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Tislelizumab (TIS) Plus Chemotherapy (Chemo) vs Placebo (PBO) Plus Chemo as First-Line (1L) Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (GC/GEJC): Patient-Reported Outcomes (PROs) in the Asian Subgroup of the RATIONALE-305 Study

Ken Kato,[1] Rui-Hua Xu,[2] Do-Youn Oh,[3] Yuxian Bai,[4] Jianhua Shi,[5] Keun-Wook Lee,[6] Hidekazu Hirano,[1] Hui Xu,[7] Tao Sheng,[7] Gisoo Barnes[8]

[1]National Cancer Center Hospital, Department of Gastrointestinal Medical Oncology, Tokyo, Japan; [2]University Cancer Center State Key Laboratory of Oncology in South China, Collaborative Innovation Center of Cancer Medicine, Department of Medical Oncology, Guangzhou, China; [3]Seoul National University Hospital Cancer Research Institute, Seoul National University College of Medicine, Department of Internal Medicine, Seoul, Republic of Korea; [4]Harbin Medical University Cancer Hospital, Department of Gastrointestinal Oncology, Harbin, China; [5]Linyi Cancer Hospital, Department II of Medical Oncology, Linyi, China; [6]Seoul National University College of Medicine, Seoul National University Bundang Hospital, Department of Medical Oncology (Internal Medicine), Seongnam, Republic of Korea; [7]BeiGene (Beijing) Co., Ltd., Beijing, China; [8]BeiGene USA, Inc., San Mateo, CA, USA.

Declaration of Interests

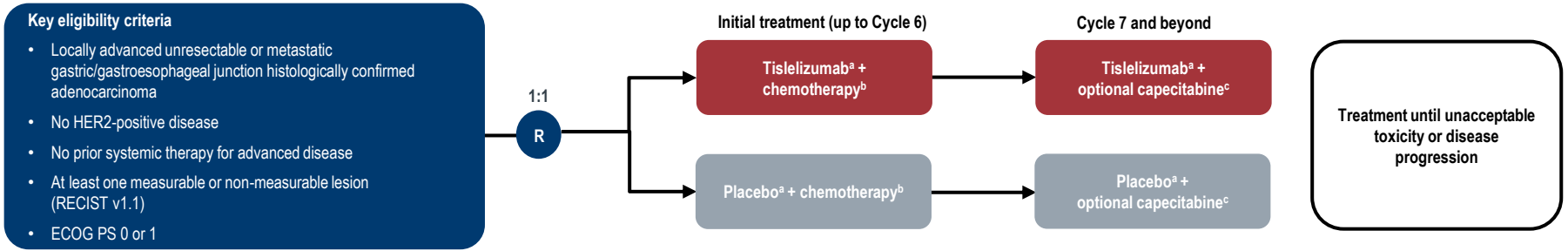
Ken Kato reports consultancy or advisory roles for Amgen, AstraZeneca, Bayer AG, BeiGene, Bristol Myers Squibb, Daiichi Sankyo, Merck and Co, Merck Biopharma, Novartis, ONO Pharmaceuticals, and Taiho; and grant/research funding from AstraZeneca, Bayer AG, BeiGene, Chugai, Janssen Pharmaceuticals, Merck & Co, Oncolys BioPharma, ONO Pharmaceuticals, and Taiho.

Background

- RATIONALE-305 (NCT03777657) demonstrated statistically significant and clinically meaningful improvements in OS (HR, 0.80 [95% CI, 0.70-0.92]) and PFS (HR, 0.78 [95% CI, 0.67-0.90]) with T+C versus P+C as 1L treatment in patients with advanced GC/GEJC
- Compared with the P+C group, patients in the T+C group experienced improvement or maintenance of PROs
    - Lower risk for deterioration of GHS/QoL (HR, 0.77 [95% CI, 0.60-0.98]), physical functioning (0.72 [0.57-0.92]), EORTC QLQ-STO22 index score (0.64 [0.45-0.92]), pain/discomfort (0.74 [0.58-0.96]), and upper gastrointestinal symptoms (0.73 [0.56-0.95])
- The current analysis examined PROs in the Asian subgroup of RATIONALE-305

Abbreviations: C, chemotherapy; CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; 1L, first-line; GC/GEJC, gastric/gastroesophageal junction cancer; GHS/QoL, global health status/quality of life; HR, hazard ratio; OS, overall survival; P, placebo; PFS, progression-free survival; PRO, patient-reported outcome; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; T, tislelizumab.

