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Nivolumab (NIVO) plus chemotherapy (Chemo) or ipilimumab (IPI) vs chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): CheckMate 649 study

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Background

CheckMate 649, a randomized, global phase 3 study of 1L programmed death (PD) 1 inhibitor-based therapies in advanced GC/GEJC/EAC, demonstrated superior overall survival (OS) with NIVO + chemo vs chemo, leading to US FDA approval. We report longer-term follow-up for NIVO + chemo vs chemo and first results for NIVO + IPI vs chemo.

Methods

Adults with previously untreated, unresectable advanced or metastatic GC/GEJC/EAC were enrolled regardless of PD-ligand 1 (PD-L1) expression. Patients (pts) with known HER2-positive status were excluded. Pts were randomized to NIVO (360 mg Q3W or 240 mg Q2W) + chemo (XELOX Q3W or FOLFOX Q2W), NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses, then NIVO 240 mg Q2W), or chemo. Dual primary endpoints were OS and progression-free survival (PFS; per blinded independent central review [BICR]) for NIVO + chemo vs chemo in pts with PD-L1 combined positive score (CPS) ≥ 5. Hierarchically tested secondary endpoints included OS in NIVO + chemo vs chemo (PD-L1 CPS ≥ 1, then all randomized) and OS in NIVO + IPI vs chemo (PD-L1 CPS ≥ 5, then all randomized).

Results

Of 2031 pts, 1581 (60% with PD-L1 CPS ≥ 5) were concurrently randomized to NIVO + chemo or chemo and 813 (58% with PD-L1 CPS ≥ 5) to NIVO + IPI or chemo. NIVO + chemo continued to show improvement in OS vs chemo alone with an additional 12-mo follow-up from the primary analysis (Table). The secondary endpoint of OS in pts with PD-L1 CPS ≥ 5 for NIVO + IPI vs chemo group was not met (minimum follow-up, 35.7 mo; Table); other endpoints in the hierarchy were not tested. No new safety signals were identified. Additional results are shown in the table.

Conclusions

NIVO + chemo continued to demonstrate clinically meaningful long-term survival benefit vs chemo and an acceptable safety profile with additional follow-up, further supporting its use as a new standard 1L treatment in pts with advanced GC/GEJC/EAC.Table: LBA7

	NIVO + chemo	Chemo	NIVO + IPI	Chemo
PD-L1 CPS ≥ 5	N = 473	N = 482	N = 234	N = 239
mOS, mo (95% CI)	14.4 (13.1–16.2)	11.1 (10.0–12.1)	11.2 (9.2–13.4)	11.6 (10.1–12.7)

	NIVO + chemo	Chemo	NIVO + IPI	Chemo
HR	0.70 (95% CI 0.61–0.81)	0.89 (96.5% CI 0.71–1.10; *P* = 0.2302)		
ORR[a]	N = 378	N = 390	N = 196	N = 183
% (95% CI)	60 (55-65)	45 (40-50)	27 (20-33)	47 (40-54)
All randomized	N = 789	N = 792	N = 409	N = 404
mOS, mo (95% CI)	13.8 (12.4–14.5)	11.6 (10.9–12.5)	11.7 (9.6–13.5)	11.8 (11.0–12.7)
HR	0.79 (95% CI 0.71–0.88)	0.91 (96.5% CI 0.77–1.07; *P* not tested)		
TRAEs, %	N = 782	N = 767	N = 403	N = 389
Any	95	89	80	92
Grade 3–4	60	45	38	46
Led to discontinuation	38	25	22	26

[a]Per BICR m, median; ORR, objective response rate; TRAE, treatment-related adverse event

Clinical trial identification

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