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AdvanTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab + Tislelizumab With Chemotherapy in Patients With Metastatic Squamous and Nonsquamous Non-Small Cell Lung Cancer

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Disclosures

HRK, YYu, **DH**, **BG**, **JZ**, **YH, WZ, YYao, TYY, YL,** and **HSS** have no conflicts of interest to declare. **SK** declares invited speaker fees from AstraZeneca, BMS, MSD, Pfizer, Roche, and Specialised Therapeutics; advisory board participation for Boehringer Ingelheim, Lilly, MSD, Pfizer, Roche, Specialised Therapeutics, and Takeda; and research grants from AstraZeneca. **WX** declares invited speaker fees from AZD, Merck, and MSD; advisory board participation for Merck, MSD, and Novartis; and research grants from Merck. **JSK** declares expert testimony for CJ Healthcare; membership of the board of directors at IMBdx; research grants from Alpha Biopharma, Astellas Pharma, AstraZeneca, Boehringer Ingelheim, CJ Healthcare, IL-Yang Pharm, Lilly, Merck, MSD, Novotech, Ono Pharmaceutical, Pfizer, Sanofi, and Yuhan; and advisory roles for Abion Inc. and CJ Healthcare. **RW** declares employment at BeiGene, Ltd. **HZ** declares employment at BeiGene USA; and stocks or shares in BeiGene USA. **WT** declares employment at BeiGene, Ltd.; and stocks or shares in BeiGene, Ltd. **RG** declares employment at BeiGene, Ltd. **SL** declares invited speaker roles for AstraZeneca, Hansoh, and Roche; advisory board participation for AstraZeneca, GenomiCare, Hutchison MediPharma, InventisBio Co. Ltd., Menarini, Mirati Therapeutics Inc., Pfizer, Roche, Yuhan Corporation, and ZaiLab; research grants from AstraZeneca, BMS Hansoh, Heng Rui, BeiGene, Hutchison MediPharma, and Roche; and Principal Investigator roles for AstraZeneca, Hansoh, Hengrui, BeiGene, Hutchison MediPharma, and Roche.

Background

- Inhibition of TIGIT with anti-PD-1 is a combination that shows enhanced antitumor activity in preclinical models[1-3]
- Early studies have shown promising antitumor activity of TIGIT inhibitors in combination with PD-1/PD-L1 inhibitors in patients with NSCLC[4-6]
- Ociperlimab is a humanized, Fc-intact, IgG1 anti-TIGIT mAb that binds to TIGIT with high affinity. Tislelizumab is an anti-PD-1 mAb approved in China in combination with chemotherapy for first-line treatment of NSCLC, or as a second- or third-line treatment for patients with locally advanced or metastatic NSCLC[3,7]
- In the ongoing AdvanTIG-105 study (NCT04047862), the RP2D was 900 mg ociperlimab IV Q3W plus tislelizumab 200 mg IV Q3W. The combination was generally well tolerated, and preliminary antitumor activity was observed in patients with advanced, unresectable solid tumors[8]
- We report results from Cohorts 1 and 2 in the dose-expansion part of the phase 1b AdvanTIG-105 study

