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Domvanalimab (dom), zimberelimab (zim), and FOLFOX in first-line (1L) advanced gastric, gastroesophageal junction, or esophageal adenocarcinoma (GC/GEJC/EAC): 26-month update from EDGE-Gastric, arm A1

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Background

Long-term outcomes for 1L GC/GEJC/EAC remain poor. Dual blockade of PD-1 and T-cell immunoglobulin and ITIM domain (TIGIT) may enhance antitumor immunity. EDGE-Gastric (NCT05329766), Arm A1 evaluated the efficacy and safety of 1L dom (Fc-silent anti-TIGIT), zim (anti–PD-1), and FOLFOX (oxaliplatin, leucovorin, and fluorouracil) in patients (pts) with previously untreated advanced HER-2-negative GC/GEJC/EAC. In a previous report, with a median follow-up of 13.9 months, confirmed objective response rate (ORR) was 59% (95% CI: 42, 74), and median progression-free survival (PFS) was 12.9 (95% CI: 9.8, 13.8) months. Here, we present an update, including overall survival (OS), with median follow-up of 26.4 months.

Methods

Pts received dom 1600 mg IV once every 4 weeks (Q4W), zim 480 mg IV Q4W, and FOLFOX Q2W. Primary endpoints are safety and ORR per RECIST 1.1. Secondary endpoints include PFS and OS.

Results

Forty-one pts were enrolled; 63% had GC. At data cutoff (03 MAR 2025), median treatment duration was 49 weeks (range, <1–117). Confirmed ORR was 59% (90% CI: 45, 72). Median PFS was 13.2 months (90% CI: 9.8, 13.8), and median OS was 26.7 months (90% CI: 18.4, not estimable [NE]) . Efficacy was observed irrespective of PD-L1 cutoff (Table). In pts with PD-L1–high tumors, median PFS was 14.5 months (90% CI: 11.3, NE), and median OS was NE. Overall and grade ≥3 TEAEs were consistent with prior reports on this study. Dom/zim-related immune-mediated TEAEs and infusion-related reactions occurred in 9 (22%) and 3 (7%) pts, respectively.Table: 2112MO

	Overall[a] (N = 41)	PD-L1 Positive (TAP ≥1%) (n = 29)	PD-L1 High (TAP ≥5%) (n = 16)
Confirmed ORR, % (n) (90% CI)	59% (24)(45%, 72%)	62% (18)(45%, 77%)	69% (11)(45%, 87%)
Median PFS, months (90% CI)	12.9 (9.8, 14.6)	13.2 (11.3, 15.2)	14.5 (11.3, NE)
24 months PFS rate, % (90% CI)	25.9 (14.8, 38.5)	24.9 (12.1, 39.9)	31.3 (14.0, 50.2)
Median OS, months (90% CI)	26.7 (18.4, NE)	26.7 (19.5, NE)	NE (17.4, NE)
24 months OS rate, % (90% CI)	50.2 (36.3, 62.6)	53.8 (37.3, 67.7)	56.3 (33.9, 73.6)

[a]All pts who enrolled and received study treatment. One pt did not have tissue available for central laboratory TAP scoring (SP263 assay). Local lab results showed the pt was PD-L1 low according to 22C3 assay. TAP, tumor area positivity.

Conclusions

In this extended follow-up, 1L dom + zim + FOLFOX continues to show encouraging efficacy with median PFS of >1 year and median OS of >2 years. The safety profile was consistent with that of anti–PD-1 + FOLFOX. The phase 3 STAR-221 trial (NCT05568095) comparing 1L dom + zim + chemotherapy vs nivolumab + chemotherapy in advanced GC/GEJC/EAC is fully enrolled.

Clinical trial identification

NCT05329766.

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Legal entity responsible for the study

Arcus Biosciences and Gilead Sciences.

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Disclosure

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