Patients with advanced non-small cell lung cancer (NSCLC) often develop progressive disease, but treatment options are limited for patients heavily pretreated with anti-programmed death-ligand 1 (PD-L1) antibodies and/or chemotherapy. Sitravatinib is an oral kinase inhibitor targeting TAM (TYRO3, AXL, MER) and split tyrosine-kinase domains containing receptors. Preclinical studies demonstrated that sitravatinib reduces the number of myeloid-derived suppressor cells and regulates TAM cell function. A 1:1 ratio of MHC polarized macrophages, which may help overcome resistance to immune checkpoint inhibitors and augment antitumor immune responses. Tislelizumab is an anti-PD-1 antibody with high affinity and binding specificity for PD-1 that has been engineered to minimize binding to FcγR on macrophages to alleviate antibody-dependent phagocytosis, a potential mechanism of resistance. Combining a PD-1 inhibitor and an agent with immune modulatory and antitumor properties may enhance antitumor activity beyond that provided by either agent alone.

A Phase 1/2 study assessed the safety, tolerability, and antitumor activity of sitravatinib + tislelizumab in various tumor types. We report results from metastatic NSCLC cohorts including both anti-PD-L1-naive patients and those with tumors refractory/resistant (R/R) to anti-PD-L1 therapy.

Methods

An open-label, multicenter, non-randomized, multi-cohort, Phase 1b trial was conducted (NCT03666143). Study design and endpoints are summarized in Figure 1. CoHorts reported herein (A, B, and F) included patients with squamous or non-squamous metastatic NSCLC treated with 1–3 prior lines of systemic therapy, with or without an anti-PD-L1 inhibitor. Enrolled regardless of PD-L1 expression level.

Sitravatinib + tislelizumab in patients with metastatic non-small cell lung cancer

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Introduction

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Results

Table 1. Demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients</th>
<th>A</th>
<th>B</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Median (range)</td>
<td>65 (21–79)</td>
<td>65 (21–79)</td>
<td>65 (21–79)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>30 (39.1%)</td>
<td>10 (33.3%)</td>
<td>10 (33.3%)</td>
<td>10 (33.3%)</td>
</tr>
<tr>
<td>Male</td>
<td>47 (60.9%)</td>
<td>20 (66.7%)</td>
<td>20 (66.7%)</td>
<td>7 (22.2%)</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>59 (78.2%)</td>
<td>22 (73.3%)</td>
<td>15 (50.0%)</td>
<td>12 (40.0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>17 (22.8%)</td>
<td>8 (26.7%)</td>
<td>7 (23.3%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>B-cell PD-L1 expression, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1%</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>0%</td>
<td>75 (100.0%)</td>
<td>32 (100.0%)</td>
<td>32 (100.0%)</td>
<td>12 (100.0%)</td>
</tr>
<tr>
<td>Prior n of lines of systemic therapy</td>
<td>Median (range)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>Prior n of anti-PD-L1 therapy</td>
<td>Median (range)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
</tr>
</tbody>
</table>

Efficacy: Tumor response by PD-L1 expression

• Defined as complete (CR), partial (PR), or progressive disease (PD).

• No association was observed between ORR and PD-L1 expression subgroups.

• Further exploration is required in a larger population.

• OS data are not mature (median follow-up duration: 14.1 months).

Efficacy: Survival

• In the overall population, confirmed progression-free survival (PFS) was 5.5 months (95% CI: 4.1, 7.0) (Figure 3A).

• Median OS was 11.9 months (95% CI: 10.1, 18.8) in the overall population (Figure 3B).

• 0.1% of patients with no post-baseline tumor assessment due to early death were not included in this figure.

• Two patients with no post-baseline tumor assessment due to early death were not included in this figure.

References

7. Acknowledgments

• All authors contributed to the design of the study, collection and analysis of data, and the writing of the manuscript.

• The study was conducted, analyzed, and interpreted independently of the authors.

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