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Integrating Recent Advances into the Management of Gastroesophageal Cancers

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Disclosures

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Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

Module 6: Clinician Survey Results

Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

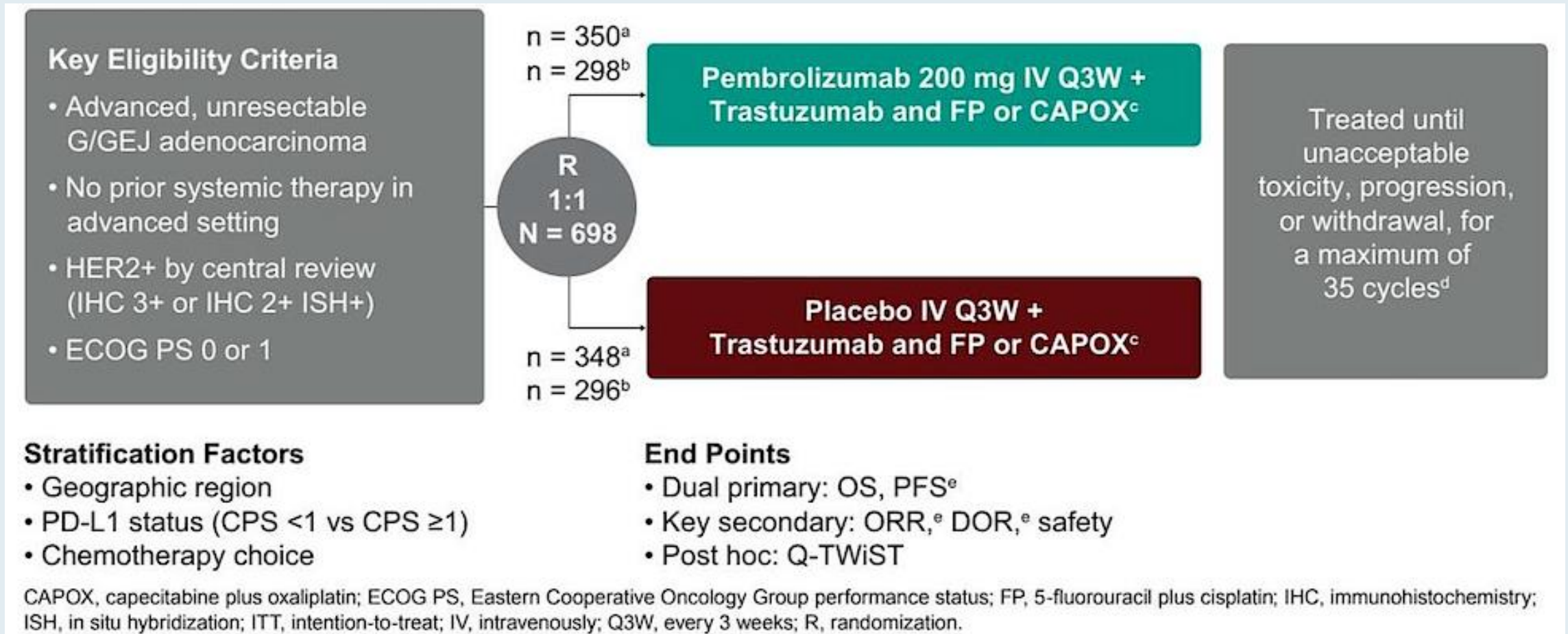
Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

