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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

SHK: Astellas, AstraZeneca, BNS/Ono Pharma and Roche. **SL**: AstraZeneca, BeiGene, BMS, GenomiCare, Hansoh, Hengrui Therapeutics, Hutchison, InventisBio Co. Ltd., Menarini, Pfizer, Roche, Yuhan Corporation and ZaiLab. **TC**: AbbVie, Amgen, Astellas, AstraZeneca, BeiGene, BMS, Clovis, Daiichi Sankyo, Foundation Medicine, Immutep, Janssen, MSD and Pfizer. **DRS**: Aeglea Biotherapeutics, Agios, Amgen, Apollomics, Arcus, Arrys Therapeutics, Astellas, AstraZeneca, Bayer, BeiGene, BIND Therapeutics, BioNTech RNA Pharmaceuticals, Blueprint Medicine, BMS, Boehringer Ingelheim, Bristol-Myers Squibb, Calithera, Celgene, Celldex, Clovis, Curio Science, Cyteir Therapeutics, Daiichi Sankyo, Denovo Biopharma, Eisai, Elevation Oncology, EMD Serono, Evelo Biosciences, Evidera, Exelixis, G1 Therapeutics, Genentech/Roche, GlaxoSmithKline, GRAIL, Hutchison MediPharma, ImClone Systems, ImmunoGen, Incyte, Intellisphere, Ipsen, Janssen, Jazz Pharmaceuticals, Kronos Bio, Lilly, Loxo Oncology, MacroGenics, MedImmune, Merck, Molecular Partners, Mirati Therapeutics, Molecular Templates, Neon Therapeutics, Novartis, Novocure, Oncologie, Pfizer, PTC Therapeutics, Puma Biotechnology, PureTech Health, Razor Genomics, Regeneron, Repare Therapeutics, Rgenix, Sanofi-Aventis, Takeda, Tesaro, Tizona Therapeutics, Transgene, UT Southwestern and Verastem. **G-CC**: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company oncology, F. Hoffmann-La Roche, Ltd, MSD, Novartis and Pfizer. **RK**, **DZ**, **YC, MC**, **EC**, **G-WL**, **MS**, **BYS**, **T-YY**, **QW**, **GY**, and **HRK**: no conflicts of interests to declare. **RW**, **WT**, **HZ**, and **RG**: employment at BeiGene.

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 October 21, 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 nonsquamous 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]≥1% TC positive on 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; OS, overall survival; 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 cells.

Baseline Characteristics

- As of April 5, 2022, 40 patients were enrolled in Cohort 3 and received at least one dose of the study drug, comprising the safety analysis set
- 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 had ≥50% PD-L1-positive TC
- The median study follow-up was 28.1 weeks (range 3.1-61.7)

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

Antitumor Response

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

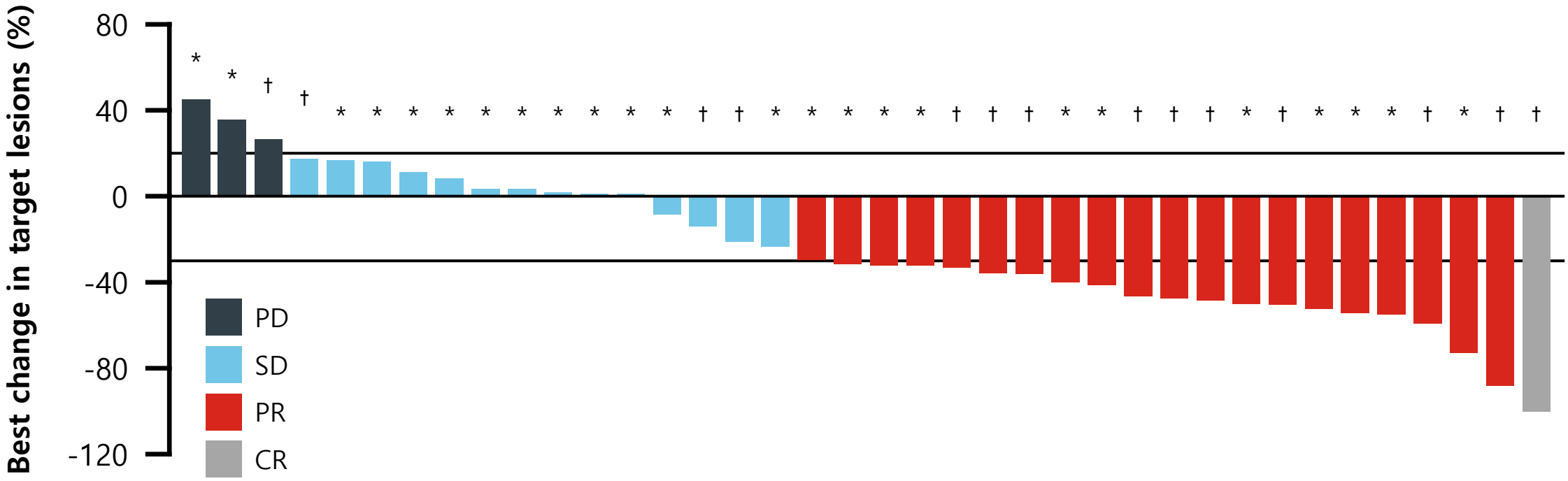
	PD-L1 TC 1-49% (n=25)	PD-L1 TC ≥50% (n=14)	Total (N=39)
ORR, n (%) (95% CI)	11 (44.0) (24.4, 65.1)	10 (71.4) (41.9, 91.6)	21 (53.8) (37.2, 69.9)
BOR, n (%)			
CR	0 (0)	1 (7.1)	1 (2.6)
PR	11 (44.0)	9 (64.3)	20 (51.3)
SD	11 (44.0)	3 (21.4)	14 (35.9)
PD	2 (8.0)	1 (7.1)	3 (7.7)
NE	1(4.0)	0 (0)	1 (2.6)

