AdvanTIG-105: Phase 1b Dose-Expansion Study of Ociperlimab Plus Tislelizumab in Patients With Checkpoint Inhibitor–Experienced Advanced NSCLC

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Poster No: 126P presented at ESMO IO 2022, Geneva, Switzerland

Conclusions

Ociperlimab plus tislelizumab demonstrated modest preliminary antitumor activity as treatment for patients with locally advanced or metastatic, CPI-experienced NSCLC.

Clinical activity of this combination was shown by an ORR of 8.0%, with two patients experiencing PRs, a disease control rate of 56%, and median PFS of almost 4 months.

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

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, due to checkpoint inhibitor (CPI) resistance and immune escape, unmet needs remain for CPI-experienced patients with NSCLC.[1]

Inhibition of T-cell immunoreceptor with immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) in combination with PD-1/PD-L1 inhibition has demonstrated antitumor activity in patients with NSCLC and advanced solid tumors.[2-5]

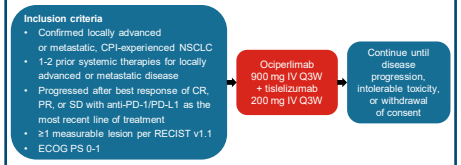
Ociperlimab is a humanized, Fc-intact, IgG1 monoclonal antibody (mAb) designed to bind to TIGIT with high specificity and affinity.[5,6] Tislelizumab, an anti-PD-1 mAb specifically designed to minimize Fc-gamma receptor binding on macrophages, is approved for the treatment of NSCLC in China.[7,8]

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.[5,9-10]

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[5]
- Here, we report data from the dose-expansion part of the phase 1b AdvanTIG-105 study in patients with CPI-experienced, advanced NSCLC (Cohort 5; **Figure 1**)

Figure 1. AdvanTIG-105 Study Design (Cohort 5)



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

Abbreviations: CPI, checkpoint inhibitor; CR, complete response; DCR, disease control rate; DoR; duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Results

Patient Disposition and Baseline Characteristics

- As of June 20, 2022, 26 patients were enrolled in Cohort 5 (safety analysis set); 25 were efficacy evaluable (≥1 evaluable postbaseline tumor response assessment)
- Median study follow-up time was 46.1 weeks (range 9.9-70.0); median age was 68.0 years (range 40-79); 30.8% of patients were female

Antitumor Activity

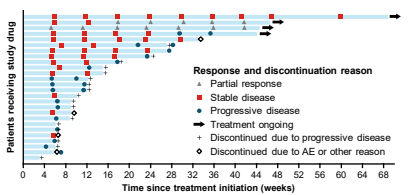
- Confirmed objective response rate (ORR) was 8.0% (95% confidence interval [CI]: 1.0, 26.0), with two partial responses (PRs) (**Figure 2** and **Table 1**)
- Median progression-free survival (PFS) was 3.8 months (**Figure 3**)

Table 1. Confirmed Antitumor Activity[a]

	Total (N=25)
ORR, n (%) [95% CI]	2 (8.0) [1.0, 26.0]
BOR, n (%)	
CR	0 (0.0)
PR	2 (8.0)
SD	12 (48.0)
PD	9 (36.0)
NE	2 (8.0)
DCR, n (%)	14 (56.0)
Median DoR, months	NE

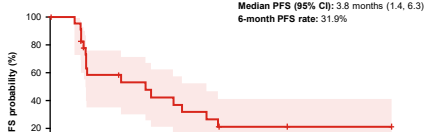
[a]Efficacy analysis set. **Abbreviations:** BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Duration of Treatment and Response[a]



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

Figure 3. Progression-Free Survival[a]



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

Safety

- Overall, 23 patients (88.5%) experienced ≥1 treatment-emergent adverse event (TEAE), 11 (42.3%) had ≥grade 3 TEAEs, and nine (34.6%) had serious TEAEs (**Table 2**)
- The most common (in ≥20% of patients) TEAEs were fatigue (30.8%), cough (26.9%), and rash (23.1%)
- Immune-mediated TEAEs were reported in 10 patients (38.5%), of whom three (11.5%) experienced ≥grade 3 events
  - Immune-mediated ≥grade 3 events included rash, immune-mediated lung disease, and immune-mediated dermatitis, in one (3.8%) patient each

Table 2. Summary of TEAEs[a]

Patients, n (%)	Total (N=26)
Patients with ≥1 AE	23 (88.5)
≥Grade 3	11 (42.3)
Serious	9 (34.6)
AE leading to ociperlimab discontinuation	4 (15.4)
AE leading to tislelizumab discontinuation	4 (15.4)
AE leading to death	0 (0.0)
Immune-mediated AE[b]	10 (38.5)
≥Grade 3	3 (11.5)

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

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Acknowledgments

This study was sponsored by BeiGene, Ltd. Medical writing support, under direction of the authors, was provided by Emma Ashman, BSc, of Ashfield MedComms, an Inizio company, and was funded by BeiGene, Ltd.

Disclosures

SF: Amtorx, Alexcobio, Monash Partners Comprehensive Cancer Consortium (MPCCC) Precision Oncology Steering Committee, MSD, Victorian Comprehensive Cancer Centre (VCCC) Accelerating Novel Therapies Steering Committee.

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