Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Gastroesophageal Cancers

A CME/MOC-Accredited Live Webinar

Tuesday, June 23, 2026

5:00 PM – 6:00 PM ET

Faculty

David H Ilson, MD, PhD

Kohei Shitara, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

Faculty

David H Ilson, MD, PhD
Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Kohei Shitara, MD
Chief of the Department of Gastrointestinal Oncology
National Cancer Center Hospital East
Kashiwa, Japan

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

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Dr Ilson — Disclosures

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Dr Shitara — Disclosures

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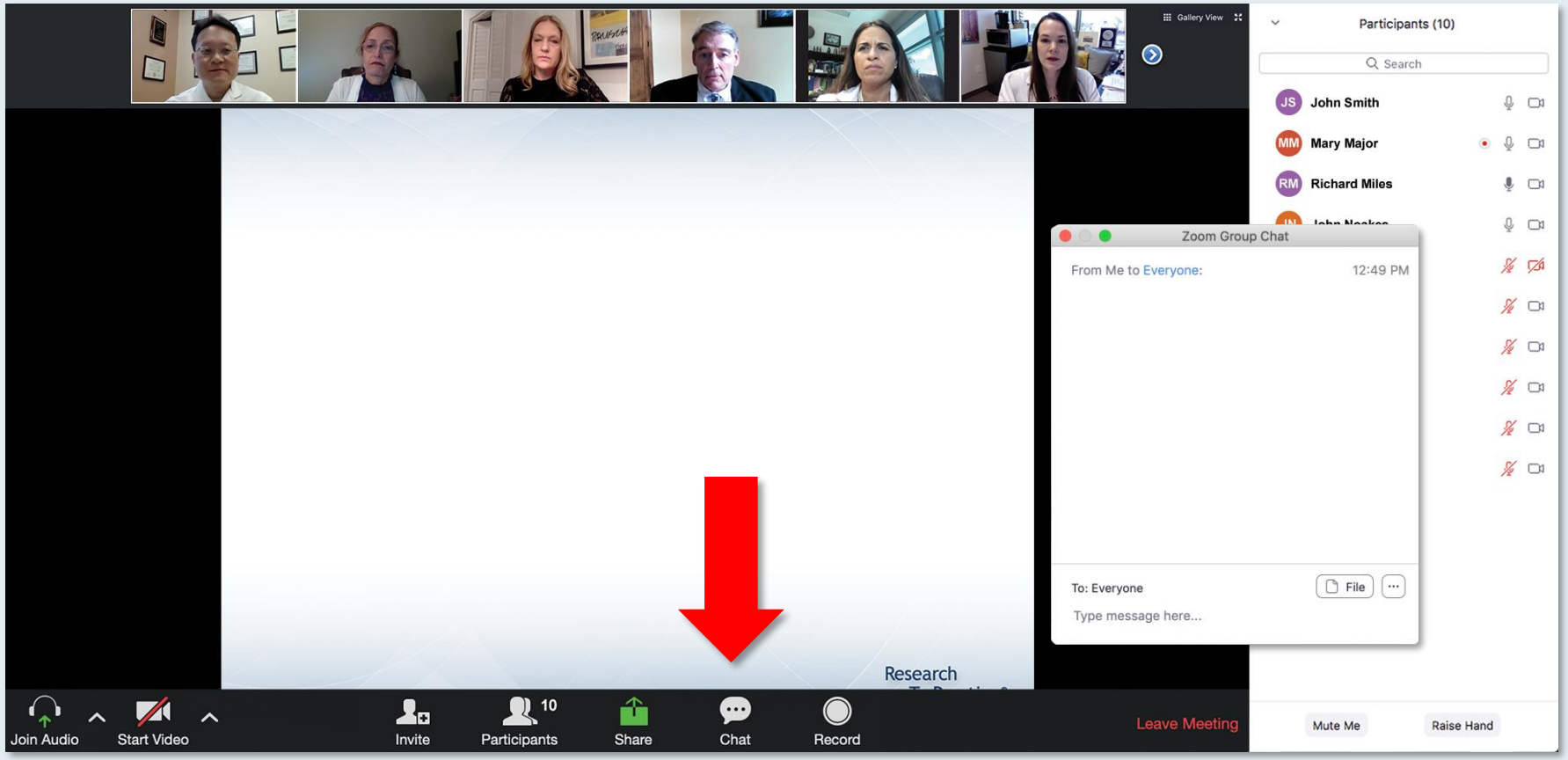

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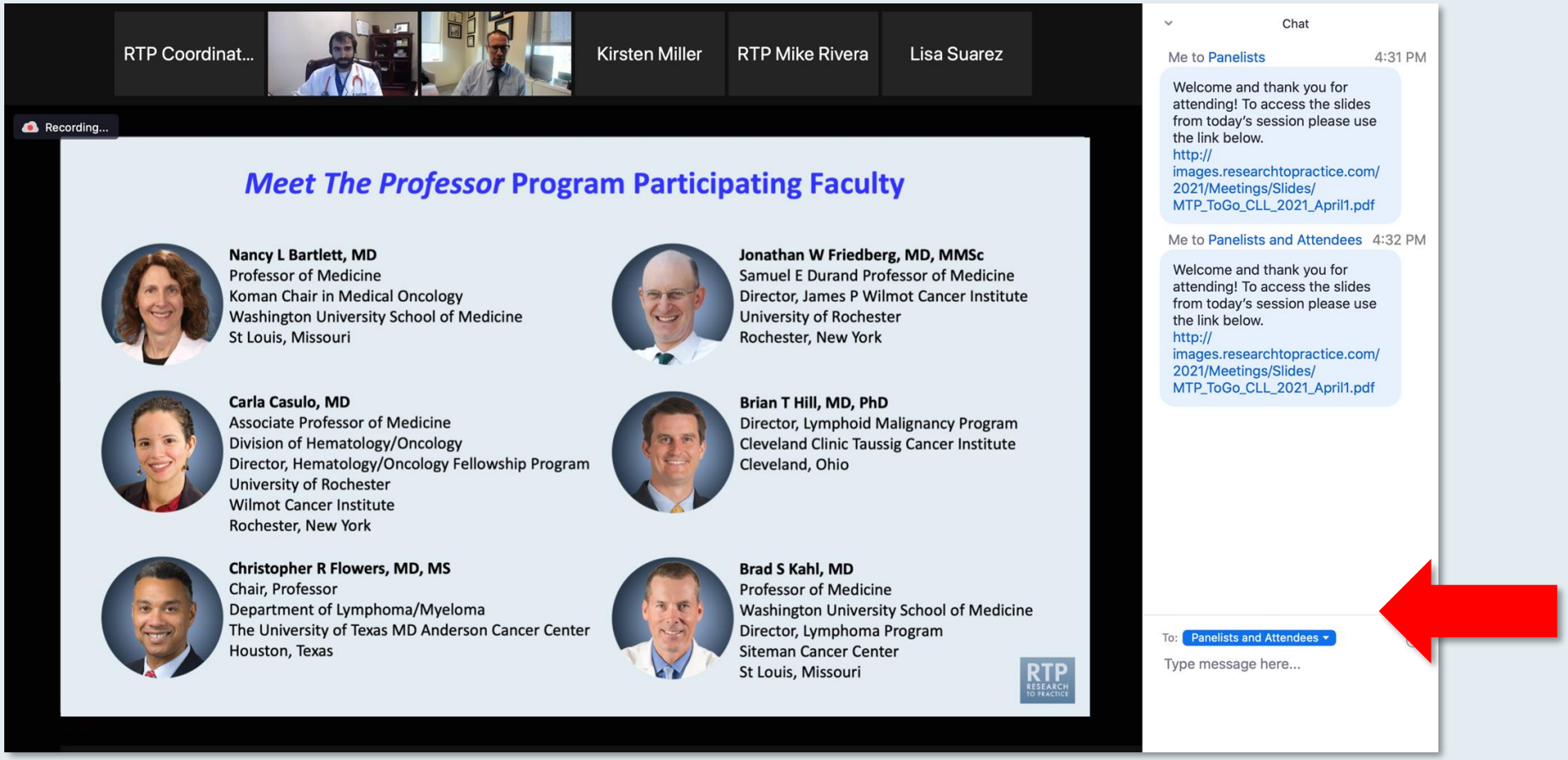

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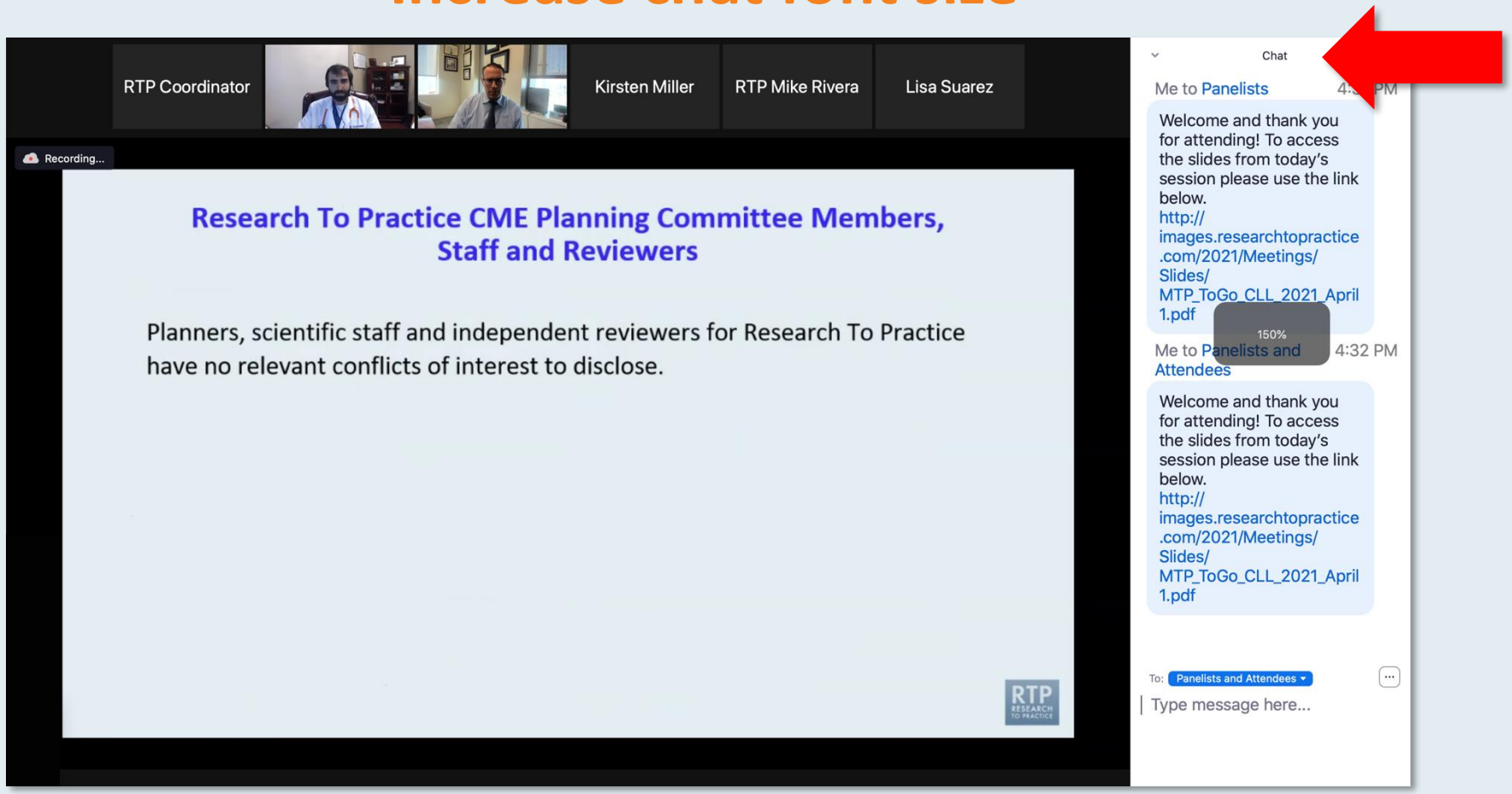

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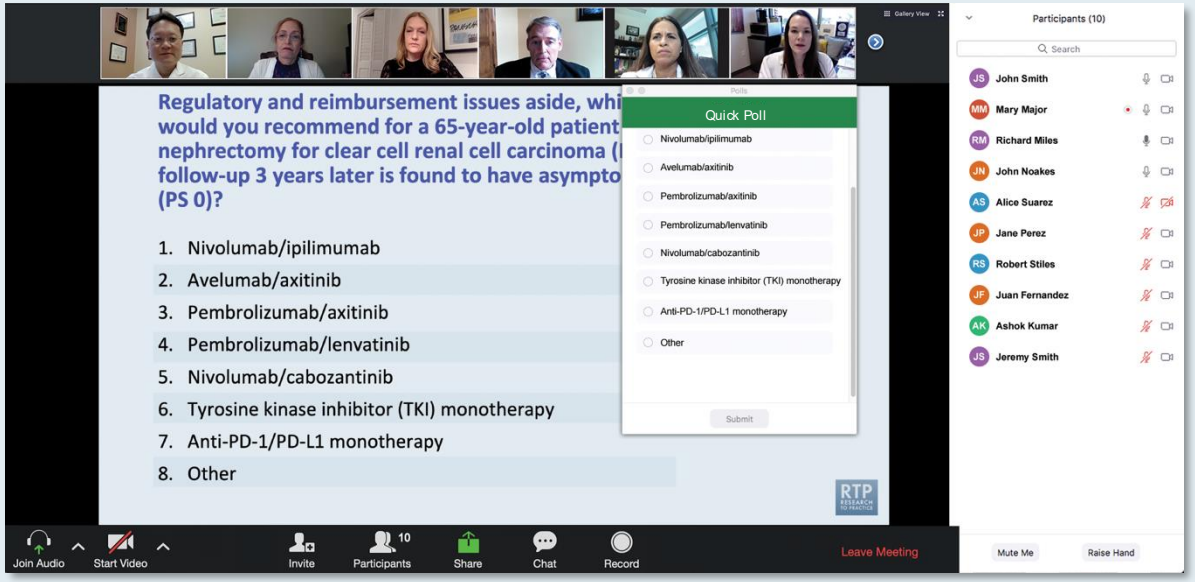

Expert Second Opinion: Investigators Discuss the Optimal Management of HER2-Positive Gastrointestinal Cancers — Proceedings from a live event held during the 2026 ASCO Gastrointestinal Cancers Symposium

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Thursday, June 25, 2026
5:00 PM – 6:00 PM ET

Faculty

Amrita Krishnan, MD
Robert Z Orlowski, MD, PhD

Moderator

Neil Love, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Therapeutic Targets Beyond EGFR for Non-Small Cell Lung Cancer

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John V Heymach, MD, PhD

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Neil Love, MD

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Patterns of Care: Exploring How Community Oncologists Manage HR-Positive, HER2-Positive Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 1, 2026

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Reshma L Mahtani, DO

Moderator

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RTP RESEARCH TO PRACTICE

Year in Review:
Gastroesophageal Cancers

INTRODUCTION

MODULE 1: Role of Immune Checkpoint Inhibitors in the Management of Gastroesophageal Cancers — Dr Ilson

MODULE 2: Other Available Therapeutic Approaches — Dr Shitara

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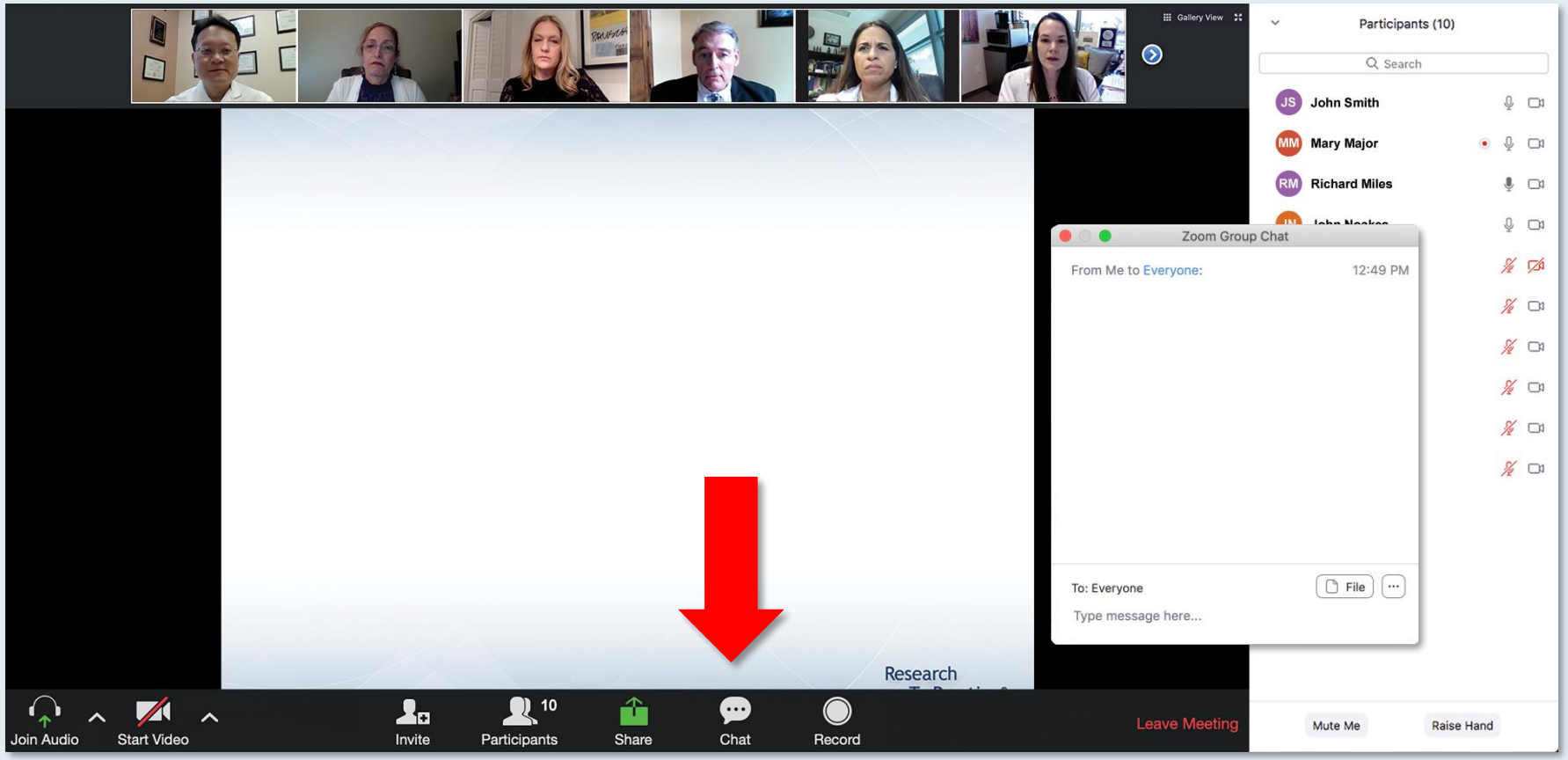

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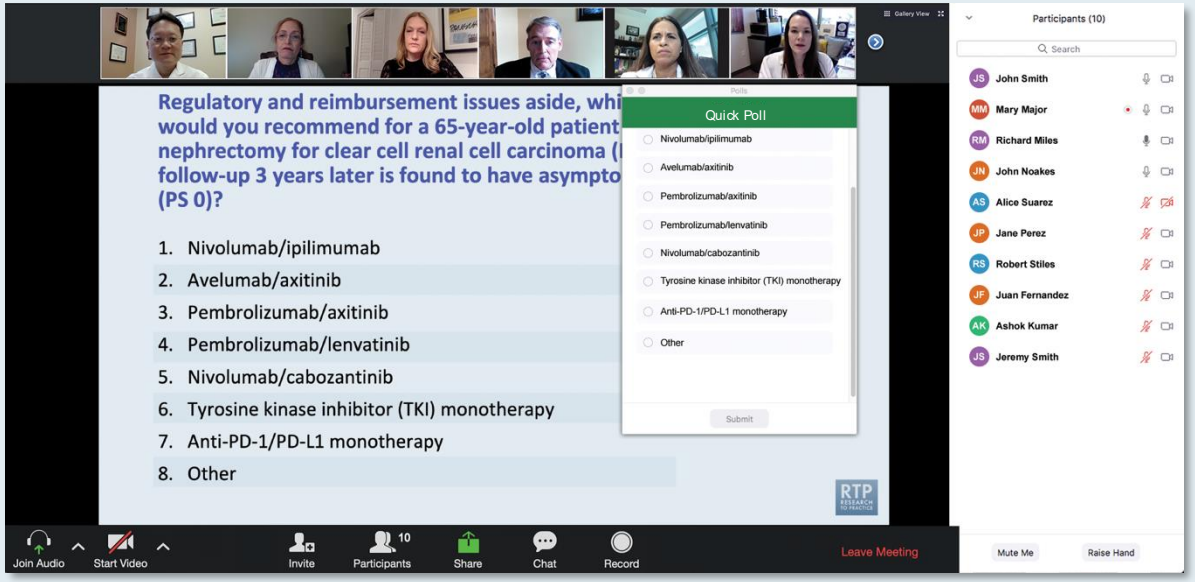

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Dr Shitara — Disclosures

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Dr Love — Disclosures

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Year in Review
(gastric/GEJ disease)

Kohei Shitara
Department of Gastroenterology
National Cancer Center Hospital East (NCCHE)

Research To Practice Gastric Cancer Updates

David H. Ilson, MD PhD
Attending Physician, Professor of Medicine
Memorial Sloan Kettering Cancer Center
Weil Cornell Medical College
New York, NY

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Key Datasets

David Ilson, MD, PhD

- Samaille T et al. Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients with localized microsatellite instability-high (MSI)/mismatch repair deficient (dMMR) oeso-gastric adenocarcinoma: Long-term follow-up of the GERCOR NEONIPIGA phase II study. ASCO 2026;Abstract 4099.
- Leone AG et al. STRIDE regimen of tremelimumab and durvalumab as non-operative management strategy of microsatellite instability-high (MSI-H) resectable gastric or gastroesophageal junction adenocarcinoma (GAC/GEJAC): Final results of the cohort 2 of INFINITY study by GONO GI. AACR 2026;Abstract CT230.
- Stein A et al. Perioperative pembrolizumab, trastuzumab and FLOT in HER2-positive localized esophagogastric adenocarcinoma: A phase 2 trial. *Nat Med* 2025;31(12):4197-204.
- Tabernero J et al. Final overall survival (OS) and the association of pathological outcomes with event-free survival (EFS) in MATTERHORN: A randomised, phase III study of durvalumab (D) plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) in resectable gastric/gastroesophageal (G/GEJ) adenocarcinoma. ESMO 2025;Abstract LBA81.
- Wainberg ZA et al. Efficacy of durvalumab and safety by treatment period in MATTERHORN: A randomized, phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) in resectable gastric/gastroesophageal junction (G/GEJ) adenocarcinoma. ASCO 2026;Abstract 4070.

Key Datasets

David Ilson, MD, PhD (continued)

- Shitara K et al. Pembrolizumab plus chemotherapy versus chemotherapy as perioperative therapy in locally advanced gastric and gastroesophageal junction cancer: Final analysis of the randomized, phase 3 KEYNOTE-585 study. *J Clin Oncol* 2025;43(29):3152-9.
- Janjigian YY et al. Nivolumab plus chemotherapy as first-line treatment for advanced gastric, gastroesophageal junction, and esophageal adenocarcinoma: 5-year follow-up results from CheckMate 649. *Ann Oncol* 2026;37(6):787-97.
- Cruz-Correa M et al. Tislelizumab + chemotherapy in gastric cancer: Long-term RATIONALE-305 randomized trial follow-up. *Adv Ther* 2026;43(1):165-83.
- Oh D-Y et al. Nivolumab plus ipilimumab combined with chemotherapy as first-line treatment for HER2-negative unresectable advanced or recurrent gastric/gastroesophageal junction cancer: A randomized phase 3 trial (ATTRACTION-6). ASCO 2026;Abstract 4006.
- Metges J-P et al. Pembrolizumab plus chemotherapy versus chemotherapy for advanced esophageal cancer: 5-year extended follow-up for the randomized phase III KEYNOTE-590 study. *ESMO Open* 2025;10(12):105854.
- Kawazoe A et al. KEYNOTE-811: 6-year median follow-up of pembrolizumab plus trastuzumab and chemotherapy for previously untreated advanced HER2-positive gastric or gastroesophageal junction adenocarcinoma. ASCO 2026;Abstract 4040.

Key Datasets

Kohei Shitara, MD

- Elimova E et al. Zanidatamab + chemotherapy (CT) ± tislelizumab for first-line (1L) HER2-positive (HER2+) locally advanced, unresectable, or metastatic gastroesophageal adenocarcinoma (mGEA): Primary analysis from HERIZON-GEA-01. Gastrointestinal Cancers Symposium 2026;Abstract LBA285.
- Rha SY et al. Zanidatamab + chemotherapy (CT) ± tislelizumab for first-line (1L) HER2-positive (HER2+) locally advanced or metastatic gastroesophageal adenocarcinoma (mGEA): PD-L1 subgroup analysis from HERIZON-GEA-01. ASCO 2026;Abstract 4010.
- Shitara K et al. Trastuzumab deruxtecan or ramucirumab plus paclitaxel in gastric cancer. *N Engl J Med* 2025;393(4):336-48.
- Janjigian YY et al. First line (1L) trastuzumab deruxtecan (T-DXd)-based regimens in advanced HER2-expressing gastric cancer (GC), gastroesophageal junction adenocarcinoma (GEJA), or esophageal adenocarcinoma (EA): Safety results from DESTINY-Gastric03 (DG-03) Part 2 arms D and F, and Part 4. ASCO 2026;Abstract 4022.
- Shah M et al. ARTEMIDE-Gastric01: A phase 3 randomized study of rilvegostomig with fluoropyrimidine and trastuzumab deruxtecan (T-DXd) as first-line (1L) treatment for locally advanced or metastatic HER2-positive gastric or gastroesophageal junction cancer (GC/GEJC). Gastrointestinal Cancers Symposium 2026;Abstract TPS460.

