Tislelizumab Versus Chemotherapy as Second-line Treatment for Advanced or Metastatic Esophageal Squamous Cell Carcinoma (ESCC, RATIONALE 302): Impact on Health-Related Quality of Life (HRQoL)

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Background

RATIONALE 302 was a global phase 3 study (NCT03430843) that investigated tislelizumab (TIS) compared with investigator-chosen chemotherapy (ICC) as second-line treatment for patients (pts) with advanced or metastatic ESCC, in which TIS demonstrated a significant and clinically meaningful improvement in overall survival hazard ratio (HR = 0.70 [95% CI 0.57–0.85], P=0.0001), and a favorable safety profile compared with ICC. Here we assess the HRQoL of pts receiving TIS vs ICC in a pt population that usually experiences HRQoL deterioration.

Methods

Adults with advanced or metastatic ESCC whose disease progressed following prior systemic therapy were randomized 1:1 to either TIS 200 mg IV every 3 weeks or ICC (paclitaxel, docetaxel, or irinotecan). HRQoL was measured using the global health status/quality of life (GHS/QoL), physical functioning, and fatigue scores from EORTC QLQ-C30 and the dysphagia, reflux, eating, and pain scores from the EORTC QLQ-OES18 from screening through Cycle 6 or until treatment discontinuation (whichever occurs first). Least-squares mean score change from baseline to Cycles 4 and 6 in HRQoL scores was assessed using a mixed model for repeated measurements. Time to deterioration (TTD) for the GHS/QoL score and the symptom scales of the QLQ-OES18 was examined using the Kaplan-Meier method.

Results

Overall, 512 pts (median age 62) were randomized to TIS (n=256) or ICC (n=256). Compared with ICC, TIS-treated pts had stable GHS/QoL and fatigue scores as well as less decline in physical functioning at Cycles 4 and 6 (table). Except for pain, the TIS arm experienced less OES18 symptoms relative to baseline than the ICC arm. TTD analysis showed pts in TIS arm

were at lower risk of worsening dysphagia (HR = 0.76 [95% CI 0.53, 1.07], P=0.0562) compared with ICC.

Conclusions

The analysis showed that ESCC pts treated with TIS in the second line had a longer maintenance of HRQoL compared to pts treated with ICC. These results, along with improved survival and favorable safety profile, suggest TIS represents a potential new second-line treatment option for pts with advanced or metastatic ESCC.

Table. Least-Square Mean Change (95% CI) From Baseline to Cycles 4 and 6

		Tislelizumab (N=256)		ICC (N=256)	
		Cycle 4	Cycle 6	Cycle 4	Cycle 6
QLQ-C30	GHS/QoL	0.0 (-2.5, 2.4)	-0.8 (-3.5, 2.0)	-5.8 (-8.8, -2.8)	-8.9 (-12.8, -4.9)
	Physical functioning	-4.0 (-6.3, -1.8)	-4.6 (-7.1, -2.1)	-6.6 (-9.3, -4.0)	-8.9 (-12.1, -5.6)
	Fatigue	3.5 (0.4, 6.6)	1.0 (-2.1, 4.2)	11.3 (7.5, 15.1)	6.4 (2.0, 10.9)
QLQ-OES18	Dysphagia	2.7 (-1.7, 7.1)	1.6 (-3.5, 6.6)	7.7 (2.2, 13.2)	1.9 (-5.5, 9.2)
	Reflux	-2.3 (-4.6, -0.1)	-1.8 (-4.7, 1.2)	1.8 (-1.1, 4.7)	-1.1 (-5.4, 3.2)
	Eating	0.0 (-2.8, 2.8)	-0.5 (-3.6, 2.6)	2.7 (-0.8, 6.2)	4.7 (0.3, 9.1)
	Pain	-1.6 (-3.4, 0.2)	-1.4 (-3.9, 1.0)	-1.1 (-3.6, 1.3)	0.2 (-3.6, 4.1)

ICC, investigator-chosen chemotherapy.