Methods A slide was produced for patients who started 1st parp inhibitor from February 2018 to May 2022, and for patients with tissues before and after 1st parp inhibitor treatment. We analyzed 20 matched tissue samples before and after progression on first exposure to PARPi among patients undergoing re-treatment with PARPi to understand the genomic changes, potential implication in resistance mechanism and response to PARPi re-treatment.

Results 10 patients were platinum sensitive and 10 patients were platinum resistant.

The histological type was identified as High grade serous carcinoma at 90% and endometrioid carcinoma at 10%.

LOH score increased in 15 patients (88%). TMB increased in 13 patients (76%). The average PARP inhibitor usage period in the platinum sensitive group was 14.65 months which is longer than that of platinum resistant group 6.15 months. Analyzing the period of use, the shorter the first PARP inhibitor, the shorter the period of use of the 2nd PARP inhibitor. The most frequently detected gene was MYC amplification and RAD 21 amplification. (n=2)

Conclusion/Implications Post-specific mutations occur and LOH and TMB increase upon progression with PARP inhibitor. Further research on resistance mechanism in case of recurrence using PARP inhibitor is needed.

Abstract EP265/#388

**Abstract EP265/#388 Figure 1**

**EP265/#388** TIMP3 ATTENUATES AGGRESSIVENESS OF OVARIAN CANCER CELLS AND ENHANCES THE SENSITIVITY TO PACLITAXEL

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**Introduction** Epithelial ovarian cancer (EOC) frequently recurs and develops chemo-resistance, resulting in cancer mortality. TIMP3 has been described as a tumor suppressor in several human malignancies, but limited scientific literature focus on the role of TIMP3 in regulating EOC progression or chemoresistance.

**Methods** Both progression-free survival (PFS) and overall survival (OS), stratified by TIMP3 level were estimated using the Kaplan-Meier method and compared using log-rank tests. To increase the expression level of TIMP3 in A2780CP70 cells, the cells were transfected with the TIMP3 expression vector. The migration and invasion abilities of the transfected cells were estimated using transwell assay. The sensitivity of transfected cells to paclitaxel and apoptotic population were evaluated by MTT assay and flow cytometry assay, respectively.

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human apoptotic array was used to screen for changes in apoptosis-related proteins.

**Results** Patients with TIMP3-overexpressed tumor had favorable long-term PFS (p <0.001) and OS (p <0.001) (figure 1A). A significant reduction in cell migration and invasion capacities was observed in TIMP3-overexpressed A2780CP70 cells (figure 1B and 1C). TIMP3 contributed to affect sensitivity of A2780CP70 cells to paclitaxel (figure 2A), rather than cisplatin. Representative apoptotic profiles showed that increased apoptotic cell populations were more apparent in TIMP3-overexpressed A2780CP70 cells, treated with paclitaxel for 48 hours when compared to its parental cells which is possibly related to down-regulation of cIAP-1, survivin, CLSPN, and HSP-27 (figure 2B and 2C).

**Conclusion/Implications** Overexpression of TIMP3 inhibited EOC aggressiveness of A2780CP70, and increased paclitaxel sensitivity. TIMP3 might be a potential target for EOC treatment.