Key Datasets

Kohei Shitara, MD (continued)

- Shitara K et al. Phase 2 ILUSTRO trial of 1L zolbetuximab plus mFOLFOX6 and nivolumab in patients with CLDN18.2+ locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ adenocarcinoma. Gastrointestinal Cancers Symposium 2026;Abstract LBA284.
- Shitara K et al. Zolbetuximab + pembrolizumab and chemotherapy as first-line treatment for patients with CLDN18.2-positive, HER2-negative, PD-L1-positive locally advanced unresectable or metastatic G/GEJ adenocarcinoma: Phase 3, double-blind, randomized trial (LUCERNA). Gastrointestinal Cancers Symposium 2026;Abstract TPS473.
- Shitara K et al. Sonesitatug vedotin (Sone-Ve) monotherapy in patients (pts) with claudin 18.2-positive (CLDN18.2+) advanced or metastatic gastric or gastroesophageal junction (GEJ) cancers: Data from CLARITY-PanTumor01. ASCO 2026;Abstract 4023.
- Shitara K et al. CLARITY-Gastric01: A randomized phase 3 study of sonesitatug vedotin (sone ve), a claudin 18.2 (CLDN18.2)-targeted antibody-drug conjugate, in second- or later-line (2L+) advanced gastric or gastroesophageal junction cancer (GJ/GEJC). Gastrointestinal Cancers Symposium 2026;Abstract TPS462.
- Lu Z et al. Izalontamab brengitecan (iza-bren) versus chemotherapy in patients with recurrent or metastatic esophageal squamous cell carcinoma (ESCC): A multicenter, randomized, open-label, phase III study. ASCO 2026;Abstract 4008.

Year in Review:
Gastroesophageal Cancers

INTRODUCTION: Biomarker Evaluation in Localized and Metastatic Disease

MODULE 1: Role of Immune Checkpoint Inhibitors in the Management of Gastroesophageal Cancers — Dr Ilson

MODULE 2: Other Available Therapeutic Approaches — Dr Shitara

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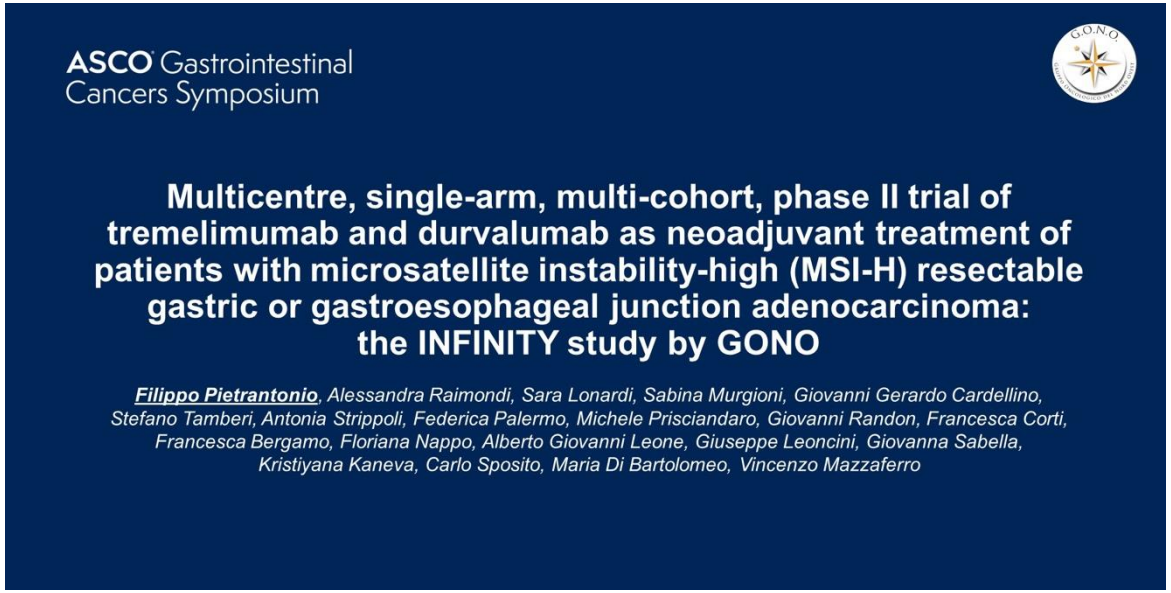
Research To Practice Gastric Cancer Updates

David H. Ilson, MD PhD
Attending Physician, Professor of Medicine
Memorial Sloan Kettering Cancer Center
Weil Cornell Medical College
New York, NY

Microsatellite Instability (MSI)-High Locally Advanced Esophagogastric Adenocarcinoma

Preoperative CPI therapy in MSI High Gastric Cancer

Andre, *JCO*. 2023;41: 255-265
ASCO GI 2022;Abstract 244



Pietrantonio, *JCO*. 2023;41(suppl 4; abstr 358)
ASCO GI 2023;Abstract 358

Preoperative CPI therapy in MSI High Gastric Cancer

Results (1): Surgery and TNM and Tumor Regression Grading (TRG)

Type of surgery (N=29)	N	%
R0	29	100
Total oesogastrectomy	1	3,5
Total gastrectomy	7	24
4/5 gastrectomy	9	31
Lewis-Santy procedure	11	38
Pancreaticoduodenectomy	1	3,5

ypT stage (N=32)	
ypT0*	19
ypT1a	1
ypT1b	2
ypT2	2
ypT3	5
unknown**	3
ypN stage (N=32)	
ypN0	23
ypN1	6
unknown*	3

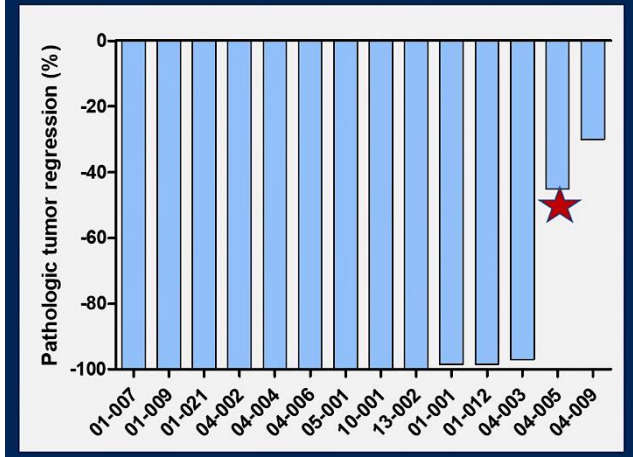
TRG Mandard (N=29)	N	%
TRG 1: complete regression/fibrosis with no tumor cells	17	58.6
TRG 2: fibrosis with scattered tumor cells	4	13.8
TRG 3: fibrosis and tumor cells with a dominance of fibrosis	2	6.9
TRG 4: fibrosis & tumor cells with dominance of tumor cells	4	13.8
TRG 5: tumor without evidence of regression	2	6.9
TRG Becker (N=29)		
TRG 1a: complete tumor regression without residual tumor	17	58.6
TRG 1b: < 10% residual tumor per tumor bed	4	13.8
TGR 2: 10% to 50% residual tumor	2	6.9
TRG 3: > 50% residual tumor cells	6	21.7

- * 2 patients ypT0 and ypN1 (residual tumoral cells < 10% in only one node)
- ** 3 patients without surgery, 1 in metastatic PD and 2 in complete response in endoscopy with no tumoral cell on biopsy

ASCO Gastrointestinal Cancers Symposium #GI22 PRESENTED BY: Thierry André, MD Abstract 244 ASCO KNOWLEDGE CONQUERS CANCER

Andre, *JCO*. 2023;41: 255-265

Primary endpoint



TRG Becker	N = 15	%
1a	9	60%
1b	3	20%
3	2	13%

1 patient did not undergo surgery for PD

Among evaluable patients, rate of pCR was 60% and rate of major to complete pathological response (<10% viable cells) was 80%.

★ Heterogeneous pMMR/dMMR status at surgery

ASCO Gastrointestinal Cancers Symposium #GI23 PRESENTED BY: Filippo Pietrantonio, MD ASCO KNOWLEDGE CONQUERS CANCER

Pietrantonio, *JCO*. 2023;41(suppl 4; abstr 358)

Pathologic CR 59%-60%, Near pCR 14-20%

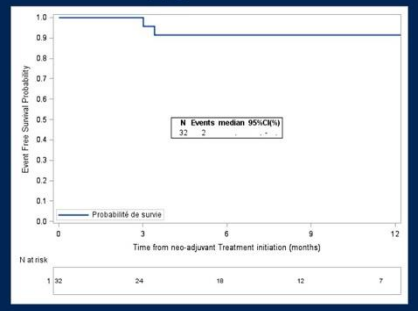
Preoperative CPI therapy in MSI High Gastric Cancer

Results (2)

6

- With a median follow-up of 12 months (95%CI: 7.8-14.2), 2 patients had events (death or relapse)
  - one death at day 3 post surgery*
  - one progressive disease with metastatic disease PD after 6 cycles (surgery not performed)
  - 31 patients alive and 30 without relapse

EFS



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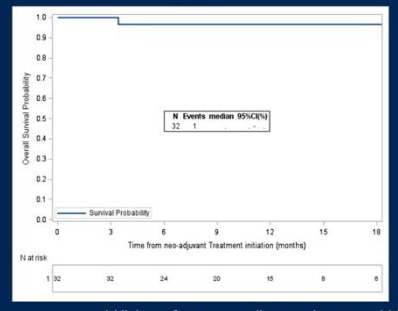

* History of severe cardio vascular co-morbidity and sudden death

ASCO Gastrointestinal Cancers Symposium #GI22 PRESENTED BY: Thierry André, MD

Abstract 244

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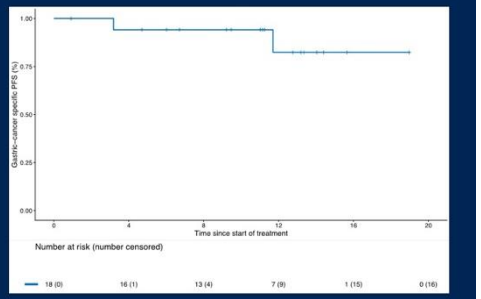
Andre JCO 41: 255-265, 2023

Survival endpoints

8

	PFS event	OS event	
01-020	Yes	No	CR to CAPOX
04-005	Yes	Yes	Heterogeneous pMMR/dMMR status
13-002	No	Yes	Late postoperative complications
01-009	No	Yes	Late postoperative complications
05-001	No	Yes	Second primary brain cancer

Gastric cancer-specific PFS



Data cutoff date: 16th December 2022, with a median follow up of 13.4 (IQR 9.7-14.2) months

ASCO Gastrointestinal Cancers Symposium #GI23 PRESENTED BY: Filippo Pietrantonio, MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Pietrantonio JCO 41: 2023 (suppl 4; abstr 358)

High Rates of pCR: Nonoperative Management?

NEONIPIGA: ASCO 2026 Update at 48 months

Abstract 550106: Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in patients (Pts) with localized microsatellite instability-high (MSI)/mismatch repair deficient (dMMR) oeso-gastric adenocarcinoma (OGA): Long-term follow-up of the GERCOR NEONIPIGA phase II study

Thomas Samaille[1], Julie Henriques[2,3], David Tougeron[4], Guillaume Piessen[5], Christelle de la Fouchardière[6], Christophe Louvet[7], Antoine Adenis[8], Marine Jary[9], Marie-Line Garcia-Larnicol[10], Romain Cohen[1], Dewi Vernerey[2,3], Jeremie H. Lefevre[11], Magali Svrcek[12], Thierry Andre[1]

GERCOR

Background

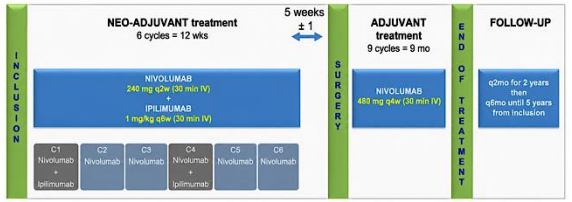
- MSI-H/dMMR status is a negative factor for chemotherapy efficacy in localized OGA and a major predictive factor for ICI efficacy.
- The NEONIPIGA study investigated peri-operative nivolumab plus ipilimumab and achieved its primary objective with a pathological complete response (pCR) of 58.6%.
- Secondary objectives included event-free survival (EFS) and overall survival (OS).

- ❖ Peri-operative nivolumab plus ipilimumab was associated with **sustained long-term survival** in MSI-H/dMMR localized OGA.
- ❖ Chemotherapy may **be avoided** in these Pts.
- ❖ Our results strongly support the development of **watch-and-wait strategies.**

Corresponding author: **thierry.andre@aphp.fr**

Methods

- Phase II, single-arm, multicentric clinical trial (NCT04006262; EUDRACT 2018-004712-22).
- Histologically proven resectable MSI-H/dMMR gastric or OGA, cT2-T4NxM0.



Results

- 32 Pts were included; 1 metastatic Pt was excluded from EFS analysis. The median age was 65 years (range 40-84).

	n	(%)		n	(%)
Male/Female	23/9	72/28	us T2/T3/not evaluable	4/22/6	12/69/16
ECOG PS 0/1	19/13	59/41	us N-/N+	9/23	28/72
Gastric/OGA	16/16	50/50	Intestinal/Diffuse/Missing	24/6/2	75/19/6

- With a median follow-up of 48.3 months, the 4-year EFS was 83.5% (95% CI, 64.8-92.8) and 4year OS was 84.1% (95% CI, 65.8-93).

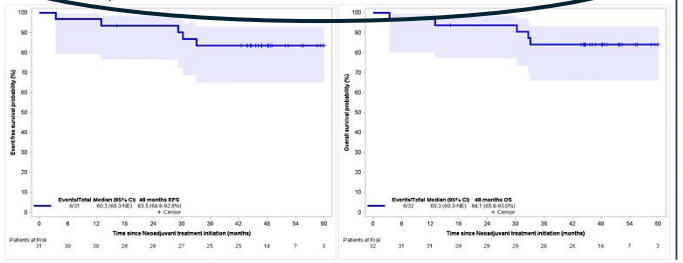


Figure 1. Kaplan-Meier curves of EFS and OS.

- Six deaths reported: 1 surgery complication, 1 cerebral relapse, 4 unrelated to treatment or cancer.

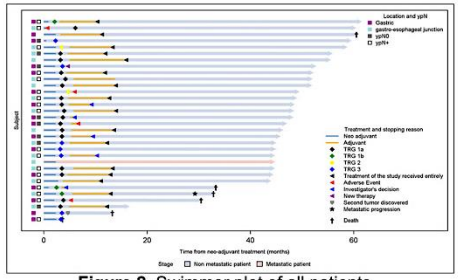


Figure 2. Swimmer plot of all patients

Future Directions for Research

- A **watch-and-wait strategy** with modalities of response assessments and surveillance scheme will be evaluated in the ongoing DEWI phase II trial (NCT06059495).

Acknowledgements

1. Sorbonne University; Department of Medical Oncology, Saint-Antoine Hospital, AP-HP, INSERM 938, SIRIC CURAMUS, Paris, France. 2. Methodology and Quality of Life Unit in Oncology, University of Besançon, Besançon, France. 3. Université Marie et Louis Pasteur, EFS, INSERM UMR1098 RIGHT, Besançon, F-25000, France. 4. Department of Hepatology and Gastroenterology, Poitiers University Hospital, Poitiers, France. 5. University of Lille, CNRS, INSERM, CHU Lille, Department of Digestive and Oncological Surgery, UMR9020-U1366-ONCOLille-CRC Lille-Team PancReaT, Lille, France. 6. Department of Medical Oncology, Institute Paoli-Calmettes Marseille France. 7. Department of Medical Oncology, Institut Mutualiste Montsouris, Paris, France. 8. Institut de Recherche en Cancérologie de Montpellier (IRCM), INSERM, University of Montpellier, Montpellier Cancer Institute (ICM), Montpellier, France. 9. Department of Digestive Oncology, University Hospital, Clermont-Ferrand, France. 10. Oncology Multidisciplinary Group (GERCOR), Paris, France. 11. Sorbonne University; Department of Digestive Surgery, Saint-Antoine Hospital, AP-HP, Paris, France. 12. Sorbonne University, Paris, Léon Bérard Comprehensive Cancer Center, Department of Pathology, Lyon, France

INFINITY AACR 2026 UPDATE

- Cohort of 17 evaluable patients with MSI esophagogastric cancers, treated with 3 months of one dose tremelimumab and monthly durvalumab
- Primary endpoint gastrectomy free survival
- 13 clinical CR, one required salvage surgery, 4 non-CR patients underwent surgery
- At median 27.1 months fu
  - PFS 94.1%
  - OS 100%
  - GFS 70.6%

Leone AACR 2026; Abstract CT230

Takeaway Messages: MSI high locally advanced esophagogastric adenocarcinoma

- From the Infinity and NEONIPIGA trials, combination anti CTLA-4 and PD-1/PD-L1 therapy achieves a high rate of pathologic and clinical complete response which appears durable in most patients.
- Consideration for treating these patients with combination checkpoint inhibitor therapy up front should be considered, with non operative management for patients achieving a clinical CR. Chemotherapy and surgery may be avoided altogether.

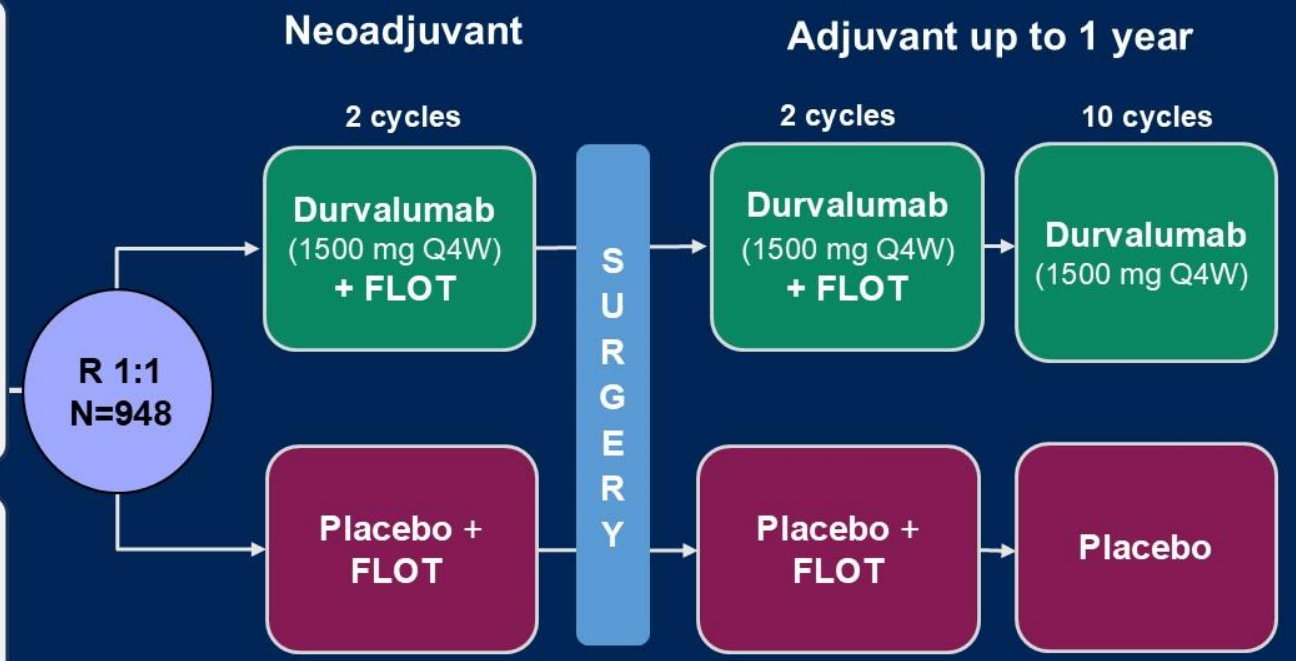
MATTERHORN and KEYNOTE-585 Trial Updates

MATTERHORN Study Design

A global, Phase 3, randomized, double-blind, placebo-controlled study

Study population
- Gastric and GEJ adenocarcinoma
- Stage II to IVa
- No evidence of metastasis
- No prior therapy
- ECOG PS 0 or 1
- Global enrollment in Asia, Europe, North & South America

Stratification factors
- Asia vs non-Asia
- Clinical N+ vs N-
- PD-L1: TAP <1% vs TAP ≥1%*



Primary endpoint:
- EFS

Secondary:
- OS
- pCR

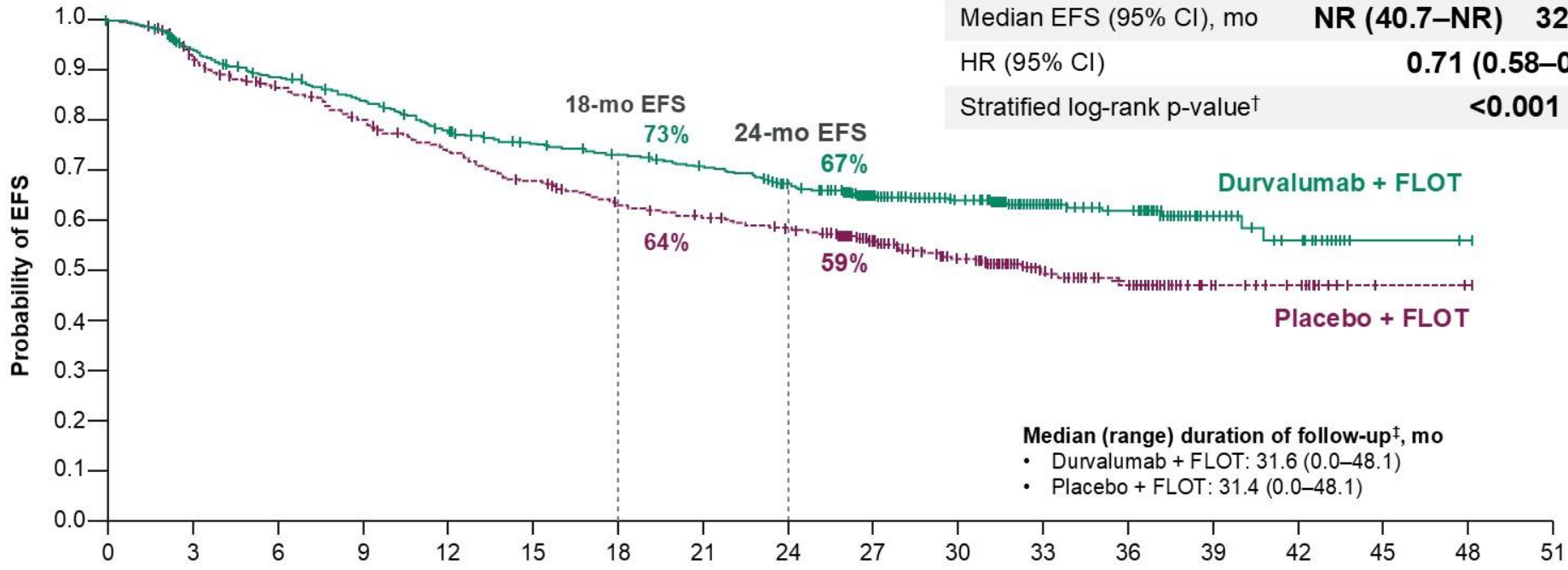
FLOT: 5-fluorouracil 2600 mg/m², leucovorin 200 mg/m², oxaliplatin 85 mg/m², docetaxel 50 mg/m², on Days 1 and 15 Q4W, 4 doses (two cycles) pre- and post-operative; durvalumab: 1500 mg on Day 1 Q4W, 2 doses (two cycles) of durvalumab or placebo pre- and post-operative, followed by 10 doses of post-operative durvalumab or placebo monotherapy. Participants underwent surgery 4–8 weeks after last dose of neoadjuvant therapy. Adjuvant therapy began 4–12 weeks post-surgery. Durvalumab / placebo monotherapy may be continued if FLOT is discontinued due to toxicity. *Measured by IHC using VENTANA PD-L1 (SP263) CDx Assay (Roche Diagnostics; IUO).
ECOG, Eastern Cooperative Oncology Group; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; GEJ, gastroesophageal junction; IHC, immunohistochemistry; IUO, investigational use only; OS, overall survival; pCR, pathologic complete response; PD-L1, programmed cell death ligand-1; PS, performance status; Q4W, every 4 weeks; R, randomized; TAP, Tumor Area Positivity.

