EDGE-Gastric Arm A1: Phase 2 study of domvanalimab (dom), zimberelimab (zim), and FOLFOX in first-line (1L) advanced gastroesophageal cancer (GEC)

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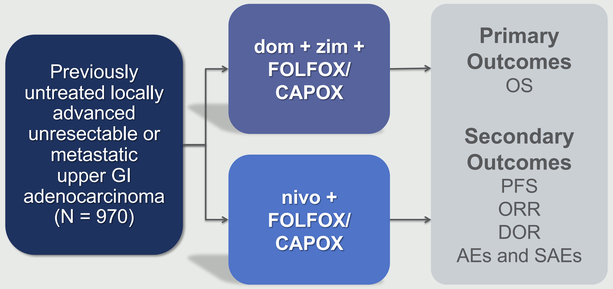
Conclusions

- Dom (anti-TIGIT) and zim (anti–PD-1) in combination with FOLFOX shows promising ORR, median PFS, and 12-month PFS in metastatic 1L gastroesophageal cancer (GEC)
- AE profile continues to be similar to prior experience with anti-PD-1 plus FOLFOX, with no new safety concerns
- Phase 3 trial (STAR-221) enrollment completed

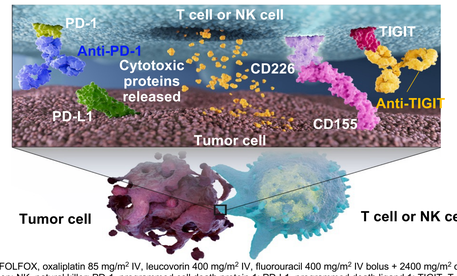
STAR-221 Phase 3 Trial (NCT05568095)



1L, first line; AE, adverse event; CAPOX, capecitabine + oxaliplatin; dom, domvanalimab; DOR, duration of response; FOLFOX, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 continuous 46-48-hour IV infusion GEC, gastroesophageal cancer; GI, gastrointestinal; nivo, nivolumab; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival, SAE, serious adverse event; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domain; zim, zimberelimab.

Background

- Anti–PD-1 treatment with chemotherapy is the current standard of care for gastroesophageal cancers, but long-term outcomes remain poor[1]
- Combined inhibition of TIGIT and PD-1 may have a synergistic effect, with robust immune activity against certain tumor cells[2]
- Here, we present the updated 12-month follow-up safety and efficacy results of 1L domvanalimab (anti-TIGIT), zimberelimab (anti–PD-1), and FOLFOX in advanced gastroesophageal adenocarcinoma from Arm A1 of the phase 2 EDGE-Gastric study



1L, first line; FOLFOX, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 continuous 46-48-hour IV infusion; NK, natural killer; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domain.

References: **1.** Janjigian Y, et al. *Lancet.* 2021;398:27–40; **2.** Johnston RJ et al. *Cancer Cell.* 2014;26:923–937.

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Methods

Arm A1: 1L Metastatic Gastric/GEJ/EAC Cohort

EDGE-Gastric (NCT05329766) is a phase 2 study evaluating the safety and efficacy of treatment combinations with and without chemotherapy in adults with advanced upper gastrointestinal tract malignancies

Key Eligibility Criteria
- 1L locally advanced unresectable or metastatic gastric/GEJ/EAC
- Measurable disease per RECIST v1.1
- ECOG 0-1
- Known HER-2–positive tumors excluded
- Regardless of PD-L1 levels

N ≈ 40

dom 1600 mg Q4W
zim 480 mg Q4W
FOLFOX Q2W

Treatment continues until PD or unacceptable toxicity

Scanning interval: Q6W for first year, and Q12W thereafter

Primary Endpoints
- Safety
- Investigator ORR

Secondary Endpoints
- Efficacy by PD-L1 (OS, PFS, DCR, DOR)
- Pharmacokinetics and biomarker data

At the 12 March 2024 data cutoff, the median follow-up was 13.9 months

1L, first line; DCR, disease control rate; dom, domvanalimab; DOR, duration of response; EAC, esophageal adenocarcinoma; ECOG, Eastern Cooperative Oncology Group; FOLFOX, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 continuous 46-48-hour IV infusion; GEJ, gastroesophageal junction; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q2W, every 2 weeks; Q4W, every 4 weeks; Q6W, every 6 weeks; Q12W, every 12 weeks; zim, zimberelimab.