Module 6: Clinician Survey Results

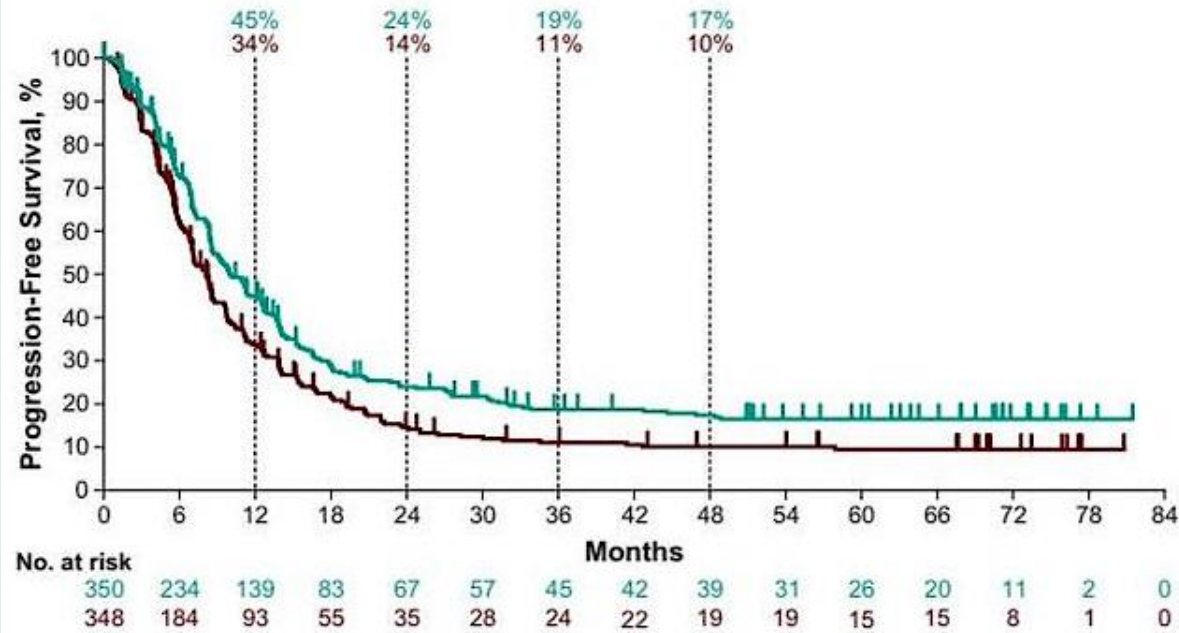
KEYNOTE-811 Phase III Trial of Pembrolizumab with Trastuzumab and Chemotherapy for Previously Untreated Advanced HER2-Positive Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma



KEYNOTE-811: Progression-Free Survival (PFS) with 6-Year Median Follow-Up

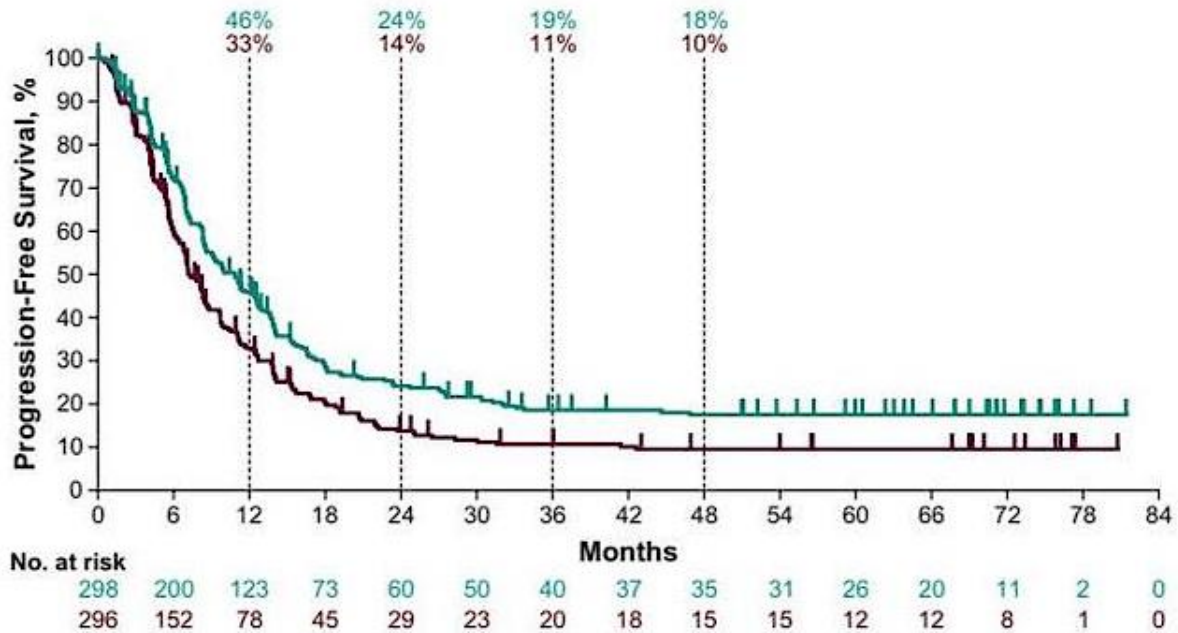
ITT

	PFS, median (95% CI), months	HR (95% CI)
Pembrolizumab group	10.0 (8.6-12.2)	0.73 (0.61-0.87)
Placebo group	8.1 (7.0-8.5)	



