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Bemarituzumab (BEMA) plus chemotherapy for advanced or metastatic FGFR2b-overexpressing gastric or gastroesophageal junction cancer (G/GEJC): FORTITUDE-101 phase III study results

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Background

BEMA is a first-in-class anti-FGFR2b antibody that blocks oncogenic signaling through FGFR2b and engages antibody-dependent cell-mediated cytotoxicity. Here, we report results of the FORTITUDE-101 trial (NCT05052801).

Methods

Patients (pts) with FGFR2b-overexpressing (>0% 2+/3+ tumor cell [TC] staining), non-HER2 positive, unresectable, locally advanced or metastatic G/GEJC were randomized to BEMA (15 mg/kg Q2W + 7.5 mg/kg on cycle 1 day 8) + mFOLFOX6 or matched placebo (PBO) + mFOLFOX6. Primary endpoint was overall survival (OS) in pts with FGFR2b ≥10% 2+/3+ TC staining. Key secondary endpoints were progression-free survival (PFS) and objective response rate (ORR) in FGFR2b ≥10% pts, and safety. Since OS efficacy boundaries were crossed and full alpha spent at the interim analysis (data cutoff Dec 9, 2024), it serves as the primary analysis (PA). A descriptive follow-up analysis (FA) was performed at data cutoff Jun 20, 2025.

Results

A total of 547 pts (68.7% male, median age, 62.0 yrs) with FGFR2b overexpression were enrolled; the FGFR2b ≥10% pt subset was 159/274 in BEMA arm and 165/273 in PBO arm. At PA (median follow-up [F/U] 11.8 mo), OS was significantly improved with BEMA vs PBO (medians 17.9 mo vs 12.5 mo; HR [95% CI], 0.61 [0.43, 0.86]; *P* = 0.005) in FGFR2b ≥10% pts. At FA (median F/U 19.4 mo), median OS was 14.5 mo vs 13.2 mo (HR [95% CI], 0.82 [0.62, 1.08]). The incidence of Grade ≥3 treatment-emergent adverse events (TEAEs), mainly driven by corneal adverse events, was higher in the BEMA vs the PBO arm. Key efficacy and safety data are in the table.

Conclusions

BEMA demonstrated a statistically significant survival benefit at the PA of this phase 3 trial, with attenuation of the treatment effect at a descriptive analysis after longer follow-up. Results from this trial and upcoming FORTITUDE-102 will further characterize the benefit of BEMA in G/GEJC.Table: LBA10

Efficacy for FGFR2b ≥10% 2+/3+ TC pts		
	BEMA (N = 159)	PBO (N = 165)
PA mOS (95% CI), mo	17.9 (13.0, 20.8)	12.5 (10.5, 14.7)
HR (95% CI)	0.61 (0.43, 0.86), *P* = 0.005	
PA mPFS (95% CI), mo	8.6 (7.5, 9.5)	6.7 (5.6, 7.6)
HR (95% CI)	0.71 (0.53, 0.95), *P* = 0.019	
FA[☒] mOS (95% CI), mo	14.5 (13.0, 17.9)	13.2 (10.9, 14.7)

Efficacy for FGFR2b ≥10% 2+/3+ TC pts		
	BEMA (N = 159)	PBO (N = 165)
HR (95% CI)	0.82 (0.62, 1.08)	
Safety at FA†		
	BEMA (N = 275)	PBO (N = 267)
Any grade TEAE, n (%)	274 (99.6)	262 (98.1)
Grade ≥3 TEAE, n (%)	246 (89.5)	210 (78.7)
Any grade TRAE, n (%)	245 (89.1)	177 (66.3)
Grade ≥3 TRAE, n (%)	165 (60.0)	49 (18.4)

*Descriptive. †All pts who received ≥1 dose of investigational product or mFOLFOX6 were analyzed according to treatment received. TRAE, treatment-related adverse event.

Clinical trial identification

NCT05052801.

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Disclosure

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