AdvanTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab Plus Tislelizumab in Patients with Metastatic Non-small Cell Lung Cancer

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Objectives: T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) inhibitor plus an anti-programmed cell death protein 1 (PD-1) antibody is a promising combination and shows efficacy in non-small cell lung cancer (NSCLC). Ociperlimab is a humanized Fc-intact IgG1 monoclonal antibody (mAb) designed to bind to 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 generally well tolerated, preliminary efficacy was observed, and the recommended Phase 2 dose of ociperlimab 900 mg intravenously (IV) every 3 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; non-squamous patients with *EGFR/ALK/ROS-1* wild-type tumors) were enrolled. Patients received ociperlimab 900 mg IV Q3W 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 Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Secondary endpoints included investigator-assessed duration of response (DoR) and disease control rate (DCR), both per RECIST v1.1, and safety. The association between PD-L1 expression and efficacy was also analyzed.

Results: As of April 5, 2022, 40 patients, with a median age of 65.0 years (range 46–81), were enrolled. The median study follow-up was 28.1 weeks (range 3.1–61.7). A total of 39 patients were efficacy evaluable; 14 patients (35.9%) had PD-L1 TC ≥ 50%, and 25 patients (64.1%) had PD-L1 TC 1–49%. The ORR in the efficacy-evaluable set (n=39) was 53.8% (95% CI: 37.2, 69.9); 71.4% (95% CI: 41.9, 91.6) in patients with PD-L1 TC ≥ 50%, and 44.0% (95% CI: 24.4, 65.1) in patients with PD-L1 TC 1–49%. The DCR was 89.7% (95% CI: 75.8, 97.1). In the safety analysis set (n=40), 38 patients (95.0%) experienced ≥ 1 treatment-emergent adverse event (TEAE), and 11 patients (27.5%) had ≥ Grade 3 TEAEs. Serious TEAEs occurred in 10 patients (25.0%). The most common TEAEs were pruritus (32.5%), pyrexia (30.0%), rash (20.0%), and decreased appetite (20.0%). TEAEs leading to treatment discontinuation occurred in 3 patients (7.5%). TEAEs leading to death occurred in 1 patient (2.5%), but the event (cerebral infarction) was considered not to be related to the study drugs.

Conclusions: The treatment combination of ociperlimab 900 mg IV Q3W plus tislelizumab 200 mg IV Q3W was generally well tolerated and showed antitumor activity in patients with treatment-naïve metastatic NSCLC with PD-L1 positive tumors (TC ≥ 1%). A higher ORR was observed in patients with PD-L1 TC ≥ 50% tumors than in patients with PD-L1 TC 1–49%.