

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

Rajiv Kumar^{†,1}, Se Hyun Kim^{*,2}, Shun Lu,³ Ying Cheng,⁴ Ming Chen,⁵ EunKyung Cho,⁶ Tim Clay,⁷ Gyeong-Won Lee,⁸ Meili Sun,⁹ Byoung Yong Shim,¹⁰ David R. Spiegel,¹¹ Tsung-Ying Yang,¹² Qiming Wang,¹³ Gee-Chen Chang,¹⁴ Guohua Yu,¹⁵ Ruihua Wang,¹⁶ Wei Tan,¹⁶ Hao Zheng,¹⁷ Rang Gao,¹⁶ Hye Ryun Kim^{†,18}

¹New Zealand Clinical Research, Christchurch, New Zealand and Department of Pathology, University of Otago, Dunedin, New Zealand; ²Division of Hematology and Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea; ³Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; ⁴Department of Thoracic Oncology, Jin Cancer Hospital, Changchun, China; ⁵Department of Bioinformatics, State Key Laboratory of Plant Physiology and Biochemistry, College of Life Sciences, Zhejiang University Cancer Hospital, Hangzhou, China; ⁶GI Medical Center, Gachon University College of Medicine, Incheon, Korea; ⁷Department of Medical Oncology, St John of God Subaco Hospital, Western Australia, Australia; ⁸Division of Hematology and Oncology, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsang National University College of Medicine, Jinju, Korea; ⁹Department of Oncology, Jinan Central Hospital Affiliated to Shandong First Medical University, Jinan, China; ¹⁰Division of Medical Oncology, Department of Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea; ¹¹Sarah Cannon Research Institute (SCRI) Tennessee Oncology, PLLC, Nashville, TN, USA; ¹²Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; ¹³Department of Internal Medicine, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; ¹⁴Division of Pulmonary Medicine, Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan; ¹⁵Oncology Department, Wafang People's Hospital, Wafang Medical University, Wafang, China; ¹⁶BeiGene (Shanghai) Co., Ltd., Shanghai, China; ¹⁷BeiGene USA, Inc., San Mateo, CA, USA; ¹⁸Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Centre, Yonsei University College of Medicine, Seoul, Korea. [†]Co-first author; ^{*}Presenting author; [‡]Corresponding author

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Conclusions

Ociperlimab plus tislelizumab demonstrated antitumor activity as first-line treatment for patients with metastatic NSCLC with PD-L1 positive tumors (TC $\geq 1\%$).

Antitumor activity was observed in patients with tumors with PD-L1 TC 1-49% and PD-L1 TC $\geq 50\%$, with a higher response rate in patients with high PD-L1 TC $\geq 50\%$.

The combination of ociperlimab plus tislelizumab had an acceptable safety profile, with most TEAEs being grade 1 or 2 in severity.

Background

Programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors have improved outcomes for patients with non-small cell lung cancer (NSCLC), however unmet needs remain.¹

Inhibition of T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) in combination with PD-1/PD-L1 inhibition has demonstrated antitumor activity in NSCLC.²⁻⁴

Ociperlimab is a humanized Fc-intact IgG1 monoclonal antibody (mAb) designed to bind to TIGIT with high specificity and affinity.⁵ Tislelizumab is an anti-PD-1 mAb approved for the treatment of NSCLC in China.⁶

In the ongoing phase 1/1b, open-label AdvanTIG-105 dose-escalation/-expansion (NCT04047862) study, ociperlimab plus tislelizumab was well tolerated in patients with advanced, unresectable solid tumors.⁷

Methods

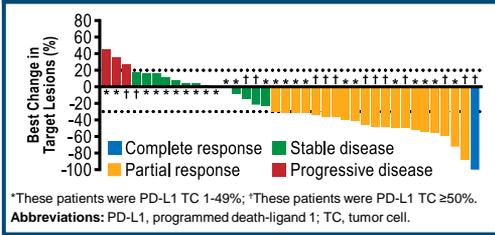
- The recommended phase 2 dose was ociperlimab 900 mg intravenously (IV) every 3 weeks (Q3W) plus tislelizumab 200 mg IV Q3W in the dose-escalation part of the study⁷
- Here we report data from the dose-expansion part (Cohort 3) of the phase 1/1b AdvanTIG-105 study, in patients with metastatic NSCLC (Figure 1)

Results

Baseline Characteristics

- As of April 5, 2022, 40 patients were enrolled in Cohort 3 and comprised the safety analysis set, who received at least one dose of the study drug
- The median age was 65.0 years (range 46-81), and 32.5% of patients were female
- In total, 35.9% (14/39) of patients were PD-L1 TC $\geq 50\%$
- The median study follow-up was 28.1 weeks (range 3.1-61.7)

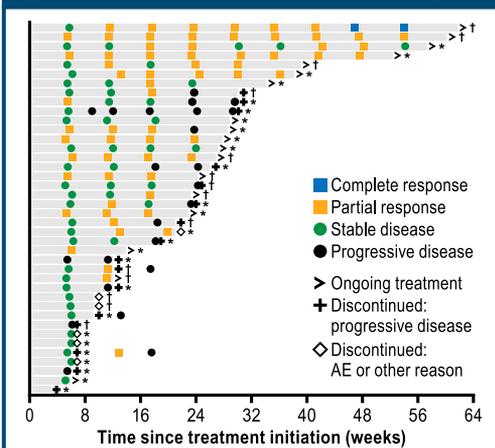
Figure 2. Best Change in Target Lesions



Antitumor activity

- In total, 39 patients were evaluable for efficacy
- The unconfirmed ORR was 53.8% (95% CI: 37.2, 69.9). In patients with PD-L1 TC 1-49% and PD-L1 TC $\geq 50\%$ subgroups, the unconfirmed ORR was 44.0% and 71.4%, respectively (Table 1)
- The median DoR was not evaluable (NE) (Table 1), and the median PFS was 5.4 months (95% CI: 4.2, NE), with 5.2 months and 5.6 months in the PD-L1 TC 1-49% and PD-L1 TC $\geq 50\%$ subgroups, respectively
- The best change in target lesions and the duration of treatment and response are shown in Figure 2 and Figure 3, respectively

