MADRID 2023 ESMO congress

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 (PDL1) Positivity

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DECLARATION OF INTERESTS

Feng Wang: *Nothing to disclose*
Chen-Yuan Lin: *Nothing to disclose*
Jong-Mu Sun: *Nothing to disclose*
Chang-Hsien Lu: *Nothing to disclose*
Xueqiang Zhu: *Nothing to disclose*
Zhendong Chen: *Nothing to disclose*
In-Ho Kim: *Nothing to disclose*
Yueyin Pan: *Nothing to disclose*
Jingdong Zhang: *Nothing to disclose*
Zhaohong Chen: *Nothing to disclose*
David Tougeron: *Has honoraria, Speaker's Bureau/Advisory Role with Amgen, Sandoz, Sanofi, BMS, Merck-Serono, MSD, Pierre Fabre, Roche and Servier*
Sung-Bae Kim: *Nothing to disclose*
Eric Van Cutsem: *Serves as a consultant or in an advisory role with Bayer, Lilly, Roche, Servier, Bristol Myers Squibb, Celgene, Merck Sharp & Dohme, Merck KGaA, Novartis, AstraZeneca, Halozyme, Array BioPharma, Biocartis, GlaxoSmithKline, Daiichi Sankyo, Pierre Fabre, Sirtex Medical, Taiho Pharmaceutical, Incyte, Astellas Pharma. He has received research funding from Amgen (Inst), Bayer (Inst), Boehringer Ingelheim (Inst), Lilly (Inst), Novartis (Inst), Roche (Inst), Celgene (Inst), Ipsen (Inst), Merck (Inst), Merck KGaA (Inst), Servier (Inst), Bristol Myers Squibb (Inst)*
Ramil Abdrashitov: *Employed by BeiGene*
Ruimin Ge: *Employed by BeiGene*
Jingchao Sun: *Employed by BeiGene*
Jiadong Zhou: *Employed by BeiGene*
Ruihua Xu*: Nothing to disclose*

Background

- Esophageal cancer (of which >80% of cases are ESCC) has a poor prognosis, including a 5-year OS of 21.7% that decreases to 5.6% with distant metastasis[1,2]
- Anti–PD-1/PD-L1 monotherapy is the recommended 2L treatment for advanced PD-L1 positive ESCC[3]
  - Only 20% of patients respond to this approach,[4] of whom most will develop acquired resistance
- **Ociperlimab (OCI)** is an IgG1 mAb engineered to bind TIGIT with high specificity and affinity[5,6]
- Tislelizumab (TIS) is an IgG4 anti–PD-1 mAb designed to minimize binding to FcγR on macrophages[7]
- Efficacy and safety of **OCI** + TIS in patients with unresectable, locally advanced, recurrent, or metastatic ESCC with PD-L1 positivity were assessed in the **phase 2, randomized, double-blind, placebo-controlled, multicenter AdvanTIG-203 trial** (NCT04732494)

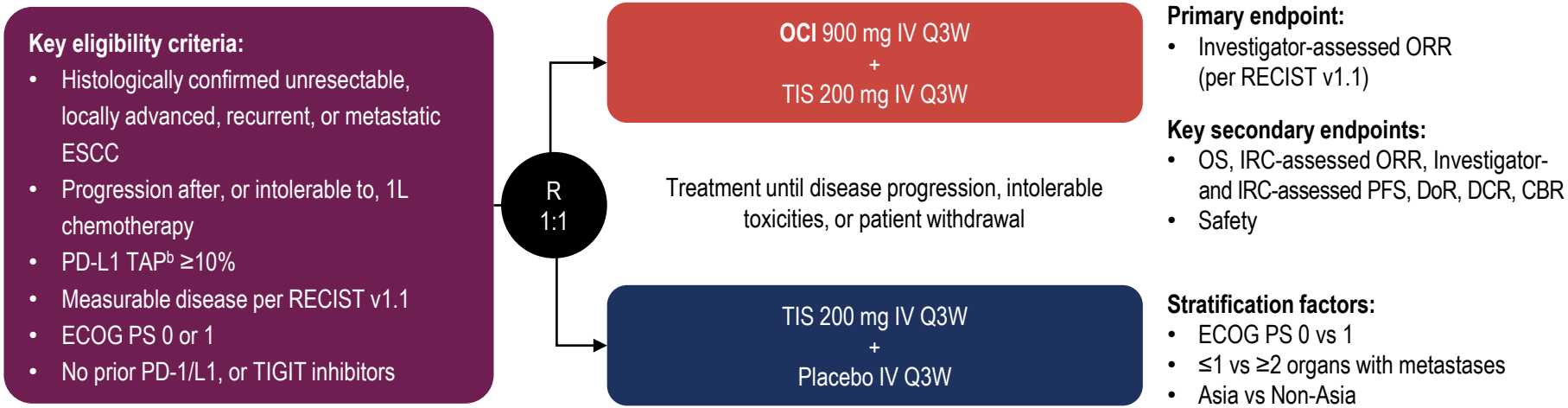
Here, we report the primary analysis of efficacy and safety outcomes from **AdvanTIG-203**

Abbreviations: 2L, second line; ESCC, esophageal squamous cell carcinoma; IgG, immunoglobulin; mAb, monoclonal antibody; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; Fc, fragment crystallizable; FcγR, Fc-gamma receptor; TIGIT, T-cell immunoreceptor with immunoglobulin and tyrosine-based inhibitory motif domains.

1. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/html/esoph.html (Accessed August 7, 2023). 2. Arnold, et al. *Gut*. 2020;69:1564-1571. 3. NCCN Clinical Practice Guidelines in Oncology. Esophageal and Esophagogastric Junction Cancers. v2.2023. 4. Kato K, et al. *Lancet Oncol*. 2019;20(11):1506-17. 5. Frentzas S, et al. *J Clin Oncol*. 2021 (Abs 2583) [presented at ASCO 2021]. 6. Chen X, et al. *Cancer Res*. 2021 (Poster 1854) [presented at AACR 2021]. 7. Zhang T, et al. *Cancer Immunol Immunother*. 2018;67(7):1079-90.

AdvanTIG-203 Study Design

Randomized, double-blind, placebo-controlled, multicenter[a] study



[a]Performed at 60 sites, including 46 in Asia (China mainland, Republic of Korea, Taiwan, and Thailand) and 14 in Europe (France and Spain). Data cutoff: February 1, 2023. [b]The TAP score is defined as the total percentage of the tumor area (tumor and any desmoplastic stroma) covered by tumor cells with PD-L1 membrane staining at any intensity and tumor-associated immune cells with PD-L1 staining at any intensity, as visually estimated by VENTANA PD-L1 (SP263) assay

Abbreviations: 1L, first line; CBR, clinical benefit rate; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; IRC, Independent Review Committee; IV, intravenously; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, once every 3 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TAP, tumor area positivity; TIGIT, T-cell immunoreceptor with immunoglobulin and tyrosine-based inhibitory motif domains.

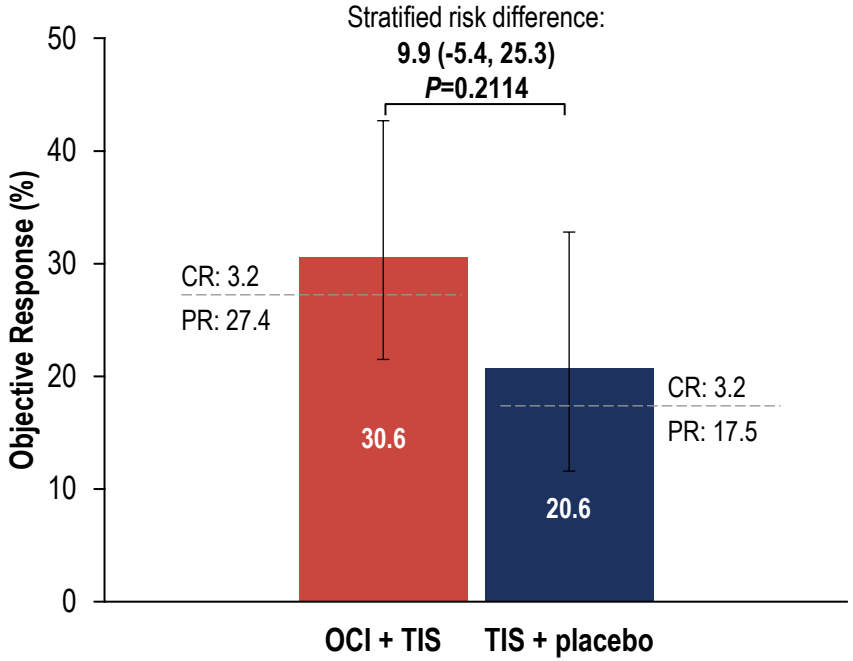
Baseline Characteristics

	OCI + TIS (n=62)	TIS + placebo (n=63)
Median (range) age, years	63.0 (42–74)	65.0 (49–81)
Male, n (%)	58 (93.5)	53 (84.1)
Race, n (%)		
Asian	55 (88.7)	54 (85.7)
White	3 (4.8)	5 (7.9)
Other/not reported	4 (6.5)	4 (6.3)
Median (range) time since ESCC diagnosis, months	9.5 (2.3–85.3)	9.9 (2.3–68.6)
Metastatic at study entry, n (%)	57 (91.9)	57 (90.5)
Median (range) time since metastatic diagnosis, months	5.0 (0.1–25.5)	3.5 (0–24.0)
ECOG PS, n (%)		
0	16 (25.8)	15 (23.8)
1	46 (74.2)	48 (76.2)
Prior therapies, n (%)		
Platinum-based chemotherapy	62 (100)	63 (100)
Radiation	43 (69.4)	40 (63.5)
Surgery	24 (38.7)	27 (42.9)

Baseline characteristics were generally well balanced between arms

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; OCI, ociperlimab; SD, standard deviation; TIS, tislelizumab.

