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

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Disclosures

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Background

- PD-1/PD-L1 inhibitors have improved outcomes for patients with NSCLC, however unmet needs remain[1]
- Inhibition of TIGIT in combination with PD-1/PD-L1 inhibition has demonstrated early efficacy in NSCLC[2-4]
- Ociperlimab is a humanized Fc-intact IgG1 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]

1. De Giglio A, et al. *Current Onc Rep*. 2021;23:126; 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://ir.beigene.com/news-details/?id=3e337eaa-a5f6-4368-95e0-3e0d35a71254. Accessed March 2022; 7. Frentzas S, et al. *J Clin Oncol*. 2021 (Abs 2583) [presented at ASCO 2021].
mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains.

AdvanTIG-105: Study Design (Cohort 3)

Open-label, Multicenter, Phase 1b Study

Inclusion criteria
- Metastatic squamous or non-squamous NSCLC
- PD-L1 positive[a]
- *EGFR/ALK/ROS1* wild-type
- No prior treatment for metastatic disease
- ECOG PS 0-1

→ Ociperlimab 900 mg IV Q3W + tislelizumab 200 mg IV Q3W → Continue until disease progression, intolerable toxicity, or withdrawal of consent

Primary endpoint:
- Investigator-assessed ORR per RECIST v1.1

Key secondary endpoints:
- Investigator-assessed PFS, DoR, and DCR per RECIST v1.1
- Safety
- Correlation of PD-L1 expression with efficacy endpoints

Key exploratory endpoint:
- OS

[a]TC ≥1% by VENTANA PD-L1 (SP263) assay by central lab.
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; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS1, c-ros oncogene 1; TC, tumor cell.

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 ≥50%
- The median study follow-up was 28.1 weeks (range 3.1-61.7)

PD-L1, programmed-death ligand 1; TC, tumor cell.

Antitumor Response

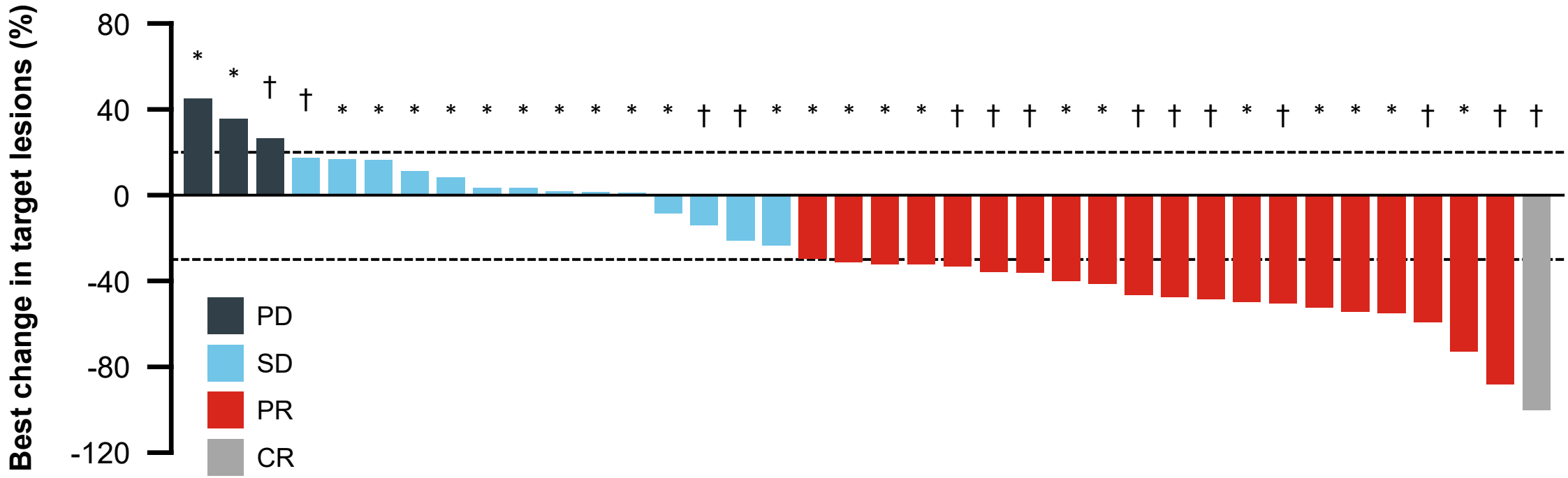
The ORR was higher in patients with PD-L1 TC ≥50% (71.4%) than in patients with PD-L1 TC 1-49% (44.0%)

	PD-L1 TC 1-49% (n=25)	PD-L1 TC ≥50% (n=14)	In Total (N=39)
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)
BOR, n (%)			
CR	0 (0)	1 (7.1)	1 (2.6)
PR	11 (44.0)	9 (64.3)	20 (51.3)
SD	11 (44.0)	3 (21.4)	14 (35.9)
PD	2 (8.0)	1 (7.1)	3 (7.7)
NE	1(4.0)	0 (0)	1 (2.6)

- Of the 39 efficacy evaluable patients, 25 patients were with PD-L1 TC 1-49% and 14 were with PD-L1 TC ≥50%
- The ORR was 44.0% (95% CI: 24.4, 65.1) in patients with PD-L1 TC 1-49% and 71.4% (95% CI: 41.9, 91.6) in patients with PD-L1 TC ≥50%
- The median DoR was not reached

BOR, best overall response; CI, confidence interval; CR, complete response; DoR, duration of response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PD-L1, programmed-death ligand 1; PR, partial response; SD, stable disease; TC, tumor cell.

