AdvantTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab + Tislelizumab With Chemotherapy in Patients With Metastatic Squamous and Nonsquamous Non-Small Cell Lung Cancer

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Background

• Inhibition of TIGIT with anti-PD-1 is a combination that shows enhanced antitumor activity in preclinical models1-3

• Early studies have shown promising antitumor activity of TIGIT inhibitors in combination with PD-1/PD-L1 inhibitors in patients with NSCLC4-6

• Ociperlimab is a humanized, Fc-intact, IgG1 anti-TIGIT mAb that binds to TIGIT with high affinity. Tislelizumab is an anti-PD-1 mAb approved in China in combination with chemotherapy for first-line treatment of NSCLC, or as a second- or third-line treatment for patients with locally advanced or metastatic NSCLC3,7

• In the ongoing AdvanTIG-105 study (NCT04047862), the RP2D was 900 mg ociperlimab IV Q3W plus tislelizumab 200 mg IV Q3W. The combination was generally well tolerated, and preliminary antitumor activity was observed in patients with advanced, unresectable solid tumors8

• We report results from Cohorts 1 and 2 in the dose-expansion part of the phase 1b AdvanTIG-105 study


IV, intravenously; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; RP2D, recommended phase 2 dose; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains.
AdvanTIG-105: Study Design and Baseline Characteristics (Cohorts 1 and 2)

Open-Label, Multicenter, Phase 1b Study

Cohort 1 inclusion criteria
- Histologically or cytologically confirmed metastatic squamous NSCLC
- No prior treatment
- ECOG PS 0-1

Cohort 1
- Ociperlimab 900 mg IV + tislelizumab 200 mg IV Q3W (+ paclitaxel/nab-paclitaxel + carboplatin)²

Continue until
- Disease progression
- Intolerable toxicity, or
- Withdrawal of consent

Cohort 2 inclusion criteria
- Histologically or cytologically confirmed metastatic nonsquamous NSCLC
- EGFR/ALK/ROS1 wild-type
- No prior treatment
- ECOG PS 0-1

Cohort 2
- Ociperlimab 900 mg IV + tislelizumab 200 mg IV + pemetrexed Q3W (+ cisplatin/carboplatin)²

Primary Endpoint:
- Investigator-assessed ORR per RECIST v1.1²

Key Secondary Endpoints:
- Investigator-assessed DoR and DCR per RECIST v1.1²
- Safety³

Baseline Characteristics:
- As of June 20, 2022, 84 patients were enrolled (Cohort 1: n=41; Cohort 2: n=43)
- The median age was 66.0 years (range: 43-82) for Cohort 1, and 63.0 years (43-79) for Cohort 2. In Cohort 1, 85.4% of patients were male, and in Cohort 2, 72.1% of patients were male
- The median study follow-up was 30.7 weeks (range: 1.1-56.0) in Cohort 1 and 30.0 weeks (range: 3.6-64.6) in Cohort 2

*Administered Q3W for 4-6 cycles during the induction phase only; ²Efficacy-evaluable analysis set included all patients who received ≥1 dose of study drugs, had evaluable disease at baseline, and ≥1 evaluable postbaseline tumor response assessment unless any clinical PD or death occurred before the first postbaseline tumor assessment; ³Safety analysis set included all patients who received ≥1 dose of study drugs.

ALK, anaplastic lymphoma kinase; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IV, intravenously; NSCLC, non-small cell lung cancer; ORR, overall response rate; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS1, c-ros oncogene 1.
Antitumor Response

The ORR was 57.5% in Cohort 1 and 54.8% in Cohort 2

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1 (n=40)</th>
<th>Cohort 2 (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR, n (%)</strong></td>
<td>23 (57.5)</td>
<td>23 (54.8)</td>
</tr>
<tr>
<td>95% CI</td>
<td>40.9, 73.0</td>
<td>38.7, 70.2</td>
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<tr>
<td><strong>BOR, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>23 (57.5)</td>
<td>23 (54.8)</td>
</tr>
<tr>
<td>SD</td>
<td>13 (32.5)</td>
<td>15 (35.7)</td>
</tr>
<tr>
<td>PD</td>
<td>1 (2.5)</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>NE</td>
<td>3 (7.5)</td>
<td>2 (4.8)</td>
</tr>
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</table>

- Of the 82 efficacy-evaluable patients, 40 patients were in Cohort 1 and 42 patients were in Cohort 2
- The ORR was **57.5%** (95% CI: 40.9, 73.0) in Cohort 1 and **54.8%** (95% CI: 38.7, 70.2) in Cohort 2
- The median DoR was not reached
Best Change in Target Lesion

Twenty-three patients in each cohort had a partial response to treatment.
Disease Response Over Time

The median duration of response was not reached in Cohorts 1 or 2.

Cohort 1
Response and reason for discontinuation
- Partial response
- Stable disease
- Progressive disease
- Treatment ongoing
- Discontinued due to progressive disease
- Discontinued due to AE or other reason

Cohort 2
Response and reason for discontinuation
- Partial response
- Stable disease
- Progressive disease
- Treatment ongoing
- Discontinued due to progressive disease
- Discontinued due to AE or other reason

AE, adverse event.
Safety

The RP2D of ociperlimab with tislelizumab and chemotherapy had a manageable safety profile.

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Cohort 1 (n=41)</th>
<th>Cohort 2 (n=43)</th>
<th>In total (n=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade TEAE</td>
<td>41 (100.0)</td>
<td>43 (100.0)</td>
<td>84 (100.0)</td>
</tr>
<tr>
<td>Grade ≥3 TEAE</td>
<td>27 (65.9)</td>
<td>24 (55.8)</td>
<td>51 (60.7)</td>
</tr>
<tr>
<td>Serious TEAE</td>
<td>15 (36.6)</td>
<td>17 (39.5)</td>
<td>32 (38.1)</td>
</tr>
<tr>
<td>TEAE leading to ociperlimab discontinuation</td>
<td>10 (24.4)</td>
<td>5 (11.6)</td>
<td>15 (17.9)</td>
</tr>
<tr>
<td>TEAE leading to tislelizumab discontinuation</td>
<td>10 (24.4)</td>
<td>4 (9.3)</td>
<td>14 (16.7)</td>
</tr>
<tr>
<td>Immune-mediated AE³</td>
<td>25 (61.0)</td>
<td>20 (46.5)</td>
<td>45 (53.6)</td>
</tr>
</tbody>
</table>

- In total, 84 patients (100.0%) experienced ≥1 TEAE. The most common TEAEs of any grade were anemia (45.2%), neutrophil count decreased (39.3%), and white blood cell count decreased (38.1%).
- Grade ≥3 TEAEs occurred in 51 patients (60.7%) and serious TEAEs occurred in 32 patients (38.1%).
- 15 patients (17.9%) experienced AEs leading to ociperlimab discontinuation, 14 patients (16.7%) experienced AEs leading to tislelizumab discontinuation.
- Immune-mediated adverse events occurred in 45 patients (53.6%).
Conclusions

- Ociperlimab and tislelizumab plus chemotherapy demonstrated antitumor activity in patients with metastatic squamous and nonsquamous NSCLC
- The RP2D of ociperlimab with tislelizumab and chemotherapy showed a manageable safety profile
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