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

Authors: Rajiv Kumar,1*† Se Hyun Kim,2* DianSheng Zhong,3* Shun Lu,4 Ying Cheng,5 Ming Chen,6 EunKyung Cho,7 Tim Clay,8 Jin-Hyoung Kang,9 Gyeong-Won Lee,10 Meili Sun,11 Byoung Yong Shim,12 David R. Spigel,13 Tsung-Ying Yang,14 Qiming Wang,15 Gee-Chen Chang,16 Guohua Yu,17 Ruihua Wang,18 Xuerui Luo,18 Hao Zheng,19 Rang Gao,18 Hye Ryun Kim20

Affiliations:

1. New Zealand Clinical Research, Christchurch, New Zealand and Department of Pathology, University of Otago, Dunedin, New Zealand
2. Division of Hematology and Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea
3. Department of Oncology, Tianjin Medical University General Hospital, Tianjin, China
4. Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China
5. Department of Thoracic Oncology, Jilin Cancer Hospital, Changchun, China
6. Department of Bioinformatics, State Key Laboratory of Plant Physiology and Biochemistry, College of Life Sciences, Zhejiang University Cancer Hospital, Hangzhou, China
7. Gil Medical Center, Gachon University College of Medicine, Incheon, Korea
8. Department of Medical Oncology, St John of God Subaico Hospital, Western Australia, Australia
9. Division of Medical Oncology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea
10. Division of Hematology and Oncology, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsang National University College of Medicine, Jinju, Korea
11. Department of Oncology, Jinan Central Hospital Affiliated to Shandong University; Jinan Central Hospital Affiliated to Shandong First Medical University, Jinan, China
12. Department of Medical Oncology, Department of Internal Medicine, St. Vincent’s Hospital, The Catholic University of Korea, Suwon, Korea
13. Sarah Cannon Research Institute (SCRI)/ Tennessee Oncology, PLLC, Nashville, Tennessee, USA
14. Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan
15. Department of Internal Medicine, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China
16. Division of Pulmonary Medicine, Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan
17. Oncology Department, Weifang People’s Hospital, Weifang Medical University, Weifang, China
18. BeiGene (Shanghai) Co., Ltd., Shanghai, China
19. BeiGene USA, Inc., San Mateo, CA, USA

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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%).