Updated Results from EDGE-Gastric Arm A1: Phase 2 Study of Domvanalimab, Zimberelimab, and FOLFOX in First-Line Advanced Gastroesophageal Cancer

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Key Takeaways

- Domvanalimab (dom; anti-TIGIT) and zimberelimab (zim; anti-PD-1) in combination with FOLFOX showed promising median PFS, and 12-month PFS, and ORR in 1L treatment of metastatic gastroesophageal cancer
  - Overall: Median PFS, 12.9 mos; 12-mos PFS rate, 58%; ORR, 59%
  - PD-L1-high: Median PFS, 13.8 mos; 12-mos PFS rate, 69%; ORR, 69%
  - PD-L1-low: Median PFS, 11.3 mos; 12-mos PFS rate, 47%; ORR, 50%
- AE profile continued to be similar to prior experience with anti-PD-1 plus FOLFOX, with no new safety concerns
- The randomized phase 3 STAR-221 trial (NCT05568095) comparing dom + zim + chemotherapy versus nivolumab + chemotherapy is underway in 1L patients with locally advanced unresectable or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma

Background

- Anti-PD-1 with chemotherapy is the current standard of care for gastroesophageal cancers (GEC) with median PFS 7.7 months and OS 13.8 months[1]; however, long-term outcomes remain poor
- Domvanalimab (dom, Fc-silent anti-TIGIT mAb) with Zimberelimab (zim, anti-PD-1 mAb) can increase tumor antigen-specific CD8+ T cell expansion with potent antitumor activity[2]
- Previously presented data of EDGE-Gastric Arm A1 of dom and zim with FOLFOX showed encouraging safety and efficacy irrespective of PD-L1 expression (cutoff: 3 September 2023)
- Here, we present the updated 12-month follow-up safety and efficacy results of 1L dom, zim, and FOLFOX in advanced gastroesophageal adenocarcinoma from EDGE-Gastric Arm A1 (enrollment completion: 3 March 2023)

1. Janjigian, Y, et al. *Lancet.* 2021;(10294):27–40. 2. Johnston RJ et al. *Cancer Cell.* 2014;26(6):923–37. 3. Janjigian Y, et al. *J Clin Oncol*. 2023;41(suppl 36):abstr 433248.

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

- First-line locally advanced unresectable or metastatic gastric/GEJ/EAC
- Measurable disease per RECIST v1.1
- ECOG 0-1
- Known HER-2-positive tumors excluded
- Irrespective 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)
- PK and biomarker data

At the 12 Mar 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; 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; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every two weeks; Q4W, every four weeks; Q6W, every six weeks; Q12W, every twelve weeks; zim, zimberelimab

Baseline Characteristics

	Arm A1 N=41, n (%)
Mean age, years (range)	61 (30 to 82)
Female	17 (41)
Country	
United States/France	22 (54)
Korea	19 (46)
Baseline ECOG performance status 1	25 (61)
Histologically confirmed diagnosis	
Esophageal	10 (24)
Gastric	26 (63)
Gastroesophageal Junction (GEJ)	5 (12)

	Arm A1 N=41, n (%)
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)*	
TAP ≥ 5%	16 (39)
TAP < 5%	24 (59)
Unavailable†	1 (2)
Microsatellite instability status	
High	1 (2)
Low/Stable	35 (85)
Unknown	5 (12)

* Ventana SP263 assay used for all TAP scores.
† 1 patient did not have tissue available for central testing.
ECOG, Eastern Cooperative Oncology Group; TAP, tumor area positivity.

Study Population and Patient Disposition

- As of the 12 Mar 2024 data cutoff, all 41 patients received study treatment* and were included in the analysis of efficacy and safety
- Median treatment duration was 11.4 months
- 28 patients (68%) have discontinued all study treatments
  - Primary reason
    - Disease progression (n=20, 49%)
    - Withdrawal by patient (n=3, 7%)
    - Start of new anticancer therapy (n=2, 5%)
    - Adverse event (n=2, 5%)
    - Death (n=1, 2%)
- 13 patients (32%) discontinued from the study†

Efficacy-evaluable: all treated patients with at least 2 post-baseline disease assessments or who discontinued treatment prior to achieving 2 disease assessments

* One patient did not receive leucovorin due to institutional standard practice

† 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)

