AdvanTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab Plus Tislelizumab With Chemotherapy in Patients With Extensive-Stage Small Cell Lung Cancer

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Conclusions

Ociperlimab plus tislelizumab with cisplatin or carboplatin plus etoposide demonstrated encouraging antitumor activity as first-line treatment for patients with ES-SCLC.

Clinical activity of this combination was shown by an ORR of 65%, median duration of response >4 months, 90% disease control rate, and median PFS of almost 5 months.

The combination of ociperlimab plus tislelizumab with cisplatin or carboplatin plus etoposide was generally well tolerated with an acceptable safety profile.

Background

The addition of anti-programmed death-ligand 1 (PD-L1) therapy to first-line chemotherapy for extensive-stage small cell lung cancer (ES-SCLC) has significantly improved prognosis versus chemotherapy alone[1,2]; however, unmet needs remain.[3]

Inhibition of T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) in combination with programmed cell death protein 1 (PD-1)/PD-L1 inhibition has demonstrated antitumor activity in advanced solid tumors.[4-7]

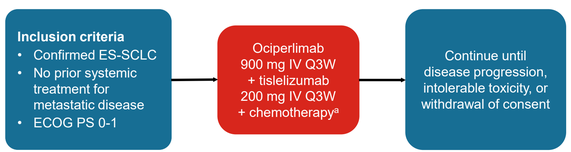
Ociperlimab is a humanized Fc-intact IgG1 monoclonal antibody (mAb) designed to bind to TIGIT with high specificity and affinity.[7,8] Tislelizumab is an anti-PD-1 mAb specifically designed to minimize Fc-gamma receptor binding on macrophages.[9]

In the ongoing phase 1/1b, open-label AdvanTIG-105 dose-escalation/expansion study (NCT04047862), ociperlimab plus tislelizumab showed preliminary antitumor activity and was well tolerated in patients with advanced solid tumors.[7,10,11]

Methods

- In dose-escalation, the established recommended phase 2 dose was ociperlimab 900 mg intravenously (IV) every 3 weeks (Q3W) plus tislelizumab 200 mg IV Q3W[7]
- Here, we report data from the dose-expansion part of the phase 1b AdvanTIG-105 study in patients with ES-SCLC (Cohort 4; **Figure 1**)

Figure 1. AdvanTIG-105 Study Design (Cohort 4)



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

Key secondary endpoints:
- Investigator-assessed PFS, DoR, and DCR per RECIST v1.1
- Safety

Key exploratory endpoint:
- OS

[a]Patients received RP2D of ociperlimab and tislelizumab plus cisplatin 75 mg/m^2 or carboplatin AUC 5 (D1) plus etoposide 100 mg/m^2 (D1, D2, D3) Q3W for 4 cycles, followed by RP2D of ociperlimab and tislelizumab.
Abbreviations: AUC, area under the curve; D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RP2D, recommended phase 2 dose.

Results

Patient Disposition and Baseline Characteristics

- As of June 20, 2022, 42 patients were enrolled in Cohort 4 (safety analysis set); 40 patients were efficacy evaluable, defined as patients with ≥1 evaluable postbaseline tumor response assessment
- Median study follow-up time was 24.9 weeks (range 3.0-67.9), median age was 65.5 years (range 40-77), and 23.8% of patients were female

Antitumor Activity

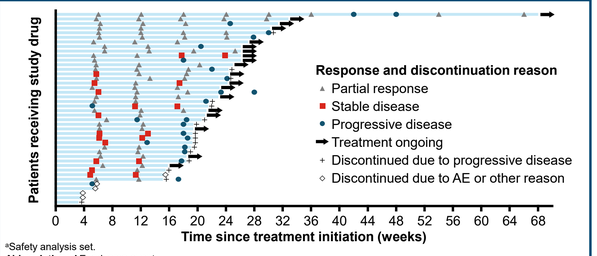
- Confirmed objective response rate (ORR) was 65.0% (95% confidence interval [CI]: 48.3, 79.4); antitumor activity is summarized in **Table 1**
- The duration of treatment and response is shown in **Figure 2**
- Median progression-free survival (PFS) was 4.9 months (**Figure 3**)

Table 1. Confirmed Antitumor Activity[a]

	Total (N=40)
ORR, n (%) (95% CI)	26 (65.0) (48.3, 79.4)
BOR, n (%)	
CR	0 (0.0)
PR	26 (65.0)
SD	10 (25.0)
PD	2 (5.0)
NE	2 (5.0)
DCR, n (%)	36 (90.0)
Median DoR, months (95% CI)	4.3 (3.2, 5.6)

[a]Efficacy evaluable set.
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; PR, partial response; SD, stable disease.