PD-L1 CPS ≥1

	PFS, median (95% CI), months	HR (95% CI)
Pembrolizumab group	10.9 (8.5-12.5)	0.72 (0.60-0.87)
Placebo group	7.3 (6.8-8.4)	

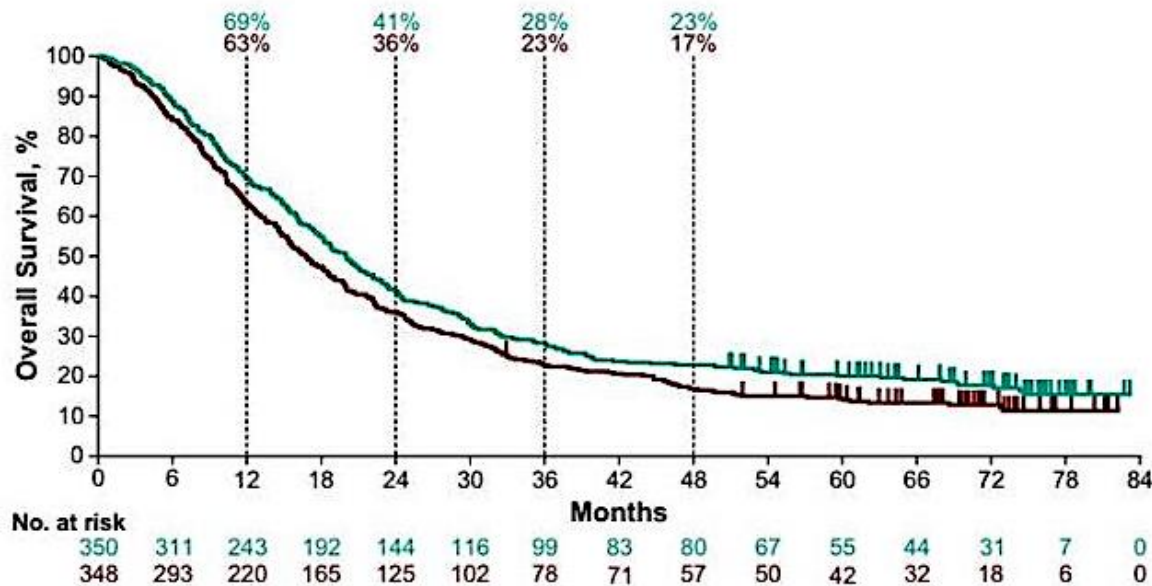


ITT = intention to treat; CPS = combined positive score; HR = hazard ratio; CI = confidence interval