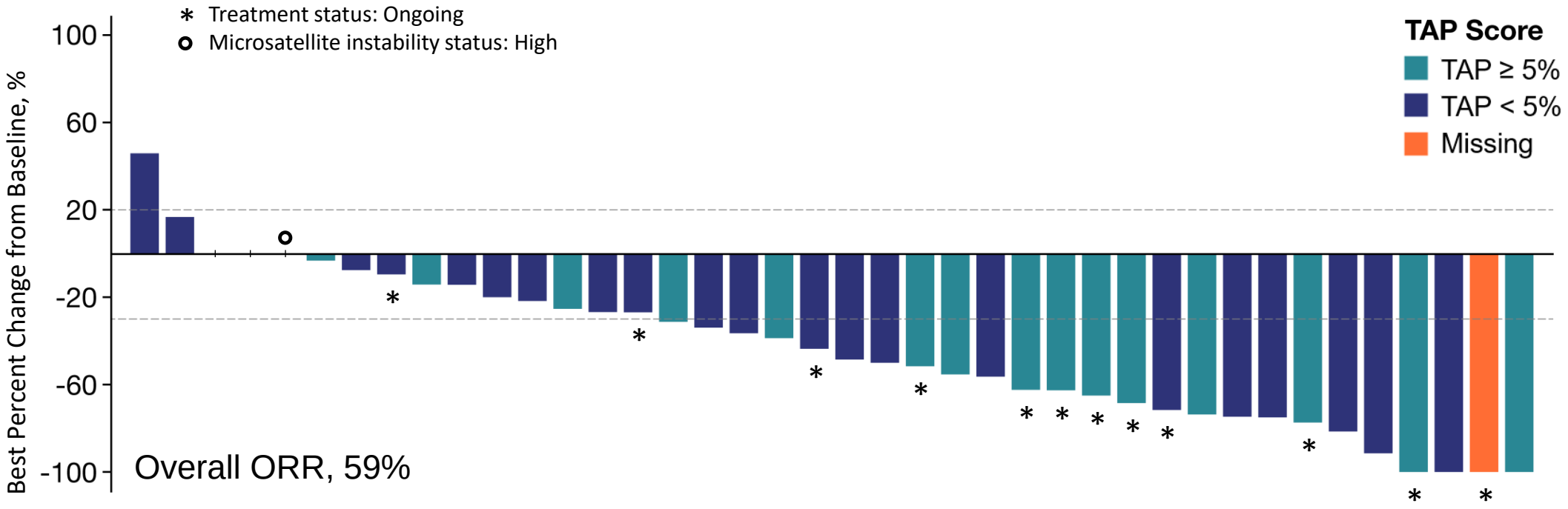
Objective Response Rate per RECIST v1.1

	Overall N=41*	TAP ≥ 5% n=16	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 post-baseline 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)

Investigator-assessed ORR is reported.
CI, confidence interval; ORR, objective response rate; NE, not evaluable; TAP, tumor area positivity.
* 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.

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

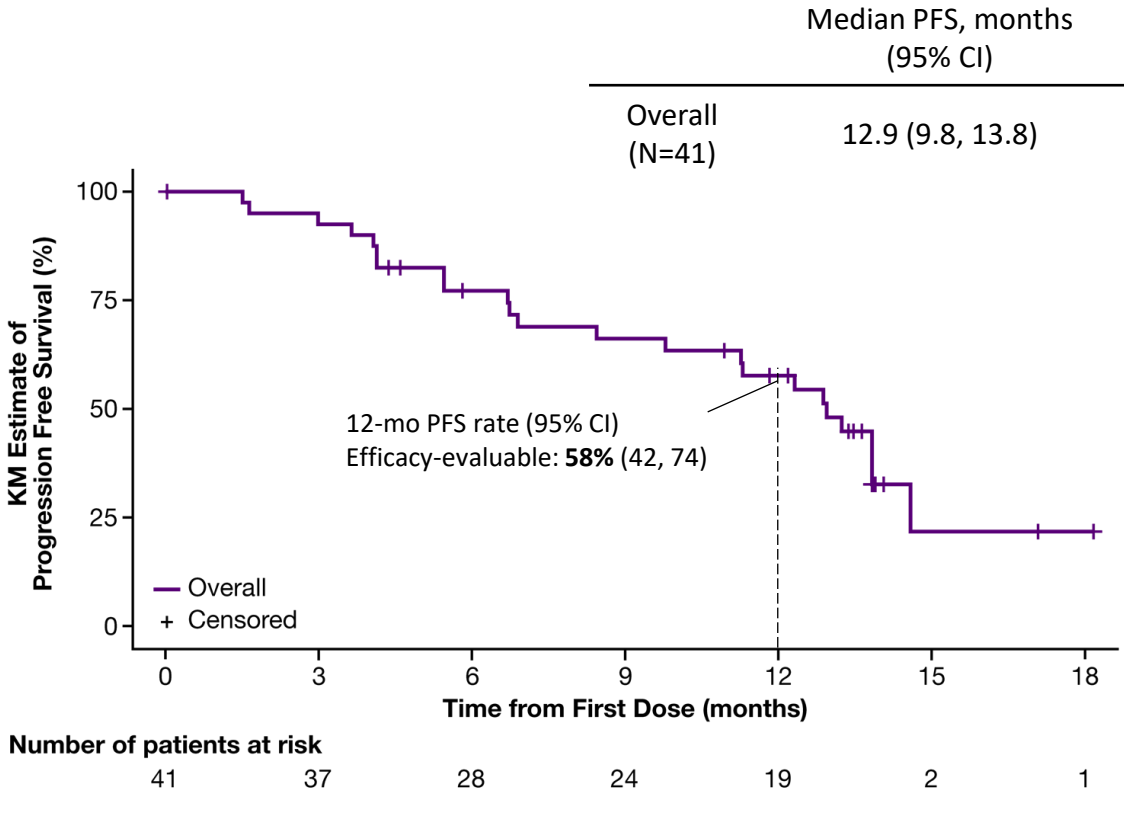
Best Percent Change in Sum of Target Lesions



