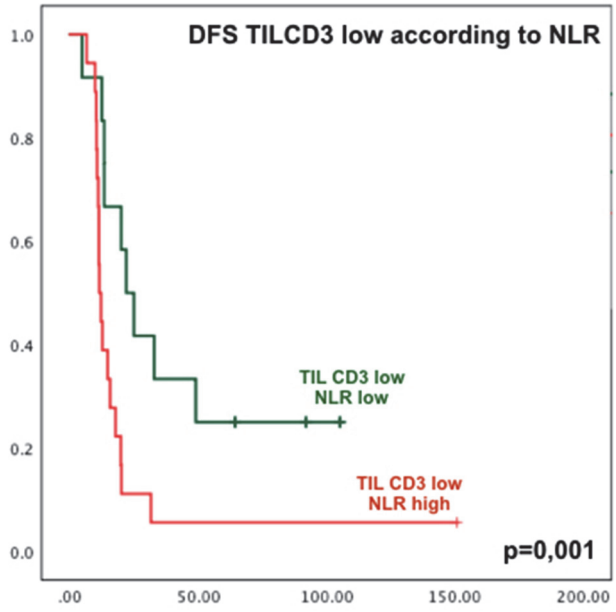

Abstract 413 Figure 2

p = 0.057), and NLR <3.72 (p = 0.004) (figure 1). The combined TIL- NLR analysis stratified patients with infiltration by TILCD3 <25% into 2 subgroups with clearly different prognoses in terms of disease-free survival (DFS) (median DFS 11.49 vs 21.94 months HR 2.74 95% CI 1.18 – 6.26; p =0.019) (figure 2). In addition, the combined analysis in the group of patients differentiated four different prognostic subgroups for OS (p = 0.05). The multivariate analysis including PS and histology showed an independent prognostic value in the variable TIL-NLR in OS (p = 0.009) and DFS (p = 0.003).

Conclusion The combination of TILCD3 and NLR increases their prognostic value in OC. Combination prognostic factor could be very useful for improving immunotherapy strategies in advanced ovarian cancer.

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416 ELUCIDATING RESISTANCE MECHANISM TO PARP INHIBITORS FOR THE DEVELOPMENT OF NOVEL THERAPEUTIC APPROACHES IN HIGH-GRADE SEROUS OVARIAN CANCER

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Introduction/Background PARP inhibitors (PARPi) have been established as a targeted therapeutic approach not only in patients with high-grade serous ovarian cancer (HGSOC) that have genetic loss of function of BRCA1/2-associated DNA repair. However, treatment efficacy varies and neither BRCA mutation, nor homolog recombination deficiency (HRD) status seem to be optimal predictors. Moreover, mechanisms of treatment resistance are poorly understood and novel approaches are urgently required.

Methodology Here we created gene expression data of HGSOC patients (n=52) before PARPi treatment to elucidate key signaling pathways of resistance to increase their efficacy in combinatorial therapeutic strategies. We performed a comprehensive bioinformatics analysis of the differentially expressed genes between the 25% extreme responders (n=26; 13 each group), including gene set enrichment analysis (GSEA) and causal inference analysis with the CARNIVAL pipeline to elucidate the underlying molecular and regulatory mechanisms governing treatment efficacy and resistance.

Results In accordance with recent publications, we found higher levels of MYC activity in non-responders and deregulation of the Wnt/ß-catenin signaling pathway resulting in PARPi treatment resistance. The pathway enrichment analysis also revealed specific pathways especially PDGFR, FGFR, PI3K/mTOR and MAPK signaling pathway associated with resistant phenotype. Furthermore, we have identified key kinases, particularly JAK1/2 and SRC that might mediate resistance to PARP inhibition. In addition, differential gene expression analysis revealed folate receptor 1 (FOLR1) to be significantly higher expressed in non-responders (logFC = 2.66; p < 0.0026) with the potential as a serum-based biomarker not only for ovarian cancer, as it correlates closely with CA125, but also PARPi treatment efficacy.

Conclusion In conclusion, these findings define a network of pathways, that are crucial to mediate mechanism of PARPi resistance and identified key signaling kinases as therapeutic targets in ovarian cancer.

Disclosures The authors declare no conflict of interest.

418 FIRST REAL-WORLD HEMATOLOGIC ADVERSE EVENTS EXPERIENCE WITH NIRAPARIB IN ADVANCED OVARIAN CANCER

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Introduction/Background Niraparib, a poly (ADP-ribose) polymerase (PARP) 1/2 inhibitor, has been approved by Food and Drug Administration (FDA) for ≥3 line recurrence ovarian cancer (OC), the platinum-sensitive recurrence maintenance treatment and new diagnosed maintenance treatment using individual starting dose (ISD, 200 mg daily for body weight <77 kg or platelet count <150,000/μL, 300 mg daily for body weight ≥77 kg and ≥150,000/μL). This study aimed to retrospectively assess the incidence of hematologic adverse events (AEs) in real-world Chinese OC patients using ISD niraparib in Zhejiang Cancer Hospital.

Methodology All medical records of OC patients with ISD niraparib in the Zhejiang Cancer Hospital from February 2019 to January 2020 were reviewed. Treatment-emergent hematologic AEs including leukopenia, anemia and thrombocytopenia were collected and analyzed.

Results A total of 43 patients with OC were included in this study. The median body weight was 50.5 (33, 75) kg. 200 mg QD was taken as ISD for all patients. Twenty seven (62.8%) patients were of BRCA wild-type, 14 (32.6%) were of BRCA mutants and 2 (4.6%) were unknown. Niraparib