KEYNOTE-811: Overall Survival (OS) with 6-Year Median Follow-Up

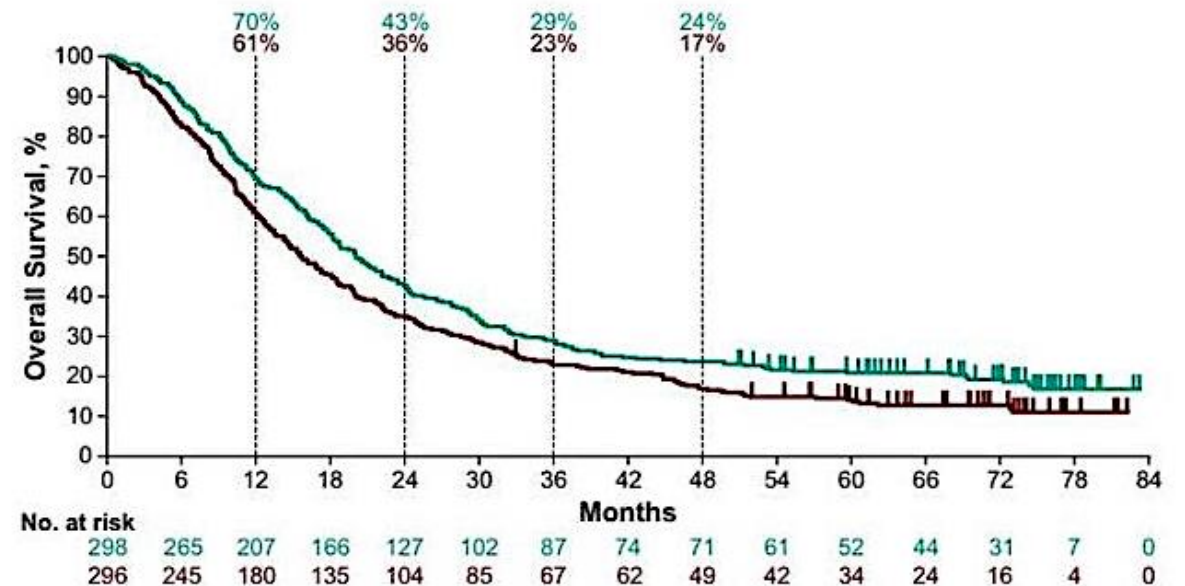
ITT

	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)	

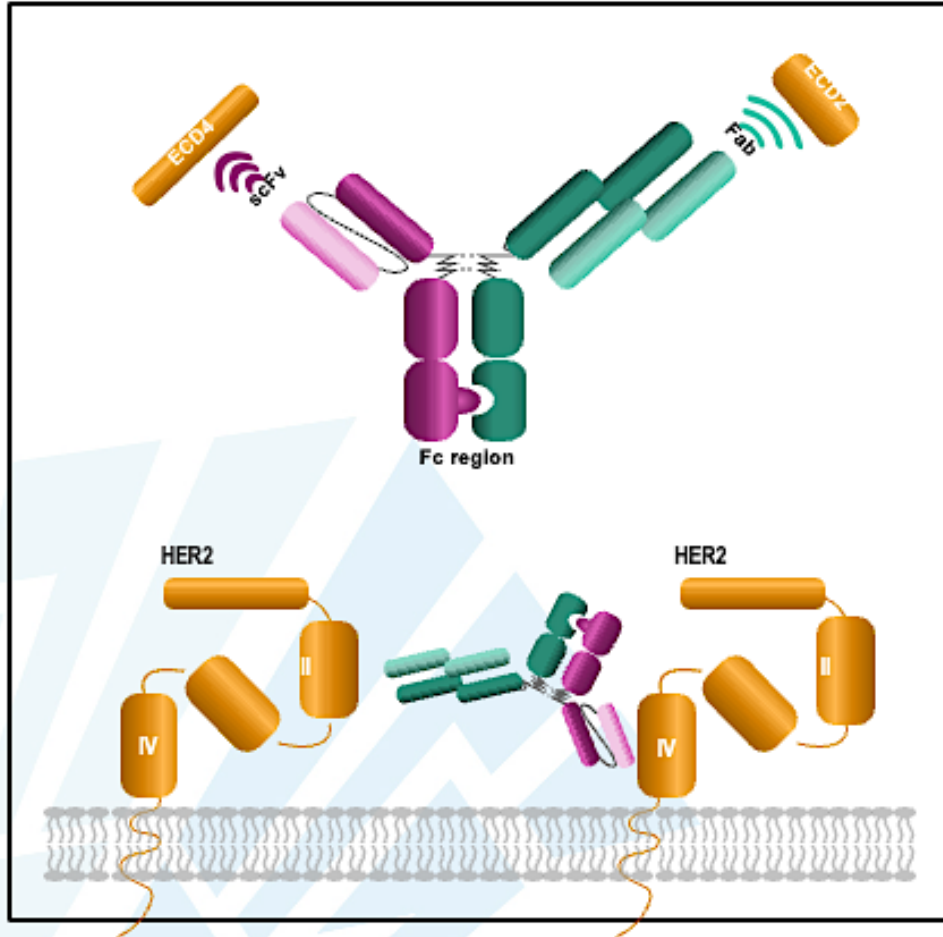


PD-L1 CPS ≥ 1

	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)	



