Abstract EP299/#540 Figure 1 Kaplan-Meier estimates of overall survival

Conclusions Despite differences in patient and treatment characteristics, OS of patients treated in the control arm of OVARPEC-1 was similar to patients treated outside the trial. This finding does not lend support for the hypothesis that the survival benefit seen in the trial was caused by inferior outcome of patients selected for the trial. These results support the administration of HIPEC in stage III EOC patients undergoing interval CRS in clinical practice.

Abstract EP299/#232 GENOMIC INSTABILITY AS A DETERMINANT OF IMMUNE ESCAPE IN OVARIAN CANCER

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10.1136/ijgc-2022-igcs.390

Objectives Genomic instability is a hallmark of human cancer, with fundamental relevance to cancer etiology and evolution, anti-tumor immunity and therapeutic response. High-grade serous ovarian cancer (HGSOC) is an archetypal cancer of genomic instability defined by distinct mutational processes, intraperitoneal spread and tumor heterogeneity. As immunotherapies have thus far proven ineffective in HGSOC, we sought to establish the determinants of immune evasion in its natural disease history.

Methods We studied the impact of mutational processes and of spatial heterogeneity on cellular phenotypes in the tumor microenvironment (TME), using genome-based stratification of homologous recombination proficient (HRP) and deficient (HRD) disease subtypes, profiling single cell phenotypes from ~1 million cells by single cell RNA sequencing, and site-matched in situ spatial imaging of 160 tumor sites obtained from 42 treatment-naive patients.

Results Mutational processes in HRD-Del (BRCA1inc-like) tumors were associated with a high neoantigen burden, cell-intrinsic JAK/STAT signaling and CD8+ T cell dysfunction; HRD-Del (BRCA2mut-like) tumors presented expanded M2-type macrophage populations; and foldback inversion (FBI, HRP) tumors were associated with cell-intrinsic TGFβ signaling, immune exclusion and predominantly naive T cells. HLA loss of heterozygosity was a common mechanism of immune escape in HRD tumors, connecting evolutionary selection with immune states. Multi-region sampling also revealed substantial spatial variation, highlighting the adnexa as an ‘immune-privileged’ site, and suggesting that organ microenvironments can direct immune pruning in patients with widespread disease.

Conclusions Our findings yield mechanistic insights linking mutational processes in HGSOC to intra- and inter-patient variation in immune resistance, which can be leveraged to optimize future immuno-therapeutic strategies.

Impact of initiation timing of Niraparib Maintenance treatment in newly diagnosed advanced ovarian cancer

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10.1136/ijgc-2022-igcs.391

Objectives PARPi maintenance treatment (MT) is indicated for patients with newly diagnosed advanced ovarian cancer (aOC) after first-line platinum-based chemotherapy (1LC). However, the impact of initiation timing of PARPi MT is unclear. This study aims to compare the efficacy and safety of niraparib MT initiated after different intervals upon completion of 1LC.

Methods This is a post hoc analysis of the PRIME phase 3 study (NCT03709316). Adults with newly diagnosed aOC and a response to 1LC were randomized 2:1 to receive niraparib or placebo within 12 weeks upon completing of 1LC. The primary endpoint was PFS by BICR. Subgroups comprised...
patients who initiated MT <9 weeks or ≥9 weeks upon completion of 1LCT.

Results Key baseline characteristics were overall balanced between groups (table 1). Median PFS (95% CI) was 29.4 months (16.9–not estimable) with niraparib versus 8.3 months (5.5–11.0) with placebo (HR =0.31; 95% CI, 0.20–0.48) for the <9 weeks group and was 24.7 months (16.5–not estimable) with niraparib versus 10.8 months (6.5–24.9) with placebo (HR=0.60; 95% CI, 0.41–0.89) for the ≥9 weeks group (figure 1). Grade ≥3 hematological adverse events occurred in similar proportions of niraparib-treated patients for the <9 weeks and ≥9 weeks groups: anemia (19.3% versus 17.0%), platelet count decreased (18.4% versus 10.6%), and neutrophil count decreased (15.8% versus 18.4%).

Conclusions Whether initiated <9 weeks or ≥9–12 weeks upon completion of 1LCT, niraparib MT conferred clinically significant benefit versus placebo to patients with newly diagnosed aOC, without significant impact on safety profile.

Abstract EP300/#876 Figure 1 PFS by BICR (intention-to-treat): initiation of maintenance treatment <9 weeks or ≥9 weeks upon completion of chemotherapy

Abstract EP300/#876 Table 1 Key baseline characteristics for groups who initiated maintenance therapy <9 weeks or ≥9 weeks upon completion of 1LCT

<table>
<thead>
<tr>
<th></th>
<th>&lt;9 weeks after 1LCT</th>
<th>≥9 weeks after 1LCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>Niraparib (N=114)</td>
<td>Placebo (N=58)</td>
</tr>
<tr>
<td>No. of patients</td>
<td>Niraparib (N=141)</td>
<td>Placebo (N=71)</td>
</tr>
<tr>
<td>Progression-free survival (%)</td>
<td>53 (46.5)</td>
<td>43 (74.1)</td>
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<tr>
<td>Hazard ratio (95% CI)</td>
<td>0.31 (0.20–0.48)</td>
<td>0.60 (0.41–0.89)</td>
</tr>
</tbody>
</table>

Objectives Patient preferences regarding management approach following frontline platinum-based chemotherapy for epithelial ovarian cancer (EOC) remain unstudied. Multiple treatment options are available, including PARP inhibitors, so understanding patient preference is critical.