Janjigian NEJM 393: 217; 2025
Janjigian ASCO 2025;Abstract LBA5

Primary Endpoint of Event-Free Survival (EFS)

A statistically significant improvement in EFS was observed with durvalumab with FLOT vs placebo with FLOT

	Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Median EFS (95% CI), mo	NR (40.7–NR)	32.8 (27.9–NR)
HR (95% CI)	0.71 (0.58–0.86)	
Stratified log-rank p-value†	<0.001	

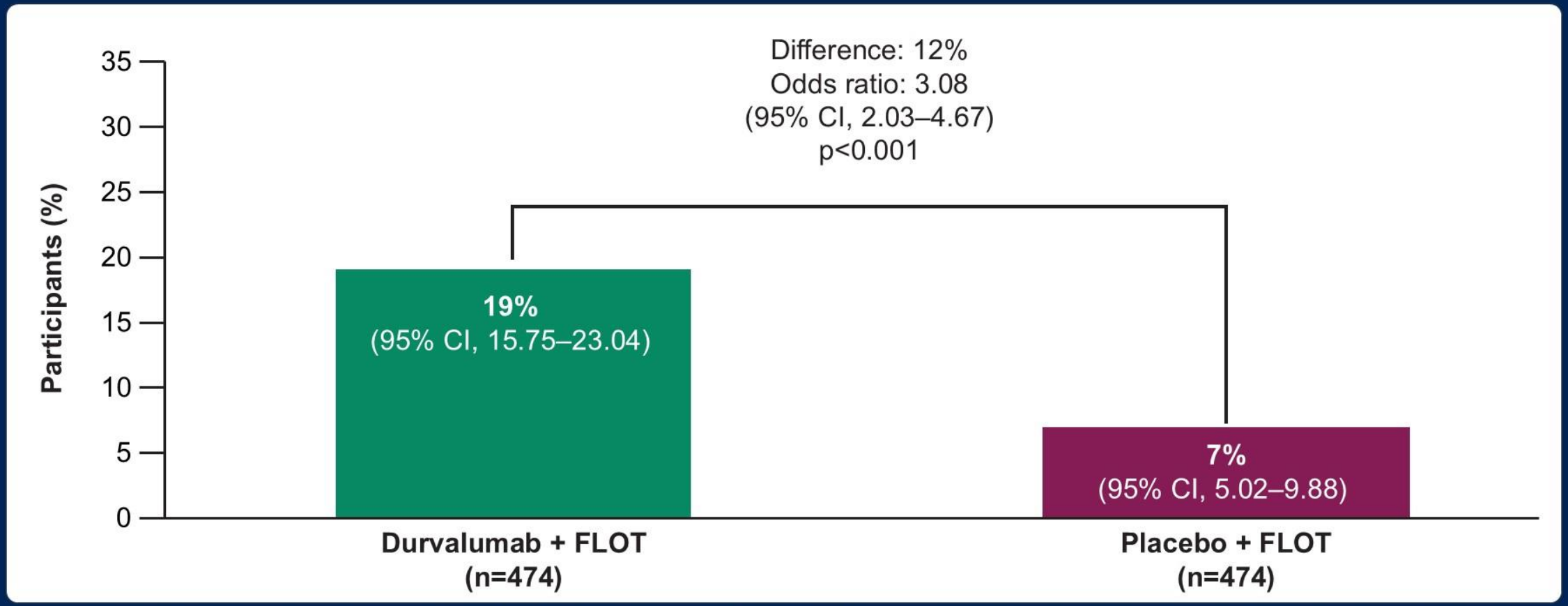


No. of participants at risk																		Total events
Durvalumab + FLOT	474	436	404	381	351	334	320	307	288	234	187	107	88	33	20	2	1	0	167
Placebo + FLOT	474	429	392	360	329	302	278	264	249	202	160	89	65	26	21	2	1	0	218

Events were defined as the earliest of RECIST v1.1 events, non-RECIST v1.1 events, or deaths of any cause. Analysis was based on BICR assessments and / or locally by pathology testing if clinically required. The HR and its CI were estimated from a Cox proportional hazards model, adjusted for geographic region, clinical lymph node status, and PD-L1 expression. The CI for the HR was calculated using a profile likelihood approach. The 2-sided p-value was calculated using a stratified log-rank test adjusted for geographic region, clinical lymph node status, and PD-L1 expression.*Full analysis set (all randomized participants, regardless of treatment received). †The threshold of significance for this analysis was 0.0239. ‡In censored participants.
BICR, blinded independent central review; CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; HR, hazard; mo, month; NR, not reached; PD-L1, programmed cell death ligand-1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

Janjigian NEJM 393: 217; 2025
Janjigian ASCO 2025;Abstract LBA5

pCR: A Statistically Significant Improvement With the Addition of Durvalumab to FLOT



Full analysis set (all randomized participants, regardless of treatment received). Threshold of significance for this analysis was 0.001. Participants had pCR if there was no residual viable tumor cells found at primary tumor and resected lymph nodes at the time of resection, meaning a pathologic regression of 100%, based on central assessment. Central review of pCR was scored using modified Ryan criteria. The analysis was performed using a stratified Cochran-Mantel-Haenszel test. The stratification factors included geographic region, clinical lymph node status, and PD-L1 expression.

CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; pCR, pathologic complete response; PD-L1, programmed cell death ligand-1.

Janjigian YY, et al. *Annal Oncol* 2023;34(suppl 2). Abs LBA73.

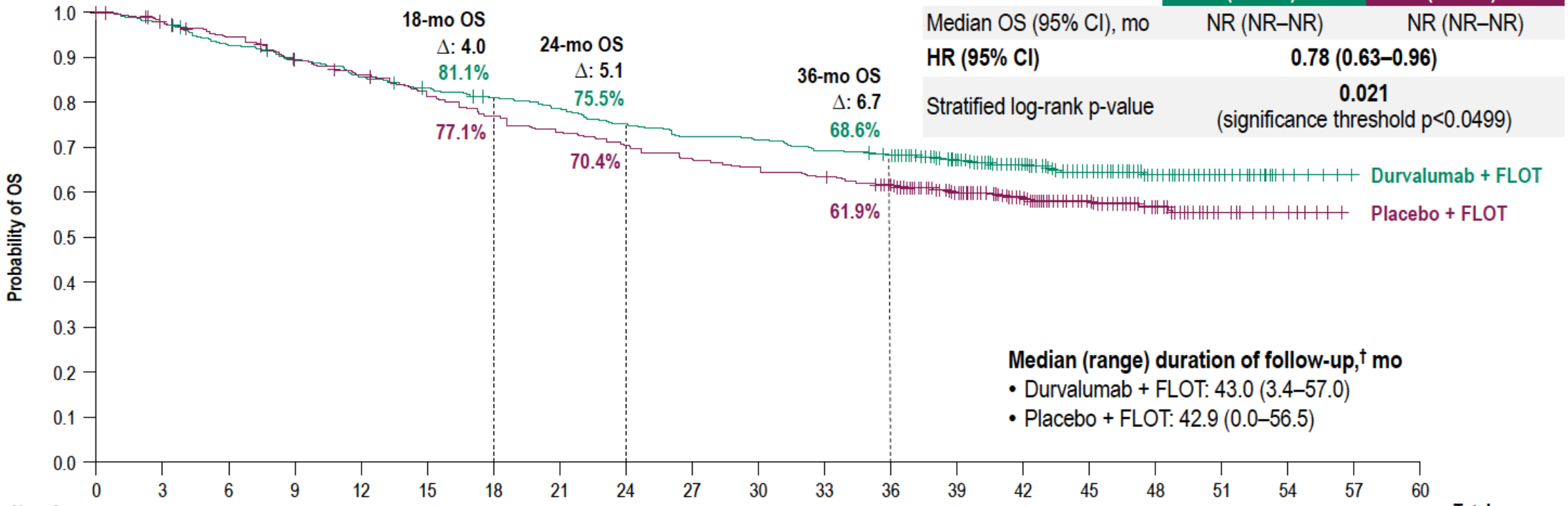
Janjigian NEJM 393: 217; 2025

Janjigian ASCO 2025;Abstract LBA5

Final OS

Durvalumab + FLOT demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo + FLOT in the intention to treat population

	Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Median OS (95% CI), mo	NR (NR–NR)	NR (NR–NR)
HR (95% CI)	**0.78 (0.63–0.96)**	
Stratified log-rank p-value	**0.021** (significance threshold p<0.0499)	



Median (range) duration of follow-up,† mo

- Durvalumab + FLOT: 43.0 (3.4–57.0)
- Placebo + FLOT: 42.9 (0.0–56.5)

No. of participants at risk																					Total no. of events
Durvalumab + FLOT	474	464	438	422	403	389	377	367	351	338	334	323	316	255	182	112	71	29	6	1	0	160
Placebo + FLOT	474	457	439	414	395	374	355	338	324	310	298	293	278	221	167	99	61	23	7	0	0	192

*Intention to treat analysis set (all randomised participants, regardless of treatment received). †In censored participants.
Data cut-off: 01 September 2025. OS maturity: 37.1%. Events were defined as time from randomisation until the date of death due to any cause. The HR and its CI were estimated from a Cox proportional hazards model, adjusted for geographic region, clinical lymph node status, and PD-L1 expression status.
The CI for the HR was calculated using a profile likelihood approach. An HR <1 favours durvalumab + FLOT. The two-sided p-value was calculated using a stratified log-rank test adjusting for geographic region, clinical lymph node status, and PD-L1 expression status.
CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1.

Josep Tabernero

MATTERHORN Study

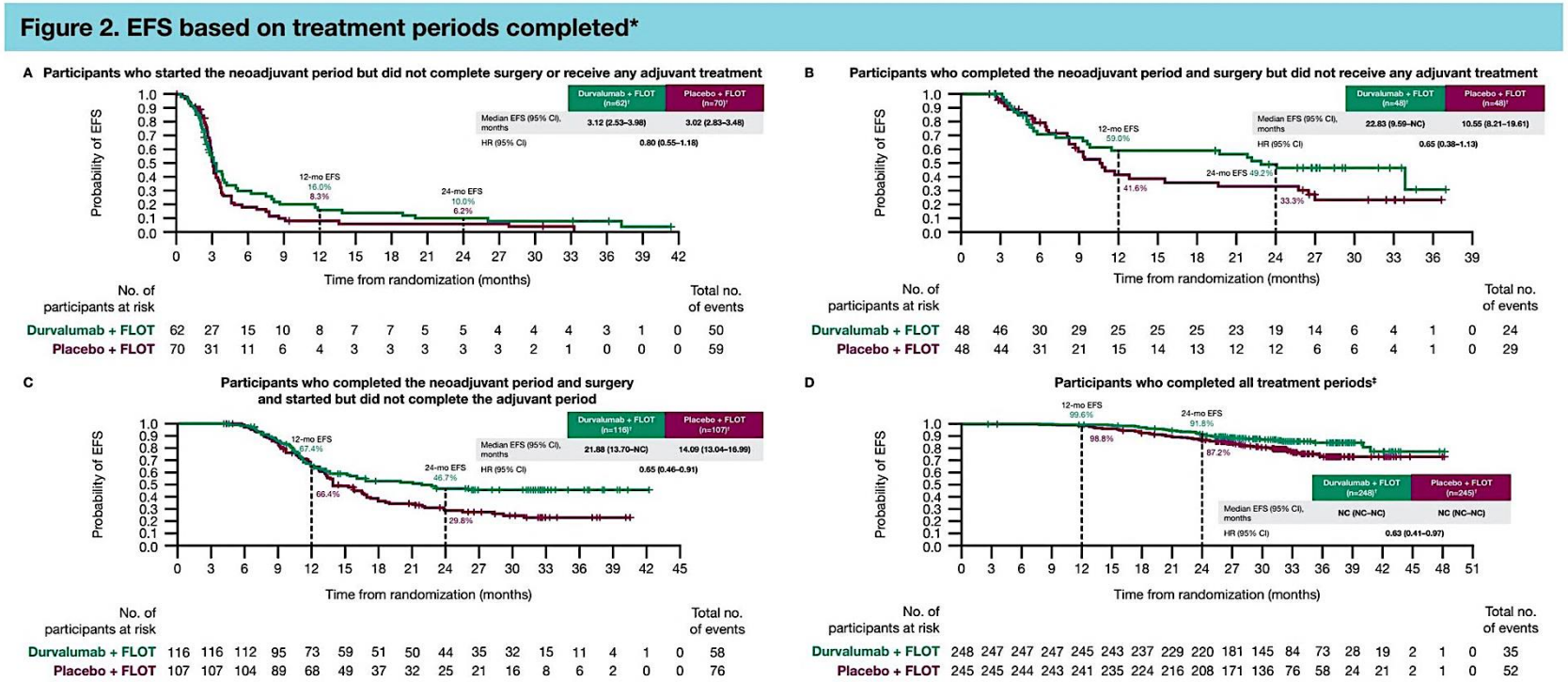
Tabernero ESMO 2025: LBA81

BERLIN 2025 ESMO congress

MATTERHORN UPDATE ASCO 2026: Abstract 470

No Surgery

No Adjuvant



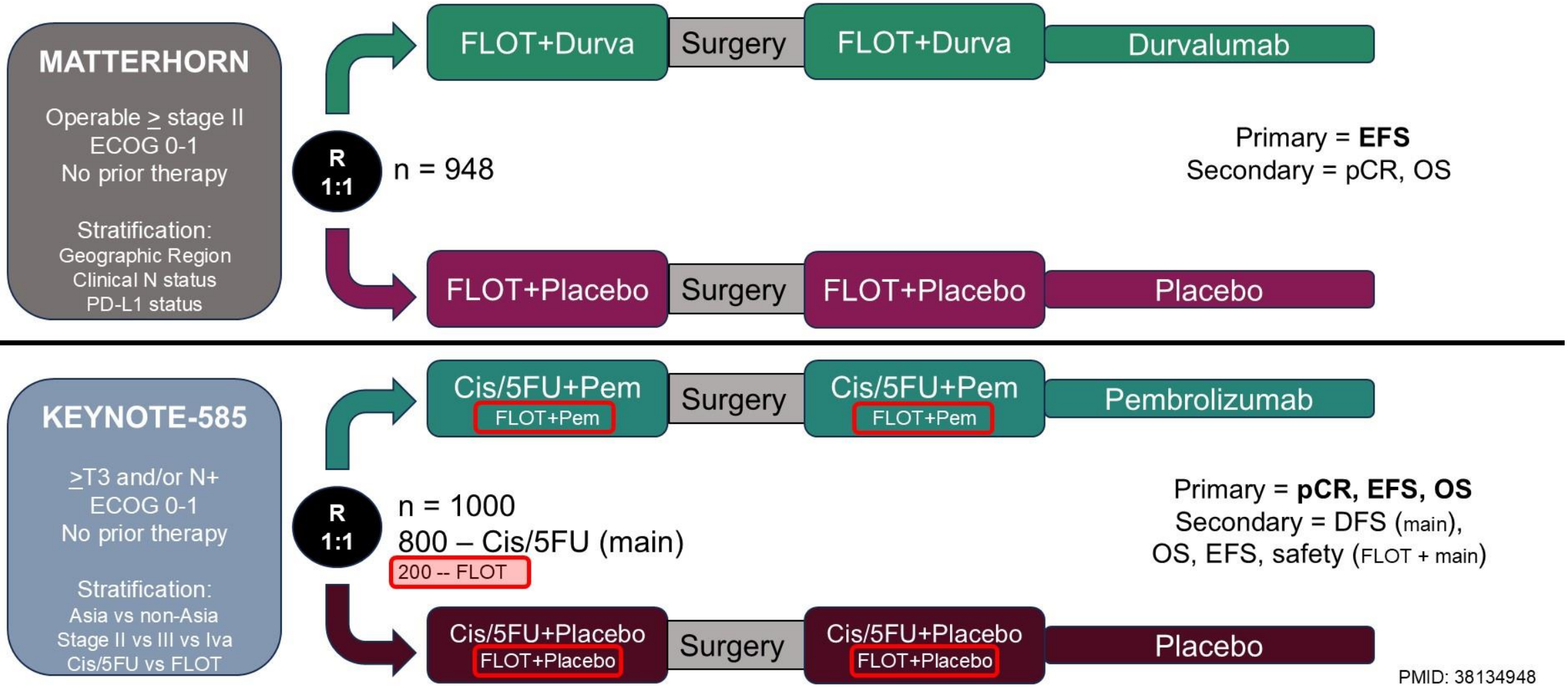
Some Adjuvant

All Adjuvant

- Greatest EFS in patients completing all planned pre and postoperative therapy
- Inferior EFS in patients receiving no or some adjuvant therapy
- Durvalumab EFS superior to placebo all patient groups

Wainberg Z et al. ASCO 2026;Abstract 4070

MATTERHORN In the Perioperative ICI Landscape



PMID: 38134948

KEYNOTE 585: EFS and OS: Main Cohort (FP) and Combined Cohort (+ FLOT)

FP

FP + FLOT

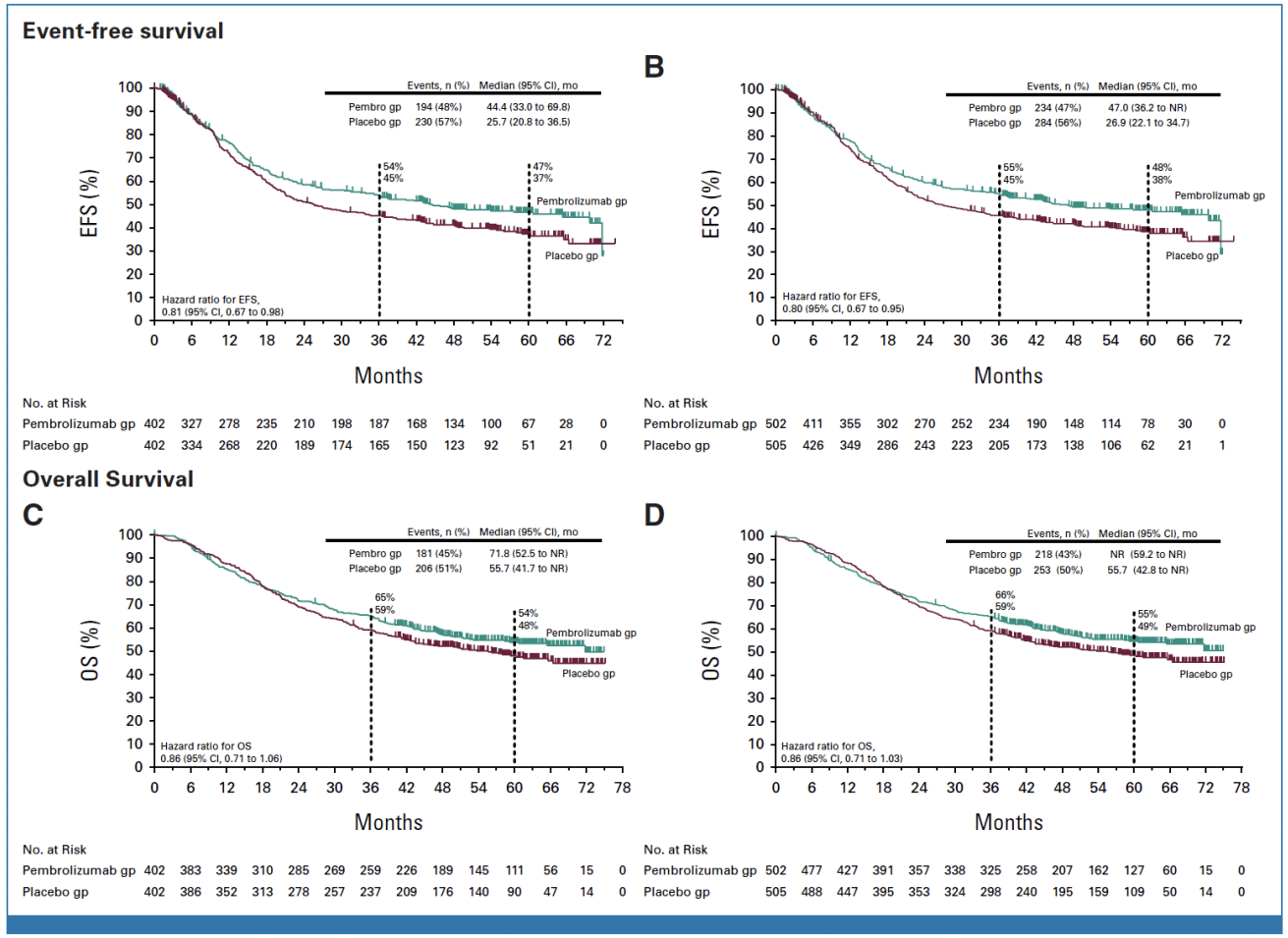


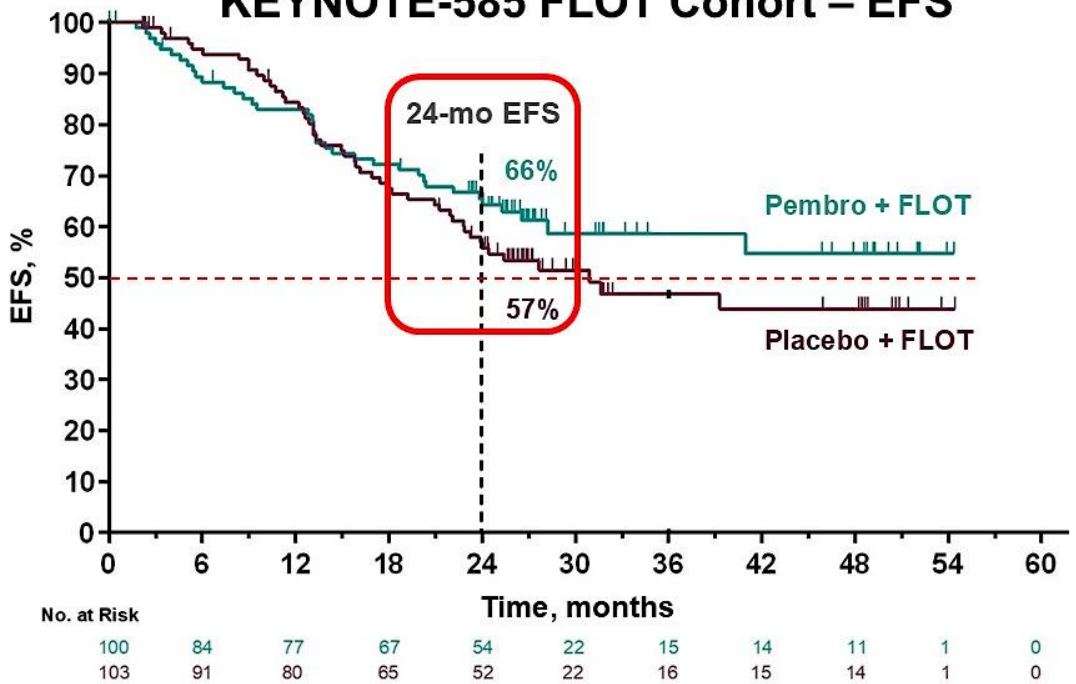
FIG 1. Kaplan-Meier estimates of EFS by investigator (A, B) and OS (C, D) in the main cohort and main plus FLOT cohorts at final analysis. Tick marks represent data censored at the time of last imaging assessment. Event-free survival was based on RECIST version 1.1 as assessed by investigator. EFS, event-free survival; HR, hazard ratio; NR, not reached; OS, overall survival.

- EFS numerically superior for pembro + FP (25.7-44.4 months), NS (HR 0.81)
- OS numerically superior for pembro + FP (55.7-71.8 months), NS (HR 0.86
- FLOT + CF: EFS (HR 0.80) and OS (HR 0.86) not changed

Shitara JCO 43: 3152; 2025

FLOT + ICI in MATTERHORN and KN-585

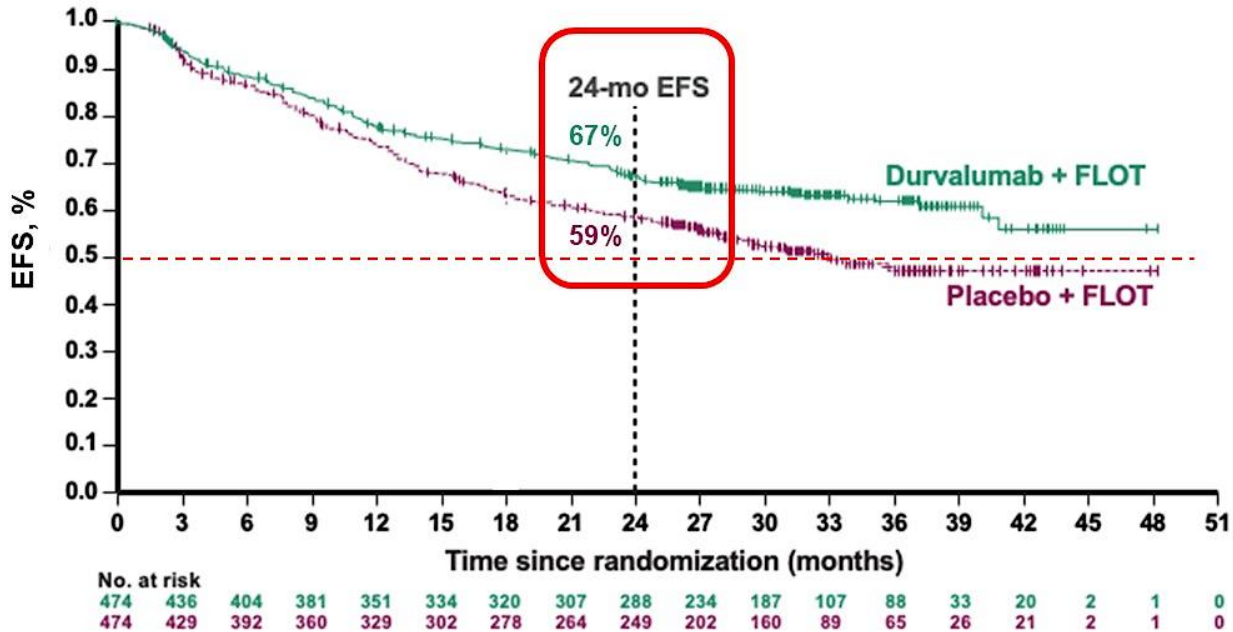
KEYNOTE-585 FLOT Cohort – EFS



GI ASCO 2024

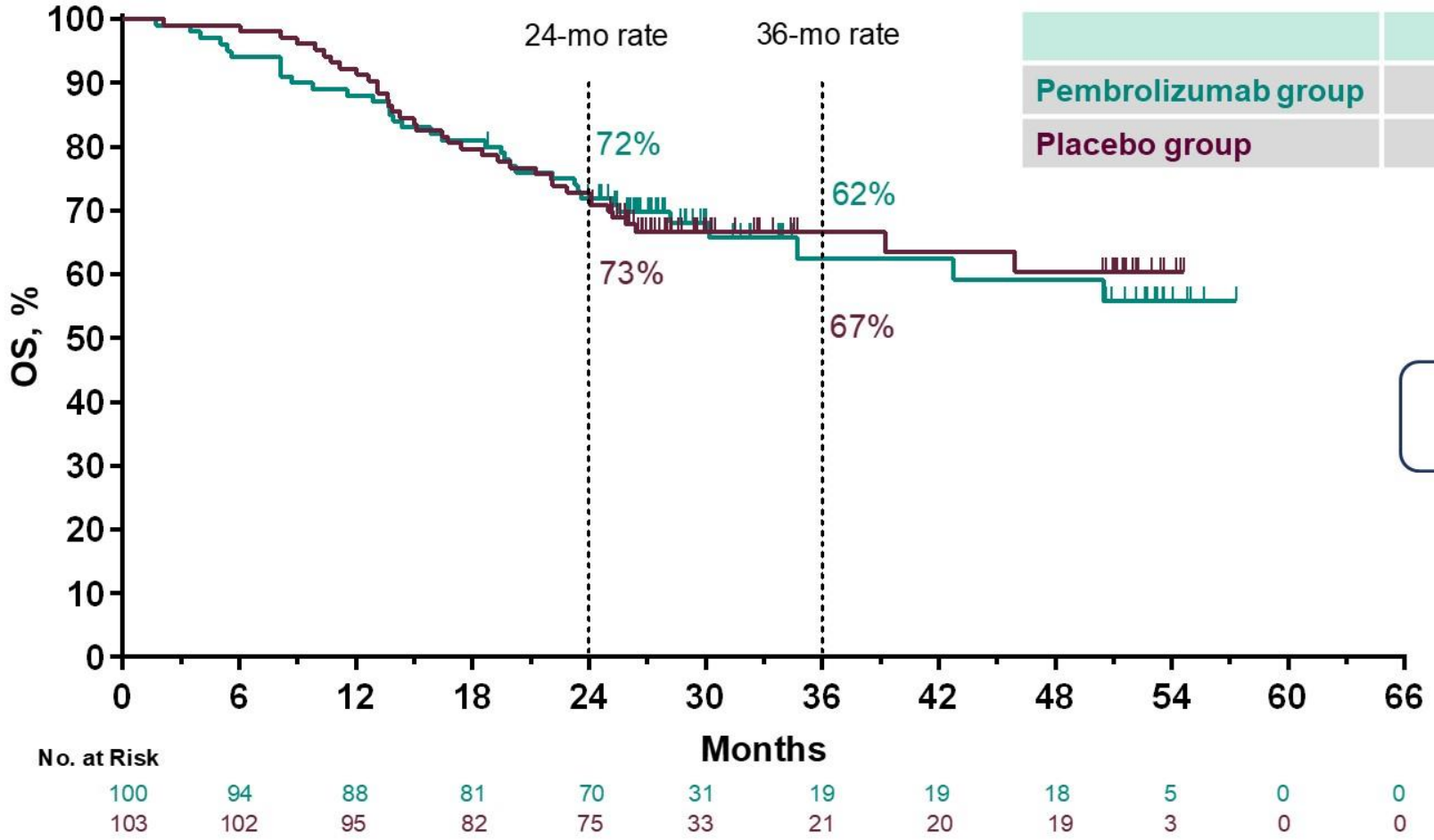
	Pembrolizumab + FLOT (n=100)	Placebo + FLOT (n=103)
Median EFS (95% CI), months	NR (28.2–NR)	30.9 (22.8–NR)
HR (95% CI)	**0.79 (0.52–1.22)**	
p-value	**NR**	

MATTERHORN – EFS



	Durvalumab + FLOT (n=474)	Placebo + FLOT (n=474)
Median EFS (95% CI), months	NR (40.7–NR)	32.8 (27.9–NR)
HR (95% CI)	**0.71 (0.58–0.86)**	
p-value	**<0.001**	

Overall Survival: FLOT Cohort



	Events	Median (95% CI), mo
Pembrolizumab group	35%	NR (34.7-NR)
Placebo group	35%	NR (45.9-NR)

HR 1.04 (95% CI, 0.66-1.66)

Data cutoff date: 09 Feb 2023. Median Follow-Up: 31.6 months (range, 24.5-57.6).