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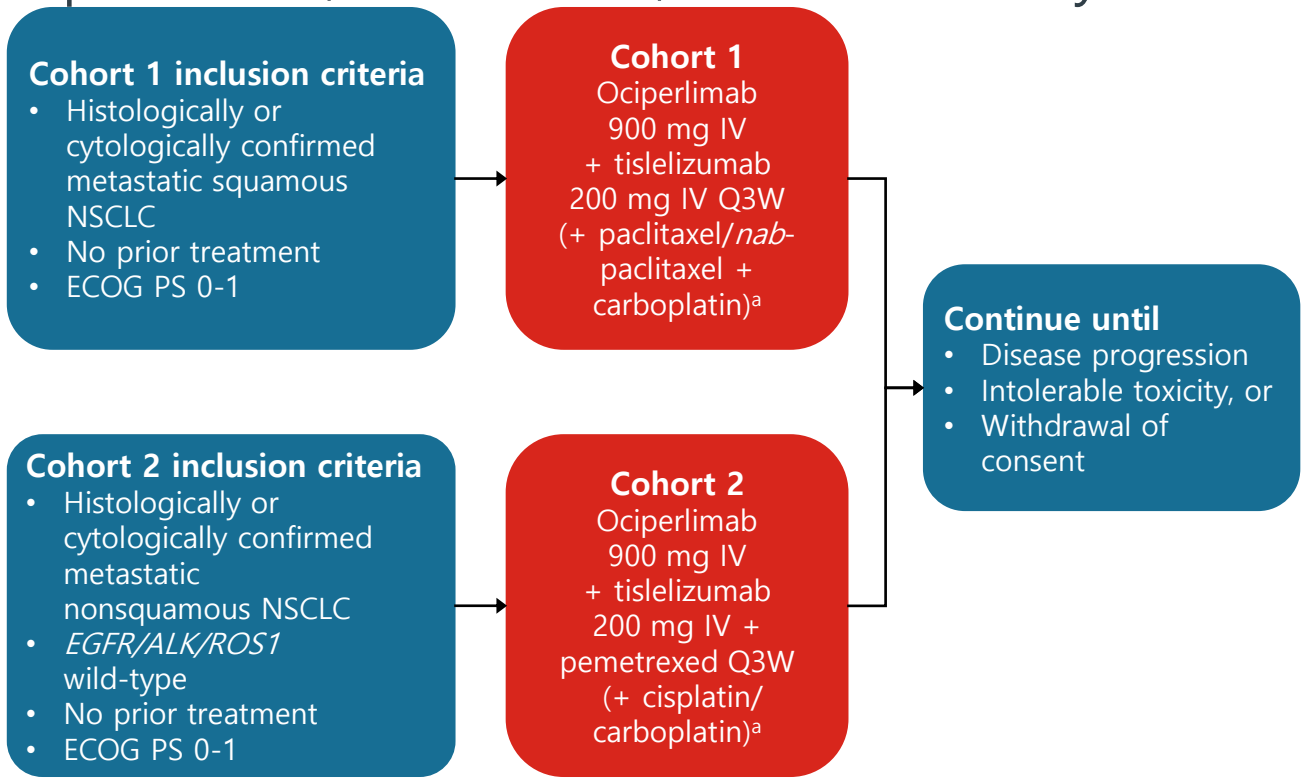
IV, intravenously; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; RP2D, recommended phase 2 dose; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains.

AdvanTIG-105: Study Design and Baseline Characteristics (Cohorts 1 and 2)

Open-Label, Multicenter, Phase 1b Study



Primary Endpoint:

- Investigator-assessed ORR per RECIST v1.1[b]

Key Secondary Endpoints:

- Investigator-assessed DoR and DCR per RECIST v1.1[b]
- Safety[c]

Baseline Characteristics:

- As of June 20, 2022, 84 patients were enrolled (Cohort 1: n=41; Cohort 2: n=43)
- The median age was 66.0 years (range: 43-82) for Cohort 1, and 63.0 years (43-79) for Cohort 2. In Cohort 1, 85.4% of patients were male, and in Cohort 2, 72.1% of patients were male
- The median study follow-up was 30.7 weeks (range: 1.1-56.0) in Cohort 1 and 30.0 weeks (range: 3.6-64.6) in Cohort 2

[a]Administered Q3W for 4-6 cycles during the induction phase only; [b]Efficacy-evaluable analysis set included all patients who received ≥1 dose of study drugs, had evaluable disease at baseline, and ≥1 evaluable postbaseline tumor response assessment unless any clinical PD or death occurred before the first postbaseline tumor assessment; [c]Safety analysis set included all patients who received ≥1 dose of study drugs.
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, overall response rate; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS1, c-ros oncogene 1.

