Tislelizumab (TIS) with or without capecitabine (CAP) continuation in gastric or gastro-oesophageal junction cancer (GC/GEJC): RATIONALE-305 post hoc analysis

Background: RATIONALE-305 demonstrated TIS + chemotherapy (CT) in patients (pts) with HER2-negative, advanced GC/GEJC is associated with improved outcomes. We explored the efficacy and safety of continued CAP + TIS/placebo (PBO) after 6 CT cycles of CAPOX (CAP + oxaliplatin) + TIS/PBO.

Methods: In RATIONALE-305 (NCT03777657), pts were randomised (1:1) to receive TIS or PBO, combined with CT (CAPOX or cisplatin + 5-fluorouracil). After 6 cycles, pts who had not progressed and received CAPOX were eligible for continued CAP + TIS/PBO. Primary endpoint was OS in PD-L1–positive (Tumour Area Positivity [TAP] score ≥5%) pts and all pts regardless of PD-L1. This post hoc analysis evaluated efficacy outcomes of continued CAP in pts who remained on study treatment after 6 cycles of CAPOX + TIS/PBO.

Results: Of 614 pts, 526 (85.7%) received CAP as continuation therapy (TIS: n=276, PBO: n=250). Baseline characteristics were similar (with CAP vs without): median age 61 vs 58.5 yr, male 68.8% vs 75.0%, East Asia region/rest of world (US, Europe) 83.3%/16.7% vs 75.0%/25.0%, Eastern Cooperative Oncology Group performance status 0/1 31.7%/68.3% vs 35.2%/64.8%. Most pts had primary GC (85.7 % vs 76.1 %) vs GEJC (14.3% vs 23.9 %), and most (54.2 % vs 60.2 %) had PD-L1 TAP scores ≥5% with CAP vs without, respectively. Median duration of treatment from randomisation (months) was longer with CAP (TIS: 10.0, PBO: 9.6) vs without (TIS: 4.4, PBO: 4.4). Continuation of CAP with TIS as opposed to PBO was associated with statistically significant OS (HR=0.78), PFS (HR=0.79), and ORR. While fewer pts did not continue CAP, TIS without CAP was associated with numerically longer PFS and higher ORR but not improved OS (Table). No new safety signals were found.

Conclusion: Continuation of CAP after induction CAPOX is a common practice. TIS with CAP is associated with improved outcomes. These findings warrant further investigation to optimise treatment strategy in this population.

Table.

Efficacy Outcomes	With CAP		Without CAP	
	TIS (n=276)	**PBO (n=250)**	**TIS (n=45)**	**PBO (n=43)**
Median OS, months (95% CI)	21.0 (18.6, 24.1)	18.1 (16.4, 20.3)	10.2 (7.2, 14.1)	12.3 (11.1, 15.2)
HR (95% CI)	0.78 (0.65, 0.95)		1.24 (0.80, 1.92)	
Median PFS, months (95% CI)	10.1 (9.0, 12.9)	9.5 (8.3, 9.8)	4.7 (4.2, 5.5)	4.3 (4.1, 4.5)
HR (95% CI)	0.79 (0.65, 0.96)		0.82 (0.52, 1.32)	
ORR, n (%)	197 (71.4)	167 (66.8)	26 (57.8)	21 (48.8)

CAP, capecitabine; CI, confidence interval; HR, hazard ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

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