KEYNOTE 585, Al-Batran JCO GI ASCO 2024

Editorials

KEYNOTE-585 Fails While Matterhorn Succeeds in Gastric Cancer: What Lessons Can We Learn?

David H. Ilson, MD, PhD[1]

J Clin Oncol 2025;43:3141-3.

“The potential superiority of preoperative and postoperative chemotherapy over adjuvant chemotherapy alone was recently evidenced from updated results from the RESOLVE trial from China and the PRODIGY trial from Japan and Korea. Therefore, perioperative FLOT, now with the addition of durvalumab, should and will be embraced globally as the standard of care in the management of operable esophagogastric cancer.”

Ilson DH. *J Clin Oncol* 2025;43:3141-43.

MATTERHORN AND KEYNOTE 585 UPDATES

- For esophagogastric adenocarcinoma, pre- and postoperative FLOT + durvalumab is the preferred standard of care treatment.
- Completing all planned therapy if possible achieves the highest event free survival.
- Two drug perioperative 5-FU/cisplatin plus pembrolizumab failed to improve survival over chemotherapy alone despite higher rates of pathologic complete response and numeric improvements in PFS and OS.

Perioperative Therapy for HER2-Positive Esophagogastric Adenocarcinoma

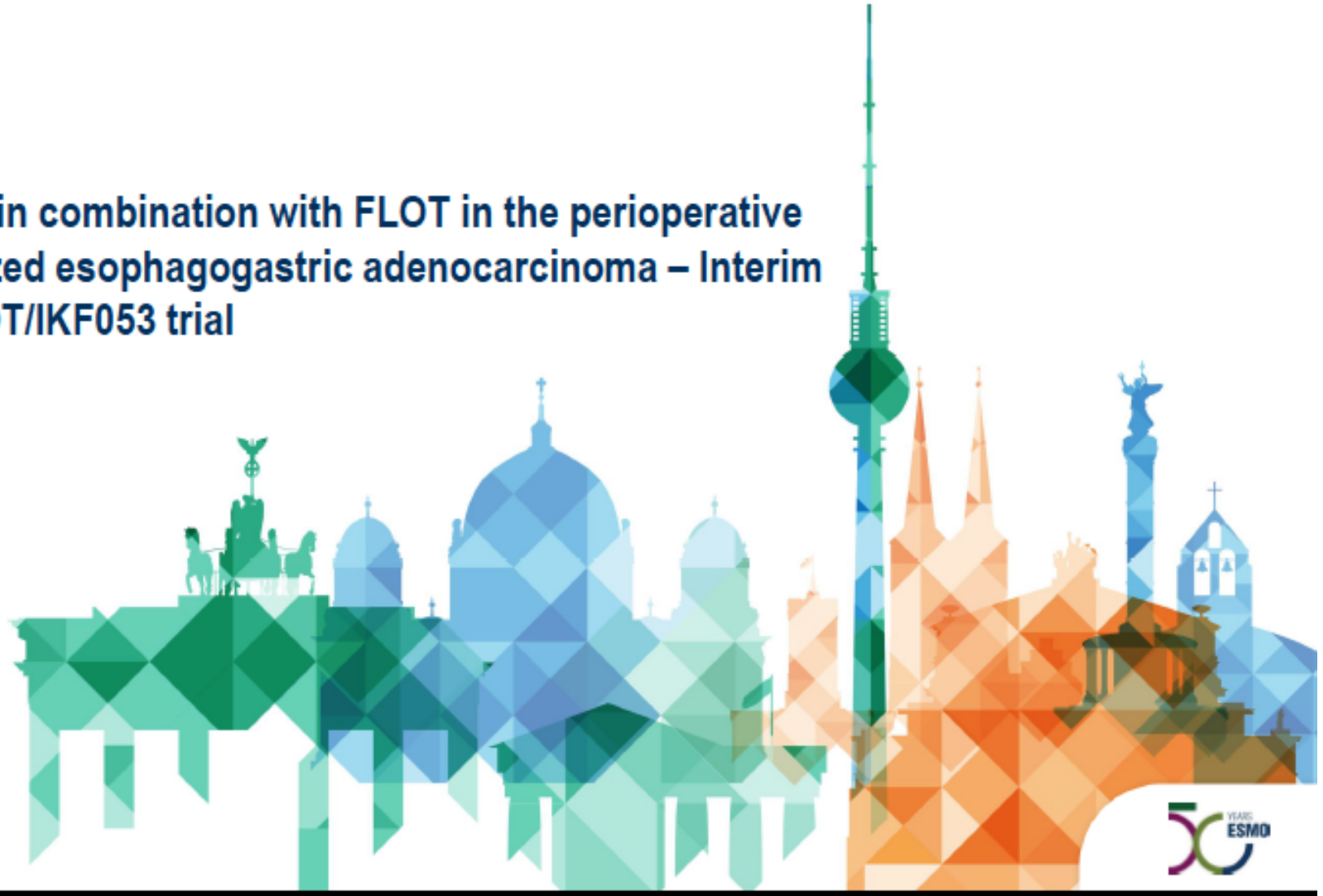
RTP Year in Review 2026

BERLIN 2025 ESMO congress

Pembrolizumab and trastuzumab in combination with FLOT in the perioperative treatment of HER2-positive localized esophagogastric adenocarcinoma – Interim Analysis of the phase II PHERFLOT/IKF053 trial

E. Goekkurt, **A. Stein**, S-E Al-Batran, N. Moosmann, T. J. Ettrich, T. Goetze, B. Gruen, N. Homann, S. Lorenzen, R.-D. Hofheinz, V. Rempel, G. Siegler, C. Müller, T. Broering, M. S. Cruz, C. Pauligk, M. Binder, **J. Tintelnot for the AIO study group (AIO STO 0321)**

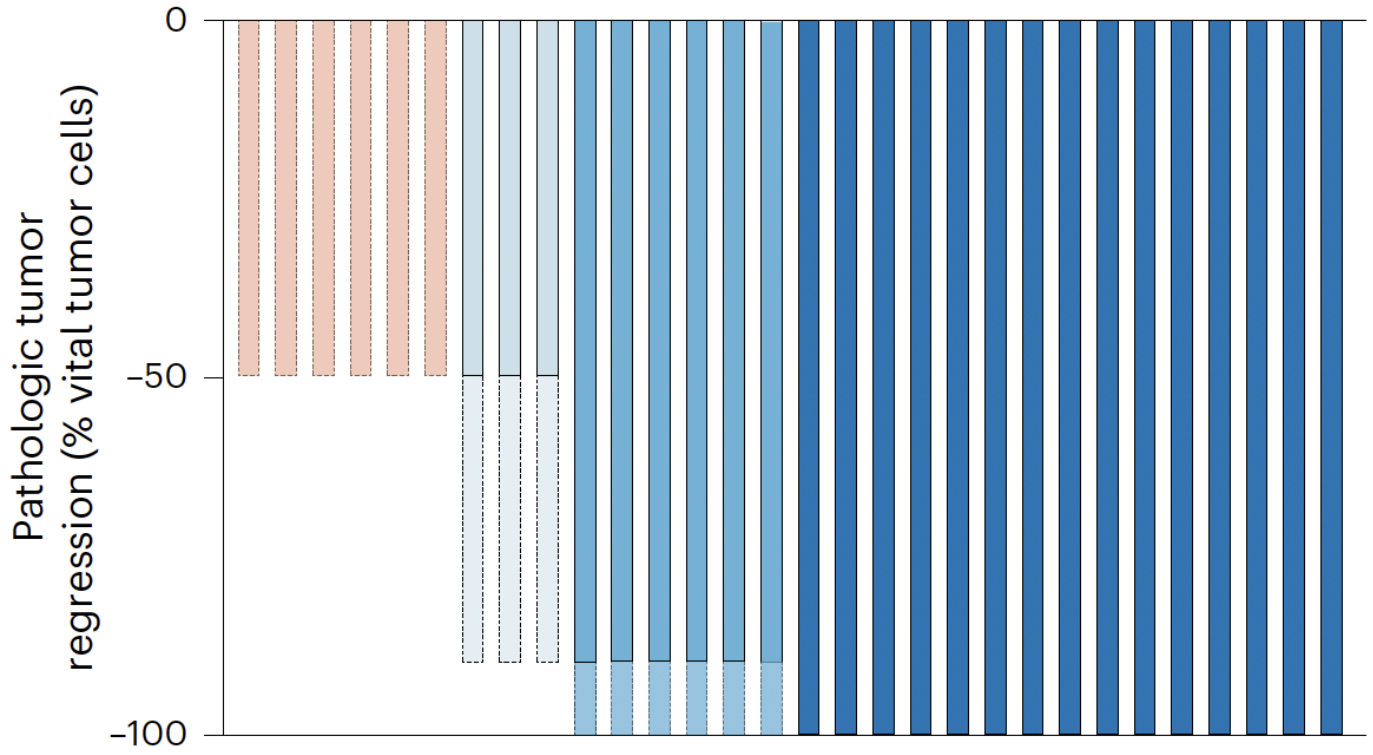
18 October 2025



Stein Nature Med 31:4197; 2025

Pathological response

All patients who consented to surgery underwent R0 resection (n=30)

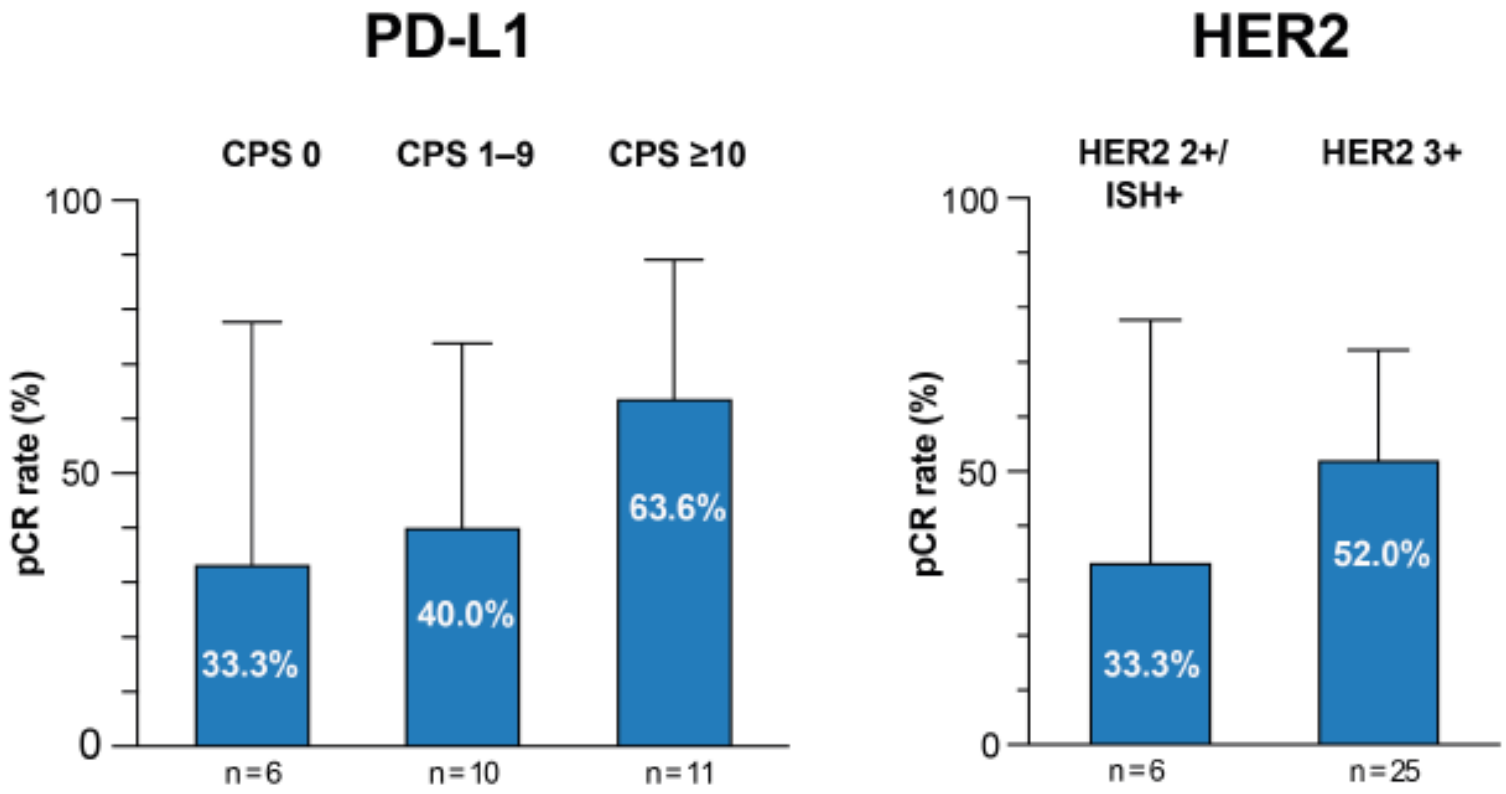


	pCR	pSR	pPR	pMR	NA
ITT, *n*=31	*n*=15, 48.4% (30.2–66.9)	*n*=6, 19.4% (7.5–37.5)	*n*=3, 9.7% (2.0–25.8)	*n*=6, 19.4% (7.5–37.5)	*n*=1, 3.2%

Stein Nature Med 31:4197; 2025

Pathological response

Subgroups



Stein Nature Med 31:4197; 2025

PERIOPERATIVE THERAPY OF HER2 + ESOPHAGOGASTRIC ADENOCARCINOMA

- The combination of FLOT, pembrolizumab and trastuzumab achieves a remarkably high rate of pathologic complete response.
- Trials may consider nonoperative management in clinical complete responders to this or similar regimens.
- Evaluation of perioperative therapy with novel and potentially more effective HER2 agents, including zanidatamab and trastuzumab deruxtecan, combined with immunotherapy, is warranted.

Long-Term Follow-Up of M1 Trials of Immunotherapy + Chemotherapy

2026 ASCO ANNUAL MEETING

Nivolumab plus ipilimumab combined with chemotherapy as first-line treatment for HER2-negative unresectable advanced or recurrent gastric/gastroesophageal junction cancer: A randomized phase 3 trial (ATTRACTION-6)

Do-Youn Oh[1*], Yoon-Koo Kang[2], Kohei Shitara[3], Li-Tzong Chen[4], Narikazu Boku[5], Min-Hee Ryu[2], Sun Young Rha[6], Jong Gwang Kim[7], Jin Young Kim[8], Sang Cheul Oh[9], Keun-Wook Lee[10], Jeeyun Lee[11], Akihito Kawazoe[3], Hirokazu Shoji[12], Kensei Yamaguchi[13], Sung Yong Oh[14], Li-Yuan Bai[15], Ming-Huang Chen[16], Jen-Shi Chen[17], Kun-Huei Yeh[18], ATTRACTION-6 Study Group

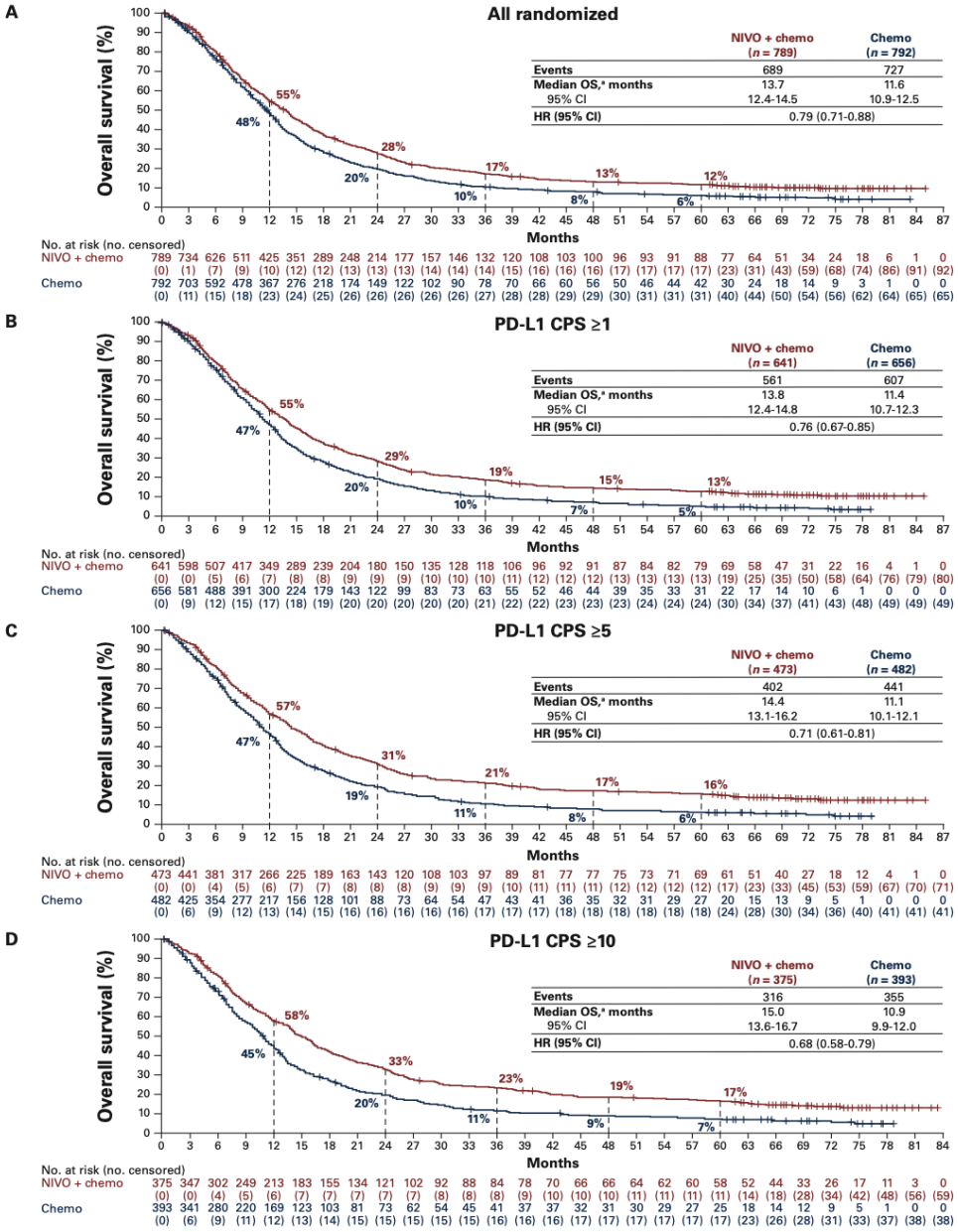
[1]Seoul National University College of Medicine, Seoul, Republic of Korea, [2]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [3]National Cancer Center Hospital East, Kashiwa, Japan, [4]Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [5]Institute of Medical Science Hospital, University of Tokyo, Tokyo, Japan, [6]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea, [7]Kyungpook National University, Daegu, Republic of Korea, [8]Keimyung University Dongsan Medical Center, Daegu, Republic of Korea, [9]Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea, [10]Seoul National University College of Medicine, Seoul, South Korea; Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [11]Samsung Medical Center, Seoul, Republic of Korea, [12]National Cancer Center Hospital, Tokyo, Japan, [13]Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan, [14]Dong-A University Hospital, Busan, Republic of Korea, [15]China Medical University Hospital, Taichung, Taiwan, [16]Taipei Veterans General Hospital, Taipei, Taiwan, [17]Chang Gung Memorial Hospital at Linkou and Chang Gung University, Tao-Yuan, Taiwan, [18]National Taiwan University Hospital, Taipei, Taiwan.

*Presenting

ATTRACTION 6

- Combined ipilimumab and nivolumab added to chemotherapy failed to improve overall survival over chemotherapy alone.
- Adding single agent checkpoint inhibitors (pembrolizumab, nivolumab, or tislelizumab) remains the standard of care
- Treatment with immune checkpoint inhibitors should be limited to tumors testing CPS or TAP > = 1%.

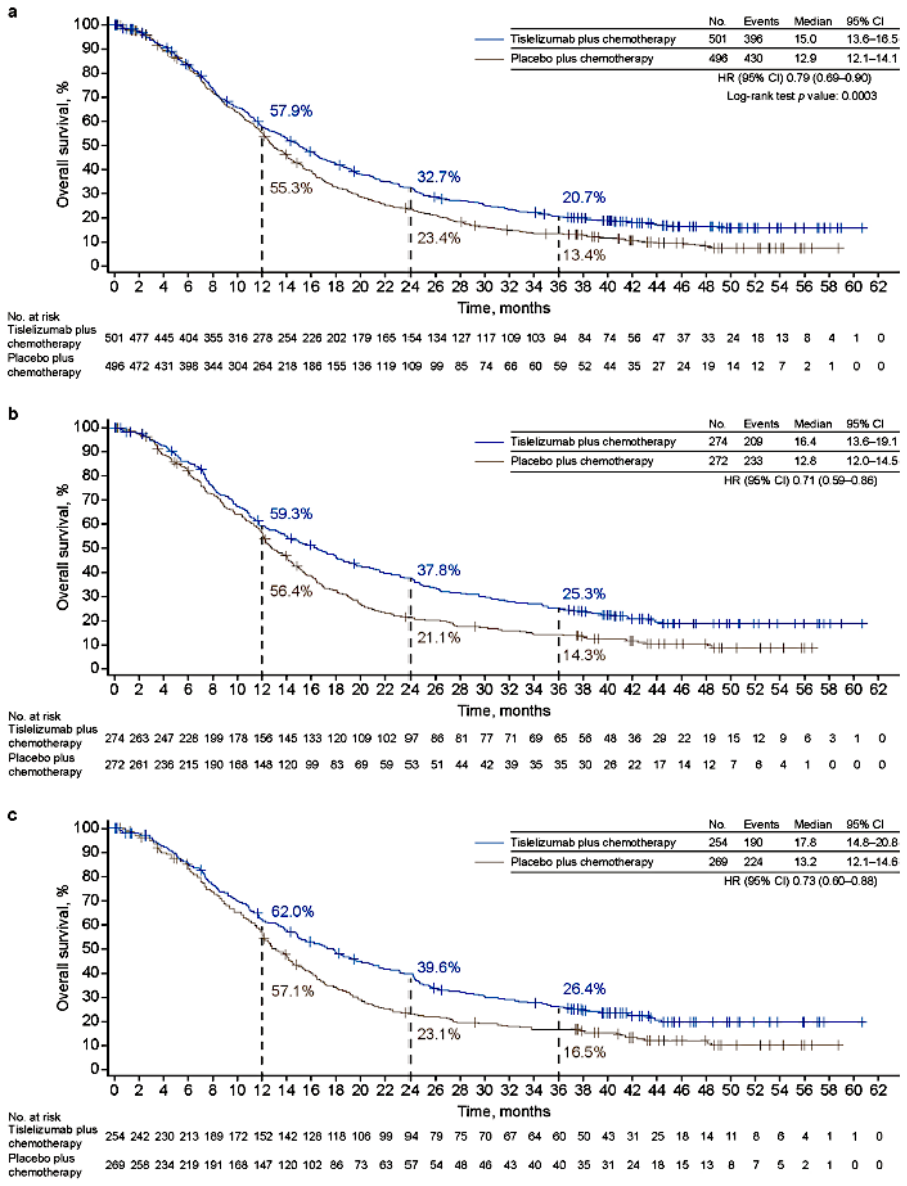
CHECKMATE 649 Long Term Follow up



- Improved long term survival with Nivolumab + Chemo
- Chemo alone 5-year OS 5%
- + Nivolumab
  - All patients: 12%
  - CPS > = 1% 13%
  - CPS > = 5% 18%
  - CPS > = 10% 17%

Janjigian Ann Oncol 37: 787; 2026

RATIONALE-305 Long Term Follow Up



- Improved long term overall survival with Tislelizumab + Chemo
- Chemo alone 3-year OS 14.3%
- + Tislelizumab
  - All patients: 20.7%
  - TAP > = 5% 25.3%
  - CPS > = 5% 26.4 %

