BACKGROUND

- Prostate cancer (PC) has a median onset age of 66, however, recent evidence suggests an increase in incidence of PC diagnosis in males <55 years of age.
- Family history and increased mutational burden has been associated with early onset PC (EOPC), nonetheless, EOPC and average onset PC (AOPC) is poorly understood.
- We characterized EOPC and AOPC, and their association with molecular and immune signature.

METHODS

- 5,305 PC samples were tested by NGS (592, NextSeq; WES, NovaSeq), WTS (NovaSeq) (Caris Life Sciences, Phoenix, AZ).
- RCA-deconvolution using QuantiSEQ was used to assess pathway enrichment was determined by GSEA (Broad Inst).
- Microsatellite-instability (MSI) was tested by fragment analysis.
- Family history and increased mutational burden has been associated with early onset PC (EOPC), nonetheless, EOPC and average onset PC (AOPC) is poorly understood.
- Immunohistochemistry (IHC), and next generation sequencing (NGS).

RESULTS

- Table 1: Patient demographics

<table>
<thead>
<tr>
<th>Term</th>
<th>FDR</th>
<th>NES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloid Dendritic Cells</td>
<td>0.06</td>
<td>1.37</td>
</tr>
<tr>
<td>Epithelial Myeloid Differentiation</td>
<td>0.00</td>
<td>1.50</td>
</tr>
</tbody>
</table>

- EOPC had lower frequency of APC (4.2% vs 5.4%), RET (2.3% vs 4.7%) and AR (1% vs 4.0%) mutation, compared to AOPC (*p<0.05).
- EOPC had higher expression of PSA (1.3-fold, p<0.05) and reduced AR expression (1.3-fold, p<0.01), however, there was no difference in IHC-AR (p>0.05).
- There was no difference in IHC-PD-L1 frequency of (3.4% vs 1.6%), and dMMR/MSI-H (2.1% vs 4.0%) compared to AOPC.
- EOPC had higher expression of TNF (1.2-fold, p<0.05) and reduced AR expression (1.3-fold, p<0.01), however, there was no difference in IHC-AR (p>0.05).

CONCLUSIONS

- Our data suggest that EOPC is enriched in fusion events including TMPRSS2, ETV1, ETV4 and BRAF. Distinct transcriptomic features seen in EOPC included neuroendocrine differentiation, MAPK activations, immunomodulatory gene expression, and increased infiltration of NK cells and dendritic cells, suggesting inherent molecular differences and differential tumor immune microenvironment in EOPC and AOPC.