versus intraperitoneal cisplatin/paclitaxel chemotherapy without bevacizumab as the frontline treatment in women with advanced ovarian, fallopian tube and primary peritoneal cancer.

Methods
All consecutive women with stage II–IV cancer treated with either frontline intraperitoneal cisplatin/paclitaxel without bevacizumab (IP group) or intravenous carboplatin/paclitaxel with bevacizumab (IVB group) at a tertiary referral center were reviewed.
Results
A total of 59 women (IP group, n=44; IVB group, n=15) were reviewed. There was no significant difference in the progression-free survival (median: 33.6 versus 14.8 months, p=0.13). However, overall survival (OS) was significantly higher in the IP group, compared with the IVB group (median: not reached versus 31.7 months, p=0.02; adjusted hazard ratio (HR)=0.35, 95% confidence interval (CI)=0.10 to 0.87, p=0.006, figure 1). Additional predictors for OS include cancer stage and the number of chemotherapy cycles. Besides, the standard dose of 100 mg/m² cisplatin was a predictor for OS, compared with other intraperitoneal regimens (adjusted HR=0.14, 95% CI=0.02 to 0.87, p=0.03, figure 2).

Conclusion/Implications
Intraperitoneal cisplatin/paclitaxel chemotherapy without bevacizumab seems to be better in OS, compared to intravenous carboplatin/paclitaxel chemotherapy with bevacizumab in the frontline treatment of women with advanced ovarian cancer.

LIMITATION OF CA125 IN PREDICTING COMPLETE RESECTION AFTER NEOADJUVANT CHEMOTHERAPY IN ADVANCED OVARIAN CANCER

Introduction
The optimal timing of interval debulking surgery (IDS) after neoadjuvant chemotherapy (NACT) in advanced epithelial ovarian cancer (EOC) is uncertain. Hence, there is a need to have a reliable test that can predict the feasibility of CC0.

Methods
Patients with stage III/IV EOC, fallopian tube, or primary peritoneal cancer treated in 2016–2021 were reviewed from a single institution. Their clinical parameters and surgical records reviewed retrospectively.

Results
260 eligible patients were identified. 125 patients (54.3%) received NACT, among which 2 (1.6%) had non-evaluable CA125 (i.e., baseline is <2x upper normal limit), and 14 (11.2%) could not undergo IDS due to disease burden. Finally, 100 patients with documentation on the CC0 were included in the analysis (table 1). CC0 rate was 67%.

Univariate analysis showed that the presence of ascites, diaphragmatic and mesentery masses, median change of CA125 level, median Fagott’s score based on pre-operative imaging, were significantly associated with CC0. Multivariate analysis showed that the change of CA125 level was not significant (p=0.069, odds ratio (OR) 0.968; 95% confidence interval (CI) 0.934–1.003), and the only significant parameter was pre-operative radiological Fagotti’s score (p=0.008; OR 1.521; 95% CI 1.117–2.071). Receiver operating characteristics (ROC) curve analysis showed that the area under the curve (AUC) of CA125 in predicting CC0 was 0.678 and 0.740 respectively (figure 1), and the estimated sensitivity of CA125 was 0.53 only.

Conclusion/Implications
The result highlighted the insufficiency of CA125 in predicting CC0. More simple and novel markers are needed to predict the feasibility of CC0.

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