Cruz-Correa Adv Ther 43: 165: 2026

KEYNOTE 590 Long Term Follow Up: Esophageal Adenocarcinoma and SCC

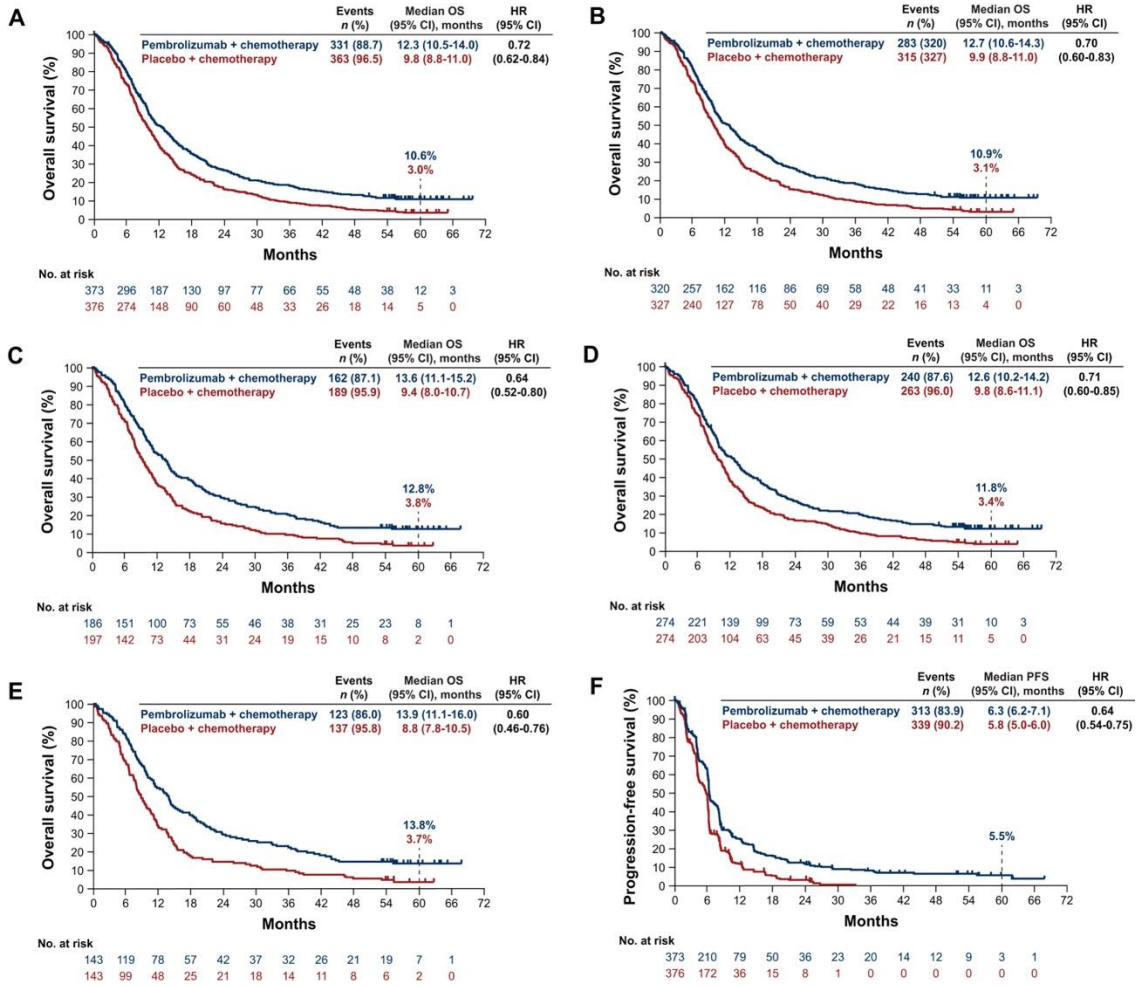


Figure 2 Efficacy outcomes. (A-E) Kaplan–Meier estimates of overall survival in (A) all randomly assigned participants in the intention-to-treat population, (B) participants with PD-L1 CPS ≥1, (C) participants with PD-L1 CPS ≥10, (D) participants with ESCC, and (E) participants with ESCC PD-L1 CPS ≥10. (F-I) Kaplan–Meier estimates of progression-free survival in (F) all randomly assigned participants in the intention-to-treat population, (G) participants with PD-L1 CPS ≥1, (H) participants with PD-L1 CPS ≥10, and (I) participants with ESCC. The intention-to-treat population included all randomly assigned participants. CI, confidence interval; CPS, combined positive score; ESCC, esophageal squamous-cell carcinoma; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

- Improved long term overall survival with Pembrolizumab + Chemo
- Chemo alone 5-year OS 3.0%
- + Pembrolizumab
  - All patients: 10.6%
  - CPS > = 1%, 10.9%
  - CPS > = 10%, 12.8 %

Metges ESMO Open 10: 1; 2025

KEYNOTE 811 Long Term Follow Up; ASCO 2026

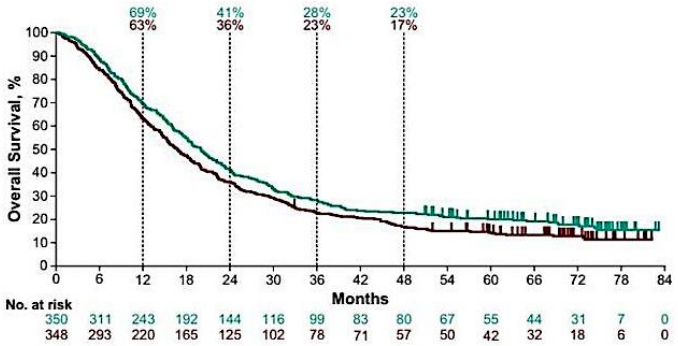
Data are n (%), unless otherwise specified.

Efficacy

Figure 3. Kaplan-Meier estimates of OS in the (A) ITT and (B) PD-L1 CPS ≥1 populations

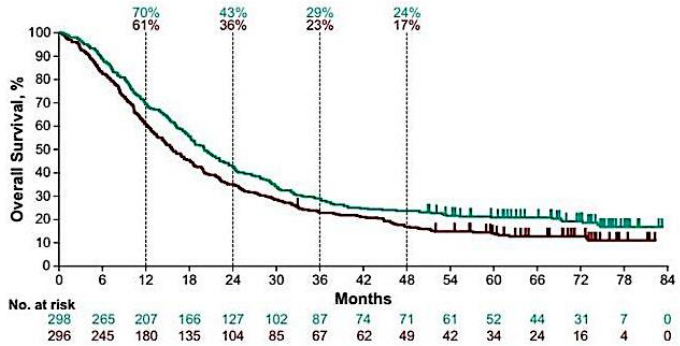
A

	OS, median (95% CI), months	HR (95% CI)
Pembrolizumab group	20.0 (17.8-22.1)	0.81 (0.69-0.95)
Placebo group	16.8 (14.9-18.7)	



B

	OS, median (95% CI), months	HR (95% CI)
Pembrolizumab group	20.1 (17.9-22.9)	0.79 (0.66-0.94)
Placebo group	15.7 (13.5-18.5)	



- Improved long term overall survival with Pembrolizumab + Chemo/Tras
- Chemo/Tras alone 4-year OS 17.0%
- + Pembrolizumab
  - All patients: 23.0%
  - CPS > = 1%, 24.0%
  - CPS < 1%: survival detriment

Kawazoe ASCO 2026 Abstract 4040

LONG TERM FU OF M1 TRIALS OF IMMUNOTHERAPY + CHEMOTHERAPY

- All trials indicate a significant improvement in long term survival with front line addition of immunotherapy (tislelizumab, pembrolizumab, or nivolumab) to chemotherapy
- Benefits are limited to cancers testing CPS positive with regulators stipulating a cutoff of 1% or higher for positive scores.

Year in Review:
Gastroesophageal Cancers

INTRODUCTION: Biomarker Evaluation in Localized and Metastatic Disease

MODULE 1: Role of Immune Checkpoint Inhibitors in the Management of Gastroesophageal Cancers — Dr Ilson

MODULE 2: Other Available Therapeutic Approaches — Dr Shitara

RTP Year in Review 2026

Year in Review
(gastric/GEJ disease)

Kohei Shitara

Department of Gastroenterology

National Cancer Center Hospital East (NCCHE)

What we will cover today

Section A · HER2-positive G/GEJ

From "trastuzumab + chemo" to dual-epitope + ADC

1L — **HERIZON-GEA-01** primary + PD-L1 subgroup
Elimova ASCO GI 2026 · Rha ASCO 2026 · Shitara NEJM 2026

2L — **DESTINY-Gastric04** T-DXd vs ram/pac
Shitara NEJM 2025 / ASCO GI 2026 update

1L — **DESTINY-Gastric03** safety (Arms D, F, Part 4)
Janjigian ASCO 2025 poster 4022

TiP — **DESTINY-Gastric05 (T-DXd+Pembro+Cape)**
Shitara ASCO 2025 poster
ARTEMIDE-Gastric01 (rilvegostomig + T-DXd)
Xu ASCO 2025 poster

Section B · CLDN18.2-positive G/GEJ

Antibody vs. ADC: two ways to drug claudin 18.2

1L — **SPOTLIGHT & GLOW** pivotal context (zolbetuximab + chemo)
Shitara Lancet 2023 · Shah Nat Med 2023

1L — **ILUSTRO** zolb + mFOLFOX6 + nivo, Cohort 4
Shitara ASCO GI 2026 · Nat Med 2026

TiP — **LUCERNA** zolb + pembro + chemo (CPS ≥1)
Shitara ASCO GI 2026

ADC — **CLARITY-PanTumor01** & **CLARITY-Gastric01**
Sonesitatug vedotin (Sone-Ve / AZD0901)

Section C · ESCC & synthesis

A new bispecific ADC in ESCC, and the cross-cutting themes

2L+ — **Iza-bren in r/m ESCC**
Lu Z, ASCO 2026 abs 4008 · BL-B01D1-305

Resistance to Trastuzumab in Gastric Cancer

Why HER2-targeted therapy fails in gastric cancer: multiple escape routes

Intratumoral heterogeneity/HER2 Loss

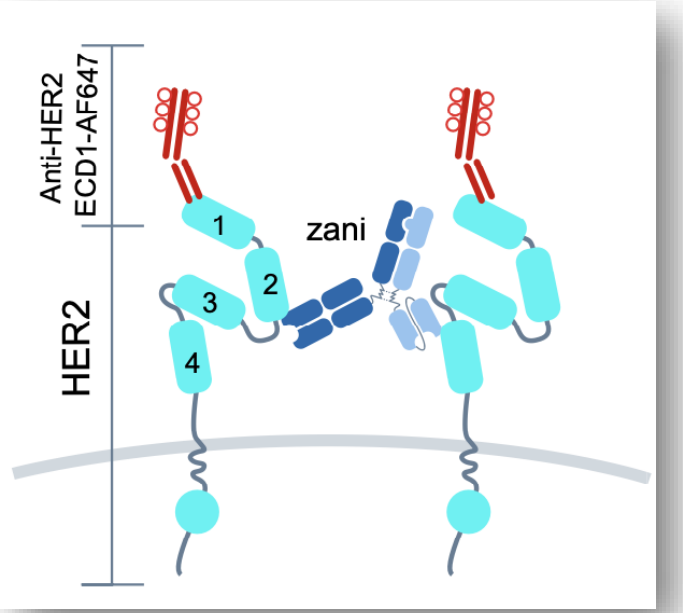
- HER2 heterogeneity is more common in gastric cancer than breast cancer
- Around 50% of patients have reduced or lost HER2 expression after chemotherapy plus trastuzumab

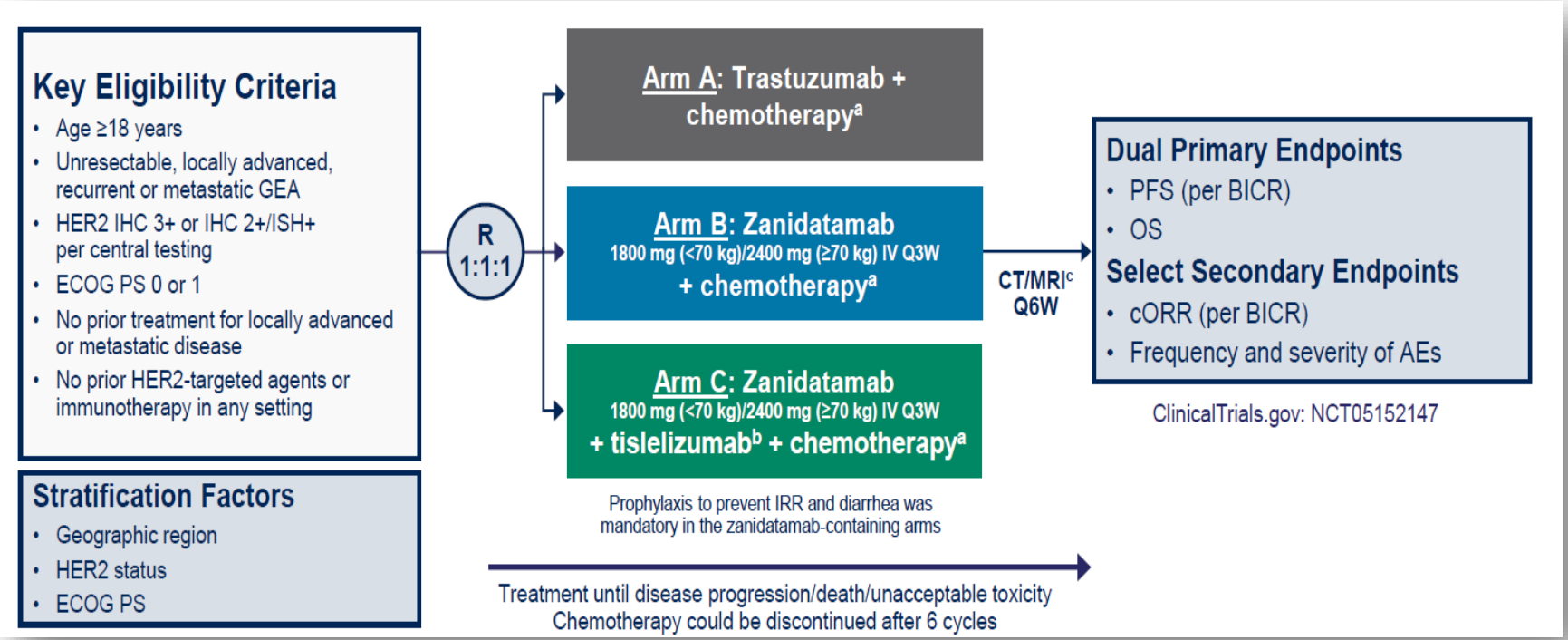
Heterodimer formation between HER2 and EGFR or HER3

- Single-agent trastuzumab cannot completely block these pairings

Trial 1: HERIZON-GEA-01 Phase III Trial of Zanidatamab + Chemotherapy ± Tislelizumab

Trial 1: HERIZON-GEA-01 Phase 3 of zanidatamab ± tisle + chemo





- Forms trans-bridging HER2 clusters with topology disruption
- Heterodimer blockade
- Complement dependent cytotoxicity

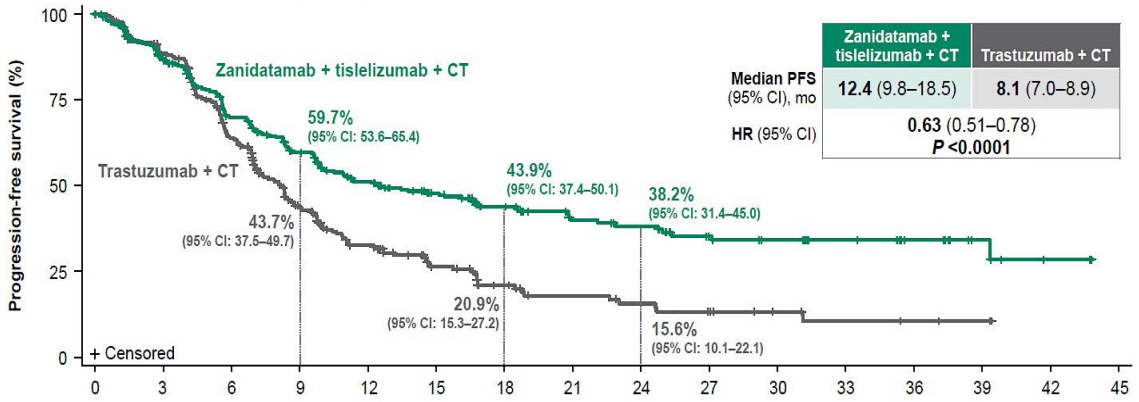
- N=914 pts (Dec 2021-Feb 2025)
  - ➢ Comparison with ToGA regimen
  - ➢ KN 811 approval by FDA in May 2021 and EMA in Aug 2023
- Asia 53%, IHC3+ 83%, TAP>1% 60%, CapeOX 90%
- Ongoing treatment: 29% (triplet), 23% (doublet) vs 12% (control)

Shitara K, et al. NEJM 2026; Elimova E, et al. ASCO-GI 2026

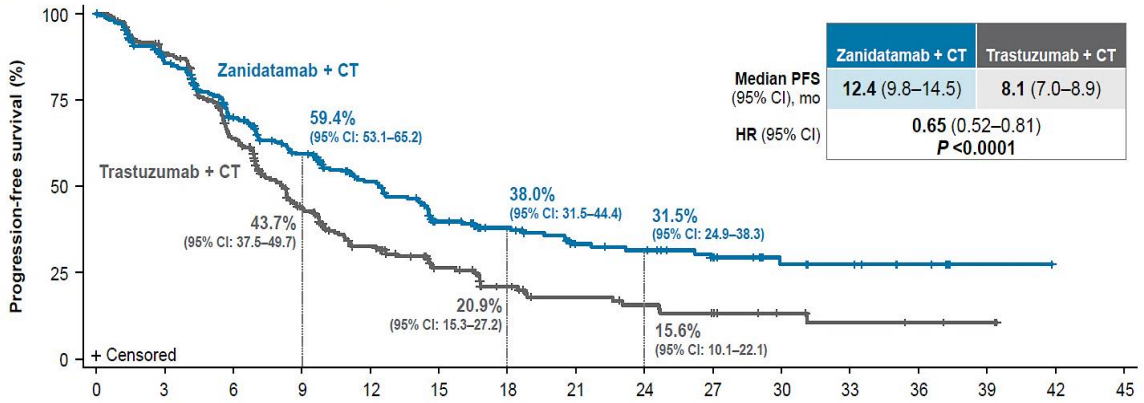
Trial 1: HERIZON-GEA-01 Phase 3 of zanidatamab ± tisle + chemo

Primary Endpoint: PFS per BICR

Statistically significant and clinically meaningful improvement in PFS with zanidatamab + tislelizumab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



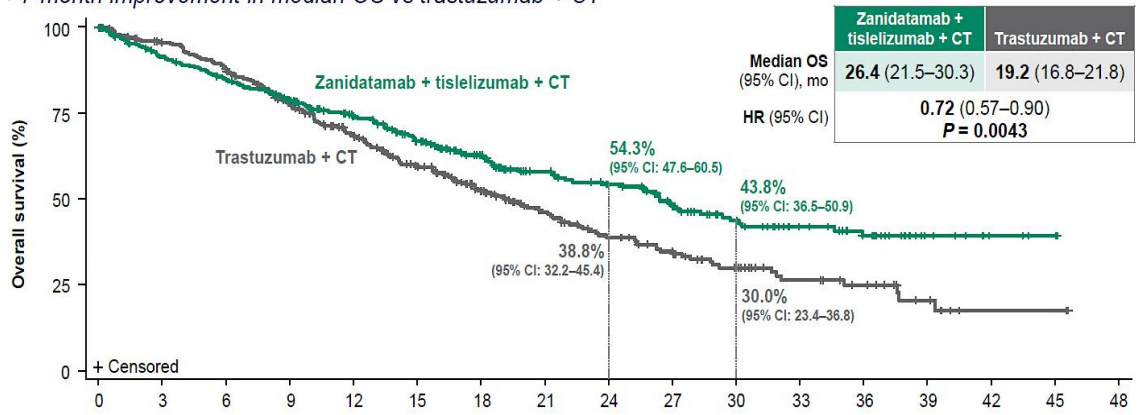
Statistically significant and clinically meaningful improvement in PFS with zanidatamab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



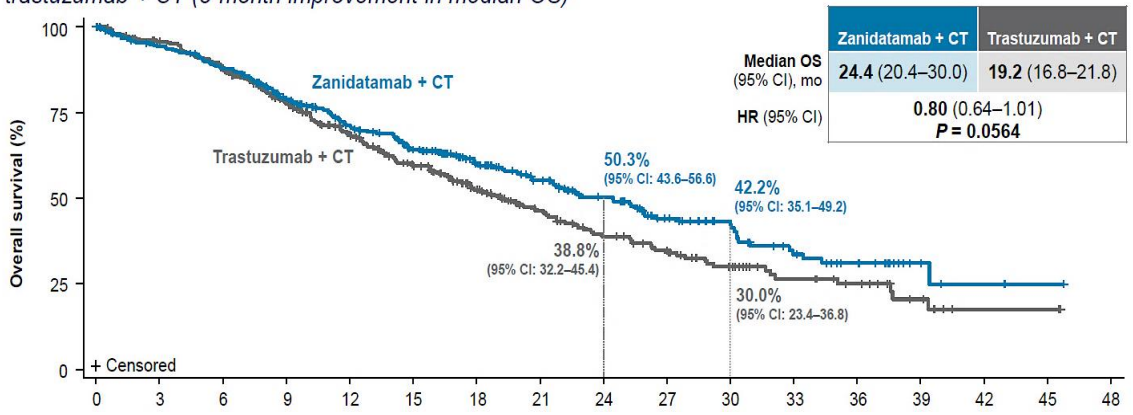
- PFS improved with both chemo+Zani+Tisle and chemo+Zani
  - mPFS+4.3 ms (HR 0.63 with triplet and 0.65 with doublet)
  - ORR 70.7%/69.6%/65.7%
  - mDOR 20.7 / 14.3 / 8.3 ms

Primary Endpoint: Overall Survival

Zanidatamab + tislelizumab + CT demonstrated a statistically significant and clinically meaningful OS benefit with a >7-month improvement in median OS vs trastuzumab + CT



At this interim analysis, there was a strong trend toward significance for OS favoring zanidatamab + CT vs trastuzumab + CT (5-month improvement in median OS)

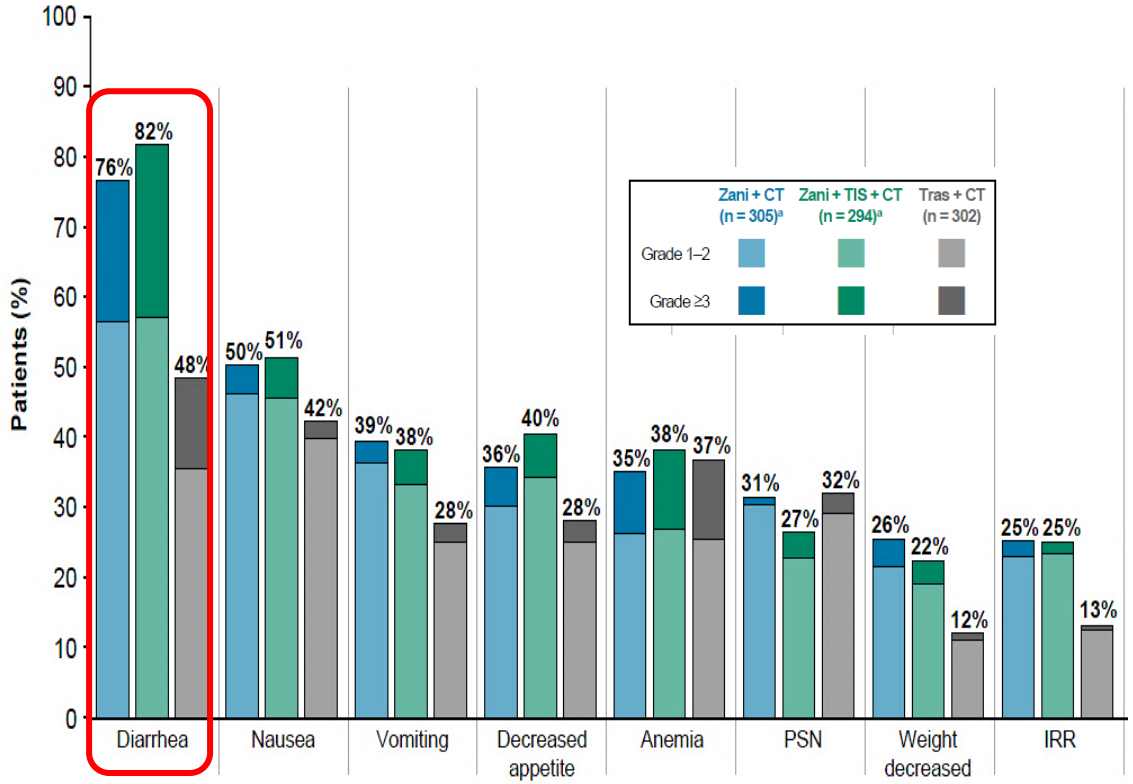


- OS improved by chemo+Zani+Tisle: mOS 26.4 (+7.2ms, HR 0.72)
- OS not conclusive by chemo+Zani; mOS 24.4 (+5.2ms, HR 0.80)
  - Follow up still ongoing for next analysis

Shitara K, et al. NEJM 2026; Elimova E, et al. ASCO-GI 2026

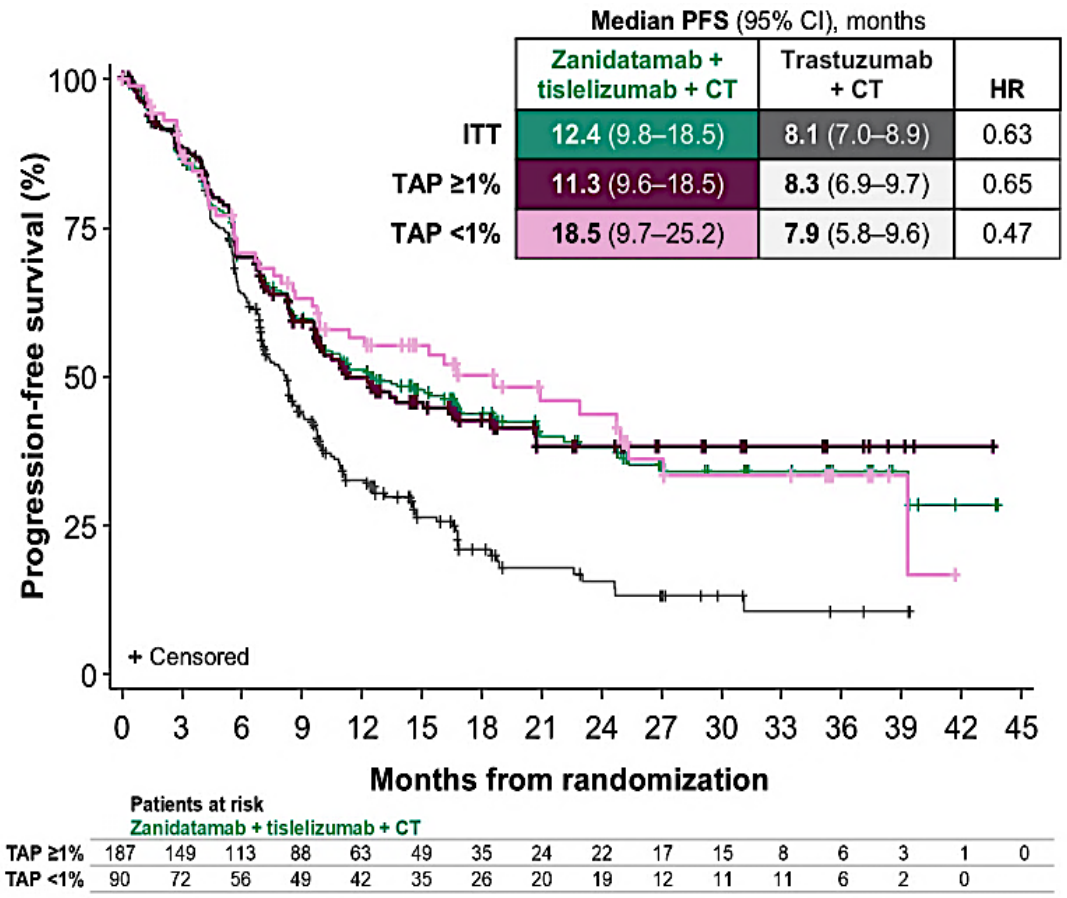
Trial 1: HERIZON-GEA-01 Phase 3 of zanidatamab ± tisle + chemo

Common TRAEs



- Diarrhea: +30% increase (+10% ≥Grade3)
- Occurred early: 7 days
- Loperamide prophylaxis mandatory for 7days in cycle 1
- Zani discontinuation by diarrhea: 4%

PFS subgroup by PDL1 TAP



- Consistent benefit in most of the subgroups
- Benefit regardless of PD-L1 status

Shitara K, et al. NEJM 2026; Elimova E, et al. ASCO-GI 2026; Rha SY, et al. ASCO 2026 #4010

Trial 1: HERIZON-GEA-01 Phase 3 of zanidatamab ± tislelizumab + chemo

Implications

- Phase 3 study to demonstrate PFS and OS superiority of a **zanidatamab**-based regimen in 1L HER2+ G/GEJ.
- Zanidatamab + chemotherapy improved PFS, supporting the biological advantage of **biparatopic HER2** targeting.
- Addition of **tislelizumab** further improved OS, with more durable response
- Benefit appeared consistent across PD-L1 subgroups, including TAP or CPS<1%.
- Diarrhea management is essential
- Comparator caveat: the control arm did not include pembrolizumab.