Figure 2. Duration of Treatment and Response[a]

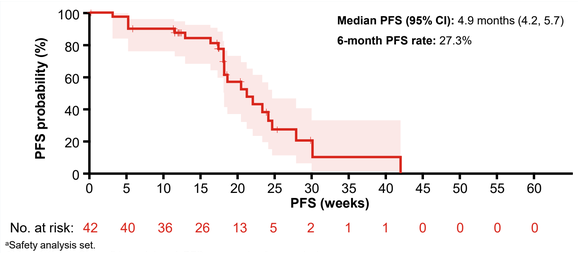


[a]Safety analysis set.
Abbreviation: AE, adverse event.

Safety

- All 42 patients experienced ≥1 treatment-emergent adverse event (TEAE), 25 (59.5%) had ≥grade 3 TEAEs, and 17 (40.5%) had serious TEAEs (**Table 2**)
- The most common (≥20%) TEAEs were anemia and neutrophil count decreased (both 54.8%), white blood cell count decreased (38.1%), platelet count decreased (26.2%), and constipation (23.8%)
  - Of the ≥grade 3 TEAEs, the most common (≥15%) were neutrophil count decreased (33.3%) and white blood cell count decreased (16.7%)
- Immune-mediated TEAEs were reported in 12 patients (28.6%), of which two (4.8%) were ≥grade 3
- Two patients (4.8%) died due to AEs (pneumonia [unrelated to treatment] and cardiac arrest; n=1 each)

Figure 3. Progression-Free Survival[a]



[a]Safety analysis set.
Abbreviations: CI, confidence interval; PFS, progression-free survival.

Table 2. Summary of TEAEs[a]

Patients, n (%)	Total (N=42)
Patients with ≥1 AE	42 (100.0)
≥Grade 3	25 (59.5)
Serious	17 (40.5)
AE leading to ociperlimab discontinuation	2 (4.8)
AE leading to tislelizumab discontinuation	2 (4.8)
AE leading to chemotherapy discontinuation	2 (4.8)
AE leading to death	2 (4.8)
Immune-mediated AE[b]	12 (28.6)
≥Grade 3	2 (4.8)

[a]Safety analysis set. [b]Immune-mediated adverse events are based on investigator's assessments.
Abbreviations: AE, adverse event; TEAE, treatment-emergent adverse event.

References
1. Paz-Ares L, et al. *Lancet.* 2019;394(10212):1929-1939.
2. Horn L, et al. *N Engl J Med.* 2018;379(23):2220-2229.
3. Povsic M, et al. *PLoS One.* 2019;14(7):e0219622.
4. Rodriguez-Abreu D, et al. *J Clin Oncol.* 2020 (Abs 9503) [presented at ASCO 2020].
5. Niu J, et al. *Ann Oncol.* 2020 (Abs 1410P) [presented at ESMO 2020].
6. Ahn M-J, et al. *Ann Oncol.* 2020 (Abs 1400P) [presented at ESMO 2020].
7. Frentzas S, et al. *J Clin Oncol.* 2021 (Abs 2583) [presented at ASCO 2021].
8. Chen X, et al. Data presented at AACR 2021. Poster 1854.
9. Zhang T, et al. *Cancer Immunol Immunother.* 2018;67:1079-1090.
10. Kumar R, et al. *J Thorac Oncol.* 2022 (Abs 1315) [presented at WCLC 2022].
11. Yu Y, et al. *Ann Oncol.* 2022 (Abs 1156) [presented at ESMO 2022].

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Disclosures
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