Comparative efficacy and safety of tislelizumab versus anti-PD-1 treatments in second line esophageal squamous cell carcinoma: simulated treatment comparisons

Authors: Elizabeth Smyth[1], Jaffer A. Ajani[2], Kaijun Wang[3], JeanPierre Coaquira Castro[3], Maximiliano Augusto Novis de Figueiredo[4], Jong-Mu Sun[5], Konstantinos Soulanis[6], Anastasios Tasoulas[6], Georgios F. Nikolaidis[7], Eugenia Priedane,[8] Lin Zhan[3]

Affiliations:

[1]Oxford University Hospitals NHS Foundation Trust
[2]Department of Gastrointestinal Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center;
[3]BeiGene USA, Inc., Emeryville, CA, USA;
[4]Department of Internal Medicine, Faculty of Medical Sciences, Universidade Estadual de Campinas (UNICAMP), Campinas, Brazil;
[5]Division of Hem/Oncology, Samsung Medical Center;
[6]IQVIA, Athens, Greece;
[7]IQVIA, London, UK;
[8]BeiGene UK, London, UK.

Background: Tislelizumab has demonstrated survival benefit over chemotherapy in previously treated advanced esophageal squamous cell carcinoma (ESCC) in an open-label phase 3 study (RATIONALE 302, N=512, NCT03430843). In the absence of head-to-head studies, anchored simulated treatment comparisons (STCs) estimated the relative effect of tislelizumab versus other anti-PD-1 treatments approved in the European Union and United Kingdom.

Methods: Individual patient data from RATIONALE 302 were adjusted to aggregate data in each comparator study using STC. Clinical expert input, statistical analyses and literature searches determined important effect modifiers. Depending on data availability, STCs for overall survival (OS) and progression-free survival (PFS) were adjusted for Eastern Cooperative Oncology Group performance status (ECOG-PS), disease status, PD-1 expression status, liver and lung metastasis; whereas STC for treatment-related adverse event (TRAE) grade ≥ 3 analysis was adjusted for age, ECOG-PS, PD-1 expression, liver metastasis, and previous therapies. Additional sensitivity analyses along with subgroup analyses (PD-1 category and baseline ECOG-PS) were considered. These analyses were also conducted using the latest DCO (Dec 28, 2022).

Results: Comparator studies were similar to RATIONALE 302 with comparable control arms. After adjustment, no significant differences were estimated in PFS, OS, or TRAEs between tislelizumab and anti-PD-1 comparators (**Table**). Results from sensitivity, subgroup and latest DCO aligned with the base case.

Conclusions: The STCs showed comparable efficacy and safety between tislelizumab, pembrolizumab, and nivolumab.

Table. Population-adjusted relative effects in the base case.

Tislelizumab (RATIONALE 302) versus Comparator (study)	OS	PFS	TRAE grade ≥3
	HR (95% CI)	HR (95% CI)	OR (95% CI)
Nivolumab (ATTRACTION-3)	0.88 (0.65, 1.19)	0.79 (0.59, 1.07)	1.30 (0.68, 2.48)
Pembrolizumab (KEYNOTE-181)	0.94 (0.67, 1.32)	0.95 (0.63, 1.43)	Not feasible*

CI, Confidence Interval; HR, Hazard ratio; OR, Odds ratio. *TRAE data was not available for pembrolizumab. DCO=Dec 01, 2020