Bottom line

- **Practice-changing**
- Likely to become a **new first-line** standard, pending **regulatory approval**.

Trial 2: DESTINY-Gastric04 Phase III Trial Comparing Trastuzumab Deruxtecan (T-DXd) to Ramucirumab + Paclitaxel

Trial 2: DESTINY-GC04 phase 3 comparing T-DXd vs. Ram + PTX

DESTINY-Gastric04: A Global, Multicenter, Randomized, Phase 3 Trial (NCT04704934)

Patient Population

- HER2+ (IHC 3+ or IHC 2+/ISH+)[a] GC/GEJA
- HER2 status confirmed locally or centrally[b] on a recent biopsy obtained after progression on trastuzumab
- ECOG PS 0 or 1
- No clinically active CNS metastases[c]

R 1:1

- T-DXd 6.4 mg/kg Q3W
- RAM + PTX[d]

Stratification factors

- HER2 status (IHC 3+ vs IHC 2+/ISH+)
- Geography (Asia [excluding mainland China] vs Western Europe vs mainland China/rest of world)
- Time to progression on 1L therapy (<6 months vs ≥6 months)

Primary Endpoint

- OS

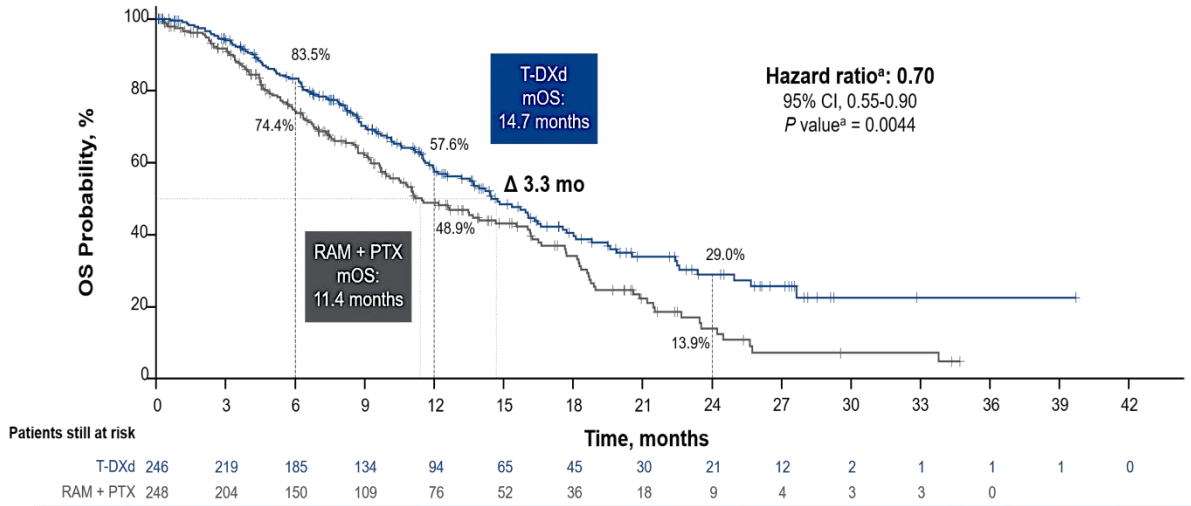
Secondary Endpoints

- PFS (INV)[e]
- Confirmed ORR (INV)[e]
- DCR (INV)[e]
- DOR (INV)[e]
- Safety

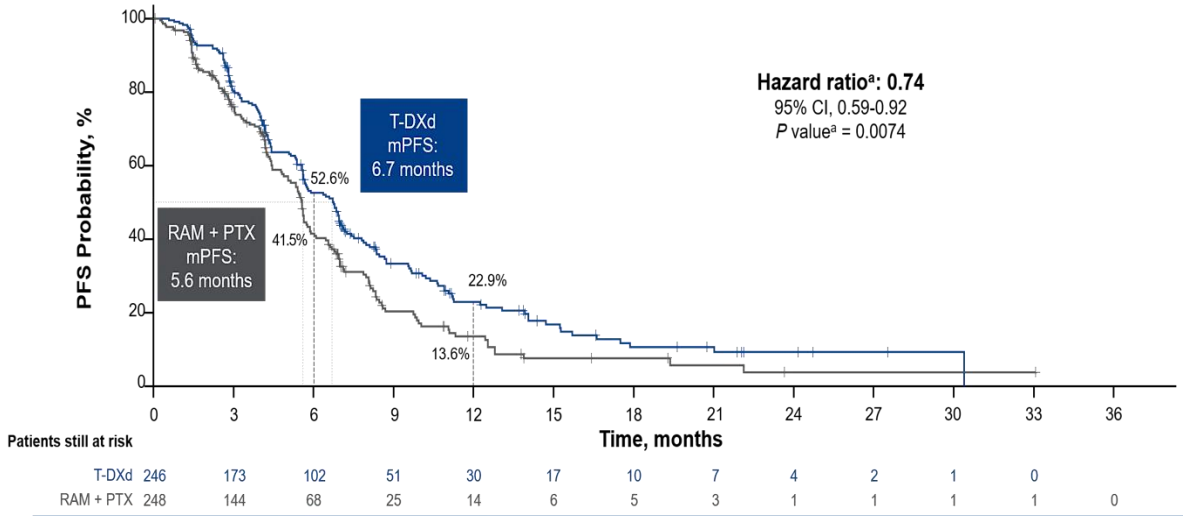
Exploratory Endpoints

- PROs[f]

	T-DXd n = 246	RAM + PTX n = 248
Confirmed ORR (95% CI),[c] %	**44.3 (37.8-50.9)**	**29.1 (23.4-35.3)**
P value[d]	0.0006	
Difference (95% CI),[e] %	15.1 (6.1-24.2)	
DOR, median (95% CI), mo	**7.4 (5.7-10.1)**	**5.3 (4.1-5.7)**
DCR (95% CI), %	**91.9 (87.7-95.1)**	**75.9 (70.0-81.2)**
Confirmed BOR, n (%)		
CR[f]	7 (3.0)	3 (1.3)
PR	97 (41.3)	66 (27.8)
SD[g]	112 (47.7)	111 (46.8)
PD	13 (5.5)	22 (9.3)
NE	6 (2.6)	35 (14.8)



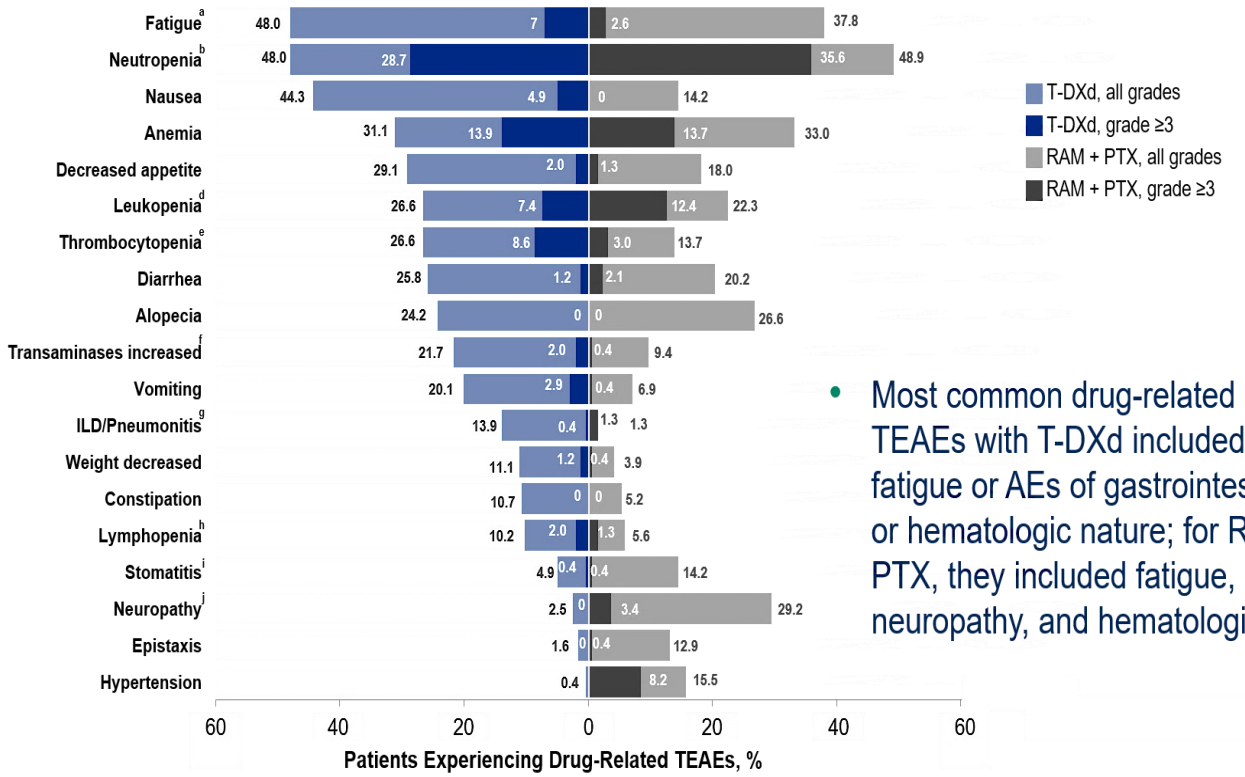
T-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with RAM + PTX in HER2+ GC/GEJA, showing a 30% reduction in risk of death



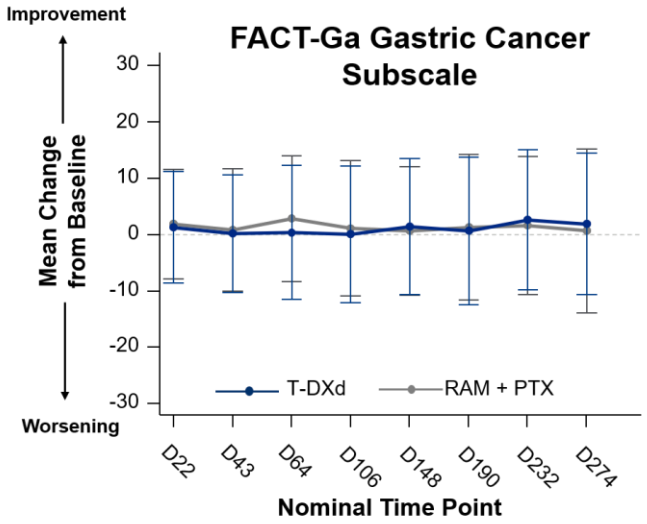
T-DXd demonstrated a statistically significant improvement in PFS compared with RAM + PTX in HER2+ GC/GEJA, showing a 26% reduction in risk of progression or death

Shitara K, et al. ASCO 2025; NEJM 2025

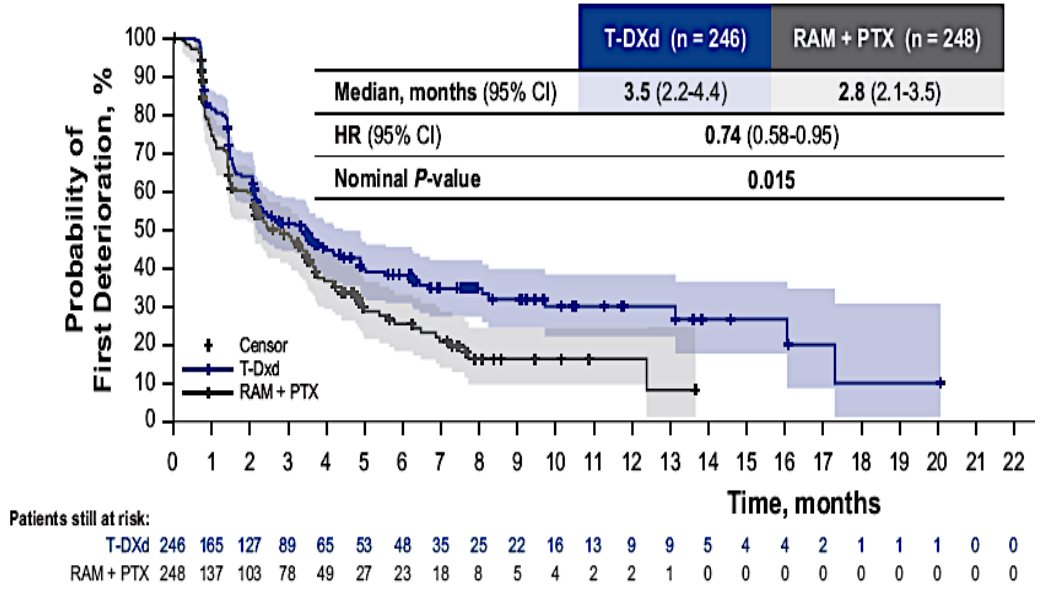
Trial 2: DESTINY-GC04 phase 3 comparing T-DXd vs. Ram + PTX



- Most common drug-related TEAEs with T-DXd included fatigue or AEs of gastrointestinal or hematologic nature; for RAM + PTX, they included fatigue, neuropathy, and hematologic AEs



C) FACT-G total score[c]



- Drug related SAE: 18% vs 18%
- ILD: 14% vs 1.3 % (grade≥3: 0.4 vs 1.3%)
- Patient reported outcomes: comparable
- Time to function deterioration; Favored T-DXd

Shitara K, et al. ASCO 2025, 2026: NEJM 2025

Trial 2: DESTINY-GC04 phase 3 comparing T-DXd vs. Ram + PTX

Implications

- First global randomized **phase 3** confirmation of **2nd-line T-DXd** in HER2-positive gastric cancer.
- T-DXd significantly improved OS, PFS, and ORR versus ramucirumab plus paclitaxel.
- **HER2 re-confirmation** at progression should be considered whenever feasible.
- **ILD** remains the key toxicity requiring proactive monitoring.

Bottom line

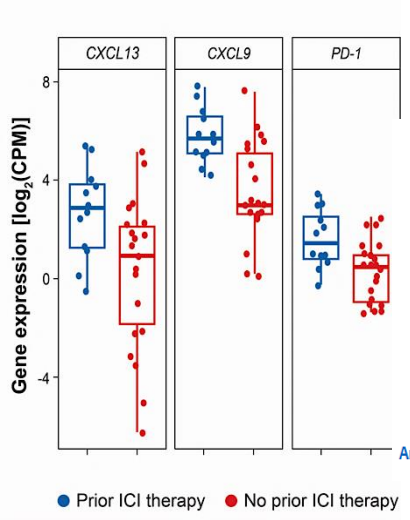
- **Practice-changing**
- **Re-biopsy HER2** at progression and **use T-DXd** as preferred 2L therapy if HER2 is retained.

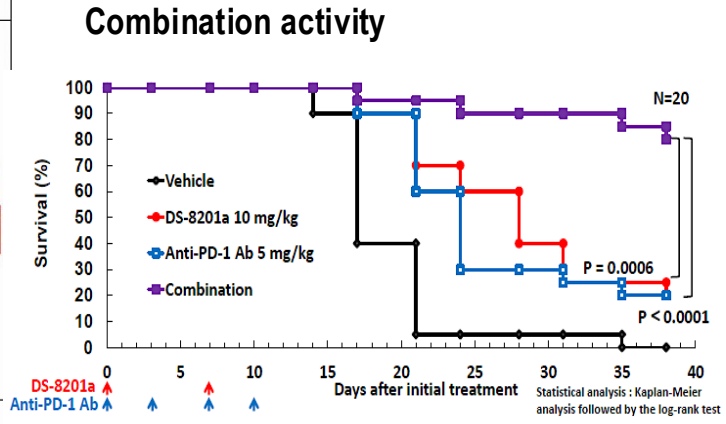
Trial 3: DESTINY-Gastric03 — T-DXd + Chemotherapy ± Anti-PD-1 Antibody

Trial 3: DESTINY-Gastric03: T-DXd plus chemo +/- anti-PD1

Rationales: analysis from DG-01 study

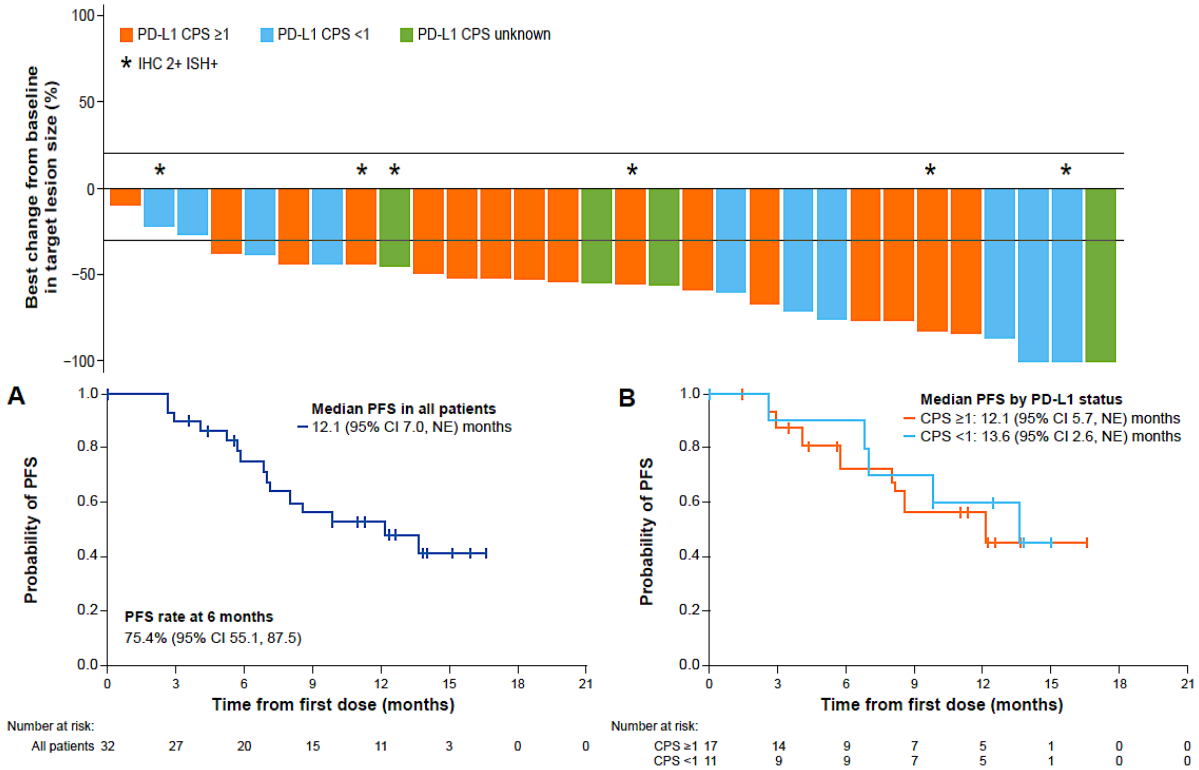
	Prior ICI		No Prior ICI	
Efficacy	**T-DXd n = 44**	**Chemo n = 17**	**T-DXd n = 81**	**Chemo n = 45**
Confirmed ORR, %	**56.8**	18.5	**34.7**	10.0
Median OS, months	16.6	8.6	10.3	8.4
	HR, 0.31		HR, 0.83	





- T-DXd showed trend of higher ORR after anti-PD1
- CXCL13, CXCL9, and PD-1 showed higher expression in pts after prior ICI such as
- T-DXd activated DC and ↑ MHC-I, resulted in combination activity

DESTINY-Gastric03: T-DXd5.4mg/kg+reduced FU/cape (750mg/bid)+pembro



- Reduced T-DXd+Capecitabine+pembro was feasible
- ORR 75%, median PFS 12.1 ms and median DOR 12.3 ms
- No increase T-DXd incidence compared with T-DXd monotherapy
- T-DXd+with bispecific (PD-1xCTLA4, PD-1xTIGIT) also showed acceptable safeties and promising activities

Shitara K, et al. ASCO-GI 2022; Iwata et al, Mol Cancer Ther. 2018; Jajigian Y, et al. ESMO Asia 2025: ASCO 2026 #4022

DESTINY-Gastric03 Safety Results

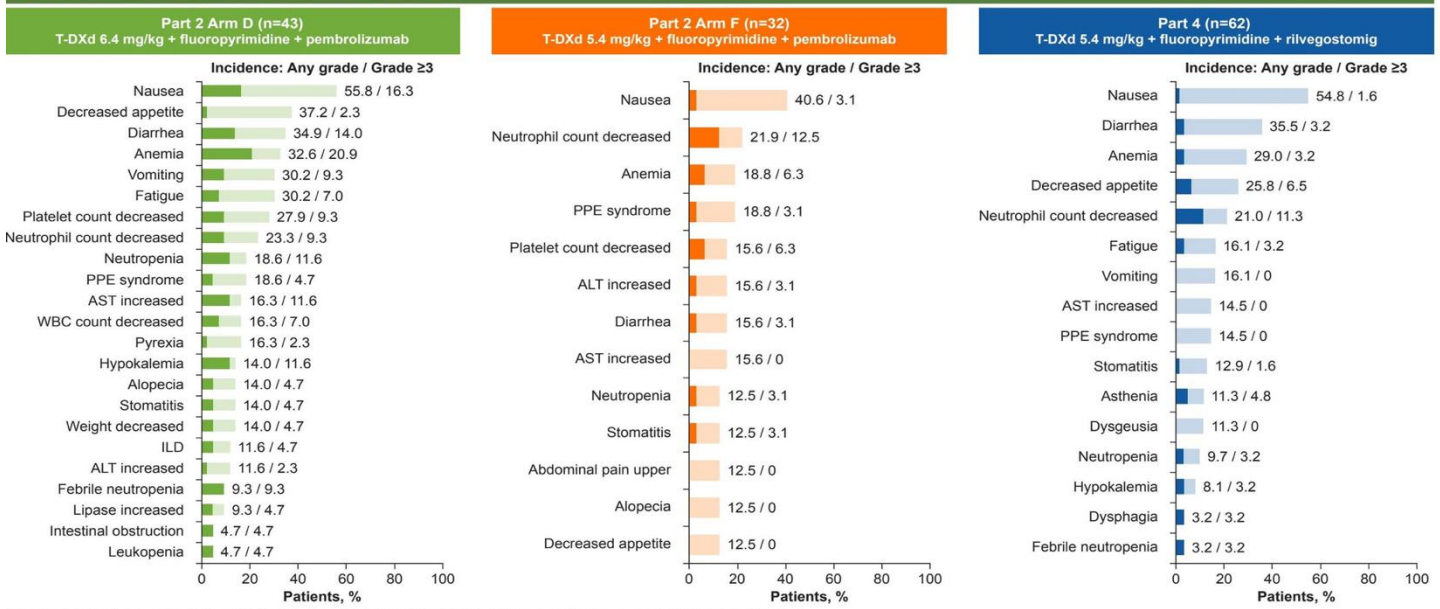
Safety summary

- In Part 2 Arm D, median treatment duration was 6.1 months (range, 0.5–13.3) for both T-DXd and pembrolizumab
- In Part 2 Arm F, median treatment duration was 6.9 months (range, 0.7–10.3) for T-DXd and 7.5 months (range, 0.7–10.3) for pembrolizumab
- In Part 4, median treatment duration was 6.5 months (range, 0.7–14.7) for both T-DXd and rilvegostomig
- Rates of Grade ≥3 AEs, serious AEs, and AEs leading to dose modifications were numerically lower in Part 2 Arm F and Part 4 (T-DXd 5.4 mg/kg–based regimens) than in Part 2 Arm D (T-DXd 6.4 mg/kg–based regimen; **Table 2**)

Table 2. Safety summary

Patients, n (%)	Part 2 Arm D (n=43) T-DXd 6.4 mg/kg + fluoropyrimidine + pembrolizumab	Part 2 Arm F (n=32) T-DXd 5.4 mg/kg + fluoropyrimidine + pembrolizumab	Part 4 (n=62) T-DXd 5.4 mg/kg + fluoropyrimidine + rilvegostomig
All-causality AEs	43 (100)	31 (96.9)	60 (96.8)
Treatment related*	40 (93.0)	27 (84.4)	55 (88.7)
Grade ≥3 AEs	38 (88.4)	15 (46.9)	31 (50.0)
Treatment related*	33 (76.7)	11 (34.4)	24 (38.7)
Serious AEs†	25 (58.1)	12 (37.5)	22 (35.5)
Treatment related*†	19 (44.2)	5 (15.6)	12 (19.4)
AEs associated with death	4 (9.3)	0	2 (3.2)
Treatment related*	4 (9.3)‡	0	1 (1.6)§
AEs leading to discontinuation of any investigational product	16 (37.2)	7 (21.9)	7 (11.3)
Treatment related*	15 (34.9)‖	6 (18.8)¶	6 (9.7)**
AEs leading to discontinuation of T-DXd	10 (23.3)	2 (6.3)	2 (3.2)
AEs leading to discontinuation of pembrolizumab (Part 2) or rilvegostomig (Part 4)	9 (20.9)	2 (6.3)	2 (3.2)
AEs leading to dose reduction of T-DXd	13 (30.2)	5 (15.6)	13 (21.0)
AEs leading to dose interruption of T-DXd††	23 (53.5)	9 (28.1)	24 (38.7)
AEs leading to dose interruption of pembrolizumab (Part 2) or rilvegostomig (Part 4)†††‡‡	26 (60.5)	12 (37.5)	25 (40.3)

Figure 2. Most common treatment-related AEs in each group*



Janjigian Y et al ASCO 2026;Abstract 4022

Trial 3: DESTINY-Gastric03: T-DXd plus chemo +/- anti-PD1

Implications

- Demonstrated **feasibility** of **combining T-DXd with immunotherapy and chemotherapy** in 1L.
- **Dose reduction** of both T-DXd and fluoropyrimidine substantially improved tolerability.
- Safety profiles were generally consistent with those of the individual components
- No unexpected safety signals emerged beyond known ADC toxicities.

