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LBA6_PR

Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): First results of the CheckMate 649 study

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Background

Standard 1L chemo options for advanced or metastatic HER2-negative GC/GEJC result in poor overall survival (OS; median < 1 year). CheckMate 649 is the largest randomized, global phase III study of programmed death (PD)-1 inhibitor-based therapies in 1L GC/GEJC/EAC. We report OS at a pre-specified interim analysis and progression-free survival (PFS) at final analysis from the NIVO + chemo vs chemo arms in patients (pts) whose tumors expressed PD-ligand 1 (L1) combined positive score (CPS) ≥ 5.

Methods

Adults with previously untreated, unresectable advanced, or metastatic GC/GEJC/EAC were enrolled, regardless of PD-L1 expression. Pts with known HER2-positive status were excluded. Pts were randomized to receive NIVO (360 mg Q3W or 240 mg Q2W) + chemo (XELOX Q3W or FOLFOX Q2W), NIVO + ipilimumab, or chemo. Dual primary endpoints for NIVO + chemo vs chemo were OS and PFS by blinded independent central review, in pts whose tumors expressed PD-L1 CPS ≥ 5.

Results

1581 pts were concurrently randomized in nivo+chemo and chemo arms, including 955 pts (60%) with PD-L1 CPS ≥ 5. With a minimum follow-up of 12 months (mo), NIVO + chemo showed a statistically significant improvement in OS and PFS vs chemo in pts whose tumors expressed PD-L1 CPS ≥ 5 (OS, HR 0.71 [98.4% CI 0.59–0.86; *P* < 0.0001] and PFS, HR 0.68 [98% CI 0.56–0.81; *P* < 0.0001]). Statistically significant OS benefit was also observed in pts with PD-L1 CPS ≥ 1 and the all-randomized population (Table). No new safety signals were identified. Safety results are described in the table.Table: LBA6_PR

Efficacy PD-L1 CPS ≥ 5	NIVO + chemo N = 473	Chemo N = 482
Median OS, mo (95% CI)	14.4 (13.1–16.2)	11.1 (10.0-12.1)
HR (98.4% CI; *P* value)	0.71 (0.59-0.86; *P<0.0001)*	
Median PFS, mo (95% CI)	7.7 (7.0-9.2)	6.1 (5.6-6.9)
HR (98.0% CI; *P* value)	0.68 (0.56-0.81; *P*<0.0001)	
PD-L1 CPS ≥ 1	N = 641	N = 655
Median OS, mo (95% CI)	14.0 (12.6-15.0)	11.3 (10.6-12.3)
HR (99.3% CI; *P* value)	0.77 (0.64–0.92; *P* = 0.0001)	

Efficacy	NIVO + chemo	Chemo
PD-L1 CPS ≥ 5	N = 473	N = 482
All randomized	N = 789	N = 792
Median OS, mo (95% CI)	13.8 (12.6–14.6)	11.6 (10.9-12.5)
HR (99.3% CI; *P* value)	0.80 (0.68-0.94; *P* = 0.0002)	
Safety: Treatment-related events, n (%)		
PD-L1 CPS ≥ 5	N = 468	N = 465
Any grade	444 (95)	407 (88)
Grade 3-4	277 (59)	203 (44)
Leading to discontinuation	178 (38)	115 (25)
Deaths	8 (2)	4 (<1)

Conclusions

NIVO is the first PD-1 inhibitor to demonstrate superior OS and PFS in combination with chemo vs chemo alone in previously untreated pts with advanced GC/GEJC/EAC, with a manageable safety profile. NIVO + chemo represents a potential new standard 1L treatment option for these pts.

Clinical trial identification

NCT02872116.

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