First-line (1L) nivolumab (NIVO) plus chemotherapy (chemo) versus chemo in advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma (GC/GEJC/EAC): Expanded efficacy and safety data from CheckMate 649.

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Background: CheckMate 649 is the largest randomized, global phase 3 study of 1L programmed death (PD)-1 inhibitor–based therapy in GC/GEJC/EAC. 1L NIVO + chemo demonstrated superior overall survival (OS) vs chemo, with progression-free survival (PFS) benefit and an acceptable safety profile in pts whose tumors expressed PD-ligand (L)1 at combined positive score (CPS) ≥ 5 and ≥ 1, and in all randomized pts (Moehler et al. *Ann Oncol* 2020). We report additional data for all randomized pts. **Methods:** Eligible pts had previously untreated, unresectable advanced or metastatic GC/GEJC/EAC. Known HER2-positive pts 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 central review in PD-L1 CPS ≥ 5 pts. Hierarchically tested secondary endpoints were OS in PD-L1 CPS ≥ 1 and all randomized pts. **Results:** At 12-month minimum follow-up for 1581 randomized pts, NIVO + chemo had a statistically significant OS benefit vs chemo (HR 0.80 [99.3% CI 0.68–0.94; $P = 0.0002$]) in all randomized pts; PFS benefit was also seen (HR 0.77 [95% CI 0.68–0.87]). OS benefit was observed in multiple prespecified subgroups, consistent with the primary population. Grade 3–4 treatment-related adverse events (TRAEs) were reported in 59% (NIVO + chemo) and 44% (chemo) of pts. TRAEs with potential immunologic etiology (select TRAEs; sTRAEs) are shown in the table. Pts in the NIVO + chemo arm had decreased risk of symptom deterioration on treatment vs those in the chemo arm (HR 0.77 [95% CI 0.63–0.95; $P = 0.0129$]). Tolerability as measured by the FACT-Ga GP5 item was similar in both treatment groups. **Conclusions:** The addition of NIVO to chemo demonstrated improved OS and PFS benefit in all randomized pts, along with an acceptable safety profile and maintained tolerability as well as QoL, providing further support for NIVO + chemo as a standard 1L treatment for advanced GC/GEJC/EAC. Clinical trial information: NCT02872116. Research Sponsor: Bristol Myers Squibb.

sTRAEs (NIVO + chemo, N = 782).

	Pts with sTRAEs, n (%)		Median time to onset (range), weeks	Median time to resolution (range),[b] weeks	Pts with resolution of sTRAEs,[b] n (%)
	Any grade	Grade 3–4[a]			
Endocrine	107 (14)	5 (< 1)	15.0 (2.0–124.3)	72.1 (0.4–139.1+)	46 (43)
GI	262 (34)	43 (5)	4.3 (0.1–93.6)	1.6 (0.1–117.6+)	228 (87)
Hepatic	203 (26)	29 (4)	7.9 (0.1–61.3)	10.1 (0.4–150.6+)	156 (78)
Pulmonary	40 (5)	14 (2)	23.9 (1.6–96.9)	10.1 (0.3+ to 121.3+)	28 (70)
Renal	26 (3)	6 (< 1)	12.4 (1.7–59.4)	3.1 (0.1–42.4+)	19 (73)
Skin	214 (27)	26 (3)	9.6 (0.1–97.4)	23.4 (0.1–153.6+)	124 (58)

[a]There were no grade 5 events; [b]Events without a stop date or where stop date was death date were considered unresolved. Events without worsening from baseline were excluded.

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