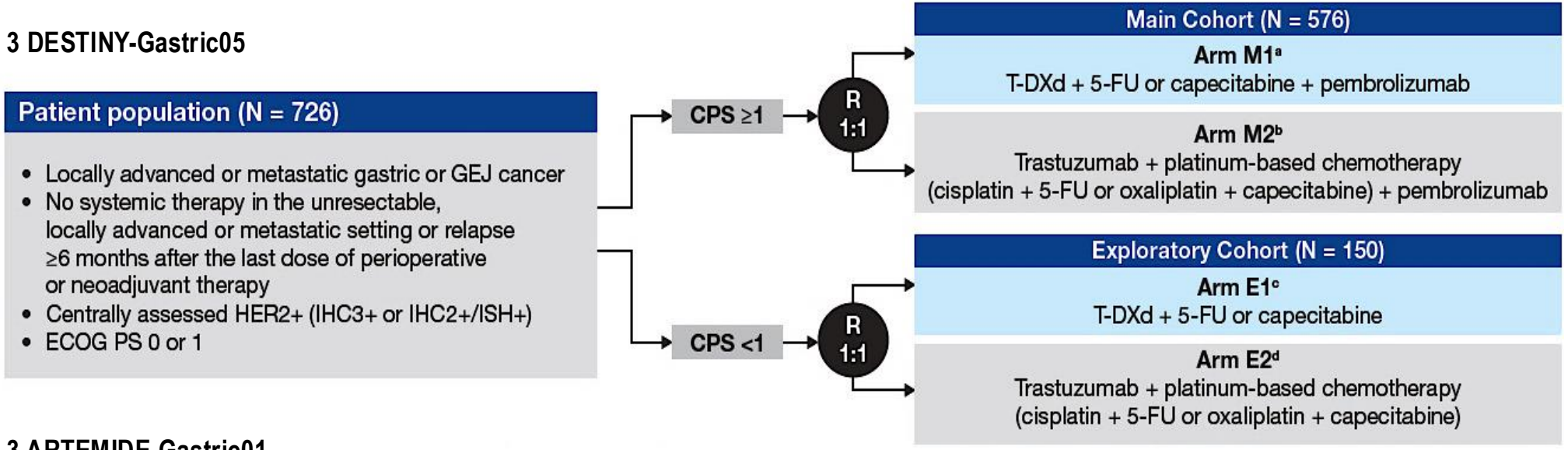
Bottom line

- Evidence tier: Signal-seeking / dose-selection
- Provides the **rationale for phase 3** development of T-DXd-based first-line combinations.

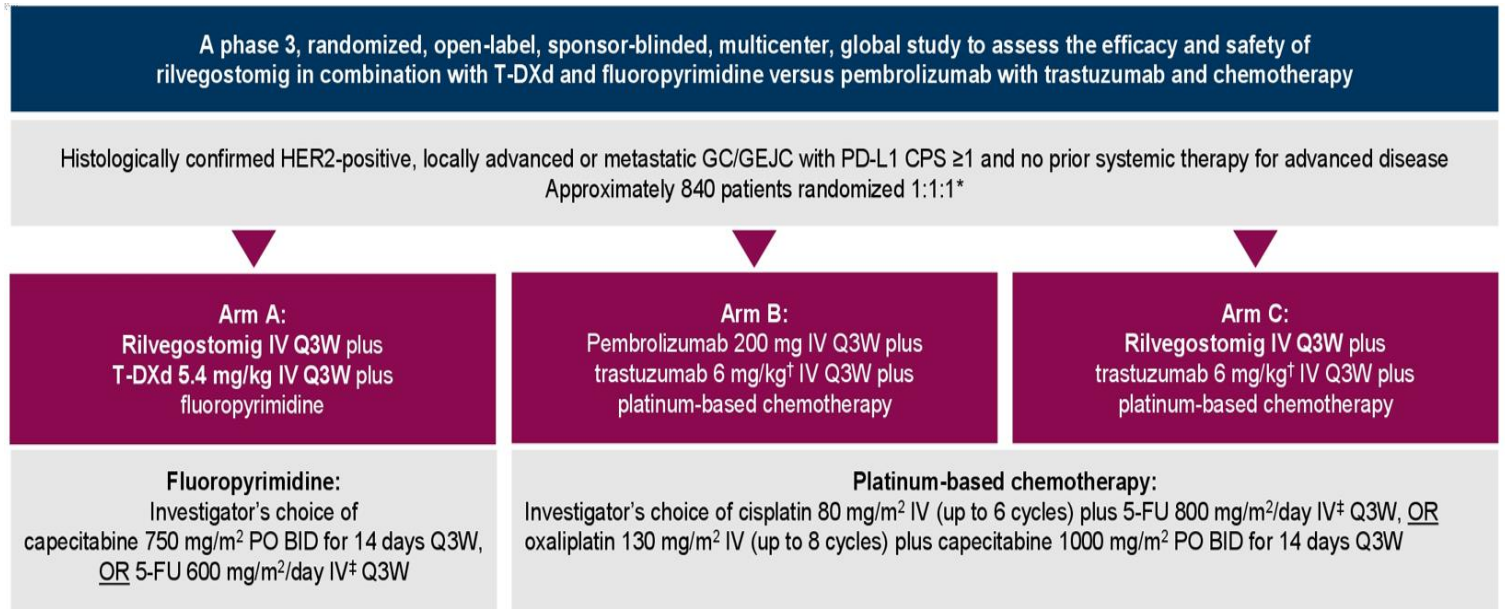
Trials 4 and 5: Phase III DESTINY-Gastric05 and ARTEMIDE-Gastric01

Trials 4 and 5: Phase 3 DESTINY-Gastric05 and ARTEMIDE-Gastric01

Phase 3 DESTINY-Gastric05



Phase 3 ARTEMIDE-Gastric01



Shitara K, Jajigian Y, et al. ASCO 2025; Shah M, et al. ASCO GI 2026 TPS460

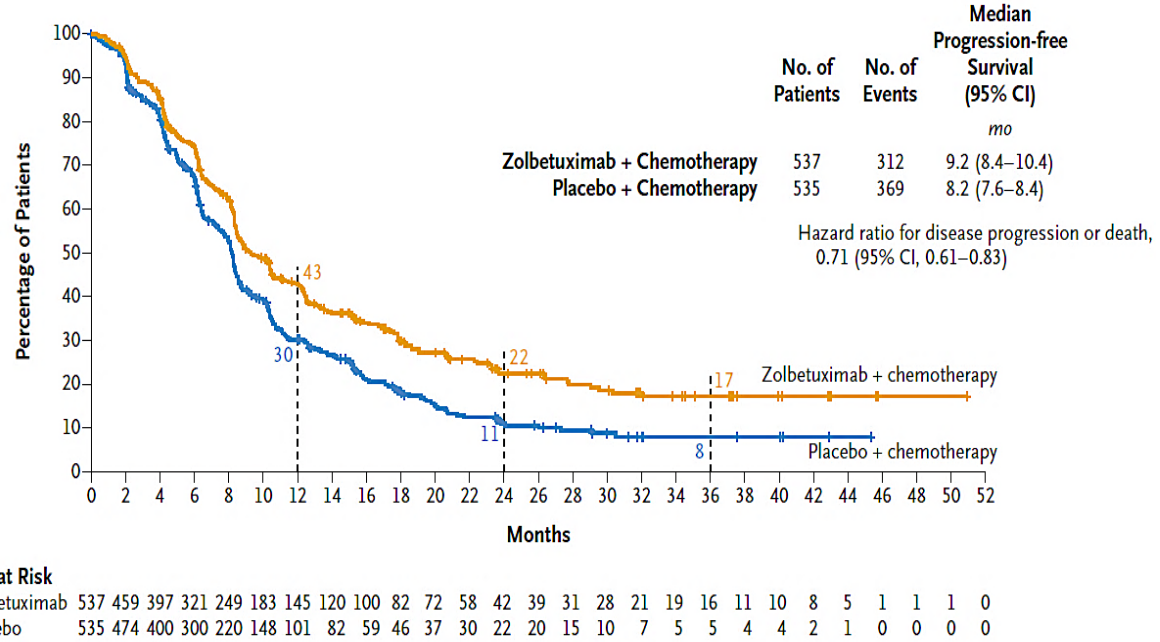
Trials 6 and 7: Zolbetuximab + Chemotherapy in the Phase III SPOTLIGHT and GLOW Trials

CLDN18.2: Non-Oncogenic Targets and Tumor-Specific Vulnerability

- Tight junction protein usually located at the apical site of normal epithelial gastric stomach cells
- During malignant transformation it is exposed to the tumor cell surface with the disruption of the tight junction – becomes an accessible target for cancer treatment
- Around 40% of patients maintain high expression of claudin 18.2, so it is a relatively prevalent biomarker for this disease

Trials 6 and 7: Zolbetuximab + chemotherapy in phase 3 SPOTLIGHT + GLOW

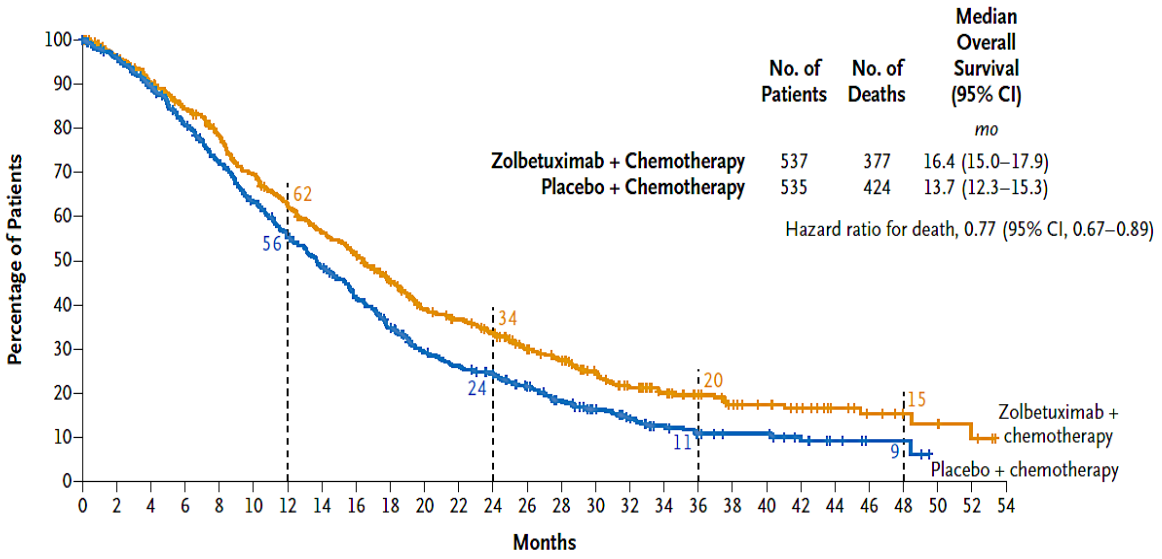
PFS of combined population



No. at Risk

Zolbetuximab	537	459	397	321	249	183	145	120	100	82	72	58	42	39	31	28	21	19	16	11	10	8	5	1	1	1	0
Placebo	535	474	400	300	220	148	101	82	59	46	37	30	22	20	15	10	7	5	5	4	4	2	1	0	0	0	0

OS of combined population



No. at Risk

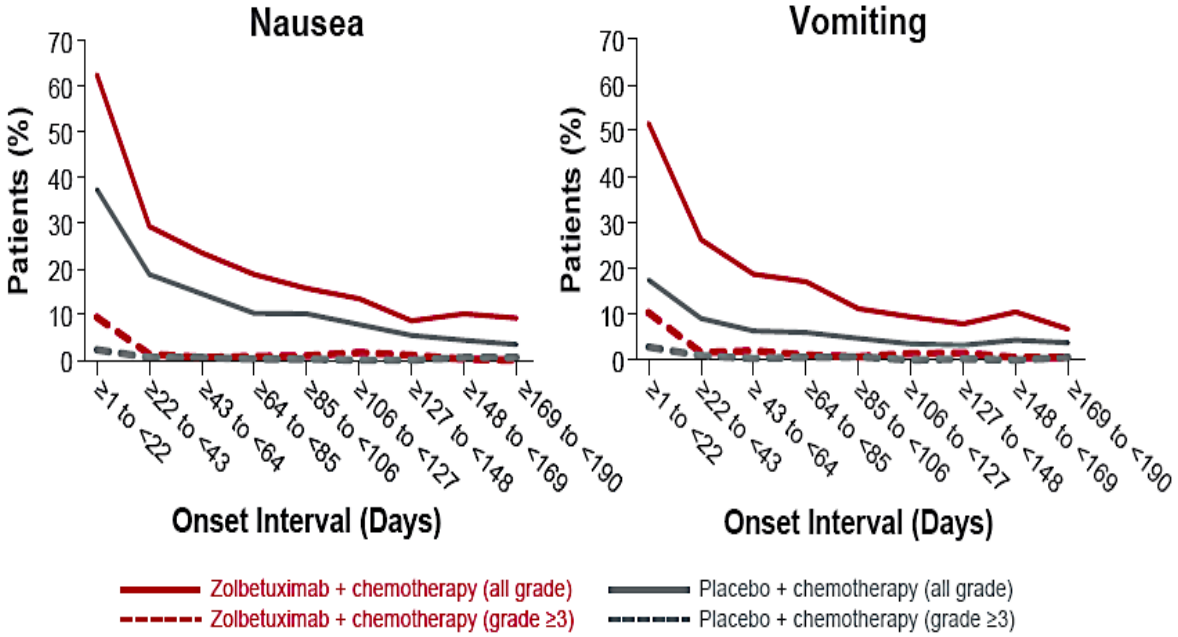
Zolbetuximab	537	497	462	427	387	343	303	273	249	213	174	159	140	109	96	75	60	47	39	30	25	20	14	10	7	6	3	0
Placebo	535	506	463	409	362	317	278	239	204	169	135	119	102	85	65	50	38	28	21	17	17	11	6	3	3	0	0	0

- Enrolled pts with CLDN18.2 IHC 2+/3+ in ≥75%
- PFS and OS improved
- No increase of response rate, suggesting a mechanism beyond direct cytotoxicity
- Approval in Japan, UK, EU and US (FDA) etc.

Shitara K, et al. Lancet 2023, Shah M, et al. Nature Med 2023; Shitara K, et al. NEJM 2024

GI toxicities with zolbetuximab

All occurrences of nausea or vomiting in SPOTLIGHT and GLOW



Use of prophylactic antiemetics, *n* (%)	*n*	With vomiting	Without vomiting
Any antiemetics	521	213	308
Yes	8	4	4
No			
Standard antiemetic regimens[a]	377	139 (36.9)	238 (63.1)
Two-drug antiemetic regimens			
NK-1 receptor antagonist + 5-HT3 receptor antagonist	187	70 (37.4)	117 (62.6)
5-HT3 receptor antagonist + steroids	93	45 (48.4)	48 (51.6)
Three-drug antiemetic regimens			
NK-1 receptor antagonist + 5-HT3 receptor antagonist + steroids	97	24 (24.7)	73 (75.3)
Other antiemetic regimens[b]	144	74 (51.4)	70 (48.6)

- Nausea/Vomiting common in pts without gastrectomy
- Incidence was high in 1st cycle and decreased later
- ➢ Infusion rate adjustment and anti-emetics were needed

- Use of NK1, 5-HT3 and steroid was associated with less vomiting

Shitara K, et al. ASCO-GI 2024; ESMO open 2026

Trials 6 and 7: Zolbetuximab + chemotherapy in phase 3 SPOTLIGHT + GLOW

Implications

- Established **CLDN18.2** as a validated therapeutic **target** in gastric cancer.
- Zolbetuximab plus chemo is now a standard first-line option for CLDN18.2-high disease.
- Two independent phase 3 trials consistently demonstrated **PFS and OS** benefit**.**
- **Nausea and vomiting** remain the major treatment-limiting toxicities.

Bottom line

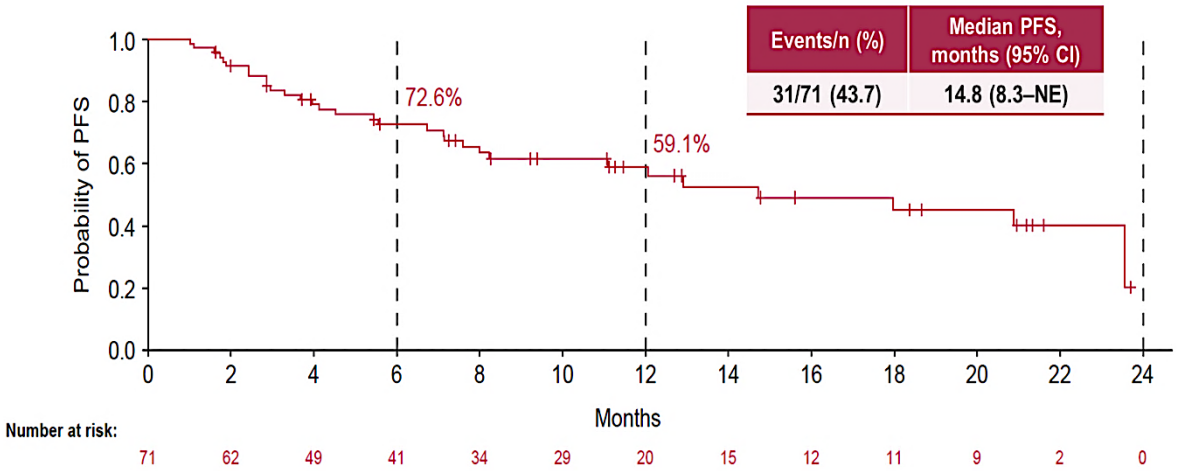
- **Practice-changing**
- Test CLDN18.2 routinely at diagnosis and proactively manage nausea/vomiting.

Trial 8: Phase II ILUSTRO Trial Cohort 4 — FOLFOX + Zolbetuximab + Nivolumab

Trial 8: Phase 2 ILUSTRO Cohort 4: FOLFOX + Zolbe + Nivo

PFS in Cohort 4B

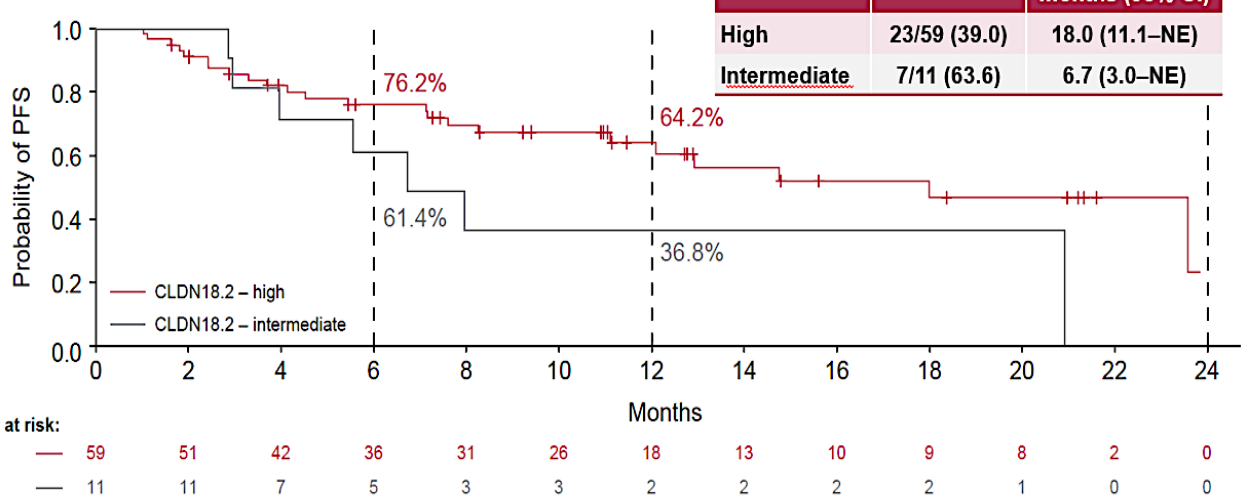
Median PFS was 14.8 months with zolbetuximab + mFOLFOX6 + nivolumab



Events/n (%)	Median PFS, months (95% CI)
31/71 (43.7)	14.8 (8.3–NE)

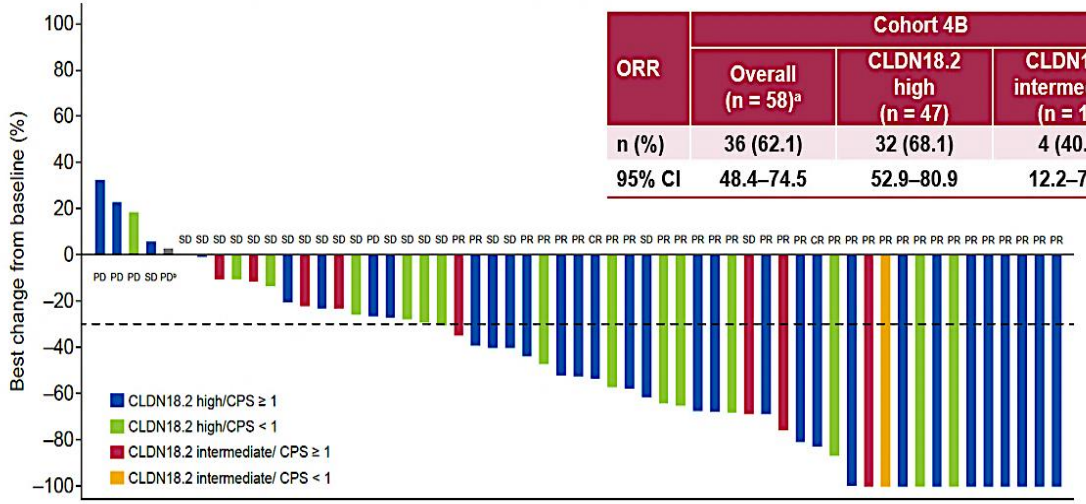
PFS Stratified by CLDN18.2 Expression in Cohort 4B

Median PFS was 18.0 months in the CLDN18.2-high population



CLDN18.2	Events/n (%)	Median PFS, months (95% CI)
High	23/59 (39.0)	18.0 (11.1–NE)
Intermediate	7/11 (63.6)	6.7 (3.0–NE)

ORR was 68.1% in patients in the CLDN18.2-high group



ORR	Cohort 4B		
	Overall (n = 58)[a]	CLDN18.2 high (n = 47)	CLDN18.2 intermediate (n = 10)
n (%)	36 (62.1)	32 (68.1)	4 (40.0)
95% CI	48.4–74.5	52.9–80.9	12.2–73.8

- N=71 pts for cohort B (dose expansion)
- mOS 18ms in CLDN high and 23ms in CLDN high+CPS≥1
- ORR 62% in all pts / 68% in CLDN high
- Discontinue by AE: Zolbe 5% Nivo 9%
- Nausea 81% (no G3) Vomiting 38% (G3: 4%)
- Phase 3 LUCERNA is ongoing

Shitara K, et al. ASCO-GI 2026 LBA284, Nature Med 2026

Trial 8: Phase 2 ILUSTRO Cohort 4: FOLFOX + Zolbe + Nivo

Implications

- First substantial dataset combining zolbetuximab, chemotherapy, and PD-1 blockade.
- Demonstrated encouraging efficacy, particularly in CLDN18.2-high tumors
- Supports the hypothesis that **CLDN18.2 targeting and PD-1 inhibition may be complementary**.
- Manageable safety profiles

Bottom line

- Evidence tier: Signal-seeking
- Supports ongoing **phase 3** evaluation of zolbetuximab plus chemo-immunotherapy.