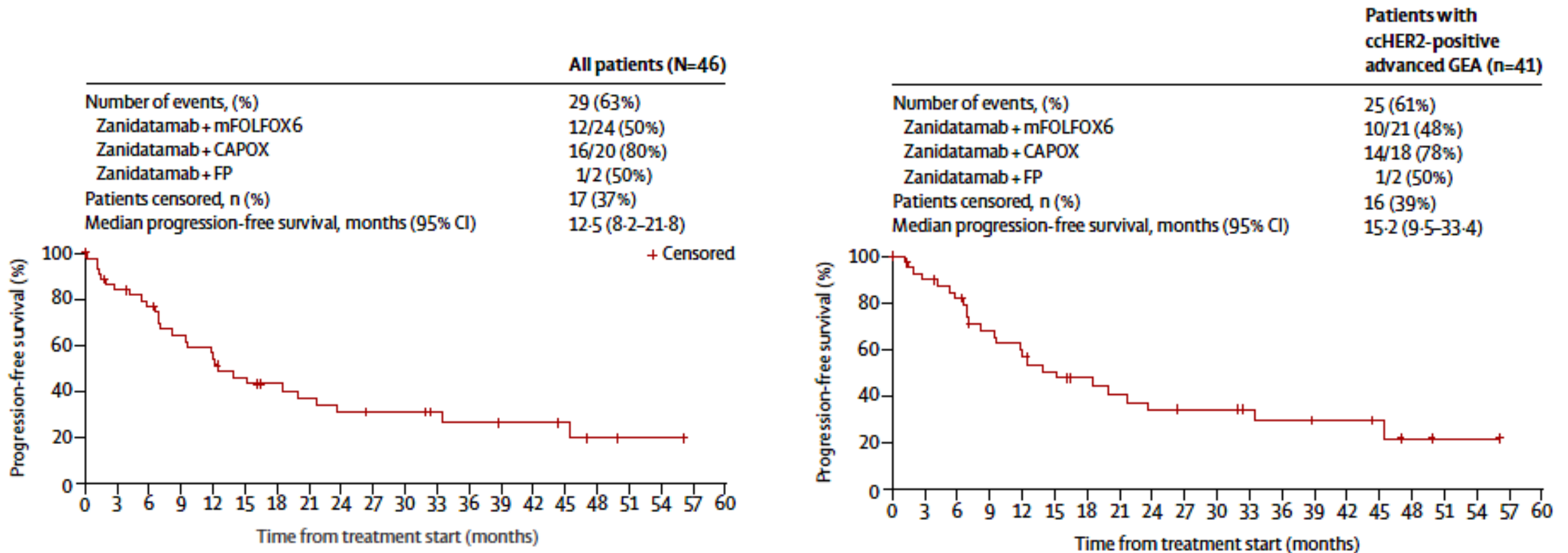
Zanidatamab Mechanism of Action



- ❑ Zanidatamab is a humanized dual HER2-targeted bispecific IgG1-like antibody that binds to the HER2 juxtamembrane domain (ECD4) and dimerization domain (ECD2)
- ❑ This biparatopic binding enables zanidatamab to crosslink neighboring HER2 proteins, leading to receptor clustering
- ❑ The clustering induces potent complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC)

