AdvanTIG-105: Phase 1b Dose-expansion Study of Ociperlimab Plus Tislelizumab With Chemotherapy in Patients With Metastatic Esophageal Squamous Cell Carcinoma and Esophageal Adenocarcinoma

Meili Sun,[1*] David Spigel,[2] Young Joo Lee,[3] Harry Yoon,[4] Ying Liu,[5] Elizabeth Ahern,[6] Samuel Harris,[7] Gyeong-Won Lee,[8] Dong Yan,[9] Jianhua Chen,[10] Her-Shyong Shiah,[11] Ting Deng,[12] Hao Zheng,[13] Wei Tan,[14] Ziqi Zhou,[14] Ruihua Wang,[14] Yi Ba[12]

[1]Department of Oncology, Jinan Central Hospital (affiliated with Shandong First Medical University), Shandong University; Jinan, China; [2]Department of Medical Oncology, Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN, USA; [3]Division of Hematology and Oncology, Department of Internal Medicine, National Cancer Center, Goyang, Republic of Korea; [4]Department of Oncology, Mayo Clinic, Rochester, MN, USA; [5]Department of Internal Medicine, the Affiliated Cancer Hospital of Zhengzhou University and Henan Cancer Hospital, Zhengzhou, China; [6]Medical Oncology, Monash Health, Clayton, VIC, Australia; [7]Department of Medical Oncology, Bendigo Health, Bendigo, VIC, Australia; [8]Division of Hematology and Oncology, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsang National University College of Medicine, Jinju, Korea; [9]Department of Oncology, Beijing Luhe Hospital, Capital Medical University, Beijing, China; [10]Department of Thoracic Medical Oncology, Hunan Cancer Hospital, the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [11]Division of Hematology and Oncology, Department of Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan; [12]Department of GI Medical Oncology, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin, China; [13]BeiGene USA, Inc., San Mateo, CA, USA; [14]BeiGene (Shanghai) Co., Ltd, Shanghai, China. *Presenting author.

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Conclusions

These study results demonstrate that ociperlimab (OCI) + tislelizumab (TIS) + chemotherapy (CT) show promising antitumor activity in patients with stage IV esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC).

This finding is encouraging because these patients continue to have poor prognosis and limited treatment options.

OCI + TIS + CT was generally well tolerated, with an acceptable safety profile consistent with previous reports; study follow-up is ongoing.

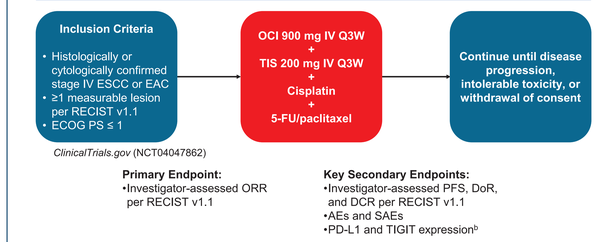
Background

- ESCC is the predominant histologic subtype in esophageal cancer, accounting for 85% of cases; EAC accounts for another 14% of cases worldwide[1]
- The prognosis for advanced ESCC and EAC remains poor, with a 5-year survival rate of 16% and 21%, respectively[2]
- Standard of care for advanced disease includes blockade of programmed cell death protein 1/programmed death-ligand 1 (PD-1/PD-L1) plus cytotoxic T-lymphocyte associated protein 4 inhibitors[3]; however, resistance is seen with PD-1/PD-L1 blockade[4]
- T cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domains (TIGIT) is a coinhibitory immune checkpoint receptor that is upregulated on T cells and natural killer cells in multiple malignancies[5]; blockade of TIGIT in combination with PD-1/PD-L1 has elicited anticancer responses in preclinical[6,7] and clinical studies[8,9]
- OCI (BGB-A1217) is a novel, humanized monoclonal antibody (mAb) that binds to TIGIT with high affinity and specificity, efficiently blocking interaction with its ligands while inducing antibody-dependent cellular cytotoxicity[9]
- TIS is an anti–PD-1 mAb engineered to minimize binding to Fcγ receptors on macrophages, diminishing antibody-dependent phagocytosis (a potential mechanism for resistance to anti–PD-1 therapy)[10]
- The dose-escalation[9] part of the phase 1/1b study, AdvanTIG-105 (NCT04047862), demonstrated that OCI + TIS administered with standard-of-care agents showed encouraging antitumor activity in patients with advanced, metastatic, unresectable solid tumors
- Here, we report efficacy and safety results from the dose-expansion part of the study in patients with ESCC (cohort 6) and EAC (cohort 7)

