Molecular and immune characterization of squamous cell ovarian cancers for identification of therapeutic targets

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Background:
- Squamous cell carcinoma (SCC) represents <1% of all ovarian cancers (OC) and is associated with poor prognosis.
- It is thought to arise predominantly from malignant transformation of mature cystic teratomas (MCT) but can also arise from Brenner’s tumors (BT) and endometriosis.
- This study seeks to identify prognostic factors and molecular markers associated with OSCC compared to Endometrioid OC (EOC), Clear Cell OC (CCOC), HPV16/18-negative vulvar SCC (VSCC) and HPV16/18-negative cervical SCC (SCS). It is thought to arise predominantly from malignant transformation of mature cystic teratomas (MCT) but can also arise from Brenner’s tumors (BT) and endometriosis.

Methods:
- 812 EOC, 846 CCOC, 32 OSCC, 15 malignant BT, 500 HPV16/18-CCSC, and 472 HPV16/18-VSCC were analyzed using next-generation sequencing of DNA (NextSeq, 500 genes and NovaSeq, WES) and RNA (NovaSeq, WTS) (Caris Life Sciences, Phx, AZ).
- Tumor mutational burden (TMB) was measured by totaling all somatic mutations (mt) per tumor (TMB<20 to >10 mt/MB).
- PD-L1 IHC positivity was determined by a cut-off of >1% CPS (Cosmic, Agilent) and >2% (SP142, Spring Biosciences).
- HPV status determined by WES for HPV16 and 18.
- Statistical significance determined using chi-square and Mann-Whitney U test and adjusted for multiple comparisons (p<0.05).
- UMAP was used to visualize differences or similarities in transcriptomic profiles.
- Real-world overall survival (rOS) obtained from insurance claims data and calculated from first treatment to last contact.
- Hazard ratio (HR) was calculated by Cox proportional hazards, with p-value calculated using log-rank test.

Table 1. Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Endometrioid OC</th>
<th>Clear Cell OC</th>
<th>Squamous OC</th>
<th>Malignant Brenner</th>
<th>HPV16/18-Cervix</th>
<th>HPV16/18- VSCC</th>
<th>Q-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>56 (23-89)</td>
<td>37 (21-89)</td>
<td>55.5 (31-76)</td>
<td>63 (52-87)</td>
<td>59 (20-89)</td>
<td>70 (26-89)</td>
<td>1.13E-45</td>
</tr>
</tbody>
</table>

Fig 1. Mutational Landscape

Fig 2. IO Biomarkers

Fig 3. Tumor mutational burden

Fig 4. ER and PR IHC Staining

Fig 5. IFN Score

Fig 6. UMAP (k-means clustering) to visualize transcriptomic differences.

Fig 7. Real-world Overall Survival (First of Carboplatin to Last Contact)

Conclusion:
- The molecular and transcriptomic profile of OSCC is distinct from EOC, CCOC, and BT but similar to CSCC and VSCC.
- OSCC demonstrated a more immune hot phenotype.
- Further studies are needed to investigate the potential use of immunotherapy in OSCC.