Abstracts

DEMONSTRATION OF THE UTILITY OF REAL-WORLD PROGRESSION-FREE SURVIVAL (rwPFS) BY APPLICATION OF AN IFN-γ-RELATED SIGNATURE IN A REAL-WORLD COHORT OF PATIENTS WITH MELANOMA

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Background The rapid advancement of immunotherapies in oncology precipitates the need for clinicogenomic databases to verify published findings and to augment related discoveries. Growing bodies of real-world data (RWD) present such opportunities. We used one RWD source, Aster Insights’ ORIEN Avatar® database, to develop criteria for estimating real-world progression-free survival (rwPFS) endpoints and applied these criteria to a melanoma cohort, investigating association of rwPFS with a published, validated, prognostic, IFN-γ-related gene signature developed from clinical trial patients.

Methods A cohort of 239 patients with melanoma and RNA-seq data were identified from the ORIEN Avatar® database (April 2023 release). This pan-cancer database is maintained by Aster Insights, which receives specimens and data submissions (comprised of whole-exome tumor/germline sequencing, RNA sequencing, and lifetime follow-up) from ORIEN members, a consortium research network of 18 U.S. cancer centers. Melanoma samples were collected from either the primary tumor site or a metastasis.

rwPFS endpoints were identified from normalized clinical data. The following were considered uncensored events: 1) annotated progression/recurrence in clinical records, 2) drug therapy annotated as stopped due to progression, 3) identification of new metastases, and 4) death. Patients without an event were right-censored at last follow-up.

RNA-seq analysis utilized a pipeline incorporating RSEM. Gene expression was quantified as Transcript Per Million (TPM), log2(TPM+1) transformed, and ComBat normalized to adjust for batch effects related to preservation method. A summary score was calculated for an 18 gene, IFN-γ-related signature previously reported to predict clinical response in PD-1 blockade.

Results 112 patients in the melanoma cohort had immune-checkpoint inhibitor (ICI) therapy, RNA-seq prior to ICI therapy, and an evaluable rwPFS endpoint. Patient characteristics are shown in table 1. Median follow-up for the cohort was 4.4 years; median rwPFS was 1.5 years. Groups derived from a median cut of the IFN-γ-related signature demonstrated a marginally significant association with rwPFS (p=0.059).

Conclusions The observation of longer rwPFS in the high IFN-γ-related signature group corresponds with the original report of the signature, in which high expression of the signature was associated with a favorable response to ICI treatment.1 Derivation of PFS endpoints from real-world data has recently been demonstrated; the current study provides additional confirmation of the utility of rwPFS.

REFERENCES

Ethics Approval For this study, ORIEN members utilized a standard protocol, Total Cancer Care (TCC®; NCT03977402), to which patients provided an IRB-approved written informed consent at their participating institutions.

Abstract 898 Table 1 Patient characteristics of ICI-treated Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Male</th>
<th>Female</th>
<th>Site of collection</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>52</td>
<td>15</td>
<td>62</td>
<td>20</td>
</tr>
<tr>
<td>Low</td>
<td>57</td>
<td>18</td>
<td>56</td>
<td>20</td>
</tr>
</tbody>
</table>

Abstract 898 Figure 1 rwPFS for IFN-gamma-Related Signature Groups

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