Introduction Compared with HRD-negative ovarian cancer patients, HRD-positive patients are more sensitive to platinum-based chemotherapy and benefit from PARPi is more significant. However, there are still some HRD-positive patients with platinum and PARPi resistance, resulting in a poor prognosis.
Methods In this study, a key differential gene, Oxysterol binding protein like 10 (OSBPL10), was identified by bioinformatics analysis of platinum-resistant and platinum-sensitive HRD-positive ovarian cancer patients after first-line chemotherapy in TCGA database. Western Blot and Immunohistochemistry were performed on tumor tissues from Qilu Hospital of Shandong university to verify the differential expression of OSBPL10. Target genes of OSBPL10 were identified by RNA-seq and validated by RIP. In addition, we established PDX models for high-grade serous ovarian cancer (HGSOC) patients to validate the efficacy of targeting OSBPL10.
Results The expression of OSBPL10 in platinum-resistant HRD-positive ovarian cancer patients were significantly higher than that in platinum-sensitive patients. Inhibiting OSBPL10 enhanced the sensitivity to cisplatin and Niraparib of ovarian cancer cells. Apolipoprotein E (APOE), as a target gene of OSBPL10, was involved in lipid transport and lipoprotein metabolism. Overexpression of OSBPL10 could active the expression of APOE, enhance DNA damage repair function, and up-regulate cholesterol levels in intracellular, extracellular and tumor microenvironment, leading to increased exhaustion of $CD8^+$ T cells, and further promoting resistance to cisplatin and Niraparib. Combined with Niraparib, OSBPL10 adenovirus (shRNA- OSBPL10) was more effective in repressing tumor growth of PDX models than Niraparib monotherapy.
Conclusion/Implications OSBPL10-APOE pathway regulated DNA damage repair and cholesterol metabolism, leading to cisplatin and Niraparib resistance of HRD-positive HGSOC.

EP280/#231 RESPONSE TO SUBSEQUENT PLATINUM-BASED CHEMOTHERAPY POST PARP INHIBITOR IN RECURRENT EPITHELIAL OVARIAN CANCER

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Introduction Maintenance therapy with PARP inhibitors (PARPi) can increase progression free survival (PFS) in recurrent or metastatic platinum-sensitive epithelial ovarian cancer (EOC), though some evidence suggests a decreased response to subsequent platinum-based chemotherapy. This study assessed real-world response rates to platinum-based chemotherapy for recurrent high grade EOC following treatment with a PARPi.
Methods Single center retrospective cohort study of patients prescribed a PARPi as maintenance therapy for recurrent or metastatic EOC, including 54 patients on niraparib and 36 patients on olaparib. Median duration of follow-up after PARPi initiation was 16.3 months.
Results Of the 91 patients included in the analysis, 54 (59.3%) experienced disease progression after PARPi therapy, including 10 (11.0%) who progressed within 6 months of their penultimate therapy. Of the 44 patients with disease progression more than 6 months following penultimate therapy, 32 (72.7%) were rechallenged with platinum-based chemotherapy. Of these, 14 (43.8%) further progressed within 6 months of their platinum rechallenge. Median PFS following platinum rechallenge was 4.4 months. Incidence of platinum resistance was 26.4% in the overall population and 44.4% in those with disease progression after initiation of PARPi therapy.
Conclusion/Implications Disease progression following PARPi therapy showed a poor response to subsequent platinum-based chemotherapy, even when progression occurred more than 6 months after the penultimate platinum-based chemotherapy. This supports the theory that PARPi resistance correlates with platinum resistance and raises concern for possible contribution of PARPi in the induction of platinum resistance in recurrent EOC.

EP282/#263 ONCOLOGIC OUTCOME OF PRIMARY TREATMENT IN PATIENTS DIAGNOSED WITH EPITHELIAL OVARIAN/TUBAL/PERITONEAL CARCINOMA WHOM UNDERWENT SUBOPTIMAL SURGERY

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Introduction To evaluate the response rate of primary treatment, its predicting factors, and to analyze survival outcomes in patients with epithelial ovarian/tubal/primary peritoneal carcinoma whom underwent suboptimal surgery.
Methods This study included women whom received suboptimal surgery between May 2006 and December 2020. The data of patient's clinical information, histopathology, tumor stage, surgical methods and outcomes, adjuvant treatment, and primary treatment outcomes were collected. Follow-up data was documented until 31 March 2023. The oncologic outcomes were analyzed.
Results Total of 320 study patients, overall response rate was 58.1%. The median progression free survival (PFS) duration was 13.167 months [6.675–20.583], and the median overall survival (OS) was 32.850 months [15.008–53.642]. The factors significantly associated with response were received neoadjuvant chemotherapy (NAC) with adjusted odd ratio (aOR) 3.342 (95% CI 1.619–6.900, P=0.001), and high-grade serous carcinoma (HGSC) (aOR 0.153, 95% CI 0.092–0.255, P<0.001). HGSC associated with longer median PFS (15.9 months vs 7.2 months, P<0.001) and median OS (35.221 months vs 11.994 months, P<0.001) compared to non-HGSC.
Conclusion/Implications The oncologic outcomes of study patients were comparable to the landmark trials. HGSC has higher response rate, longer PFS and OS than non-HGSC.