Results

Baseline Characteristics

Characteristic, n (%)	Arm A1 N = 41
Age, years, mean (range)	61 (30 to 82)
Sex	
Male	24 (59)
Female	17 (41)
Country	
United States/France	22 (54)
Korea	19 (46)
ECOG performance status 1	25 (61)
Histologically confirmed diagnosis	
Esophageal	10 (24)
Gastric	26 (63)
Gastroesophageal junction	5 (12)

Characteristic, n (%)	Arm A1 N = 41
Current disease status	
Locally advanced unresectable disease	3 (7)
Metastatic disease	38 (93)
Liver metastases	13 (32)
Peritoneal metastases	15 (37)
TAP category (Central Lab)[a]	
TAP ≥ 5%	16 (39)
TAP < 5%	24 (59)
Unavailable[b]	1 (2)
Microsatellite instability status	
High	1 (2)
Low/stable	35 (85)
Unknown	5 (12)

ECOG, Eastern Cooperative Oncology Group; TAP, tumor area positivity. [a]Ventana SP263 assay used for all TAP scores.[b]One patient did not have tissue available for central testing.

Study Population and Patient Disposition

12 March 2024 Data Cutoff Date

Primary reason for discontinuation from all study treatments	Patients, n (%) (N = 41)
Disease progression	20 (49%)
Withdrawal	5 (12%)
Adverse event	2 (5%)
Death	1 (2%)

- All 41 patients received study treatment[a] and were included in the analysis of safety and efficacy
- Median treatment duration was 11.4 months
- 28 (68%) patients have discontinued all study treatments
- 13 (32%) patients discontinued from the study[b]

[a]One patient did not receive leucovorin due to institutional standard practice.
[b]Reasons for discontinuation from study were death (n = 8) and withdrawal from study by patient (n = 5). Reasons for withdrawal from study were patient withdrawal of consent (n = 3), patient relocation (n = 1), and patient refusal of further study procedure (n = 1).

Results

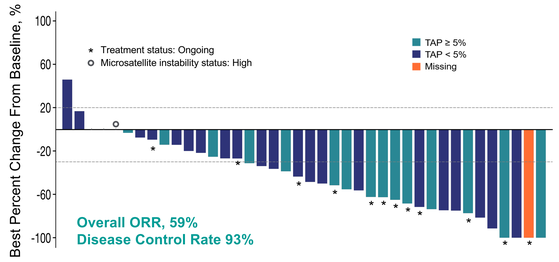
Objective Response Rate per RECIST v1.1

Parameter	Overall N = 41[a]	PD-L1 High (TAP ≥ 5%) n = 16	PD-L1 Low (TAP < 5%) n = 24
Confirmed ORR, % [95% CI]	59 [42, 74]	69 [41, 89]	50 [29, 71]
Complete response, n (%)	3 (7)	1 (6)	1 (4)
Partial response, n (%)	21 (51)	10 (63)	11 (46)
Stable disease, n (%)	14 (34)	5 (31)	9 (38)
Progressive disease, n (%)	2 (5)	0	2 (8)
No postbaseline scan, n (%)	1 (2)	0	1 (4)
Median duration of response, months (95% CI)	12.4 (9.9, NE)	NE (11.5, NE)	10.2 (4.0, 12.4)

- As of the 12 March 2024 data cutoff date, 13 (32%) patients continued study treatment

ORR, objective response rate; NE, not evaluable; PD-L1, programmed death ligand 1; TAP, tumor area positivity.
[a]One patient had no tissue available for TAP central lab testing. From local lab results, the patient was PD-L1 low via 22-C3 assay. Investigator-assessed ORR is reported.

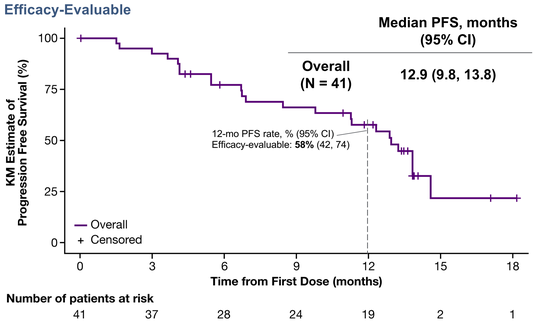
Best Percent Change in Sum of Target Lesions



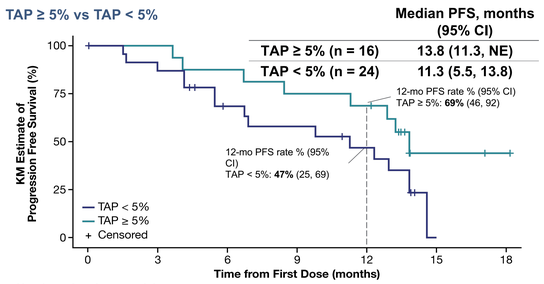
ORR, objective response rate; TAP, tumor area positivity.
One patient (missing; orange bar) had no tissue available for TAP central lab testing. From local lab results, the patient was PD-L1 low via 22-C3 assay.