Trial 9: Ongoing Phase III LUCERNA Trial (NCT06901531)

Trial 9: Phase 3 LUCERNA (NCT0690151) is ongoing

Key inclusion criteria

- Adult[a] patients with LA unresectable or mG/GEJ adenocarcinoma
- HER2–[b]
- CLDN18.2+[c]
- PD-L1+ (CPS ≥ 1)[d]
- ECOG PS 0–1

Key exclusion criteria

- Receipt of prior systemic chemotherapy and/or immunotherapy[e]
- Receipt of prior CLDN18.2-targeted therapy

Stratification factors

- Region (Asia vs non-Asia)
- PD-L1 CPS (≥ 1 to < 10 vs ≥ 10)

Planned (N ≈ 500)

R 1:1

Zolbetuximab IV
800 mg/m² Cycle 1 Day 1 → 400 mg/m² Q2W or 600 mg/m² Q3W
Pembrolizumab IV
200 mg Q3W or 400 mg Q6W
CAPOX[f] / mFOLFOX6[g]
Cycles 1–4 (42 days/cycle)

→

Zolbetuximab IV
400 mg/m² Q2W or 600 mg/m² Q3W
Pembrolizumab IV
200 mg Q3W or 400 mg Q6W[h]
Capecitabine[i] / folinic acid + fluorouracil[i]
Cycles 5+ (42 days/cycle)

Placebo IV Q2W or Q3W
Pembrolizumab IV
200 mg Q3W or 400 mg Q6W
CAPOX[f] / mFOLFOX6[g]
Cycles 1–4 (42 days/cycle)

→

Placebo IV Q2W or Q3W
Pembrolizumab IV
200 mg Q3W or 400 mg Q6W[h]
Capecitabine[i] / folinic acid + fluorouracil[i]
Cycles 5+ (42 days/cycle)

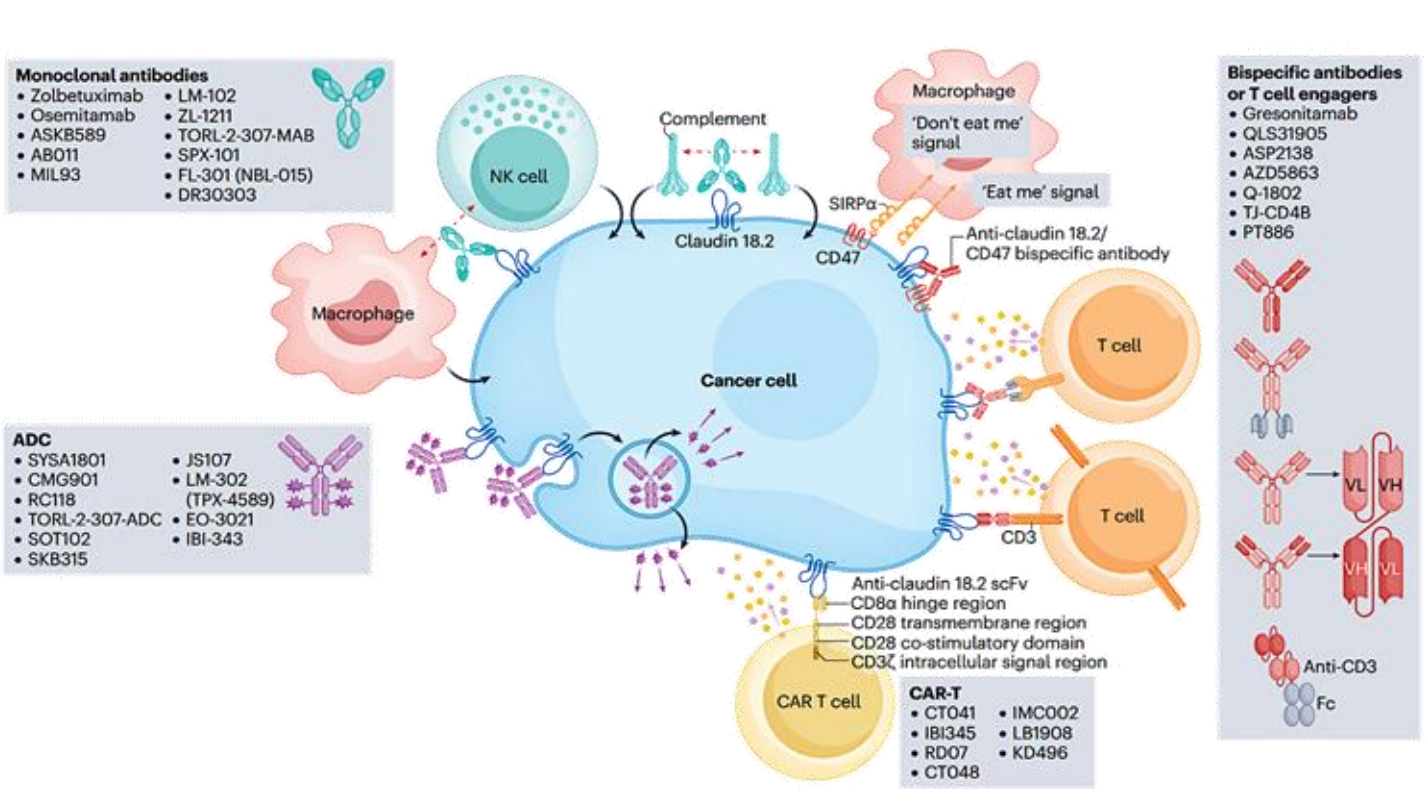
Primary endpoint	Secondary endpoints	Exploratory endpoints
• OS	• PFS[j] • DOR[j] • Safety • ORR[j] • PK • Immunogenicity	• HRQoL • PFS2 • Biomarkers

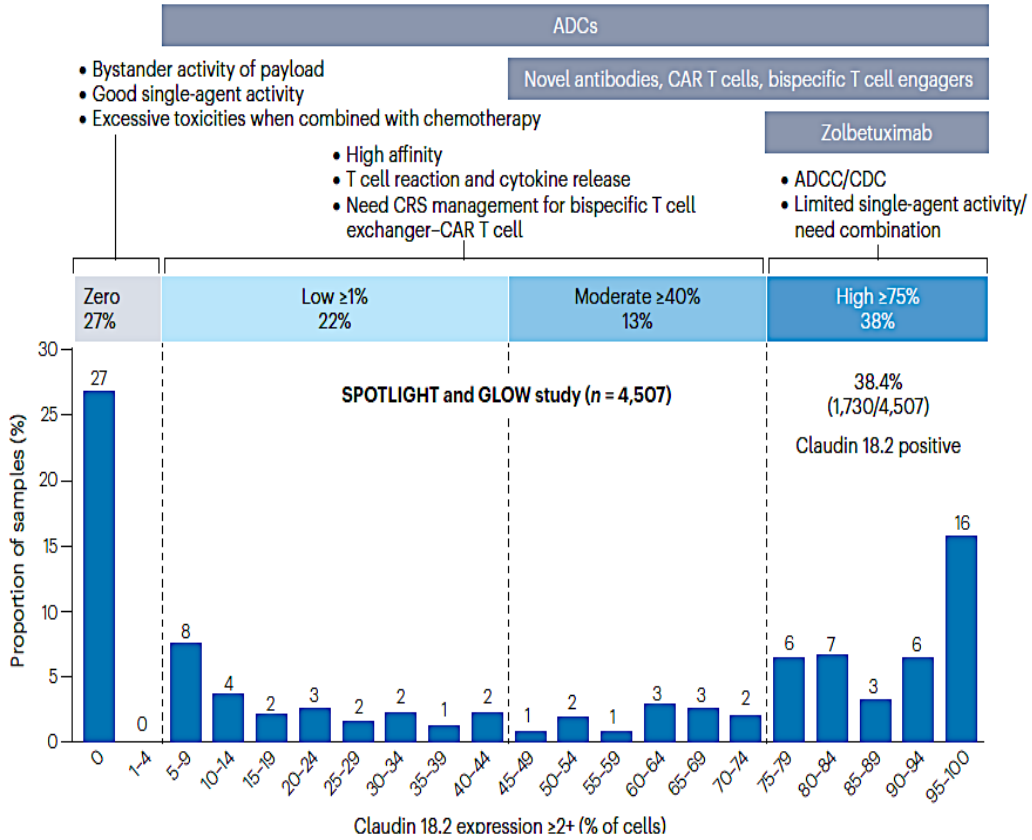
- Key question: Does zolbetuximab add benefit beyond pembrolizumab + chemotherapy?

Shitara K, et al. ASCO-GI 2026 TPS473

Trial 10: Phase II CLARITY-PanTumor01 Trial with AZD0901 (Sonesitatug Vedotin)

Emerging CLDN18.2 Targeted treatments



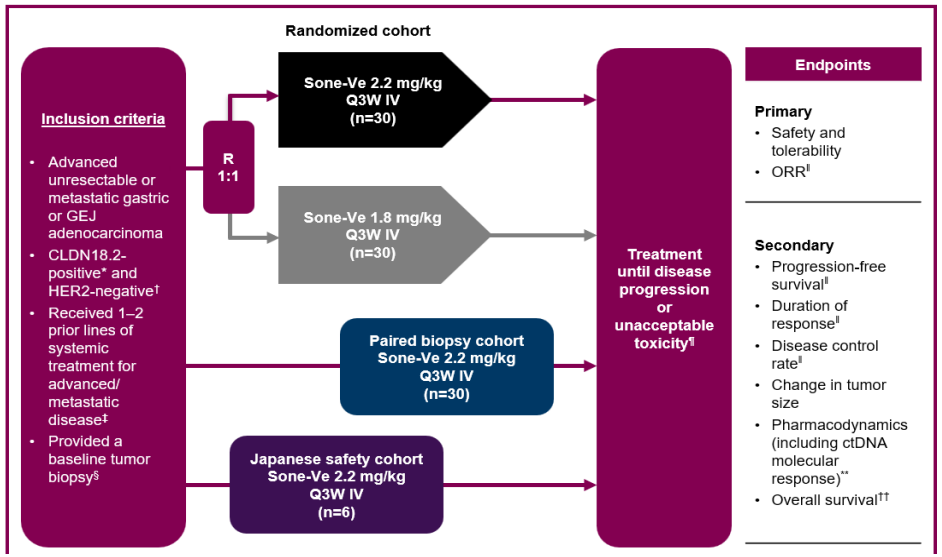


- >30 agents have been tested in clinical trials
- ADCs, T-cell engager, CAR-T may expand indication of CLDN targeted agents

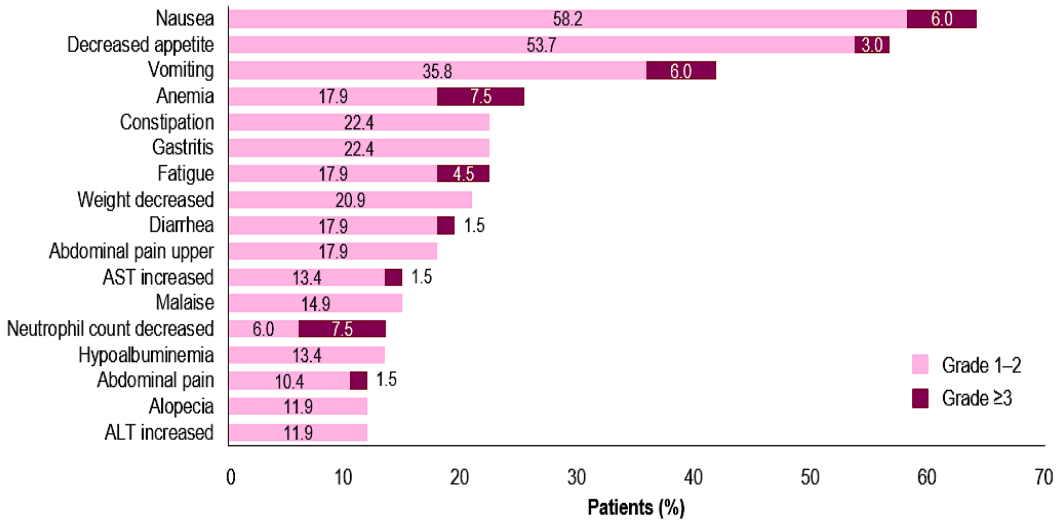
Nakayama I, Shitara K. et al. Nature Revise Clinical Oncol. 2024

Trial 10: Phase 2 CLARITY-Pan tumor 01 trial with AZD0901 (Sone-Ve)

Figure 1. CLARITY-PanTumor01 substudy 1 schema

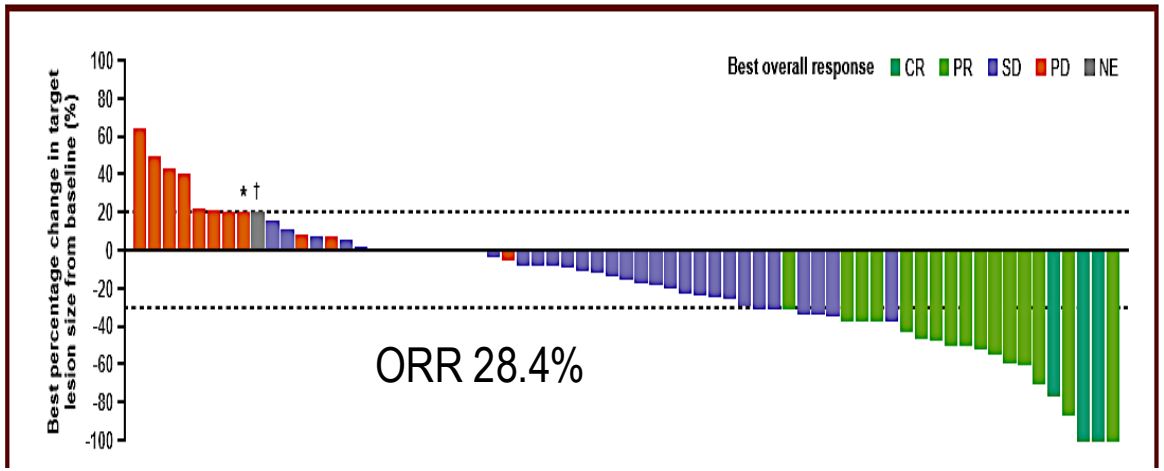


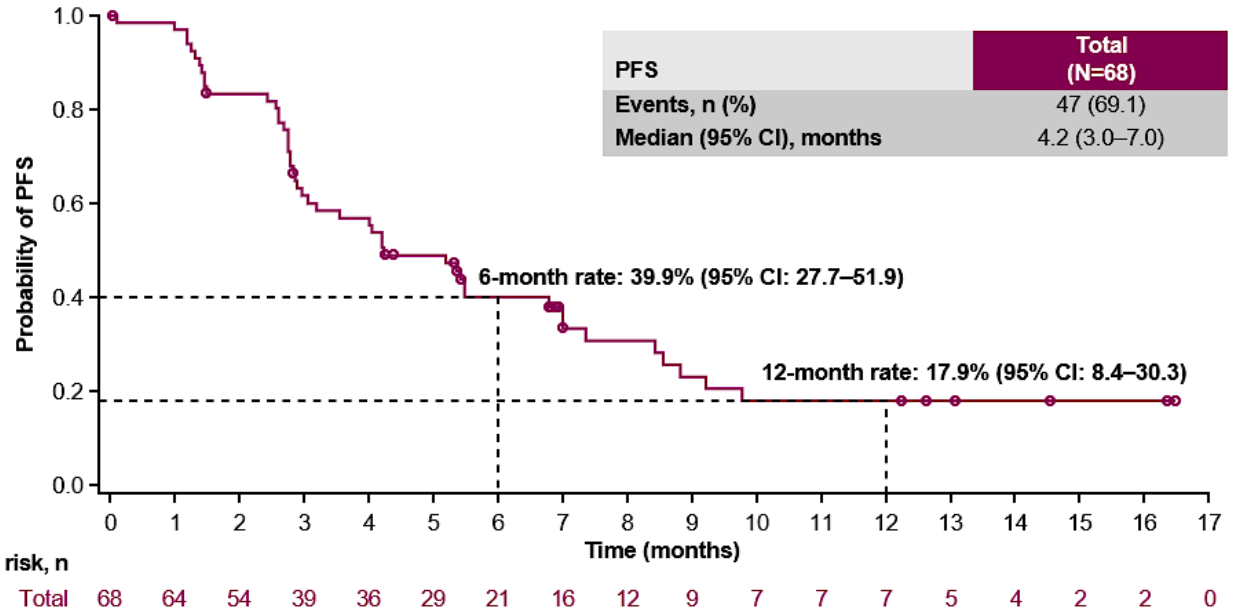
CLDN18.2 >25% with any intensity, 2nd or later line



Premedication for Nausea is essential

Figure 3. Best percentage change in target lesion size from baseline (investigator-assessed per RECIST v1.1)





PFS	Total (N=68)
Events, n (%)	47 (69.1)
Median (95% CI), months	4.2 (3.0–7.0)

Shitara K, et al. ASCO 2026 #4023

Trial 10: Phase 2 CLARITY-Pan tumor 01 trial with AZD0901 (Sone-Ve)

Implications

- Represents the next generation of CLDN18.2-directed therapy using an ADC approach.
- Early studies demonstrate substantial activity in heavily pretreated patients.
- May provide deeper and more durable responses than antibody-based approaches.
- Nausea and vomiting remain important but manageable toxicities.

Bottom line

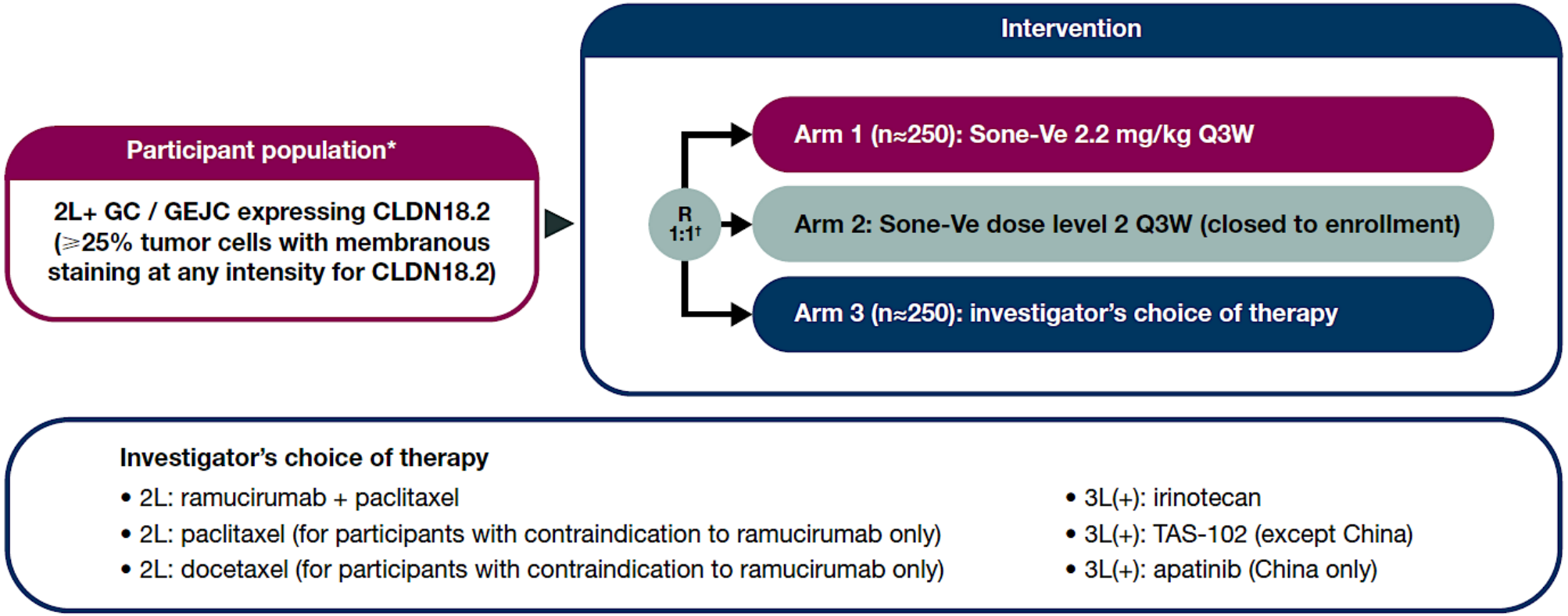
- Evidence tier: Early signal
- Support the ongoing phase 3 study

Trial 11: Ongoing CLARITY-Gastric01 Phase III Study

Trial 11: ongoing CLARITY-Gastric 01 phase 3 study

CLARITY-Gastric01: Phase 3 AZD0901 vs 2nd or 3rd line chemo (NCT06346392)

CLARITY-Gastric 01 was designed as a three-arm study containing two Sone-Ve dose levels. As planned, an independent committee determined the optimal Sone-Ve dose (2.2 mg/kg), and the arm containing the non-selected dose was closed for enrollment



- Key question: Can ADCs outperform antibodies in CLDN18.2-positive disease?

Shitara K, et al. ESMO-GI 2024; ASCO-GI 2026 TPS462

Trial 12: Izalontamab Brengitecan versus Chemotherapy for Recurrent/Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

Trial 12: Izalontamab brengitecan vs. chemotherapy in recurrent/metastatic ESCC

PANKU-Esophagus01 Study Design

A multicenter, randomized, open-label, phase III study conducted at 80 study centers across China.

Key eligibility criteria

- Histologically or cytologically confirmed recurrent/metastatic ESCC
- Measurable lesion per RECIST v1.1
- Progressed after first-line treatment with a PD-1/PD-L1 inhibitor plus platinum-based chemotherapy
- ECOG PS 0-1

Treatment until
Disease progression per RECIST v1.1 or intolerable toxicity

R 1:1
N=488

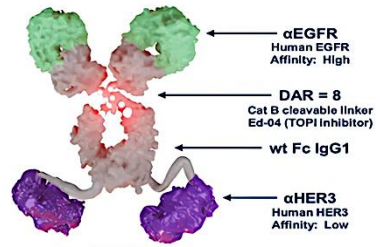
- **Iza-bren** 2.5 mg/kg D1D8 Q3W
- **Chemotherapy**
  - Irinotecan, D1D8 Q3W
  - Paclitaxel, Q3W
  - Docetaxel, Q3W

Stratified by
- Baseline ECOG PS (0 vs 1)
- Definitive treatment (surgery or radiotherapy for the primary tumor, yes vs no)

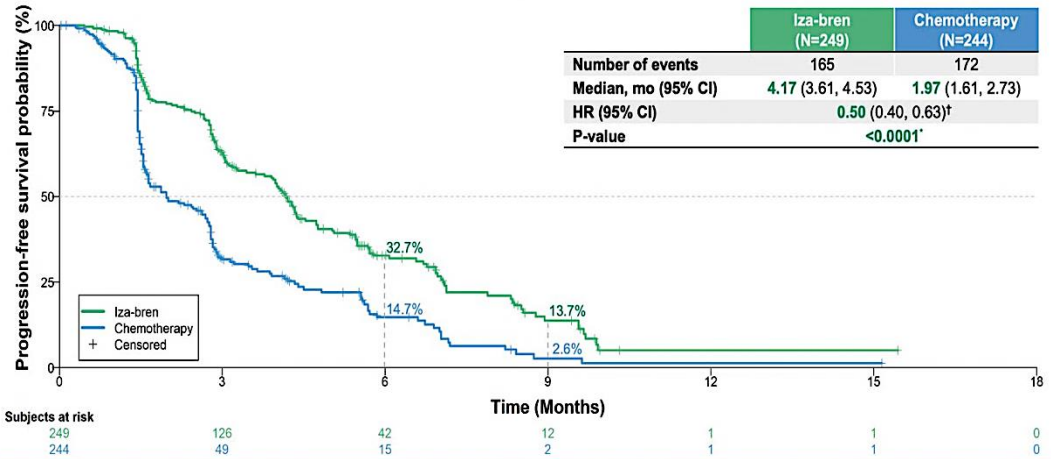
Dual primary endpoints
PFS (BICR) & OS
H_{PFS} α=0.005
H_{OS} α=0.020

Secondary endpoints
ORR (BICR)
PFS (INV)
DCR, DoR, Safety, PK, Immunogenicity

iza-bren (BL-B01D1)
EGFR x HER3 bispecific ADC



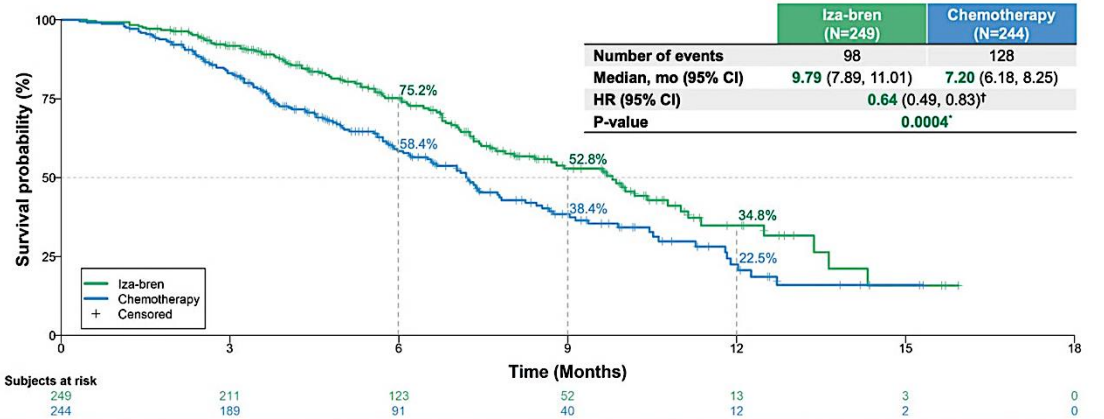
PFS (BICR): Dual Primary Endpoint



	Iza-bren (N=249)	Chemotherapy (N=244)
Number of events	165	172
Median, mo (95% CI)	4.17 (3.61, 4.53)	1.97 (1.61, 2.73)
HR (95% CI)	0.50 (0.40, 0.63)†	
P-value	<0.0001*	

Iza-bren showed statistically significant and clinically meaningful improvement in PFS vs chemotherapy (median Δ 2.20 mo).

OS: Dual Primary Endpoint



	Iza-bren (N=249)	Chemotherapy (N=244)
Number of events	98	128
Median, mo (95% CI)	9.79 (7.89, 11.01)	7.20 (6.18, 8.25)
HR (95% CI)	0.64 (0.49, 0.83)†	
P-value	0.0004*	

Iza-bren showed statistically significant and clinically meaningful improvement in OS vs chemotherapy (median Δ 2.59 mo).

- PFS and OS improved
- ORR by BICR 35.3 vs 13.1%
- Grade 3 related AEs 85% vs 60%
- AEs leading to discontinuation 2% vs 3.3%
- ILD 1.6% with Iza-Bren

Lu et al. ASCO 2026 #4008

Trial 12: Izalontamab brengitecan vs. chemotherapy in recurrent/metastatic ESCC

Implications

- Demonstrates meaningful activity of EGFR × HER3 bispecific ADC therapy in ESCC
- Responses appear durable and clinically relevant in refractory disease.
- Safety profile is manageable and consistent with prior BL-B01D1 experience.
- A promising new ADC option that may expand treatment choices in ESCC

Bottom line

- **Potentially practice-changing**
- Warrants confirmation in global cohorts

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Thursday, June 25, 2026
5:00 PM – 6:00 PM ET

Faculty

Amrita Krishnan, MD
Robert Z Orlowski, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2026

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