Study Design and Patient Population



Stratification factors

- Regions of enrollment
- Peritoneal metastasis
- PD-L1 expression score (≥5% vs <5%)[d]
- Investigator-chosen chemotherapy (XELOX or FP)

Endpoints

- **Primary endpoint:** OS in PD-L1 score ≥5% and ITT populations
- **Secondary endpoints:** HRQoL, PFS, ORR, DoR, and safety

- Of 997 randomized patients, 748 (T+C: n=376; P+C: n=372) were enrolled from Asia; of these, 403 had a PD-L1 score of ≥5%
- The Asian subgroup comprised patients from China (including Taiwan), Japan, and South Korea
- As of data cutoff of final analysis (February 28, 2023), median study follow-up in the Asian subgroup was 14.5 months (range, 0.1-50.1) and minimum study follow-up in this subgroup was 24.6 months
- PROs assessed HRQoL using the EORTC QLQ-C30 (measures overall cancer-related HRQoL) and its stomach cancer module, the EORTC QLQ-STO22
- A mixed model for repeated measures was used for PRO endpoints at treatment cycles 4 and 6, and time to deterioration was analyzed

[a]Tislelizumab 200 mg or placebo Q3W (Day 1). [b]Oxaliplatin 130 mg/m² IV (Day 1) and oral capecitabine 1000 mg/m² twice daily (14 consecutive days from Day 1) Q3W (XELOX), or cisplatin 80 mg/m² IV (Day 1) and 5-fluorouracil 800 mg/m²/day IV (Days 1-5) Q3W (FP). [c]Capecitabine as maintenance therapy was optional and only for XELOX-treated patients. [d]PD-L1 score was determined using the VENTANA PD-L1 (SP263) assay by tumor area positivity score.

Abbreviations: C, chemotherapy; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EORTC, European Organisation for Research and Treatment of Cancer; FP, 5-fluorouracil and cisplatin; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; ITT, intent-to-treat; IV, intravenous; ORR, objective response rate; OS, overall survival; P, placebo; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, once every 3 weeks; QLQ-C30, Quality of Life Questionnaire Core-30; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; T, tislelizumab; XELOX, capecitabine and oxaliplatin.

Demographics and Baseline Characteristics

The baseline characteristics were similar between the arms

	Asian Subgroup ITT Population		Overall ITT Population	
	T+C (n=376)	P+C (n=372)	T+C (n=501)	P+C (n=496)
Age, median (range), years	59.0 (23.0-86.0)	61 (25.0-83.0)	60.0 (23.0-86.0)	61.0 (25.0-86.0)
Sex, male, n (%)	258 (68.6)	261 (70.2)	346 (69.1)	346 (69.8)
ECOG PS, n (%)				
0	120 (31.9)	102 (27.4)	169 (33.7)	154 (31.0)
1	256 (68.1)	270 (72.6)	332 (66.3)	342 (69.0)
Primary tumor location, n (%)[a]				
Stomach	329 (87.5)	319 (85.8)	405 (80.8)	395 (79.6)
GEJ	47 (12.5)	52 (14.0)	96 (19.2)	100 (20.2)
PD-L1 TAP score, n (%)				
≥5%	202 (53.7)	201 (54.0)	274 (54.7)	272 (54.8)
<5%	174 (46.3)	171 (46.0)	227 (45.3)	224 (45.2)
Metastatic disease, n (%)	373 (99.2)	369 (99.2)	494 (98.6)	490 (98.8)
Peritoneal metastasis, n (%)	165 (43.9)	160 (43.0)	220 (43.9)	214 (43.1)
Investigator-chosen chemotherapy, n (%)				
Oxaliplatin/capecitabine	370 (98.4)	367 (98.7)	466 (93.0)	465 (93.8)
Cisplatin/5-fluorouracil	6 (1.6)	5 (1.3)	35 (7.0)	31 (6.3)