Kaplan-Meier Estimate of Progression-Free Survival per RECIST v1.1

Efficacy-Evaluable



TAP ≥ 5% vs TAP < 5%

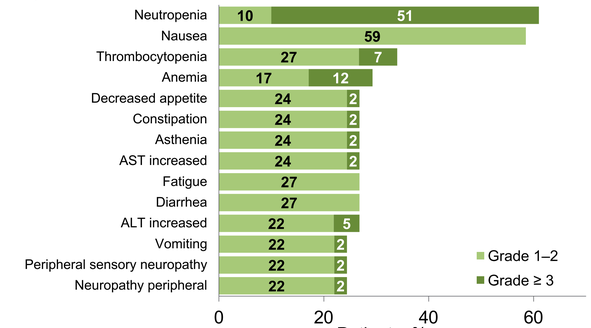


mo, month; NE, not estimable; PFS, progression-free survival; TAP, tumor area positivity.
Median follow-up time for the efficacy-evaluable population was 13.9 months (95% CI: 13.5, 14.1).

Overall Safety Summary

Safety Evaluable Population, n (%)	Arm A1 (N = 41)
Any TEAE	41 (100)
TEAEs related to any study drug[a]	40 (98)
Grade ≥ 3 TEAEs	30 (73)
Grade ≥ 3 TEAEs related to dom/zim	6 (15)
Grade ≥ 3 TEAEs related to FOLFOX	24 (59)
Serious TEAEs	15 (37)
Serious TEAEs related to dom/zim	0
Serious TEAEs related to FOLFOX	2 (5)
TEAEs leading to discontinuation of any study drug	27 (66)
TEAEs leading to discontinuation of dom/zim	4 (10)
TEAEs leading to discontinuation of FOLFOX	26 (63)
TEAEs leading to discontinuation all study drugs	1 (2)
TEAEs leading to dose modification/interruption from any study drug	35 (85)
TEAEs resulting in death[b]	1 (2)

Any Grade TEAEs[c] in ≥ 20% of Patients

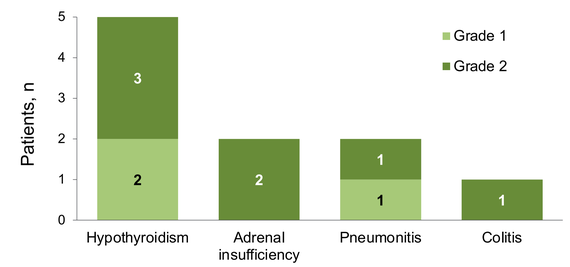


ALT alanine aminotransferase; AST, aspartate aminotransferase; dom, domvanalimab; FOLFOX, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 continuous 46-48-hour IV infusion TEAE, treatment-emergent adverse event; zim, zimberelimab.
[a]TEAEs related to zim (n = 32), dom (n = 32), and FOLFOX (n = 39).
[b]Event term is "Death" and assessed as not related to any study medications; query pending.
[c]"Neutropenia" and "Neutrophil count decreased" were coded to separate Preferred Terms and combined post hoc. "Thrombocytopenia" and "Platelet count decreased" were coded to separate Preferred Terms and combined post hoc.

Infusion-Related Reactions and Immune-Mediated AEs

Safety Evaluable Population, n (%)	Arm A1 (N = 41)
All infusion-related reactions[a]	8 (20)
Infusion-related reactions related to components of FOLFOX	7 (17)
All immune-mediated AEs	10 (24)
Hypothyroidism	5 (12)
Adrenal insufficiency	2 (5)
Pneumonitis	2 (5)
Colitis	1 (2)
Grade ≥ 3 immune-mediated AEs	0
Serious immune-mediated AEs	0

Any Grade Immune-Mediated TEAEs



AEs, adverse events; dom, domvanalimab; FOLFOX, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 continuous 46-48-hour IV infusion TEAE, treatment-emergent AE; zim, zimberelimab.
[a]Infusion-related reactions as assigned by investigator.
Two patients reported infusion-related reactions related to dom/zim (pruritus n = 1; pyrexia n = 1).

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