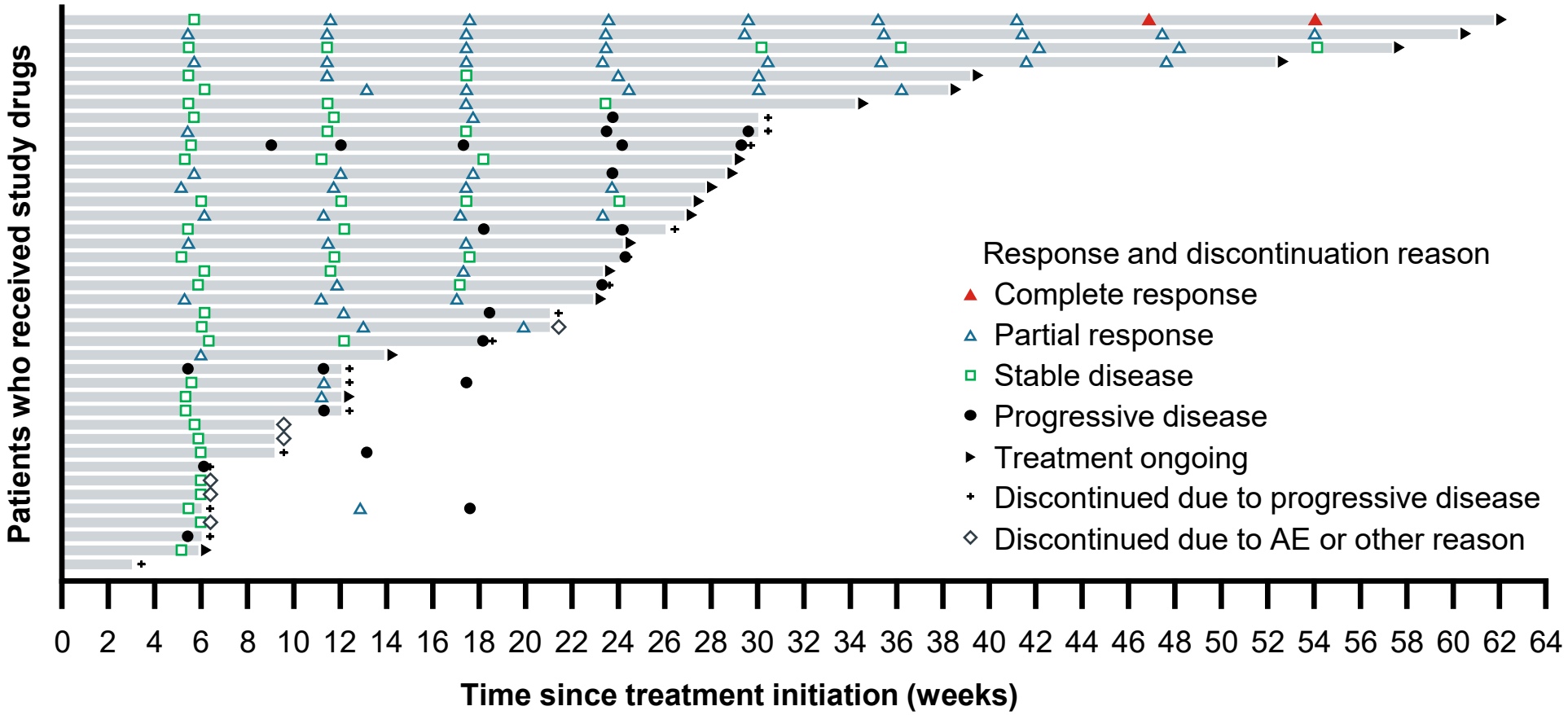
Best Change in Target Lesion



*These patients were PD-L1 TC 1-49%; †These patients were PD-L1 TC ≥50%.
CR, complete response; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; TC, tumor cell.

Disease Response Over Time

Duration of Treatment and Response



*These patients were PD-L1 TC 1-49%; †These patients were PD-L1 TC ≥50%.
AE, adverse event; PD-L1, programmed-death ligand 1; TC, tumor cell.

Safety

The RP2D of ociperlimab with tislelizumab had a manageable safety profile

Patients, n (%)	N=40 TEAEs
Patients with at least one AE	38 (95.0)
Grade ≥3 AE	11 (27.5)
Serious AE	10 (25.0)
AE leading to ociperlimab discontinuation	3 (7.5)
AE leading to tislelizumab discontinuation	3 (7.5)
Immune-mediated AE[a]	22 (55.0)

- The most common TEAEs were pruritus (32.5%), pyrexia (30.0%), decreased appetite (20.0%), rash (20.0%), anemia (17.5%), nausea (17.5%), and dyspnea (17.5%)
- The most common grade ≥3 TEAEs were pneumonia (7.5%) and anemia (5.0%)
- 3 patients (7.5%) experienced AE leading to ociperlimab discontinuation
- 3 patients (7.5%) experienced AE leading to tislelizumab discontinuation
- 22 patients (55.0%) experienced immune-mediated AE

[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 plus tislelizumab demonstrated antitumor activity as first-line treatment for patients with metastatic NSCLC with PD-L1 positive tumors (TC ≥1%)
- Antitumor activity was observed in patients with tumors with PD-L1 TC 1-49% and PD-L1 TC ≥50%, with a higher response rate in patients with high PD-L1 TC ≥50%
- The combination of ociperlimab plus tislelizumab had a manageable safety profile, with most TEAEs being grade 1 or 2 in severity
- Ociperlimab in combination with tislelizumab is also being investigated in patients with NSCLC in a randomized phase 3 study (AdvanTIG-302; NCT04746924)

NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; TC, tumor cell; TEAE, treatment-emergent adverse event.

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