AdvanTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab plus Tislelizumab in Patients with Metastatic NSCLC

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Abstract:

Introduction: T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) inhibitor plus an anti-programmed cell death protein 1 (PD-1) antibody is a promising combination and shows potent efficacy in non-small cell lung cancer (NSCLC). Ociperlimab is a humanized IgG1 monoclonal antibody (mAb) designed to bind to Fc-intact TIGIT with high affinity and specificity. Tislelizumab is an anti-PD-1 mAb approved for the treatment of NSCLC in China. AdvanTIG-105 is a Phase 1/1b open-label study designed to assess the safety and preliminary antitumor activity of ociperlimab plus tislelizumab in patients with advanced, metastatic unresectable solid tumors (NCT04047862). In the dose-escalation part, ociperlimab plus tislelizumab was well tolerated, preliminary efficacy was observed, and the recommended Phase 2 dose of ociperlimab 900 mg intravenously (IV) every three weeks (Q3W) plus tislelizumab 200 mg IV Q3W was established. Here we report results from the dose-expansion part (Cohort 3) of the AdvanTIG-105 study.

Methods: Treatment-naïve adult patients with histologically or cytologically confirmed metastatic squamous or non-squamous NSCLC with programmed death-ligand 1 (PD-L1) positive (tumor cell [TC] ≥ 1% by VENTANA PD-L1 [SP263] Assay) and non-squamous patients with *EGFR/ALK/ROS-1* wild-type tumors were enrolled. Patients received ociperlimab 900 mg IV plus tislelizumab 200 mg IV Q3W until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was investigator-assessed objective response rate (ORR) per RECIST v1.1. Secondary endpoints included investigator-assessed duration of response (DoR), disease control rate (DCR) per RECIST v1.1, and safety. The association between PD-L1 expression and efficacy was also analyzed.

Results: As of December 27, 2021, 36 patients, with a median age of 65.0 years (range 46–81), were enrolled. The median study follow-up time was 15.9 weeks (range 6.1–47.6). All 36 patients were efficacy evaluable; the confirmed ORR was 22.2% (95% confidence interval [CI]: 10.1, 39.2) and the unconfirmed ORR was 44.4% (95% CI: 27.9, 61.9). The DCR was 88.9% (95% CI: 73.9, 96.9). The confirmed ORR in PD-L1 TC ≥ 50% (n=13) was 23.1%, while the confirmed ORR in PD-L1 TC 1–49% (n=23) was 21.7%. The unconfirmed ORR in PD-L1 TC ≥ 50% was 53.8%, while the unconfirmed ORR in PD-L1 TC 1–49% was 39.1%. In total, 33 patients (91.7%) experienced ≥ 1 treatment-emergent adverse event (TEAE), and 10 patients (27.8%) had ≥ Grade 3 TEAEs. Serious TEAEs occurred in eight patients (22.2%). The most common TEAEs were pyrexia (30.6%), pruritus (22.2%), and nausea (19.4%). TEAEs leading to treatment discontinuation occurred in two patients (5.6%). TEAEs leading to death occurred in one patient (2.8%), but the event (cerebral infarction) was not related to the study drugs.

Conclusion: The treatment combination of ociperlimab 900 mg plus tislelizumab 200 mg IV Q3W was well tolerated and showed antitumor activity in patients with treatment-naïve metastatic squamous or non-squamous NSCLC with PD-L1 positive tumors (TC ≥ 1%).