Antitumor Response

The ORR was 57.5% in Cohort 1 and 54.8% in Cohort 2

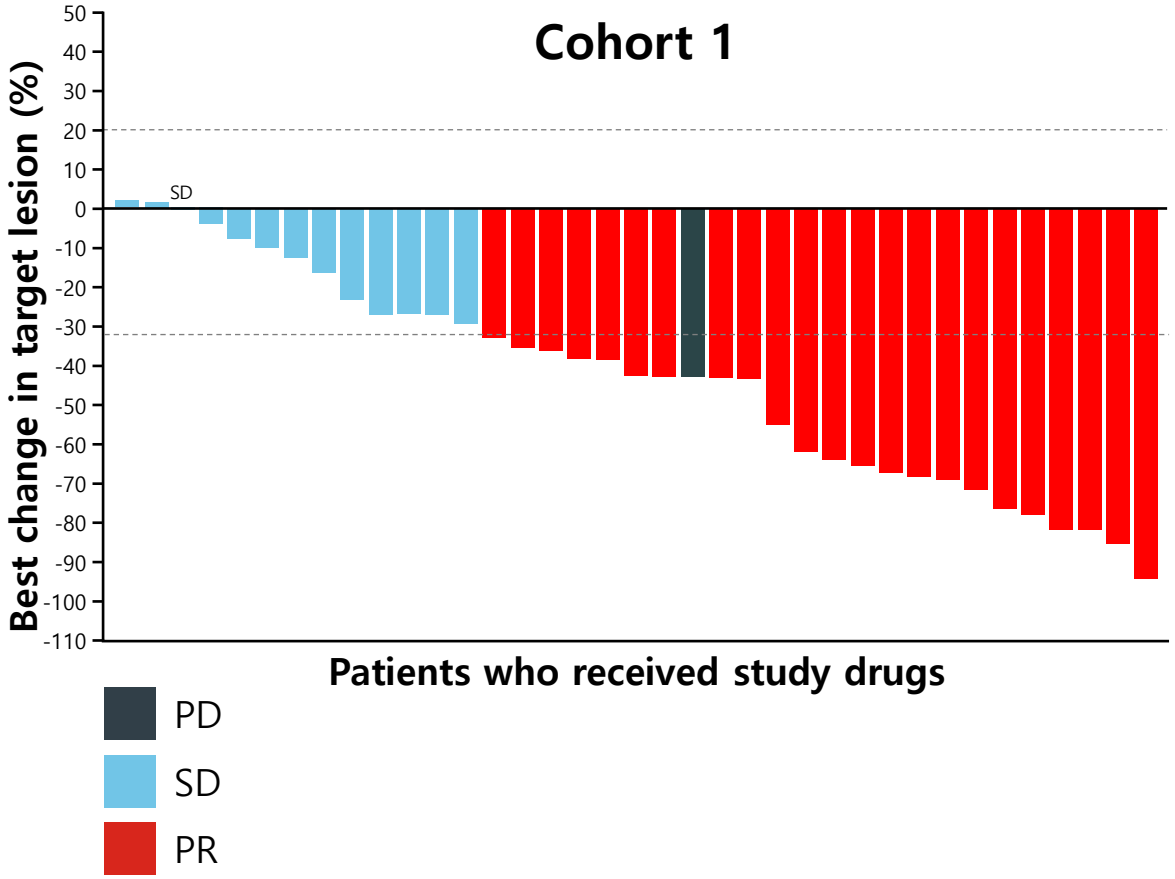
	Cohort 1 (n=40)	Cohort 2 (n=42)
ORR, n (%)	23 (57.5)	23 (54.8)
95% CI	40.9, 73.0	38.7, 70.2
BOR, n (%)		
PR	23 (57.5)	23 (54.8)
SD	13 (32.5)	15 (35.7)
PD	1 (2.5)	2 (4.8)
NE	3 (7.5)	2 (4.8)

