Methods The American Association for Cancer Research’s (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) database version 13.1 was queried via cBioPortal (http://genie.cbioportal.org) for the following gynecologic tumors: epithelial ovarian, sex-cord stromal, germ cell, endometrial, uterine sarcoma, cervical and vulvar/vaginal tumors. PGV frequencies of 27 HRD genes were descriptively reported among these tumors: ATM, ARID1A, ATRX, BRCA1, BRCA2, BARD1, BRIP1, BLM, BAP1, CHEK1, CHEK2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCL, MRE11, NBN, PALB2, RAD50, RAD51, RAD51B, RAD51C, RAD51D, WRN.

Results A total of 13,312 tumors from 12,804 patients were included for analysis. At least one PGV in an HRD gene was found in 29.6% (3946/13,312) of all samples analyzed, with the highest frequency observed in endometrial tumors (2156/5087, 42.4%), uterine sarcomas (196/704, 27.8%), and epithelial ovarian tumors (1402/6052, 23.2%). There were also substantial rates of HRD PGVs in cervical and vulvar/vaginal tumors, and comparatively lower rates among germ cell and sex cord/stromal tumors (table 1). Across all tumors, HRD genes with the highest frequencies of PGVs were ARID1A (19.6%), BRCA1 (3.9%), BRCA2 (3.7%), and ATM (3.7%).

Conclusion/Implications NGS data demonstrate a substantial rate of somatic PGVs in HRD genes across most types of gynecologic tumors analyzed. These data suggest the need to expand routine functional HRD status assessment beyond epithelial ovarian tumors, and also suggest the need for clinical trials evaluating the efficacy of HRD targeting agents in these cancers.
cancer and to determine the possibility of inhibiting ovarian cancer progression using novel therapeutics.

**Methods**

In this study, we analyzed the conditioned media in SKOV3 ovarian cancer cell line treated with catecholamine to identify secreted proteins responding to chronic stress.

**Results**

We observed that epinephrine and norepinephrine enhanced the secretion and mRNA expression of CXC-chemokines (CXCL1, 2, 3, and 8). Neutralizing antibody to CXCL8 and CXCL8 receptor (CXCR2) inhibitors significantly reduced catecholamine-mediated invasion of SKOV3 cells. Finally, we found that the concentration of CXCL1 and CXCL8 in the plasma of ovarian cancer patients increased with stage progression.

**Conclusion/Implications**

Therefore, not only can CXCL1 and CXCL8 be used as diagnostic markers for ovarian cancer, but their inhibition also holds promise as a potential therapeutic option for suppressing ovarian cancer progression. Taken together, these findings suggest that stress-related catecholamines may influence ovarian cancer progression through the secretion of CXC-chemokines.

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**PR003/#357**

**PERIPHERAL PD-1+REGULATORY T CELLS FOR PREDICTING TREATMENT RESPONSE TO PARPi INHIBITOR MAINTENANCE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER**

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**Introduction**

Poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitors (PARPi) are becoming the standard of care for epithelial ovarian cancer (EOC). Recently, clinical trials of triple maintenance therapy (PARPi+anti-angiogenic agent+anti-PD-1/L1) are actively ongoing. Here, we investigated the immunological effects of PARPi or triple maintenance therapy on T cells and their impact on clinical responses.

**Methods**

We collected serial blood from EOC patients receiving PARPi therapy (cohort 1: PARPi, n=49; cohort 2: olaparib+bevacizumab+pembrolizumab, n=31). Peripheral T cells were analyzed using flow cytometry and compared according to the PARPi response. Progression-free survival (PFS) was assessed according to predictive biomarkers identified in a comparative analysis.

**Results**

Regulatory T cells (Tregs) were suppressed by PARPi therapy, whereas PD-1 was not significantly changed. Short PFS group exhibited a higher percentage of baseline PD-1+Tregs than long PFS group, and the patients with high percentage of PD-1+Tregs before treatment showed poor PFS in cohort 1. However, the expression of PD-1 on Tregs significantly decreased after receiving triple maintenance therapy, and the reduction in PD-1+Tregs was associated with superior PFS in cohort 2 (P=0.0078).

**Conclusion/Implications**

PARPi suppresses Tregs, but does not affect PD-1 expression. Addition of PD-1 blockade to PARPi decreases PD-1+Tregs, which have negative predictive value for PARPi monotherapy. Our data suggest that addition of PD-1 blockade to PARPi maintenance therapy is a promising option to improve survival outcomes for high-risk patients with ovarian cancer.

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**PR004/#458**

**CELL-FREE DNA FROM ASCITES IDENTIFIES CLINICALLY RELEVANT VARIANTS AND TUMOUR EVOLUTION IN A COHORT OF PATIENTS WITH ADVANCED OVARIAN CANCER**

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**Introduction**

Poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitors (PARPi) are becoming the standard of care for epithelial ovarian cancer (EOC). Recently, clinical trials of triple maintenance therapy (PARPi+anti-angiogenic agent+anti-PD-1/L1) are actively ongoing. Here, we investigated the immunological effects of PARPi or triple maintenance therapy on T cells and their impact on clinical responses.