AdvanTIG-105: A Phase 1 Dose Verification Study of Ociperlimab in Combination with Tislelizumab in Advanced Solid Tumors in Chinese Patients

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Objective: T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) inhibitor in combination with an anti-programmed cell death protein 1 (PD-1) monoclonal antibody (mAb) is an emerging treatment of solid tumors. AdvanTIG-105 is a Phase 1/1b dose-escalation, -verification and -expansion study investigating an anti-TIGIT mAb ociperlimab as a monotherapy, and in combination with an anti-PD-1 mAb tislelizumab, in patients with unresectable advanced, or metastatic solid tumors (NCT04047862). During dose-escalation, conducted in Australia, ociperlimab (50–1800 mg) administered in combination with tislelizumab 200 mg every 3 weeks (Q3W) was generally well tolerated and showed promising antitumor activity in patients with solid tumors. Ociperlimab, across the dosing range, demonstrated linear and dose proportional pharmacokinetics (PK) profile, as well as complete peripheral TIGIT receptor occupancy. Based on the dose-escalation phase, the recommended Phase 2 dose (RP2D) was established as 900 mg ociperlimab in combination with 200 mg tislelizumab (Q3W). The objective of the dose-verification phase of this study was to confirm the safety and efficacy profile of the RP2D in Chinese patients.

Methods: Adult patients (aged ≥ 18 years) with histologically/cytologically confirmed unresectable locally advanced, or metastatic solid tumors, with an Eastern Cooperative Oncology Group performance status of ≤ 1, and no prior anti-TIGIT therapy were enrolled. Patients were treated with the RP2D of ociperlimab (900 mg, intravenous [IV], Q3W), with or without 200 mg tislelizumab (IV, Q3W). Treatment continued until disease progression, unacceptable toxicity, or voluntary withdrawal. The primary endpoint of the study was safety, and the secondary endpoints were objective response rate (ORR), duration of response (DoR), and disease control rate (DCR), all assessed by RECIST v1.1.

Results: As of April 5, 2022, 20 Chinese patients were enrolled into the dose-verification phase (monotherapy: n=9; combination: n=11). The median study follow-up for all patients was 9.2 weeks (range: 1.4–48.0). Within the safety analysis set (N=20), all patients (100%) experienced at least 1 treatment-emergent adverse event (TEAE), and 9 patients (45.0%) had Grade ≥ 3 TEAEs. Serious TEAEs occurred in 9 patients (45.0%), and no patients had a dose limiting toxicity event. Treatment-related adverse events (TRAEs) were experienced by 18 patients (90.0%), including Grade ≥ 3 TRAEs in 2 patients (10.0%), and serious TRAEs in 1 patient (5.0%). No TRAEs led to treatment discontinuation or death.

In the ociperlimab monotherapy arm (n=9), all patients (100%) had at least 1 TEAE, with 4 patients (44.4%) experiencing a Grade ≥ 3 TEAE. The most common any grade TEAE was hyponatremia (44.4%), and the most common Grade ≥ 3 TEAE was dyspnea (22.2%).

A total of 7 patients (77.8%) receiving monotherapy experienced at least 1 TRAE, 1 patient (11.1%) experienced a Grade ≥ 3 TRAE, and no patients had a serious TRAE. An increase in gamma-glutamyltransferase was the most common any grade TRAE (33.3%).

In the ociperlimab plus tislelizumab arm (n=11), all patients (100%) had at least 1 TEAE, with 5 patients (45.5%) experiencing a Grade ≥ 3 TEAE. The most common any grade TEAEs were an increase in blood bilirubin (45.5%), and hypoalbuminemia (45.5%), and there were no Grade ≥ 3 TEAEs that occurred in more than one patient each (9.1%). One death that occurred as the result of an adverse event within 30 days of the last dose (9.1%) was determined to be unrelated to treatment, and related to disease per investigator assessment (Grade 5 gastrointestinal hemorrhage; patient with esophageal cancer).

A total of 11 patients (100%) receiving ociperlimab plus tislelizumab experienced at least 1 TRAE, 1 patient (9.1%) experienced a Grade ≥ 3 TRAE and serious TRAE, respectively. The most common any grade TRAEs were an increase in blood bilirubin (45.5%), an increase in aspartate aminotransferase (27.3%), decreased appetite (27.3%), and chills (27.3%).

Immune-mediated adverse events (imAE) were experienced by 8 patients; 2 patients (22.2%) in the monotherapy arm, and 6 patients (54.5%) in the combination arm. All imAEs were Grade 1 and 2, and none led to treatment discontinuation or death.

There were 15 patients in the efficacy evaluable set. In the monotherapy arm (n=6), 1 patient had stable disease (SD; patient with cervical cancer) and no patients achieved a PR, resulting in a DCR of 16.7% (95% confidence intervals [CI]: 0.0, 64.1). The longest duration of SD in the monotherapy arm was 42 weeks. In the ociperlimab plus tislelizumab arm (n=9), the ORR was 11.1% (n=1/9) with 1 patient achieving partial response (PR; patient with non-squamous non-small cell lung cancer). The DoR in the combination arm was 7.0 months (95% CI: not estimable [NE], NE). An additional 4 patients had SD (44.4%), resulting in a DCR of 55.6% (95% CI: 21.2, 86.3). The longest duration of SD in the combination arm was 36 weeks.

Preliminary pharmacokinetic analysis (N=19) indicates that ociperlimab PK was comparable between the dose-escalation (conducted in Australia) and dose-verification (conducted in China) populations. No patients were found to be ociperlimab anti-drug antibody (ADA)-positive. Tislelizumab ADA-positive rate was comparable with historical data.

Conclusion: The ociperlimab RP2D 900 mg plus tislelizumab IV Q3W was generally well tolerated and showed preliminary antitumor activity in Chinese patients with unresectable advanced, or metastatic solid tumors.