AdvanTIG-105: Phase 1b Dose-expansion Study of Ociperlimab Plus Tislelizumab With Chemotherapy in Patients With Stage IV Gastric/Gastroesophageal Adenocarcinoma

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Conclusions

Ociperlimab plus tislelizumab and chemotherapy demonstrated encouraging antitumor activity in patients with stage IV gastric/gastroesophageal adenocarcinoma (GC/GEJC).

Clinical activity of this combination was shown by an overall response rate (ORR) of 57.6%; this response was maintained regardless of programmed death-ligand 1 (PD-L1) tumor area positivity (TAP) status.

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

Background

Programmed cell death protein 1 (PD-1) inhibitors have demonstrated improved outcomes for patients with advanced GC/GEJC; however, some patients do not respond and/or experience relapse.[1-3]

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

Ociperlimab is a humanized Fc-intact immunoglobulin gamma 1 (IgG) monoclonal antibody (mAb) designed to bind to TIGIT with high specificity and affinity.[7,8] Tislelizumab is a humanized IgG4 anti-PD-1 mAb specifically designed to minimize Fcɣ receptor binding on macrophages.[7,9]

In the ongoing phase 1/1b, open-label AdvanTIG-105 dose-escalation/expansion study (NCT04047862), ociperlimab plus tislelizumab and chemotherapy 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 stage IV GC/GEJC (Cohort 9; **Figure 1**)

Figure 1. AdvanTIG-105 Study Design (Cohort 9)

Inclusion criteria
- Histologically or cytologically confirmed stage IV HER2-negative GC/GEJC
- No prior therapy for metastatic disease
- ≥1 measurable lesion per RECIST v1.1
- ECOG PS 0-1

→ Ociperlimab 900 mg IV Q3W + tislelizumab 200 mg IV Q3W + chemotherapy[a] → 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

Key exploratory endpoint:
- OS

[a]Patients received either RP2D of ociperlimab and tislelizumab (D1), alongside chemotherapy of oxaliplatin 130 mg/m^2 (D1) plus capecitabine 1000 mg/m^2 (D1-14) Q3W for 6 cycles (C), followed by maintenance therapy with RP2D of ociperlimarb and tislelizumab, plus capecitabine Q3W, or the RP2D of ociperlimab and tislelizumab with cisplatin 75 mg/m^2 (D1) plus 5-fluorouracil 750-800 mg/m^2 (D1-5) Q3W for 6 C. **Abbreviations:** D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GC/GEJC, gastric/gastroesophageal adenocarcinoma; HER2, human epidermal growth factor receptor 2; IV, intravenous; ORR, overall 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 February 2, 2023, 60 patients were enrolled in Cohort 9 (safety analysis set); 59 patients were efficacy evaluable, defined as patients with ≥1 evaluable postbaseline tumor response assessment unless any clinical disease progression or death occurred before the first postbaseline tumor assessment
- Median study follow-up time was 44.2 weeks (range 1.4-79.6), median age was 61.5 years (range 35-82), and 26.7% of patients were female

Antitumor Activity

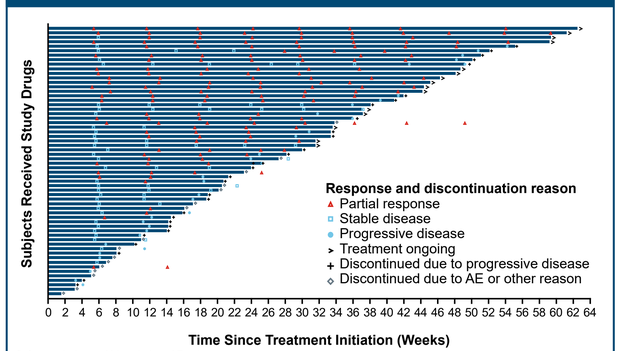
- ORR was 57.6% (95% confidence interval [CI]: 44.1, 70.4) (**Table 1**)
- The duration of treatment and response is shown in **Figure 2**
- Median progression-free survival (PFS) was 7.3 months (95% CI: 5.2, 9.8; **Figure 3**)
- In a subgroup analysis, the ORR in PD-L1 TAP score ≥5% and <5% subgroups was 63.0% (95% CI: 42.4, 80.6; n=27) and 57.1% (95% CI: 37.2, 75.5; n=28), respectively