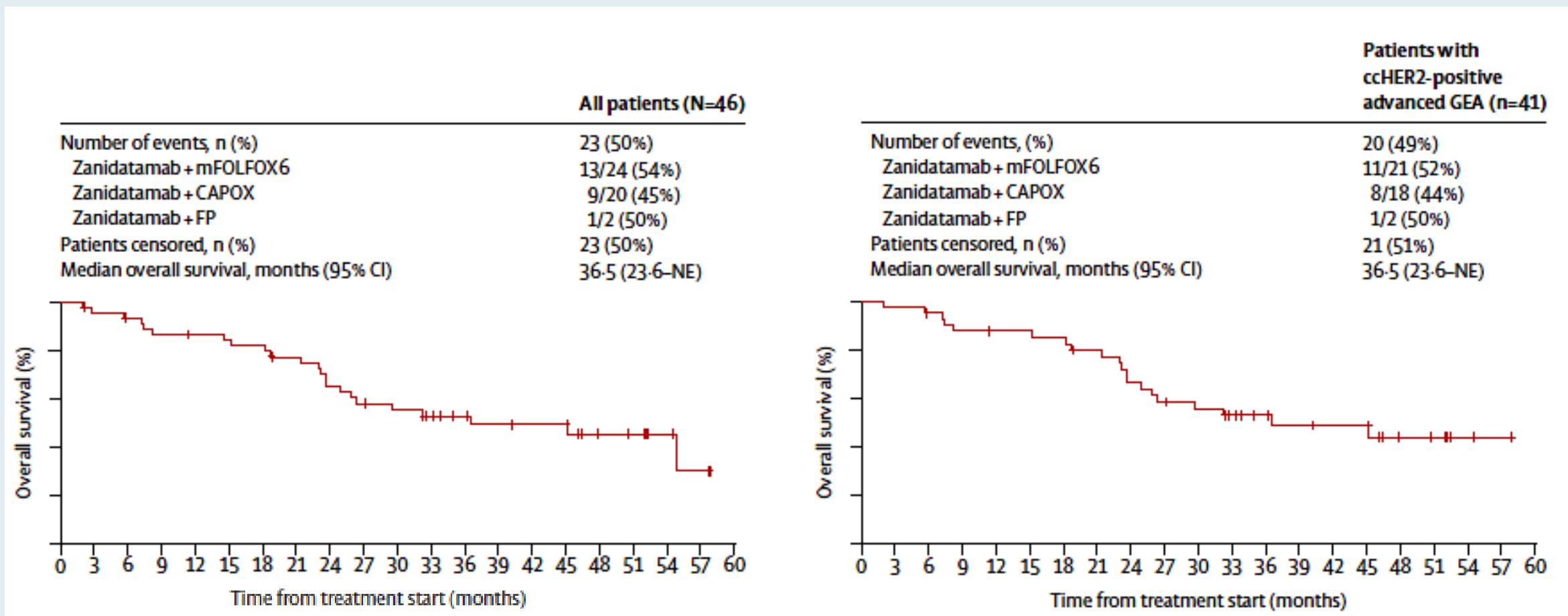
Weisser N et al. *Nat Commun* 2023.

Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers: PFS



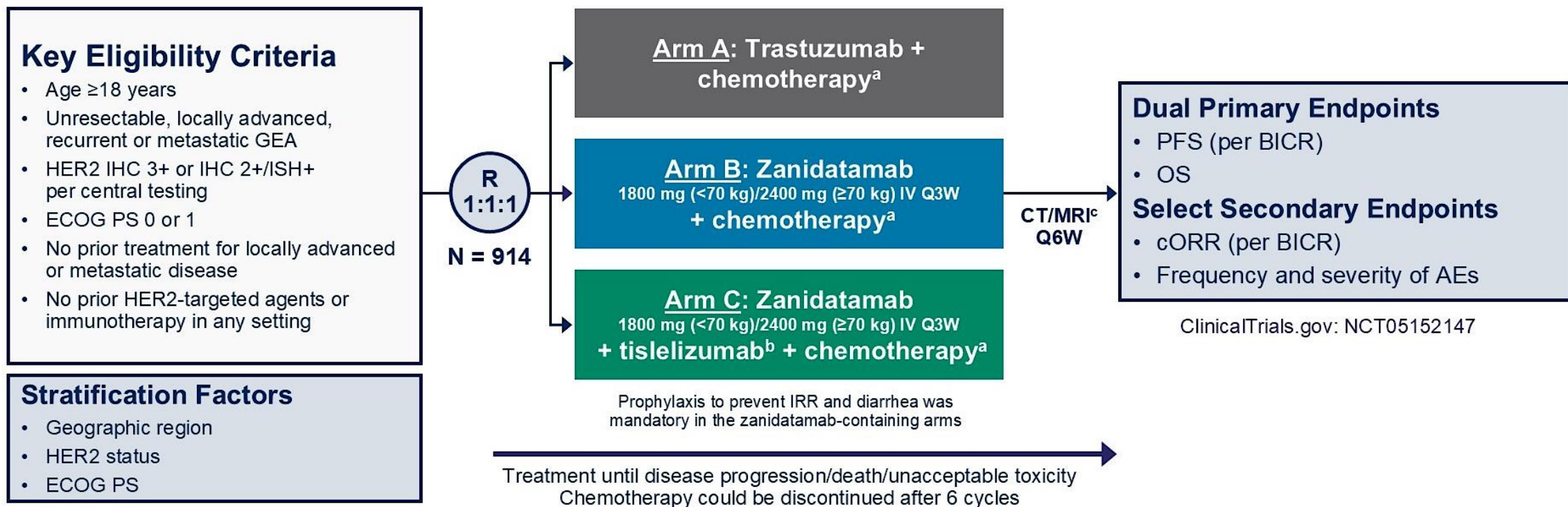
ccHER2+ = centrally confirmed HER2-positive; GEA = gastroesophageal adenocarcinoma