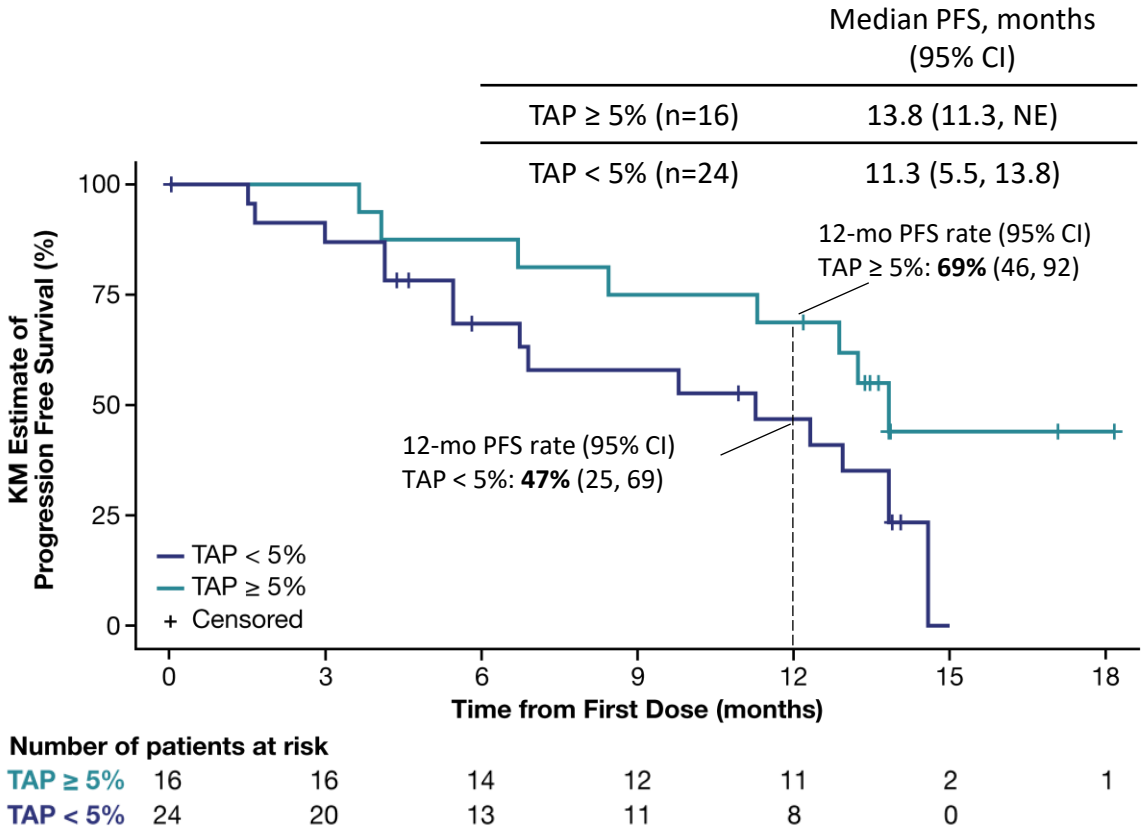
One patient (missing; orange bar) had no tissue available for TAP central lab testing. From local lab results, the patient was PD-L1 low via 22-C3 assay.
TAP, tumor area positivity.