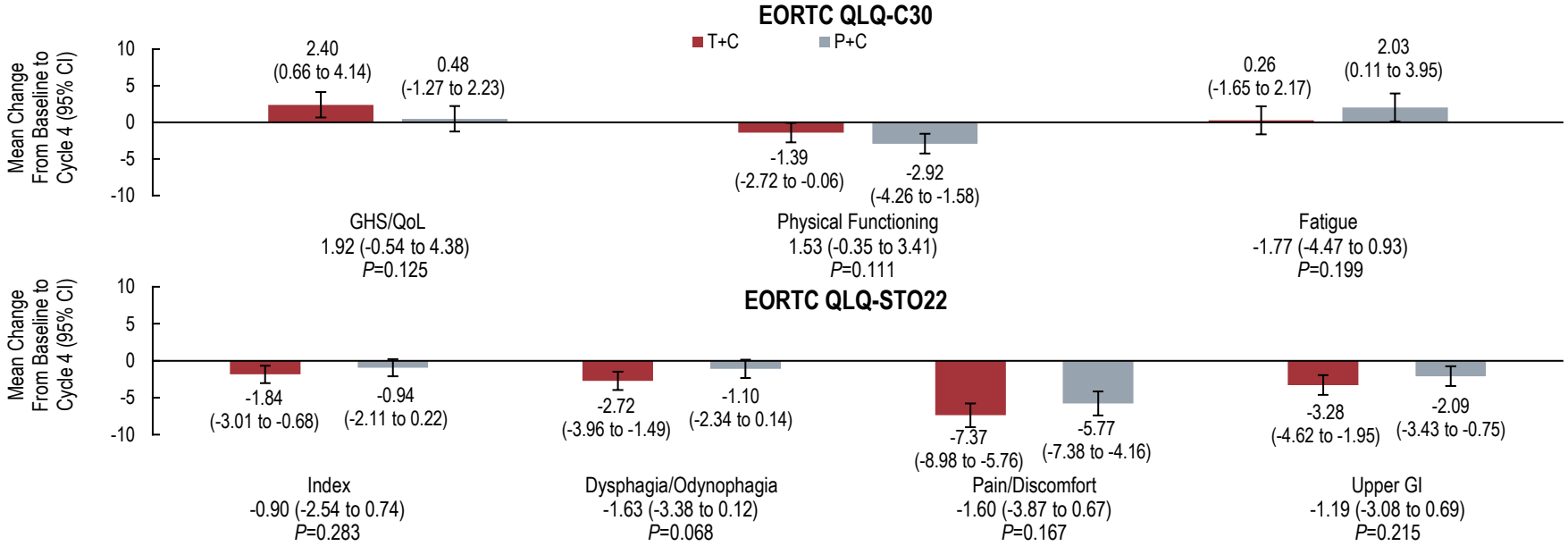
Data cutoff: February 28, 2023.

[a]The diagnosis of one patient was updated from gastric adenocarcinoma to be pancreatic cancer after randomization and the patient remained in the ITT population.

Abbreviations: C, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GEJ, gastroesophageal junction; ITT, intent-to-treat; P, placebo; PD-L1, programmed death-ligand 1; T, tislelizumab; TAP, tumor area positivity.

Change From Baseline to Cycle 4: Asian Subgroup in ITT Population

- Both arms experienced clinically meaningful improvements/reductions in pain with a greater reduction for T+C
- Other PRO key endpoints were maintained in both arms, with more improvements for T+C