Phase II Study of First-Line Zanidatamab and Chemotherapy for HER2-Positive Advanced GEJ Cancers: OS



Phase III HERIZON-GEA-01 Trial of Zanidatamab with or without Tislelizumab for HER2-Positive Gastroesophageal Cancer

Global phase 3 trial of zanidatamab + chemotherapy ± tislelizumab vs trastuzumab + chemotherapy in previously untreated patients with HER2+ mGEA



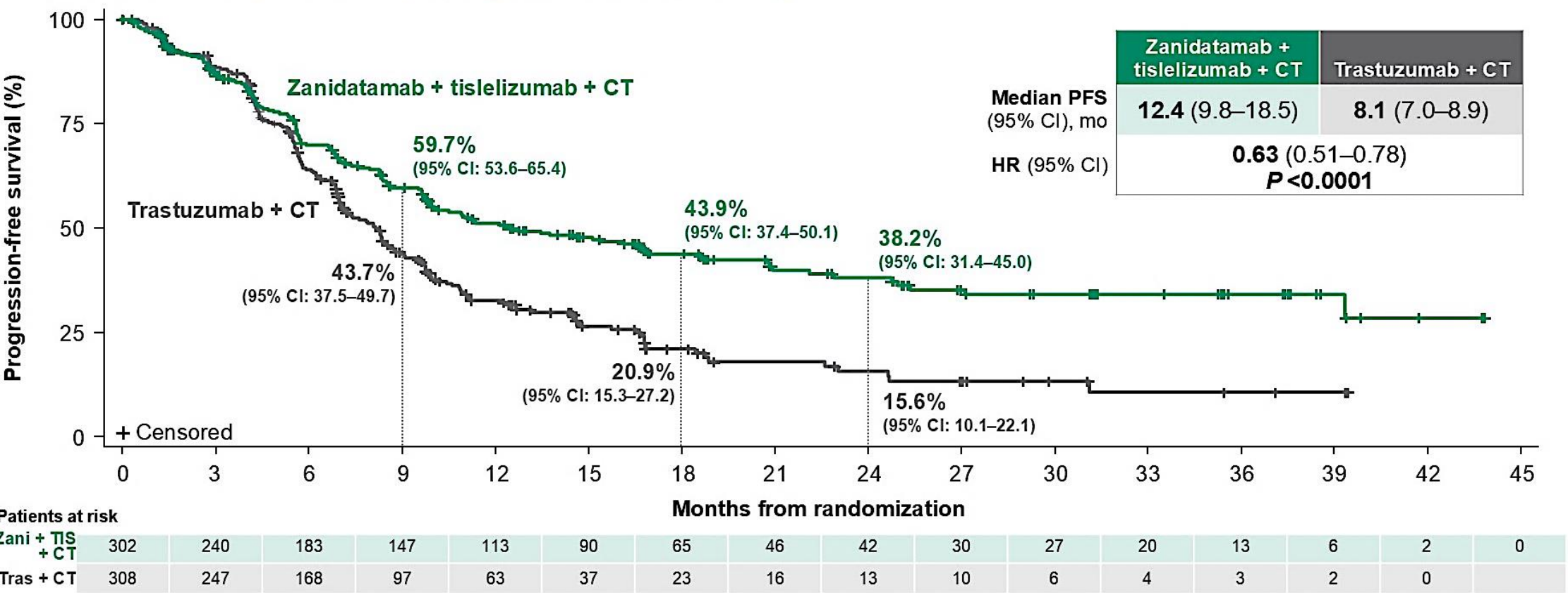
^aPhysician's choice of capecitabine plus oxaliplatin or 5-fluorouracil plus cisplatin. Chemotherapy was administered for at least 6 cycles or until disease progression, unacceptable toxicity, or another criterion for treatment discontinuation was met.

