Tislelizumab (TIS) Plus Chemotherapy (Chemo) vs Placebo (PBO) Plus Chemo as First-Line (1L) Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (GC/GEJC): Health-Related Quality of Life (HRQoL) Outcomes in the RATIONALE-305 Study

Authors:

Marcia Cruz Correa, University of Puerto Rico, School of Medicine, San Juan, Puerto Rico
Rui-Hua Xu, University Cancer Center State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Department of Medical Oncology, Guangzhou, China
Markus Moehler, Johannes Gutenberg-University Clinic, Department of Internal Medicine I, Mainz, Germany
Do-Youn Oh, Seoul National University Hospital Cancer Research Institute, Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Republic of Korea
Ken Kato, National Cancer Center Hospital, Department of Gastrointestinal Medical Oncology, Tokyo, Japan
David Spigel, Sarah Cannon Research Institute, Nashville, TN, USA
Hendrik-Tobias Arkenau, Sarah Cannon Research, London, England
Josep Tabernero, Vall d'Hebron University Hospital, Department of Medical Oncology, Barcelona, Spain
Anastasia V. Zimina, BIH Of Omsk Region, Clinical Oncology Dispensary, Omsk Oblast, Russia
Yuxian Bai, Harbin Medical University Cancer Hospital, Department of Gastrointestinal Oncology, Harbin, China
Jianhua Shi, Linyi Cancer Hospital, Department II of Medical Oncology, Linyi, China
Keun-Wook Lee, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Department of Medical Oncology (Internal Medicine), Seongnam, Republic of Korea
Hidekazu Hirano, National Cancer Center Hospital, Department of Gastrointestinal Medical Oncology, Tokyo, Japan
Lucjan Wyrwicz, Maria Sklodowska-Curie National Cancer Research Institute, Department of Oncology and Radiotherapy, Warsaw, Poland
Roberto Pazo Cid, Hospital Universitario Miguel Servet, Department of Medical Oncology, Zaragoza, Spain
Hui Xu, BeiGene (Beijing) Co., Ltd., Beijing, China
Tao Sheng, BeiGene (Beijing) Co., Ltd., Beijing, China
Gisoo Barnes, BeiGene USA, Inc., San Mateo, CA, USA

Background: RATIONALE-305 (NCT03777657), demonstrated statistically significant and clinically meaningful improvements in overall survival (OS) with TIS + chemo (n=501) over PBO + chemo (n=496) as 1L treatment in patients (pts) with advanced G/GEJC. This analysis examined HRQoL outcomes of the RATIONALE-305 study at final analysis.

Methods: Adults with previously untreated, unresectable, or metastatic GC/GEJC, were randomized (1:1) to TIS 200 mg or PBO IV once every 3 weeks plus investigator-choice of chemo. HRQoL was assessed using EORTC QLQ-C30 and the QLQ-STO22. A mixed model for repeated measures using PRO endpoints at clinical Cycles 4 and 6 was performed. Time to deterioration was examined.

Results: TIS + chemo had improved outcomes than PBO + chemo (see Table) as indicated by least-squares mean change from baseline to Cycle 6 for QLQ-C30 GHS/QoL (2.52 [95% CI:0.29 to 4.74]), physical functioning (2.46 [95% CI: 0.49 to 4.43]), fatigue (-3.01 [95% CI: -5.78 to -0.24]), and the STO22 index score (-1.62 [95% CI: -3.12 to -0.12]), as well as maintaining upper gastrointestinal (GI) symptoms (-1.74 [95% CI: -3.55 to 0.06)] and pain (-1.88 [95% CI: -4.03 to 0.27]). Pts receiving TIS + chemo had a lower risk for deterioration of GHS/QoL(0.77 [95% CI: 0.60 to 0.98]), physical functioning (0.72 [0.57 to 0.92]), STO22 index score (0.64 [0.45 to 0.92]), pain/discomfort (HR: 0.74 [0.58-0.96]), and upper GI symptoms (0.73 [0.56 to 0.95]).

Conclusion: Pts treated with TIS + chemo had better HRQoL outcomes vs pts treated with PBO + chemo, particularly for GHS/QoL, physical functioning, fatigue, GC/GEJC symptoms, pain/discomfort, and upper GI symptoms. These results, along with prolonging of OS and other secondary efficacy endpoints, as well as a tolerable safety profile, support the benefit of TIS + chemo as a potential 1L treatment option for GC/GEJC.

	Cycle 4 TIS + chemo n=501 Mean (95% CI)	Cycle 4 PBO + chemo n=496 Mean (95% CI)	Cycle 6 TIS + chemo n=501 Mean (95% CI)	Cycle 6 PBO + chemo n=496 Mean (95% CI)
QLQ-C30 GHS/QoL	1.35 (-0.24, 2.94)	-0.45 (-2.04, 1.13)	0.93 (-0.71, 2.57)	-1.58 (-3.24, 0.07)
Physical functioning	-2.47 (-3.77, -1.18)	-3.92 (-5.21, -2.62)	-2.76 (-4.22, -1.30)	-5.22 (-6.69, -3.75)
Fatigue	1.75 (-0.09, 3.60)	3.07 (1.23, 4.91)	1.71 (-0.32, 3.75	4.73 (2.68, 6.77)
QLQ- STO22 Index score	-1.71 (-2.77, -0.66)	-0.61 (-1.66, 0.45)	-1.84 (-2.95, -0.74)	-0.22 (-1.34, 0.89)
Dysphagia	-2.78 (-3.99, -1.57)	-1.27 (-2.48, -0.06)	-2.79 (-3.93, -1.64)	-2.01 (-3.17, -0.86)
Pain/Discomfort	-6.88 (-8.39, -5.36)	-4.64 (-6.16, -3.13)	-5.97 (-7.56, -4.38)	-4.09 (-5.69, -2.49)
Dietary restrictions	-0.31 (-1.75, 1.12)	0.61 (-0.82, 2.05)	-0.25 (-1.79, 1.30)	1.08 (-0.48, 2.63)
GI symptoms	-3.14 (-4.40, -1.87)	-1.54 (-2.80, -0.28)	-3.24 (-4.58, -1.90)	-1.49 (-2.84, -0.14)