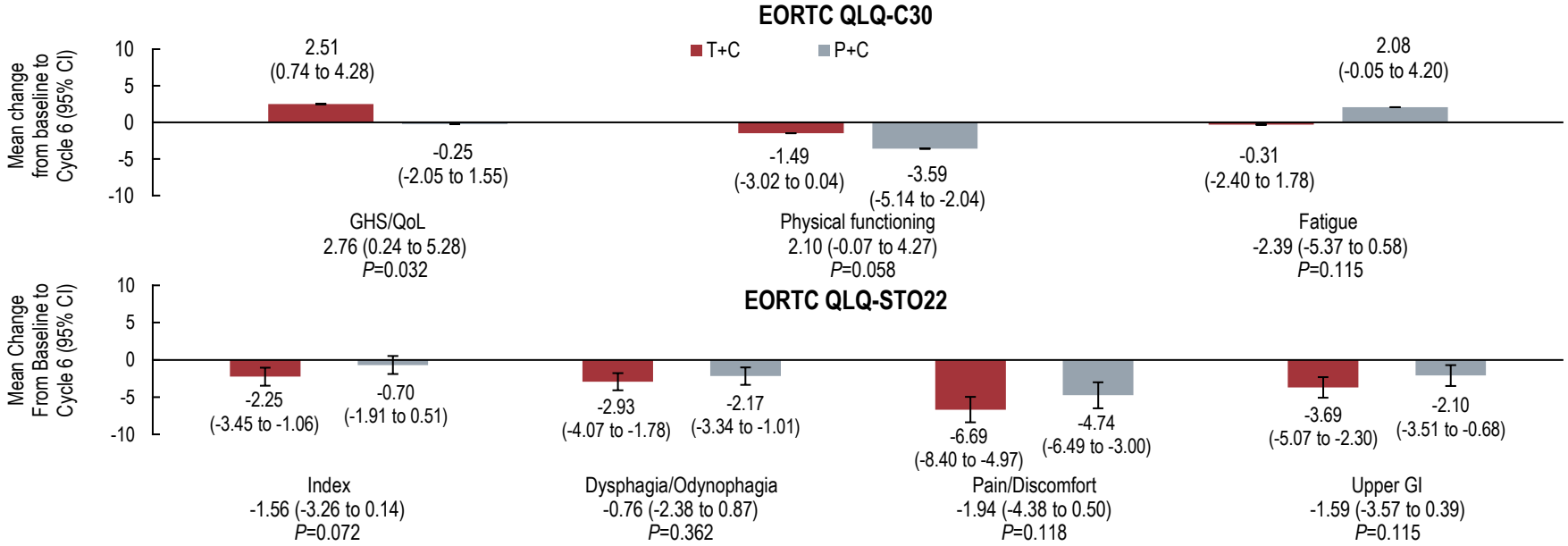


Increases in scores for GHS/QoL and physical functioning represent improvement while increases in scores for fatigue represent deterioration for the QLQ-C30. Increases in scores for the index, dysphagia/odynophagia, pain/discomfort, and upper GI symptoms represent deterioration for the QLQ-STO22.

Abbreviations: C, chemotherapy; CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; GI, gastrointestinal; ITT, intent-to-treat; P, placebo; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core-30; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; T, tislelizumab.

Change From Baseline to Cycle 6: Asian Subgroup in ITT Population

- T+C arm continued to experience clinically meaningful improvements/reduction in pain
- Other PRO key endpoints were maintained in both arms, with more improvements for T+C



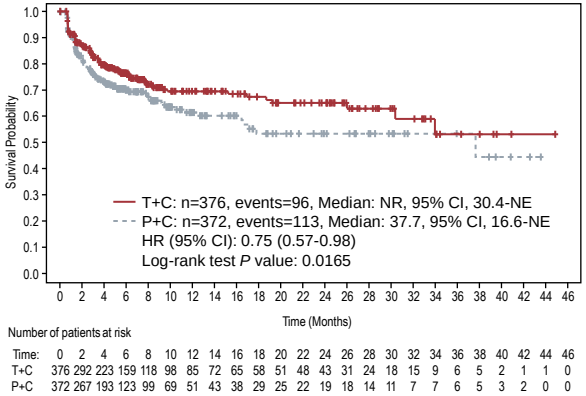
Increases in scores for GHS/QoL and physical functioning represent improvement while increases in scores for fatigue represent deterioration for the QLQ-C30. Increases in scores for the index, dysphagia/odynophagia, pain/discomfort, and upper GI symptoms represent deterioration for the QLQ-STO22.

Abbreviations: C, chemotherapy; CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; GI, gastrointestinal; ITT, intent-to-treat; P, placebo; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core-30; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; T, tislelizumab.

