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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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Conclusions

Ociperlimab and tislelizumab plus chemotherapy demonstrated antitumor activity in patients with metastatic squamous and nonsquamous NSCLC.

The recommended phase 2 dose of ociperlimab with tislelizumab and chemotherapy showed a manageable safety profile.

Ociperlimab in combination with tislelizumab is also being investigated in patients with NSCLC in a randomized phase 3 study (AdvanTIG-302; NCT04746924).

Background

Inhibition of T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) with anti-programmed cell death protein 1 (PD-1) is a combination which shows enhanced antitumor activity in preclinical models.[1-3]

Early studies have shown promising antitumor activity of TIGIT inhibitors in combination with PD-1/programmed death-ligand 1 inhibitors in patients with non-small cell lung cancer (NSCLC).[4-6]

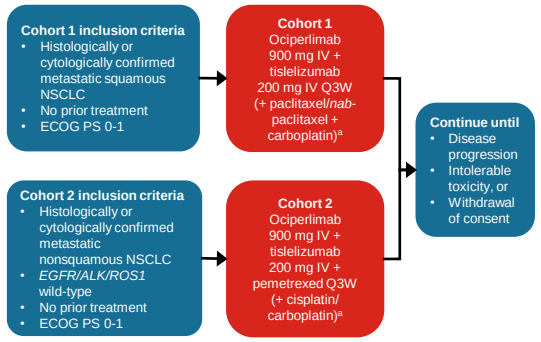
Ociperlimab is a humanized Fc-intact IgG1 anti-TIGIT monoclonal antibody (mAb) which binds to TIGIT with high affinity. Tislelizumab is an anti-PD-1 mAb approved in China in combination with chemotherapy for first-line treatment of NSCLC, or as a second- or third-line treatment for patients with locally advanced or metastatic NSCLC.[3,7]

In the ongoing AdvanTIG-105 study, the recommended phase 2 dose was 900 mg ociperlimab intravenously (IV) every 3 weeks (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]

Methods

- We report results from Cohorts 1 and 2 in the dose-expansion part of the phase 1b AdvanTIG-105 study (NCT04047862)

Figure 1. Study Design (Cohorts 1 and 2)



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]

[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.
Abbreviations: 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; PD, progressive disease; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Results

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 (3.6-64.6) in Cohort 2

Antitumor Activity

- Of the 82 efficacy-evaluable patients, 40 patients were in Cohort 1 and 42 patients were in Cohort 2. The unconfirmed objective response rate in Cohort 1 was 57.5% (95% confidence interval [CI]: 40.9, 73.0) and 54.8% (95% CI: 38.7, 70.2) in Cohort 2 (**Table 1**)
- In Cohort 2, only 6.7% of patients in the PD-L1 evaluable population (N=30) were PD-L1 ≥50%. Patients with PD-L1 TC ≥25% had a higher unconfirmed ORR (N=6, 83.3%) than patients with PD-L1 TC <25% (N=24, 41.7%)
- The limited PD-L1 evaluable patient number and low PD-L1 prevalence may limit this analysis
- The median DoR was not reached
- The best change in target lesions are shown in **Figure 2**, and the duration of treatment and response are shown in **Figure 3**

Safety

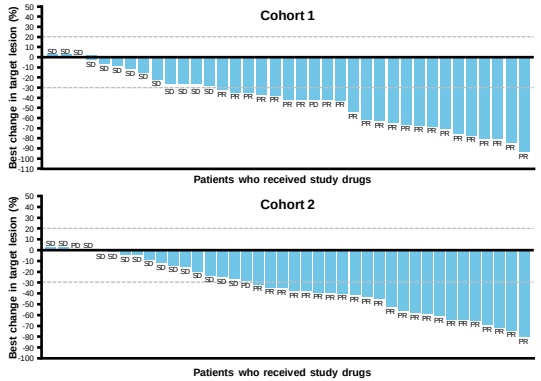
- Treatment-emergent adverse events (TEAEs) occurred in all patients in Cohorts 1 and 2 (**Table 2**)
- In total, 77 patients (91.7%) experienced ≥1 treatment-related adverse event (TRAE), and 41 patients (48.8%) had ≥grade 3 TRAEs. Serious TRAEs occurred in 14 patients (16.7%). Immune-mediated adverse events occurred in 45 patients (53.6%). The most common TRAEs of any grade were anemia (42.9%), neutrophil count decreased (39.3%), and white blood cell count decreased (36.9%). No TRAEs led to death

Table 1. Antitumor Response

	Cohort 1 (n=40)	Cohort 2 (n=42)
ORR, n (%)[a]	23 (57.5)	23 (54.8)
95% CI	40.9, 73.0	38.7, 70.2
BOR, n (%)[a,b]		
PR	23 (57.5)	23 (54.8)
SD	13 (32.5)	15 (35.7)
PD	1 (2.5)	2 (4.8)
DCR, n (%)[c]	36 (90.0)	38 (90.5)
95% CI	76.3, 97.2	77.4, 97.3
Median DoR, months[c]	NE	NE
95% CI	(4.9, NE)	(4.4, NE)

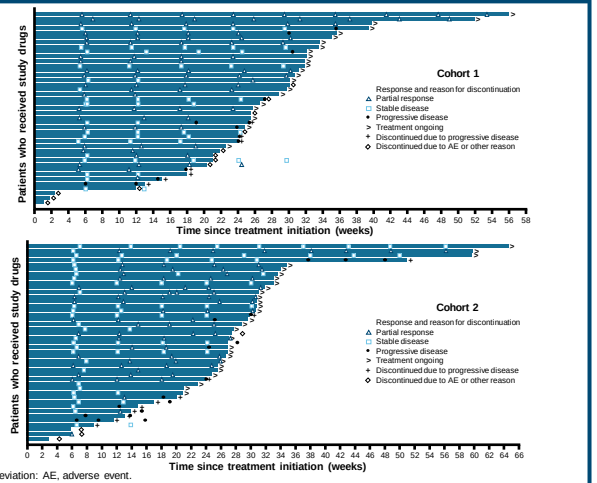
[a]Unconfirmed. [b]Three patients in Cohort 1 and two patients in Cohort 2 were NE for BoR; [c]Confirmed.
Abbreviations: BOR, best overall response; DCR, disease control rate; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Best Change in Target Lesion



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

Figure 3. Disease Response



Abbreviation: AE, adverse event.

Table 2. Summary of TEAEs (Safety Analysis Set)

Patients, n (%)	Cohort 1 (n=41)	Cohort 2 (n=43)
Any grade TEAE[a]	41 (100.0)	43 (100.0)
≥ grade 3 TEAE	27 (65.9)	24 (55.8)
Serious TEAE	15 (36.6)	17 (39.5)
TEAE leading to death[b]	1 (2.4)	1 (2.3)
TEAE leading to ociperlimab discontinuation	10 (24.4)	5 (11.6)
TEAE leading to tislelizumab discontinuation	10 (24.4)	4 (9.3)

[a]The most common TEAEs were anemia, neutrophil count decreased, and white blood cell count decreased; [b]The patients' cause of death was rectal hemorrhage in Cohort 1, and cerebrovascular accident in Cohort 2. Neither death was related to treatment.
Abbreviation: TEAE, treatment-emergent adverse event.

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Disclosures

The presenting author **Yan Yu** has no conflict to declare.

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