Primary Endpoint: Investigator-Assessed ORR



ORR was numerically improved in patients receiving **OCI** + TIS vs TIS + placebo

Data cutoff: February 1, 2023. Results presented as stratified *P*-value and risk difference (95% CI) with stratification factors at randomization (ECOG PS score and the number of organs with metastases).
Abbreviations: CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; OCI, ociperlimab; ORR, objective response rate; PR, partial response; TIS, tislelizumab.

Secondary Efficacy Endpoints

Endpoint[a]	Assessment	OCI + TIS (n=62)	TIS + placebo (n=63)	Comparison
OS, months[b]		10.1 (7.1, NE)	9.3 (6.0, NE)	0.93 (0.55, 1.58)[c]
ORR, %	IRC	32.3 (20.9, 45.3)	25.4 (15.3, 37.9)	6.6 (-9.2, 22.5)[d] *P*=0.4209
CR/PR	IRC	11.3% / 21.0%	6.3% / 19.0%	
PFS, months	Investigator	3.4 (1.8, 5.1)	3.5 (1.9, 4.1)	0.93 (0.61, 1.43)[c]
	IRC	3.6 (2.7, 5.1)	2.8 (1.9, 6.9)	1.01 (0.64, 1.59)[c]
DCR, %	Investigator	61.3 (48.1, 73.4)	58.7 (45.6, 71.0)	2.7 (-14.4, 19.9)[d]
	IRC	64.5 (51.3, 76.3)	58.7 (45.6, 71.0)	5.0 (-11.7, 21.8)[d]
CBR, %	Investigator	33.9 (22.3, 47.0)	30.2 (19.2, 43.0)	3.9 (-12.7, 20.4)[d]
	IRC	32.3 (20.9, 45.3)	27.0 (16.6, 39.7)	5.0 (-11.0, 21.0)[d]
DoR, months	Investigator	14.6 (5.7, NE)	NR (2.7, NE)	-
	IRC	14.6 (7.2, NE)	NR (4.2, NE)	-

Both treatments had similar efficacy in PFS and OS; however, OS data are immature

[a]Values expressed as median or rate (%) with 95% CI. [b]Based on event rates of 48.4% for OCI + TIS and 42.9% for TIS + placebo. [c]Stratified hazard ratio (95% CI). [d]Stratified risk difference (95% CI).
Abbreviations: CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; IRC, Independent Review Committee; NE, not estimable; NR, not reached; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; TIS, tislelizumab.

Safety

Overview	OCI + TIS (n=62)	TIS + placebo (n=63)
Patients with any TEAE	58 (93.5)	60 (95.2)
Grade ≥3 TEAE	26 (41.9)	26 (41.3)
Serious TEAE	26 (41.9)	25 (39.7)
TEAE leading to death[a]	4 (6.5)	4 (6.3)
Immune-related AE	28 (45.2)	19 (30.2)
TEAE leading to discontinuation	6 (9.7)	10 (15.9)

TEAE in >10% of patients in either arm	OCI + TIS (n=62)	TIS + placebo (n=63)
Anemia	16 (25.8)	18 (28.6)
Constipation	10 (16.1)	8 (12.7)
Weight decreased	9 (14.5)	6 (9.5)
Diarrhea	8 (12.9)	5 (7.9)
Hypoalbuminemia	8 (12.9)	10 (15.9)
Hypothyroidism	8 (12.9)	11 (17.5)
COVID-19	7 (11.3)	2 (3.2)
Cough	7 (11.3)	10 (15.9)
Hypokalemia	7 (11.3)	6 (9.5)
Decreased appetite	5 (8.1)	10 (15.9)
Hyponatremia	4 (6.5)	7 (11.1)
Pneumonia	4 (6.5)	8 (12.7)
ALT increased	3 (4.8)	9 (14.3)
AST increased	3 (4.8)	7 (11.1)

Adding **OCI** to TIS was generally well tolerated based on similar event rates between treatment arms

[a]Excludes death due to the disease under study.

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; OCI, ociperlimab; TEAE, treatment emergent adverse event; TIS, tislelizumab.

Conclusions

- In **AdvanTIG-203**, that included patients with unresectable, locally advanced, recurrent, or metastatic ESCC and PD-L1 TAP ≥10%, 2L treatment with **OCI** + TIS:
  - Resulted in a numeric increase in ORR vs TIS + placebo based on investigator assessment
  - Showed similar effects as TIS + placebo on other efficacy outcomes like PFS and OS; however, OS data were immature
  - Was generally well tolerated with manageable toxicities

Abbreviations: 2L, second line; ESCC, esophageal squamous cell carcinoma; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TAP, tumor area positivity; TIS, tislelizumab.

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Thank you!

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