AdvanTIG-105: Phase 1b dose-expansion study of ociperlimab (OCI) + tislelizumab (TIS) with chemotherapy (CT) in patients (pts) with metastatic esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC)

Authors: 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]

Affiliations:

1. Department of Oncology, Jinan Central Hospital, Shandong University; Central Hospital Affiliated to
2. Department of Medical Oncology, Sarah Cannon Research Institute, Tennessee Oncology, Nashville, Tennessee, 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, Minnesota, 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, Victoria, Australia
7. Department of Medical Oncology, Bendigo Health, Bendigo, Victoria, 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

Background

A T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) inhibitor + an anti-PD-1 antibody is a promising combination which shows potent efficacy in solid tumors. AdvanTIG-105 (NCT04047862) is a Phase 1/1b open-label study designed to assess the safety and preliminary antitumor activity of anti-TIGIT mAb OCI + anti-PD-1 mAb TIS in pts with metastatic unresectable solid tumors. OCI + TIS was well tolerated in the dose-escalation part, preliminary efficacy was observed, and the recommended Phase 2 dose (RP2D) of OCI 900 mg IV Q3W + TIS 200 mg IV Q3W was established. Here we report results from dose-expansion cohorts 6 (C6) and 7 (C7).

ESMO 2023

Methods

Treatment-naïve adult pts with histologically/cytologically confirmed metastatic ESCC (C6) or EAC (C7) were enrolled. Pts received the RP2D of OCI + TIS with cisplatin + 5-fluorouracil/paclitaxel until disease progression, intolerable toxicity, or consent withdrawal. Primary endpoint: investigator-assessed ORR per RECIST v1.1. Secondary endpoints: efficacy (PFS, DoR, DCR), safety and PD-L1 and TIGIT expression as predictive efficacy biomarkers.

Results

As of Feb 2, 2023, 27 pts (C6: n=21; C7: n=6) with a median age of 63.0 y (range C6: 51-72; C7: 58-69) were enrolled; 24 (C6: n=19; C7: n=5) were efficacy evaluable. Efficacy and safety data are summarized in the table. ORRs by biomarker subgroups: C6, 100% in pts with PD-L1 tumor area positivity (TAP) score ≥10% (n=4) vs 76.9% in pts with PD-L1 TAP <10% (n=13); 80.0% in pts with TIGIT IC score ≥5% (n=10) vs 87.5% in pts with TIGIT IC <5% (n=8). C7 had too few pts for biomarker subgroup analysis.

Conclusions

These results demonstrate that OCI 900 mg + TIS 200 mg + CT had a safety profile consistent with previous reports and showed encouraging antitumor activity in pts with stage IV ESCC and EAC.

Table. Efficacy and Safety Summary

	Efficacy Evaluable Set	
	C6	**C7**
Parameter	**n=19**	**n=5**
	% (95% CI)	
ORR	84.2 (60.4-96.6)	80.0 (28.4-99.5)
DCR	94.7 (74.0-99.9)	100 (47.8-100)
	mo (95% CI)	
Median DoR	6.7 (4.7-NE)	3.4 (1.7-NE)
Median PFS	8.1 (6.5-NE)	6.2 (3.0-NE)
	Safety Set	
Parameter	**n=21**	**n=6**
Median study follow-up (range), wks	36.1 (1.7-77.0)	29.3 (8.6-57.1)
	n (%)	
Pts with ≥1 TEAE	21 (100)	6 (100)
Grade ≥3	14 (66.7)	6 (100)
Serious	9 (42.9)	4 (66.7)
imAE	11 (52.4)	2 (33.3)

DCR, disease control rate; DoR, duration of response; imAE, immune-mediate adverse event; mo, months; NE, not estimable; ORR, objective response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event.