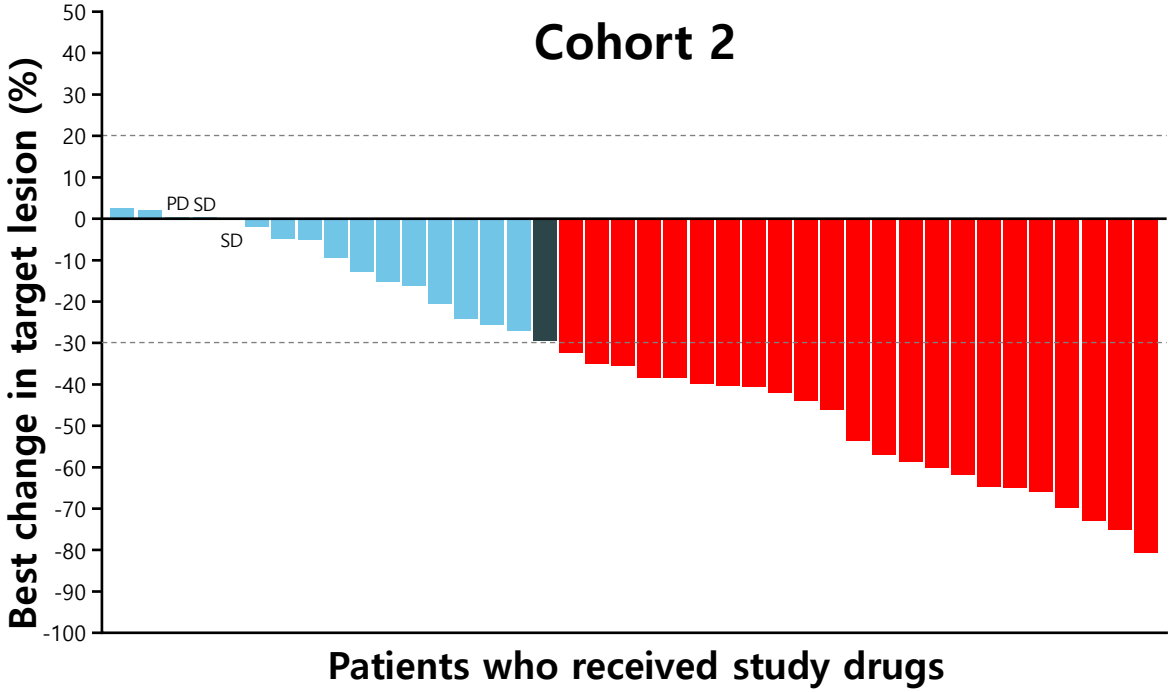
- Of the 82 efficacy-evaluable patients, 40 patients were in Cohort 1 and 42 patients were in Cohort 2
- The ORR was **57.5%** (95% CI: 40.9, 73.0) in Cohort 1 and **54.8%** (95% CI: 38.7, 70.2) in Cohort 2
- The median DoR was not reached

BOR, best overall response; CI, confidence interval; DoR, duration of response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Best Change in Target Lesion

