AdvanTIG-203: Phase 2 Randomized, Multicenter Study of Ociperlimab (OCI) + Tislelizumab (TIS) in Patients (pts) With Unresectable, Locally Advanced, Recurrent/Metastatic Esophageal Squamous Cell Carcinoma (ESCC) and Programmed Cell Death-Ligand 1 (PD-L1) Positivity

Authors: Feng Wang MD PhD,[1] Chen-Yuan Lin MD PhD,[2] Jong-Mu Sun MD PhD,[3] Chang-Hsien Lu MD,[4] Prof Xueqiang Zhu MD,[5] Zhendong Chen MD,[6] In-Ho Kim MD PhD,[7] Prof Yueyin Pan MD,[8] Prof Jingdong Zhang MD PhD,[9] Zhaohong Chen MD,[10] David Tougeron MD PhD,[11] Prof Sung-Bae Kim MD PhD,[12] Prof Eric Van Cutsem MD PhD,[13] Ramil Abdrashitov MD, PhD,[14] Ruimin Ge MBBS PhD,[15] Jingchao Sun PhD,[16] Jiadong Zhou PhD,[15] Ruihua Xu MD PhD[1]

Affiliations:

1. *Department of Medical Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China*
2. *Department of Pediatric Hematology and Oncology, China Medical University Hospital, Taiwan, China*
3. *Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Seoul, Republic of Korea*
4. *Department of Pediatric Hematology and Oncology, Chiayi Chang Gung Memorial Hospital, Taiwan, China*
5. *Department of Oncology, Sichuan Provincial People's Hospital, Chengdu, Sichuan, China*
6. *Department of Oncology, The Second Hospital of Anhui Medical University, Hefei, China*
7. *Division of Oncology, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea'', Seoul, Republic of Korea*
8. *Department of Oncology, Anhui Provincial Hospital, Hefei, China*
9. *Department of Gastrointestinal Cancer, Liaoning Cancer Hospital & Institute, Shenyang, China*
10. *Department of Oncology, People's Hospital of Deyang City, Deyang, China*
11. *Hepato-gastroenterology department, Poitiers University Hospital, Poitiers, France*
12. *Department of Oncology, Asan Medical Center, Seoul, Republic of Korea*
13. *Department of Digestive Oncology, University Hospitals Gasthuisberg Leuven and University of Leuven (KUL), Leuven, Belgium*
14. *Clinical Development, BeiGene USA, Inc., Fulton, MD, USA*
15. *Clinical Development, BeiGene (Beijing) Co., Ltd., Beijing, China*
16. *Biostatistics, BeiGene (Beijing) Co., Ltd., Beijing, China*

Background: Prognosis of unresectable ESCC is poor, with median overall survival (OS) in 2nd line (2L) of ~10 months. Anti-PD-1 agents, including TIS, have demonstrated an OS increase, albeit still unsatisfactory, in unresectable ESCC pts. In preclinical studies and clinical studies of other tumors, coinhibition of T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) and PD-1 enhances antitumor activity of anti-PD-1. AdvanTIG-203 (NCT04732494) is investigating efficacy/safety of TIS +/- OCI (anti-TIGIT) in advanced ESCC pts, progressing on/after 1st line (1L) systemic therapy.

Methods: Adult ESCC pts with PD-L1 tumor area positivity (TAP) ≥10% and progression on/after 1L systemic therapy were randomized (1:1) to OCI 900 mg + TIS 200 mg (O+T) or placebo + TIS (P+T) every 3 weeks until progression, unacceptable toxicity, or withdrawal. Primary endpoint was investigator (INV)-assessed objective response rate (ORR). Secondary endpoints included progression free survival (PFS).

Results: As of 1 Feb 2023, 125 pts (median age 64 years; 88.8% male) were randomized to O+T (n=62) or P+T (n=63). INV-assessed ORR was 30.6% with O+T vs. 20.6% with P+T; hazard ratio (HR) of INV-assessed PFS was 0.93 (95% CI: 0.61, 1.43) (**Table**). Incidence of pts with ≥1 any adverse event (AE) was comparable between O+T (93.5%) and P+T (95.2%); most common AE was anemia (O+T: 25.8%; P+T: 28.6%). Respective AE rates for O+T and P+T were 41.9% and 41.3% grade ≥3 AEs, 41.9% and 39.7% serious AEs, 9.7% and 15.9% AEs that led to treatment discontinuation, 45.2% and 30.2% immune-related AEs, and 0% and 3.2% treatment-related fatal AEs.

Conclusions: In 2L therapy of advanced ESCC pts with PD-L1 TAP ≥10%, O+T showed tolerable safety profile and trend toward better ORR, but similar PFS vs. P+T.

Table: Efficacy

	O+T (n=62)	P+T (n=63)
ORR[a], % (95% CI)		
INV[b]	30.6 (19.6, 43.7)	20.6 (11.5, 32.7)
	P[c,d]=0.2114	
IRC[e]	32.3 (20.9, 45.3)	25.4 (15.3, 37.9)
	P[c,d]=0.4209	
OS[e,f] (months), median (95% CI)	10.1 (7.1, NE)	9.3 (6.0, NE)
	HR[c] (95% CI): 0.93 (0.55, 1.58)	
	P[c,g]=0.3977	
PFS[e] (months), median (95% CI)		
INV	3.4 (1.8, 5.1)	3.5 (1.9, 4.1)
	HR[c] (95% CI): 0.93 (0.61, 1.43)	
IRC	3.6 (2.7, 5.1)	2.8 (1.9, 6.9)
	HR[c] (95% CI): 1.01 (0.64, 1.59)	

Median follow-up was 7 months.
IRC, independent review committee; NE, not estimable
[a]Confirmed per RECIST v1.1
[b]Primary endpoint
[c]Stratified
[d]2-sided; by Cochran-Mantel-Haenszel method
[e]Secondary endpoint
[f]Still immature (event rate 45.6%)
[g]1-sided; by log-rank test