Time to Deterioration: Asian Subgroup in ITT Population

- Patients receiving T+C were at lower risk for deterioration of physical functioning (HR, 0.75 [95% CI, 0.57-0.98]), QLQ-STO22 index score (0.65 [0.43-0.98]), and upper GI symptoms (0.72 [0.53-0.97])
- Risk of deterioration was similar between the arms in other PRO endpoints

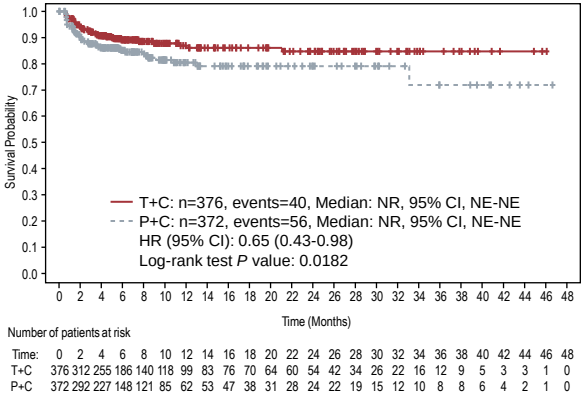
Figure 1. Physical Functioning



Number of patients at risk

Time:	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46
T+C	376	292	223	159	118	98	85	72	65	58	51	48	43	31	24	18	15	9	6	5	2	1	1	0
P+C	372	267	193	123	99	69	51	43	38	29	25	22	19	18	14	11	7	7	6	5	3	2	0	0

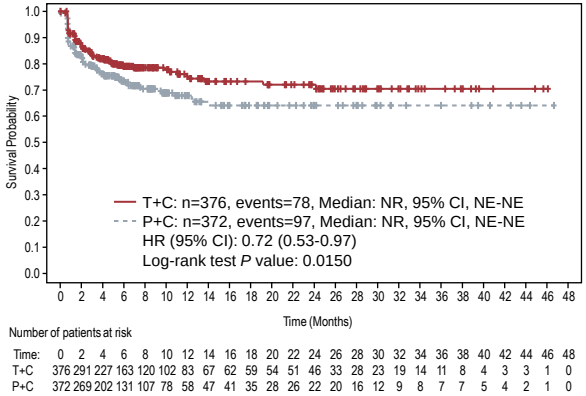
Figure 2. EORTC QLQ-STO22 Index Score (Overall GC Symptoms/HRQoL)



Number of patients at risk

Time:	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48
T+C	376	312	255	186	140	118	99	83	76	70	64	60	54	42	34	26	22	16	12	9	5	3	3	1	0
P+C	372	292	227	148	121	85	62	53	47	38	31	28	24	22	19	15	12	10	8	8	6	4	2	1	0

Figure 3. Upper Gastrointestinal Symptoms



Number of patients at risk

Time:	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48
T+C	376	291	227	163	120	102	83	67	62	59	54	51	46	33	28	23	19	14	11	8	4	3	3	1	0
P+C	372	269	202	131	107	78	58	47	41	35	28	26	22	20	16	12	9	8	7	7	5	4	2	1	0

Abbreviations: C, chemotherapy; CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; GC, gastric cancer; GI, gastrointestinal; HR, hazard ratio; HRQoL, health-related quality of life; NE, not evaluable; NR, not reported; P, placebo; PRO, patient-reported outcome; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; T, tislelizumab.

Conclusion

- Asian patients in RATIONALE-305 treated with T+C had better PROs than patients treated with P+C, especially in the symptom of pain/discomfort, and were at lower risk of clinically meaningful worsening in overall gastric cancer symptoms, upper gastrointestinal symptoms, and physical functioning
- These results were in line with the better OS (HR, 0.83 [95% CI, 0.70-0.97]) and PFS (HR, 0.76 [95% CI, 0.64-0.90]) for T+C in the Asian population of RATIONALE-305
- These results also corroborate the PRO findings in the ITT population, further supporting the benefit of T+C as a potential 1L treatment option for GC/GEJC

Abbreviations: C, chemotherapy; CI, confidence interval; 1L, first-line; GC/GEJC, gastric/gastroesophageal junction cancer; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; P, placebo; PFS, progression-free survival; PRO, patient-reported outcome; T, tislelizumab.

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SINGAPORE 2024 ESMO ASIA

European Society for Medical Oncology (ESMO)
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
esmo@esmo.org

esmo.org