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

Efficacy-Evaluable (N=41)



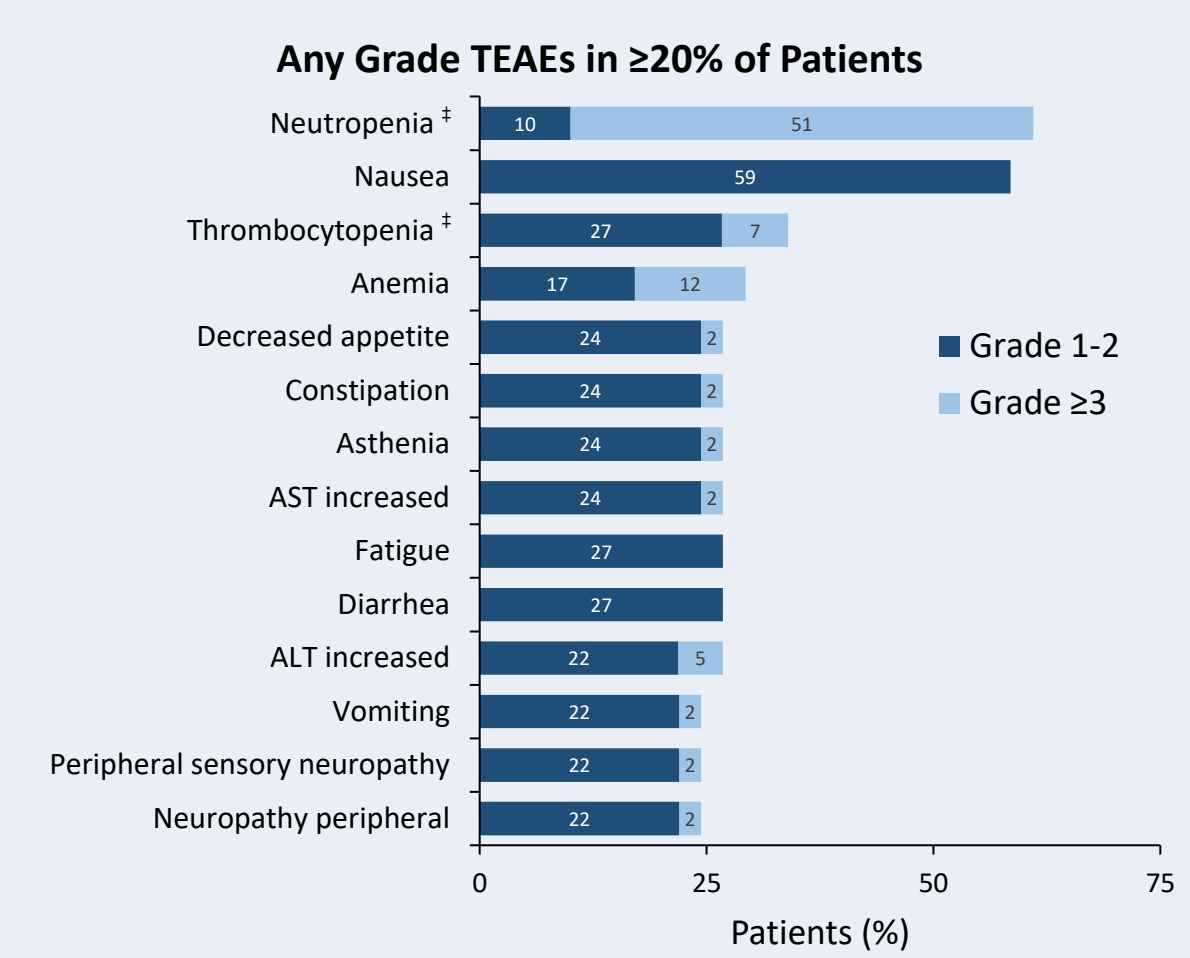
TAP ≥ 5% (n=16); TAP < 5% (n=24)



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

Overall Safety Summary

	Arm A1 N=41, n (%)
Any TEAE	41 (100)
TEAEs related to any study drug*	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†	1 (2)



* TEAEs related to zim (n=32), dom (n=32), and FOLFOX (n=39). † Event term is "Death" and assessed as not related to any study medications; query pending.
‡ '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.
ALT alanine aminotransferase; AST, aspartate aminotransferase; dom, domvanalimab; TEAE, treatment-emergent adverse event; zim, zimberelimab.

Conclusions

- Dom (anti-TIGIT) and zim (anti-PD-1) in combination with FOLFOX shows promising ORR, median PFS, and 12-month PFS in metastatic first line GEC
  - Overall: Median PFS, 12.9 mos; 12-mos PFS rate, 58%; ORR, 59%
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