Twenty-three patients in each cohort had a partial response to treatment

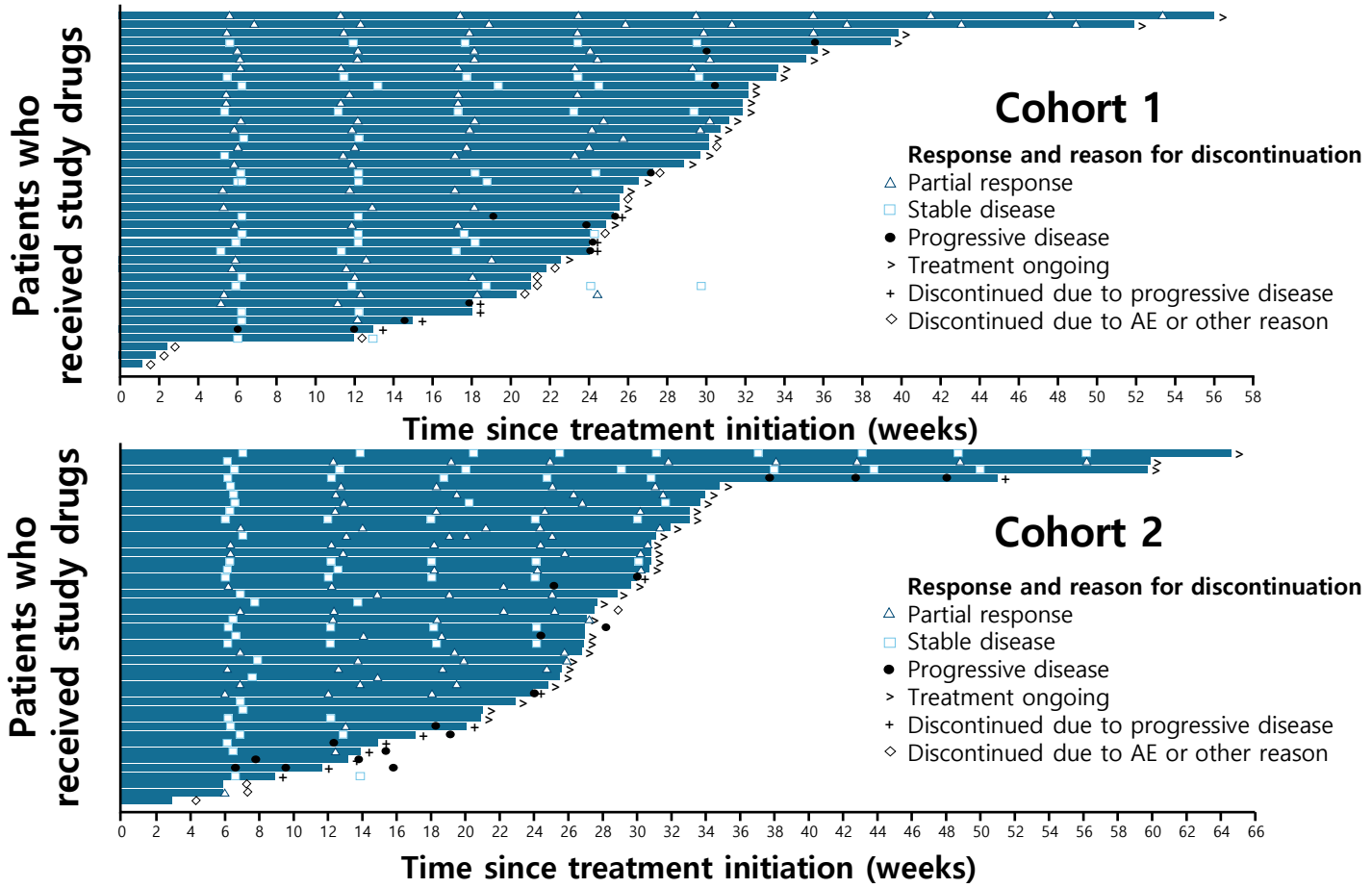




PD, progressive disease; PR, partial response; SD, stable disease.

Disease Response Over Time

The median duration of response was not reached in Cohorts 1 or 2



AE, adverse event.

Safety

The RP2D of ociperlimab with tislelizumab and chemotherapy had a manageable safety profile

Patients, n (%)	Cohort 1 (n=41)	Cohort 2 (n=43)	In total (n=84)
Any grade TEAE	41 (100.0)	43 (100.0)	84 (100.0)
Grade ≥3 TEAE	27 (65.9)	24 (55.8)	51 (60.7)
Serious TEAE	15 (36.6)	17 (39.5)	32 (38.1)
TEAE leading to ociperlimab discontinuation	10 (24.4)	5 (11.6)	15 (17.9)
TEAE leading to tislelizumab discontinuation	10 (24.4)	4 (9.3)	14 (16.7)
Immune-mediated AE[a]	25 (61.0)	20 (46.5)	45 (53.6)

- In total, 84 patients (100.0%) experienced ≥1 TEAE. The most common TEAEs of any grade were anemia (45.2%), neutrophil count decreased (39.3%), and white blood cell count decreased (38.1%)
- Grade ≥3 TEAEs occurred in 51 patients (60.7%) and serious TEAEs occurred in 32 patients (38.1%)
- 15 patients (17.9%) experienced AEs leading to ociperlimab discontinuation, 14 patients (16.7%) experienced AEs leading to tislelizumab discontinuation
- Immune-mediated adverse events occurred in 45 patients (53.6%)

[a]Immune-mediated adverse events are based on investigator's assessments.
AE, adverse event; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event.

Conclusions

- Ociperlimab and tislelizumab plus chemotherapy demonstrated antitumor activity in patients with metastatic squamous and nonsquamous NSCLC
- The RP2D of ociperlimab with tislelizumab and chemotherapy showed a manageable safety profile

NSCLC, non-small cell lung cancer; RP2D, recommended phase 2 dose.

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