Figure 3. Duration of Treatment and Response



Safety

- The safety profiles of ociperlimab and tislelizumab are shown in Table 2

Table 1. Summary of Antitumor Activity

	PD-L1 TC 1-49% (n=25)	PD-L1 TC $\geq 50\%$ (n=14)	Total (N=39)
Unconfirmed ORR, n (%) (95% CI)	11 (44.0) (24.4, 65.1)	10 (71.4) (41.9, 91.6)	21 (53.8) (37.2, 69.9)
CR	0 (0)	1 (7.1)	1 (2.6)
PR	11 (44.0)	9 (64.3)	20 (51.3)
Unconfirmed BOR, n (%)^a			
SD	11 (44.0)	3 (21.4)	14 (35.9)
PD	2 (8.0)	1 (7.1)	3 (7.7)
DCR, n (%)^b	22 (88.0)	13 (92.9)	35 (89.7)
Median DoR, months (95% CI)^b	NE (2.2, NE)	NE	NE (4.2, NE)

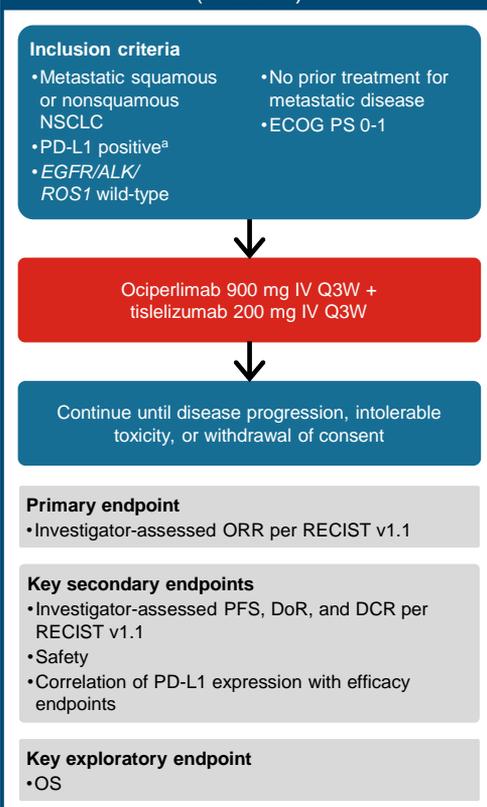
^aOne patient in the PD-L1 1-49% group was NE. This patient had symptoms which were assessed as disease progression but was not considered to have radiological progression; ^bConfirmed.
Abbreviations: BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PD-L1, programmed-death ligand 1; PR, partial response; SD, stable disease; TC, tumor cell.

Table 2. Summary of TEAEs and TRAEs (SAS)

Patients, n (%)	N=40	
	TEAEs	TRAEs
Patients with at least one AE	38 (95.0) ^a	31 (77.5)
\geq Grade 3 AE	11 (27.5) ^b	4 (10.0) ^c
Serious AE	10 (25.0)	4 (10.0)
AE leading to ociperlimab dose modification	17 (42.5)	-
AE leading to tislelizumab dose modification	17 (42.5)	-
AE leading to ociperlimab discontinuation	3 (7.5)	1 (2.5)
AE leading to tislelizumab discontinuation	3 (7.5)	1 (2.5)
AE leading to death	1 (2.5)	0 (0)

^aThe most common TEAEs were pruritus (32.5%), pyrexia (30.0%), decreased appetite (20.0%), rash (20.0%), anemia (17.5%), and dyspnea (17.5%); ^bThe most common grade ≥ 3 TEAEs were pneumonia (7.5%) and anemia (5.0%); ^cThe TRAEs were hyperglycemia, lipase increased, pruritus, acute kidney injury, and pneumonia.
Abbreviations: AE, adverse event; SAS, safety analysis set; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Figure 1. AdvanTIG-105 Study Design (Cohort 3)



^aTC $\geq 1\%$ by VENTANA PD-L1 (SP263) assay by central lab.
Abbreviations: 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, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS1, c-ros oncogene 1; TC, tumor cell.

References
1. De Giglio A, et al. *Current Oncol Rep*. 2021;23(11):126.
2. Rodriguez-Abreu D, et al. *J Clin Oncol* 2020 (Abs 9503) [presented at ASCO 2020].
3. Niu J, et al. *Ann Oncol* 2020 (Abs 1410P) [presented at ESMO 2020].
4. Ahn M-J, et al. *Ann Oncol* 2020 (Abs 1400P) [presented at ESMO 2020].
5. Chen X, et al. Data presented at AACR 2021. Poster 1854.
6. BeiGene. China NMPA approves tislelizumab as second- or third-line treatment for patients with locally advanced or metastatic non-small cell lung cancer. Available at: <https://www.beigene.com/news-details/715-3e3376ea-481c-4389-85a0-3e0d193a71254>. Accessed March 2022.
7. Frenntz S, et al. *J Clin Oncol* 2021 (Abs 2583) [presented at ASCO 2021].

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Disclosures
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Author details:
Rajiv Kumar
Rajiv.Kumar@nzcr.co.nz