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

Abstract No: 4028 presented at ASCO 2023, Chicago, IL

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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

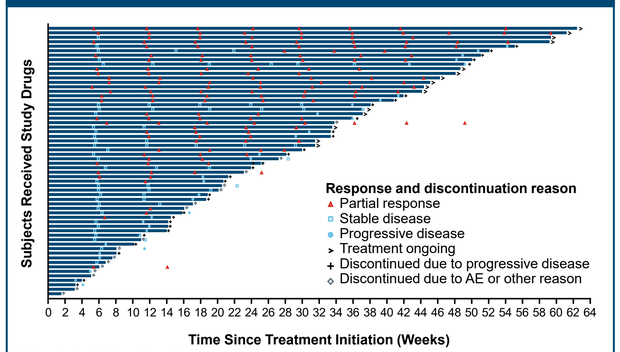
- ORR was 57.6% (95% confidence interval [CI]: 44.1, 70.4) (**Table 1**)
- The duration of treatment and response is shown in **Figure 2**
- Median progression-free survival (PFS) was 7.3 months (95% CI: 5.2, 9.8; **Figure 3**)
- In a subgroup analysis, the ORR in PD-L1 TAP score ≥5% and <5% subgroups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

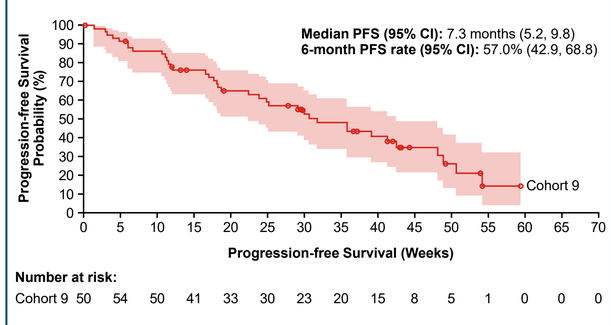
[a]According to PD-L1 TAP score in the efficacy-evaluable analysis set, four patients had missing PD-L1 TAP score. **Abbreviations:** CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NE/NA, not evaluable/not assessed; ORR, overall response rate; PD, 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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Acknowledgments

This study is sponsored by BeiGene, Ltd. Medical writing support, under the direction of the authors, was provided by Gemma Walker, BSc, of Ashfield MedComms, an Inizio company, and was funded by BeiGene, Ltd. Editorial support was provided by Elizabeth Hermans, PhD, of BeiGene, Ltd.

Disclosures

Disclosure information is available online with the abstract details.