Sitravatinib + tislelizumab in patients with anti-PD-L1 refractory/resistant metastatic non-small cell lung cancer

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Introduction

Sitravatinib in combination with tislelizumab is currently being investigated in several solid tumor types. Tislelizumab is an anti-PD-1 antibody designed to minimize binding to Programmed death protein (ligand)-1 (PD-L1). Inhibitors of PD-L1 inhibitors are effective first-line treatments for advanced non-squamous metastatic NSCLC (NSCLC). Despite this, patients ultimately relapse and treatment options are limited for patients with metastatic NSCLC that is refractory/resistant (R/R) to anti-PD(L)-1 therapy.1-3

Methods

An open-label, multicenter, non-randomized, multi-cohort, Phase 1b trial was conducted (NCT03666143). Patients with R/R metastatic NSCLC that is R/R to anti-PD-L1 therapy are enrolled. The study is non-comparative and is being conducted at 36 sites in China. All patients had NSCLC, metastatic, R/R to ≥1 line of platinum-based chemotherapy (≥1 line of therapy was a study eligibility criterion). Patients must have had ≥3 months of prior PD-(L)1 inhibitor therapy. The primary objective of the study was to assess the safety and tolerability of sitravatinib + tislelizumab in combination with tislelizumab in a diverse population of patients with R/R metastatic NSCLC.

Results

Table 1: Baseline demographic and disease characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N=47)</th>
<th>NE (n=1)</th>
<th>SD (n=32)</th>
<th>SD (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 (25-79)</td>
<td>68 (25-79)</td>
<td>55 (24-79)</td>
<td>66 (24-79)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>Male 36 (76.6)</td>
<td>24 (82.7)</td>
<td>31 (96.9)</td>
<td>24 (60.0)</td>
</tr>
<tr>
<td>Female 11 (23.4)</td>
<td>4 (17.3)</td>
<td>1 (3.1)</td>
<td>3 (9.1)</td>
<td>4 (10.0)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White 11 (23.4)</td>
<td>3 (100.0)</td>
<td>5 (15.6)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Asian 36 (76.6)</td>
<td>1 (33.3)</td>
<td>27 (84.4)</td>
<td>39 (92.3)</td>
<td>31 (75.0)</td>
</tr>
<tr>
<td>Histology, n (%)</td>
<td>NSCLC 43 (91.5)</td>
<td>1 (100.0)</td>
<td>31 (96.9)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>SCLC 4 (8.5)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
<td>1 (3.1)</td>
<td>1 (2.5)</td>
</tr>
<tr>
<td>NSclc subtype, n (%)</td>
<td>NSc 40 (85.1)</td>
<td>1 (100.0)</td>
<td>29 (89.4)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Squamous cell carcinoma 7 (14.9)</td>
<td>0 (0.0)</td>
<td>3 (9.4)</td>
<td>1 (2.5)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Performance status, n (%)</td>
<td>0 32 (68.1)</td>
<td>1 (33.3)</td>
<td>29 (89.4)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>1 15 (31.9)</td>
<td>0 (0.0)</td>
<td>3 (9.4)</td>
<td>1 (2.5)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Previous lines of therapy, n (%)</td>
<td>1 23 (48.9)</td>
<td>1 (33.3)</td>
<td>21 (65.6)</td>
<td>2 (5.0)</td>
</tr>
<tr>
<td>2 24 (51.1)</td>
<td>1 (33.3)</td>
<td>1 (3.1)</td>
<td>2 (5.0)</td>
<td>2 (5.0)</td>
</tr>
<tr>
<td>Prior treatment with sitravatinib, n (%)</td>
<td>0 40 (85.1)</td>
<td>1 (33.3)</td>
<td>29 (89.4)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>1 7 (14.9)</td>
<td>0 (0.0)</td>
<td>3 (9.4)</td>
<td>1 (2.5)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Prior treatment with tislelizumab, n (%)</td>
<td>0 40 (85.1)</td>
<td>1 (33.3)</td>
<td>29 (89.4)</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>1 7 (14.9)</td>
<td>0 (0.0)</td>
<td>3 (9.4)</td>
<td>1 (2.5)</td>
<td>3 (7.5)</td>
</tr>
</tbody>
</table>

Table 2: Summary of TEAE and TRAE incidence (safety analysis set)

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Total (n=47)</th>
<th>NE (n=1)</th>
<th>SD (n=32)</th>
<th>SD (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>47 (100.0)</td>
<td>47 (100.0)</td>
<td>36 (100.0)</td>
<td>3 (75.0)</td>
</tr>
<tr>
<td>TEAE leading to treatment discontinuation</td>
<td>9 (19.1)</td>
<td>9 (19.1)</td>
<td>6 (16.7)</td>
<td>3 (75.0)</td>
</tr>
<tr>
<td>TRAE</td>
<td>21 (44.7)</td>
<td>8 (17.0)</td>
<td>12 (37.5)</td>
<td>3 (75.0)</td>
</tr>
<tr>
<td>TRAE leading to treatment discontinuation</td>
<td>3 (6.4)</td>
<td>1 (2.1)</td>
<td>1 (3.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>TRAE leading to dose reduction/sequestration</td>
<td>13 (27.7)</td>
<td>4 (8.5)</td>
<td>8 (25.0)</td>
<td>1 (25.0)</td>
</tr>
</tbody>
</table>

Conclusions

- **Safety**: Tislelizumab and sitravatinib had a manageable safety and tolerability profile in patients with metastatic NSCLC that is R/R to prior anti-PD-L1 therapy. The combination demonstrated promising antitumor activity: patients achieved an ORR of 13.6%, DCR of 86.4%, and a median PFS of 5.2 months.

- **Efficacy**: This study supports the potential of sitravatinib in combination with tislelizumab as a potential treatment option for patients with R/R NSCLC. RECIST v1.1 is R to prior anti-PD-L1 therapy, and further investigation is warranted.

Efficacy: Survival

Median overall survival (OS) was 5.2 months (95% CI: 4.1, 5.9) (Figure 3A) and 6-12 month PFS rates were 33.9% (95% CI: 19.0, 49.4) and 64.8% (95% CI: 0.5, 23.5), respectively.

Efficacy: PDL-1 expression and tumor response

- Defined cut-offs for PD-L1 tumor cell or immune cell expression were used to investigate whether there was an association between PD-L1 expression and tumor response.

- Based on current results, no association was observed (Figure 4) and further exploration is required in a larger population.

References

4. Incidences reported above are rounded to the nearest whole number.

Acknowledgements

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