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.


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

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Abstracts

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/mc, 300 mg daily for body weight ≥77 kg and ≥150,000/mc). 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 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 improve 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.
was used as newly diagnosed maintenance treatment in 25 (58.1%) patients, as treatment for ≥3 line recurrence treat-
ment in 14 (32.6%) patients, and as platinum-sensitive recur-
rence maintenance treatment in 4 (9.3%) patients. Overall, 28
(65.1%) patients experienced ≥1 grade hematologic AEs,
which included leukopenia (37.2%), anemia (34.9%) and
thrombocytopenia (39.5%). Only 10 (23.3%) patients had
grade 3/4 AEs including leukopenia (9.3%), anemia (7.0%)
and thrombocytopenia (11.6%). Until last follow up, the
median time for the occurrence of leukopenia, anemia and
thrombocytopenia were 30 (range: 7, 162), 34 (range: 7, 108)
and 20 (range: 13, 180) days, respectively. No deaths were
reported. Of those patients who experienced AEs during treat-
ment, the dose was reduced in 4 (14.3%) patients, and treat-
ment was interrupted in 9 (32.1%) patients. Additional
recombinant human granulocyte colony stimulating factor
(n=5, 17.9%), erythrocyte (n=2, 7.1%) and recombinant
human thrombopoietin (n=5, 17.9%) were provided for treat-
ing the AEs. After intervention, 8 (18.6%) patients restart the
treatment and only 1 (2.3%) patient discontinued the
treatment.

Conclusion The incidence of hematologic AEs in real-world
experience was lower than reported by niraparib 300 mg/day
in ENGOT-OV16/NOVA trial. In addition to maintenance treatment
in the first line, the patients in platinum-sensitive recur-
cence treatment and later line treatment might benefit
from ISD niraparib.

Disclosures The authors declare that they have no competing
interests.

419 SIGNALING PATHWAYS RELATED WITH ITGBL1 IN
OVARIAN CANCER CELLS
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Bioinformatics

Introduction/Background Integrin beta-like 1 (ITGBL1) is a
poorly characterized protein comprised of ten EGF-like
repeats. Our previous studies suggested that higher ITGBL1
mRNA expression level in the tumor is related with shorter
survival of ovarian cancer patients. 1, 2 Subsequent functional in
vitro studies revealed that ITGBL1 overexpression in ovarian
cancer cells resulted in the altered adhesion, migration and
invasiveness, while it had no effect on proliferation rate and
the cell cycle. ITGBL1-overexpressing cells were significantly
more resistant to cisplatin and paclitaxel, 3 major drugs used in
OC treatment. 4 In the current study we analyzed gene expres-
sion profiles of ITGBL1-overexpressing and control ovarian
cancer cells and investigated ITGBL1 influence on ovarian
cancer cell signaling pathways.

Methodology ITGBL1 coding sequence was PCR-amplified
from cDNA and cloned into pLNCX2 vector. Retroviral sys-
tem was used to obtain two ovarian cancer cell lines: OAW42/ITGBL1(+) and SKOV3/ITGBL1(+) with overexpres-
sion of ITGBL1. Control cell lines were obtained by transduc-
tion with an empty vector. RNA was isolated from wild type,
ITGBL1-overexpressing and control cells. DNA microarray
experiment was performed using GeneChip™ Human Trans-
scriptome Array 2.0 (Affymetrix, Santa Clara, CA, USA)
according to the manufacturer’s instructions. Bioinformatical
analysis was carried out in R environment (version 3.5.3) with
Bi conductor packages.

Results Using Principal Component Analysis, an unsupervised
method of data analysis, we selected gene sets related to major
sources of variability in our dataset. Then, by perform-
ing Gene Set Enrichment Analysis we found 76 and 146 sig-
nificantly affected cellular signaling pathways (in OAW42 and
SKOV3 cell line, respectively). Majority of them (22 and 44,
respectively) were related to extracellular matrix structure and
function, integrin signaling, focal adhesion, cell junction, cellu-
lar motility, ERBB2 and ERBB4 signaling, etc.

Conclusion Global gene expression analysis revealed that sig-
naling pathways affected by ITGBL1 overexpression were
mostly those related to extracellular matrix organization and
function, integrin signaling, focal adhesion, cellular communi-
cation and motility. These results are concordant with func-
tional changes observed in ITGBL1-overexpressing cells, like
altered adhesiveness, enhanced motility and invasiveness. Over-
all, our results indicate that higher expression of ITGBL1 in
ovarian cancer cells is associated with features that may wor-
sen clinical course of the disease.

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423 FIBRONECTIN AND PERIOSTIN AS PROGNOSTIC
MARKERS IN OVARIAN CANCER
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Introduction/Background In our previous microarray study we
identified a 96-gene prognostic signature associated with the
shorter overall survival (OS) of ovarian cancer patients. 1 Two
genes from this signature, both coding for extracellular matrix
proteins, were objects of the present study: FN1 and POSTN.
We analyzed, by immunostaining, expression of encoded pro-
teins in the independent set of ovarian cancer samples and
evaluated its correlation with clinical, pathological, and molec-
ular features.

Methodology Ovarian cancer samples from 108 patients were
analyzed by immunohistochemistry using rabbit anti-human
fibronectin polyclonal antibody (1:3000 dilution, A0245,
Dako, Glostrup, USA) and rabbit anti-human peristin