- Of the 39 efficacy-evaluable patients, 25 had 1-49% PD-L1-positive TC and 14 had ≥50% PD-L1-positive TC
- The ORR was **44.0%** (95% CI: 24.4, 65.1) in patients with 1-49% PD-L1-positive TC and **71.4%** (95% CI: 41.9, 91.6) in patients with ≥50% PD-L1-positive TC
- 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 cells.

Best Change in Target Lesion

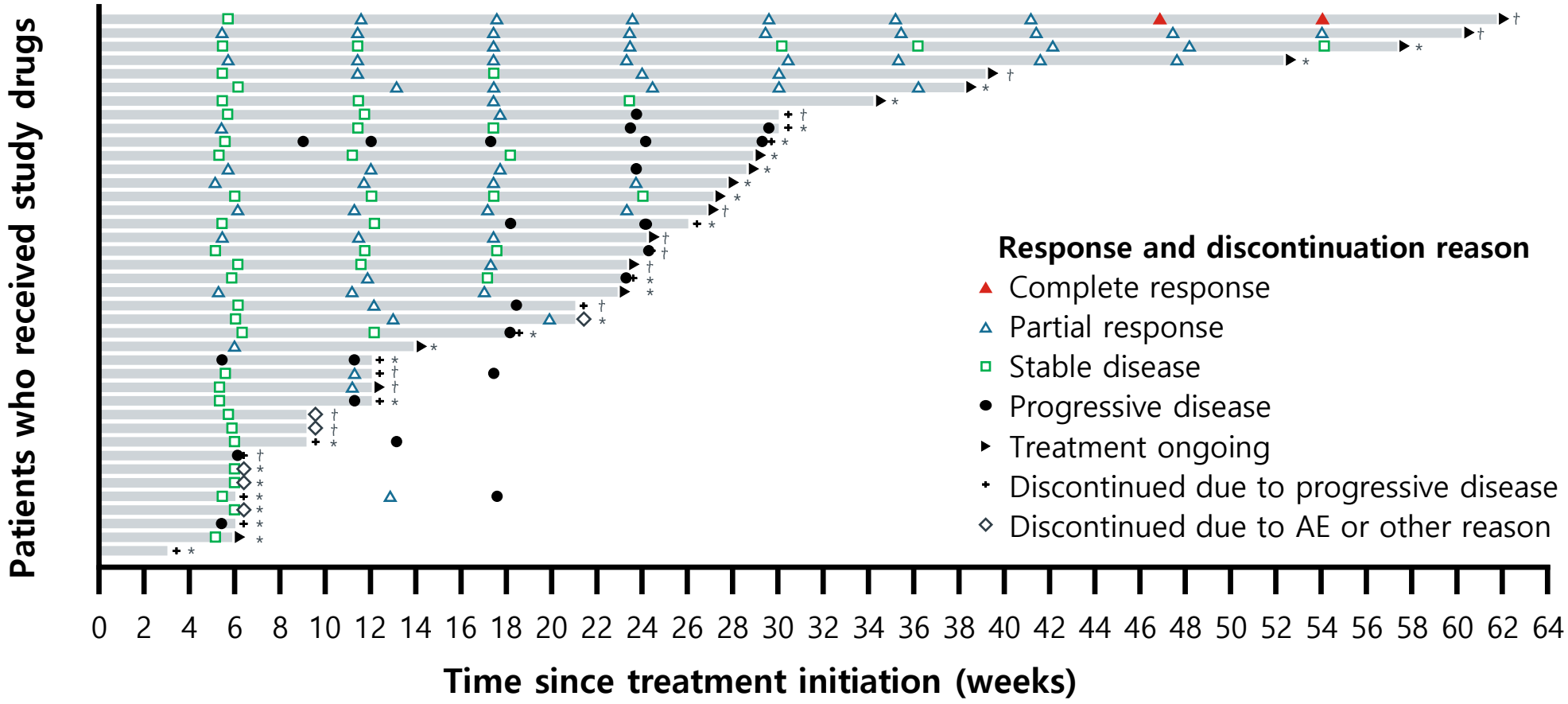
Twenty patients in this cohort had a partial response and one patient had a complete response to treatment



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

Disease Response Over Time

The median duration of response was not reached in Cohort 3



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

Safety

The RP2D of ociperlimab with tislelizumab had a manageable safety profile

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

[a]Immune-mediated AEs 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 (≥1% TC)
- Antitumor activity was observed in patients with tumors with 1-49% and ≥50% PD-L1-positive TC, with a higher response rate in patients with high PD-L1 positivity, ≥50% TC
- 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 cells; TEAE, treatment-emergent adverse event.

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