Methods

- Methodological details are summarized in **Figure 1**
- In the dose-escalation part, the established recommended phase 2 dose was OCI 900 mg intravenously (IV) every 3 weeks (Q3W) + TIS 200 mg IV Q3W[9]
- The safety analysis set included all patients who received ≥1 dose of study drug (OCI, TIS, or any CT)
- The efficacy-evaluable analysis set included all dosed patients who had evaluable disease at baseline and ≥1 evaluable postbaseline tumor response (investigator assessed per Response Evaluation Criteria in Solid Tumors version 1.1), including those who had evaluable disease at baseline and experienced clinical disease progression or death before the planned first postbaseline tumor assessment
- PD-L1 and TIGIT expression are predictive biomarkers for efficacy
  - PD-L1 score was defined by the total percentage of the tumor area with PD-L1–stained tumor cells and immune cells, visually estimated using the Tumor Area Positivity score method
  - TIGIT immune cell (IC) score was defined by the total percentage of the tumor area covered by positive immune cells, tested using Roche TIGIT (SP410) formulation locked assay

Figure 1. Dose-expansion Study Design[a]



[a]Study follow-up is ongoing. [b]PD-L1 and TIGIT expression are predictive biomarkers for efficacy.
Abbreviations: 5-FU, 5-fluorouracil; AE, adverse event; DCR, disease control rate; DoR, duration of response; EAC, esophageal adenocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; IV, intravenously; OCI, ociperlimab; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SAE, serious adverse event; TIGIT, T cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domains; TIS, tislelizumab.

Results

Patients

- As of February 2, 2023, 27 patients were enrolled (ESCC, n=21; EAC, n=6) with a median age of 63.0 years (ESCC range, 51-72 years; EAC range, 58-69 years) (**Table 1**)
- Of the 27 patients, 14 (51.9%) discontinued from the study, of whom 11 patients (40.7%) died and three (11.1%) withdrew (**Table 2**)

Table 1. Baseline Characteristics and Patient Demographics[a]

	ESCC (n=21)	EAC (n=6)
Age, median (range), years	63 (51-72)	63 (58-69)
Sex, n (%)		
Male	18 (85.7)	6 (100.0)
Female	3 (14.3)	0
Race, n (%)		
Asian	16 (76.2)	0
White	2 (9.5)	6 (100.0)
Multiple	3 (14.3)	0
Country, n (%)		
Australia	0	2 (33.3)
China	14 (66.7)	0
South Korea	4 (19.0)	0
Taiwan, China	1 (4.8)	0
United States	2 (9.5)	4 (66.7)
ECOG PS, n (%)		
0	7 (33.3)	2 (33.3)
1	14 (66.7)	4 (66.7)

[a]Safety analysis set.
Abbreviations: EAC, esophageal adenocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma.

Table 2. Patient Disposition[a]

	ESCC (n=21)	EAC (n=6)
Patients, n (%)		
Discontinued OCI	12 (57.1)	6 (100.0)
Discontinued TIS	12 (57.1)	6 (100.0)
Discontinued from study	9 (42.9)	5 (83.3)
Deaths, n (%)	6 (28.6)	5 (83.3)
Treatment follow-up, median (range), weeks	31.3 (1.7-49.1)	21.1 (3.0-30.0)
Study follow-up, median (range), weeks	36.1 (1.7-77.0)	29.3 (8.6-57.1)

[a]Safety analysis set.
Abbreviations: EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; OCI, ociperlimab; TIS, tislelizumab.