Table 1. Antitumor Activity[a]

	PD-L1 ≥5% (n=27)	PD-L1 <5% (n=28)	All Patients (N=59)
ORR, n (%) (95% CI)	17 (63.0) (42.4, 80.6)	16 (57.1) (37.2, 75.5)	34 (57.6) (44.1, 70.4)
Best overall response, n (%)			
CR	0 (0.0)	0 (0.0)	0 (0.0)
PR	17 (63.0)	16 (57.1)	34 (57.6)
SD	6 (22.2)	8 (28.6)	17 (28.8)
PD	4 (14.8)	2 (7.1)	6 (10.2)
NE/NA	0 (0.0)	2 (7.1)	2 (3.4)
DCR, n (%) (95% CI)	23 (85.2) (66.3, 95.8)	24 (85.7) (67.3, 96.0)	51 (86.4) (75.0, 94.0)
Median DoR, months (95% CI)	8.4 (7.0, NE)	4.7 (3.2, 10.0)	8.1 (4.7, 10.0)

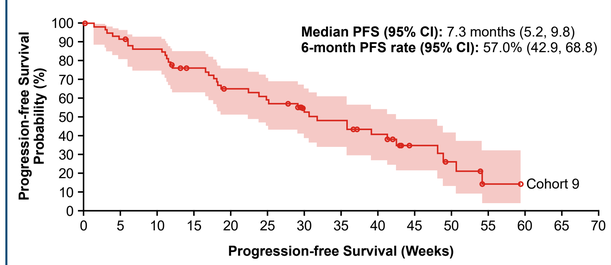
[a]According to PD-L1 TAP score in the efficacy-evaluable analysis set, four patients had missing PD-L1 TAP score. **Abbreviations:** CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE/NA, not evaluable/not assessed; ORR, overall response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; TAP, tumor area positivity.

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

- All 60 patients experienced ≥1 treatment-emergent adverse event (TEAE); 46 (76.7%) had ≥grade 3 TEAEs, and 30 (50.0%) had serious TEAEs (**Table 2**)
- The most common (in ≥30% patients) TEAEs were anemia (46.7%), platelet count decreased (41.7%), nausea (38.3%), neutrophil count decreased (33.3%), peripheral sensory neuropathy (31.7%), and white blood cell count decreased (31.7%)
- In total, five patients (8.3%) experienced TEAEs leading to discontinuation of ociperlimab and tislelizumab, two of which were treatment related
- TEAEs led to two deaths; one due to neutropenic sepsis related to chemotherapy and one due to pulmonary embolism that was not treatment-related
- Overall, 24 patients (40.0%) experienced TEAEs that were potentially immune-mediated; the most common (in ≥5% patients) were hypothyroidism (18.3%), rash (15.0%), maculo-papular rash (6.7%), adrenal insufficiency (5.0%), and immune-mediated hepatitis (5.0%)

Table 2. Summary of TEAEs[a]

Patients, n (%)	Total (N=60)
Patients with ≥1 TEAE	60 (100)
≥Grade 3	46 (76.7)
Serious	30 (50.0)
TEAE leading to ociperlimab discontinuation	5 (8.3)
TEAE leading to tislelizumab discontinuation	5 (8.3)
TEAE leading to death	2 (3.3)
Immune-mediated TEAE	24 (40.0)

[a]Safety analysis set. **Abbreviation:** TEAE, treatment-emergent adverse event.

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Disclosures

Disclosure information is available online with the abstract details.