Exploration of potential biomarkers correlated with efficacy of ociperlimab (anti-TIGIT) plus tislelizumab (anti-PD1) in 1L PD-L1+ non-small cell lung cancer (NSCLC)

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Background: PD-L1 expression was associated with anti-immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) + anti-PD-(L)1 treatment, in which a high PD-L1 subgroup showed improved efficacy. We investigated if anti-TIGIT mechanism of action (MOA)-related markers were associated with the efficacy of ociperlimab + tislelizumab in Cohort 3 (1L PD-L1+ NSCLC) of the phase 1/1b AdvanTIG-105 trial (NCT04047862) and evaluated a potential patient-enrichment strategy based on tumor tissue gene expression profile (GEP).

Methods: Tumor tissue GEP was tested using TruSeq RNA Access technology. Ventana SP263 PD-L1 immunohistochemistry (IHC) assay was used to evaluate PD-L1 expression. Median progression-free survival (mPFS) by investigator was calculated descriptively by Kaplan-Meier methodology. 95% confidence intervals for mPFS were generated using the Brookmeyer method. The primary inferential PFS comparison used unstratified log-rank test with 2-sided descriptive P-values.

Results: At data cutoff (Feb 2, 2023), 24 of 45 patients had GEP results. Anti-TIGIT MOA-related genes and signatures correlated with ociperlimab + tislelizumab treatment response. Patients with high (H) vs low (L) expression of TIGIT, CD226, CCR8, or a tumor-associated macrophage (TAM) signature had significantly longer mPFS (Table). Dual biomarkers combining both anti-PD-L1 (PD-L1 IHC) and one of the anti-TIGIT MOA-related factors (TIGIT, CCR8, TAM signature GEP) identified subgroups of PD-L1 H + TIGIT MOA-related factor H patients with improved PFS vs other subgroups (Table). A highly overlapped PD-L1 H + TIGIT H + CCR8 H + TAM signature H patient population was observed in dual biomarker analyses.
Conclusions: Anti-TIGIT MOA-related genes and signatures correlated with efficacy in ociperlimab + tislelizumab-treated 1L PD-L1+ NSCLC. Combining anti-TIGIT MOA-related factors with PD-L1 expression identified a subgroup of patients with improved efficacy.
Table. Efficacy Analyses in Patient Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>TIGIT&lt;sup&gt;a&lt;/sup&gt;</th>
<th>CD226&lt;sup&gt;b&lt;/sup&gt;</th>
<th>CCR8&lt;sup&gt;b&lt;/sup&gt;</th>
<th>TAM&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>H</td>
<td>L</td>
<td>H</td>
<td>L</td>
</tr>
<tr>
<td>mPFS, months (95% CI)</td>
<td>NR (2.6, NR)</td>
<td>5.26 (2.07, 11.86)</td>
<td>NR (4.21, NR)</td>
<td>4.68 (1.41, 15.05)</td>
</tr>
<tr>
<td>PFS, P-value</td>
<td>0.0326</td>
<td>0.0327</td>
<td>0.0131</td>
<td>0.0153</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>TIGIT&lt;sup&gt;+&lt;/sup&gt;</th>
<th>PD-L1&lt;sup&gt;c&lt;/sup&gt; + TIGIT&lt;sup&gt;a&lt;/sup&gt;</th>
<th>PD-L1&lt;sup&gt;c&lt;/sup&gt; + CCR8&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PD-L1&lt;sup&gt;c&lt;/sup&gt; + TAM&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>n</td>
<td>8</td>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>mPFS, months (95% CI)</td>
<td>NR (1.41, NR)</td>
<td>4.76 (2.6, NR)</td>
<td>8.62 (2.07, NR)</td>
<td>2.94 (1.25, NR)</td>
</tr>
</tbody>
</table>

Cutoff: *Top 1/3; #Median; TC≥25%