Antitumor Activity (Efficacy-evaluable Analysis Set)

- Among the 24 patients with ESCC (n=19) and EAC (n=5), 84.2% and 80.0% achieved partial response, respectively (**Table 3**)
- In patients with ESCC, objective response rate was 80.0% in patients with TIGIT IC score ≥5% (n=10) and 87.5% in patients with TIGIT IC <5% (n=8) (**Table 4**)
- There were too few patients with EAC to allow for biomarker subgroup analysis
- In patients with ESCC, median progression-free survival (mPFS) was 8.1 months (**Figure 2**), and median duration of response (mDoR) was 6.7 months
- In patients with EAC, mPFS was 6.2 months (95% CI: 3.0, not estimable), and mDoR was 3.4 months

Table 3. Efficacy Outcomes[a]

	ESCC (n=19)	EAC (n=5)
DCR, n (%) [95% CI]	18 (94.7) [74.0, 99.9]	5 (100) [47.8, 100]
ORR, n (%) [95% CI]	16 (84.2) [60.4, 96.6]	4 (80.0) [28.4, 99.5]
BOR, n (%)		
CR	0	0
PR	16 (84.2)	4 (80.0)
SD	2 (10.5)	1 (20.0)
PD	0	0
NA	1 (5.3)	0
DoR, median (95% CI), months	6.7 (4.7, NE)	3.4 (1.7, NE)

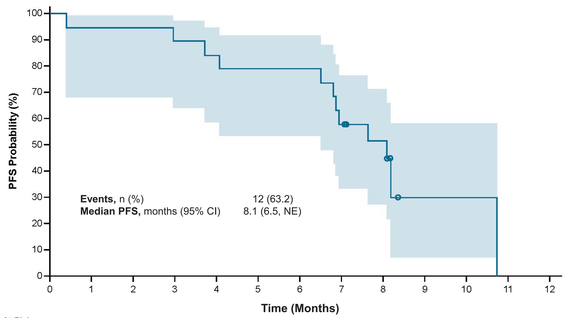
[a]Efficacy-evaluable analysis set.
Abbreviations: BOR, best overall response; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NA, not assessed or not evaluable; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial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

Table 4. Efficacy Outcomes in Patients With ESCC by PD-L1 and TIGIT Expression Status[a]

	PD-L1 TAP score ≥10% (n=4)	PD-L1 TAP score <10% (n=13)	TIGIT IC score ≥5% (n=10)	TIGIT IC score <5% (n=8)
DCR, % (95% CI)	100 (39.8, 100)	92.3 (64.0, 99.8)	100 (69.2, 100)	87.5 (47.4, 99.7)
ORR, % (95% CI)	100 (39.8, 100)	76.9 (46.2, 95.0)	80.0 (44.4, 97.5)	87.5 (47.4, 99.7)

[a]Efficacy-evaluable analysis set.
Abbreviations: DCR, disease control rate; IC, immune cell; ORR, objective response rate; PD-L1, programmed death-ligand 1; TAP, tumor area positivity.

Figure 2. Progression-Free Survival for ESCC[a,b]



[a]Efficacy-evaluable analysis set. [b]The patient numbers were too small to generate meaningful survival curves for patients with EAC (cohort 7).
Abbreviations: CI, confidence interval; EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; NE, not estimable; PFS, progression-free survival.

Safety

- Among the 27 patients, 20 (74.1%) experienced Grade ≥3 treatment-emergent adverse events (TEAEs), 13 patients (48.1%) had serious TEAEs (eight were treatment related), and one patient (3.7%) experienced a TEAE leading to death (**Table 5**)
- A total of 11 patients (52.4%) with ESCC and two patients (33.3%) with EAC experienced immune-mediated adverse events

Table 5. Overall Safety Summary[a]

	ESCC (n=21)	EAC (n=6)
Patients with ≥1 TEAE, n (%)		
Any grade	21 (100)	6 (100)
Grade ≥3	14 (66.7)	6 (100)
Serious TEAE	9 (42.9)	4 (66.7)
imAE, n (%)	11 (52.4)	2 (33.3)
TEAE leading to OCI dose modification	14 (66.7)	5 (83.3)
TEAE leading to OCI discontinuation	0	1 (16.7)
TEAE leading to TIS dose modification	14 (66.7)	4 (66.7)
TEAE leading to TIS discontinuation	0	1 (16.7)
TEAE leading to discontinuation from any study drug, n (%)	3 (14.3)	2 (33.3)
TEAE leading to death, n (%)	1 (4.8)	0

[a]Safety analysis set.
Abbreviations: EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell carcinoma; imAE, immune-mediated adverse event; OCI, ociperlimab; TEAE, treatment-emergent adverse event; TIS, tislelizumab.

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Disclosures

Meili Sun has no conflicts of interest to declare.