^bTislelizumab 200 mg was administered IV Q3W. ^cCT/MRI scans were performed every 6 weeks for the first 54 weeks, then every 9 weeks.

AE, adverse event; BICR, blinded independent central review; cORR, confirmed objective response rate; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; GEA, gastroesophageal adenocarcinoma; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IRR, infusion-related reaction; ISH, in situ hybridization; IV, intravenously; mGEA, advanced or metastatic GEA; MRI, magnetic resonance imaging; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomization.

HERIZON-GEA-01 Primary Endpoint: PFS per BICR with Zanidatamab, Tislelizumab and Chemotherapy (CT)

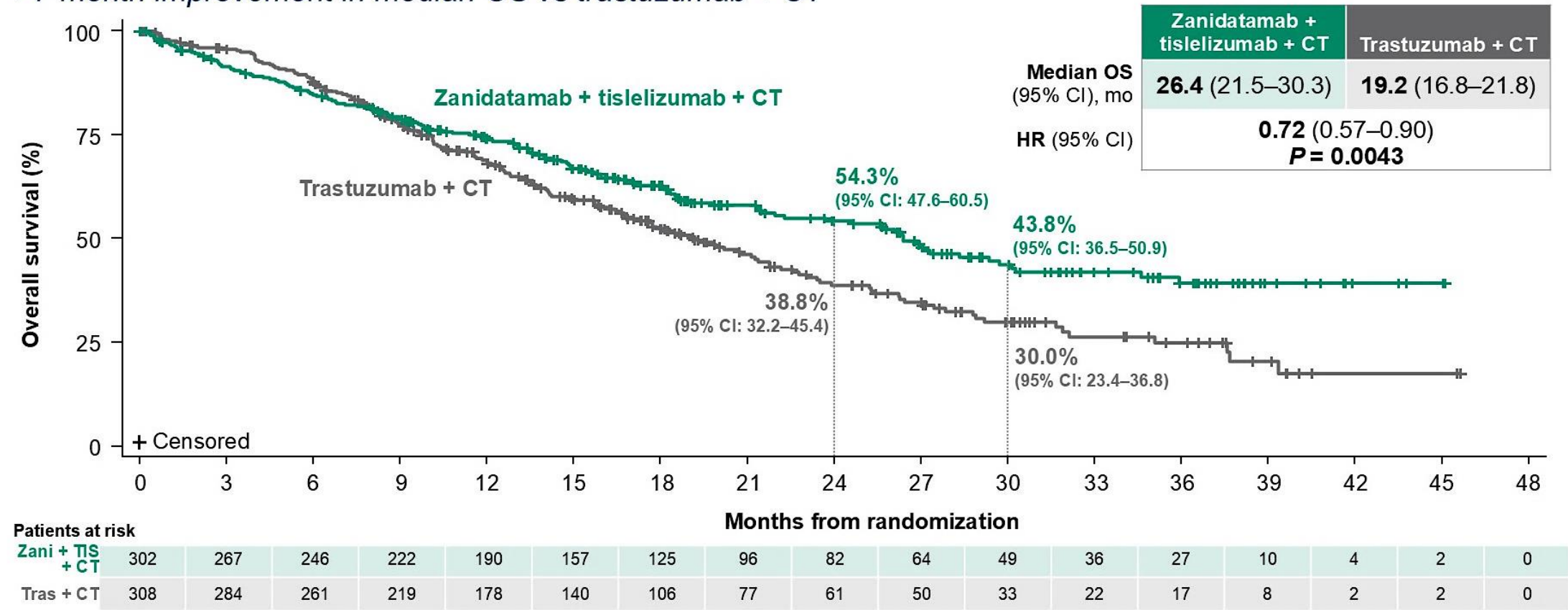
Statistically significant and clinically meaningful improvement in PFS with zanidatamab + tislelizumab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



BICR, blinded independent central review; CT, chemotherapy; HR, hazard ratio; PFS, progression-free survival; TIS, tislelizumab; Tras, trastuzumab; Zani, zanidatamab.

HERIZON-GEA-01 Primary Endpoint: Interim Analysis of OS with Zanidatamab, Tislelizumab and Chemotherapy

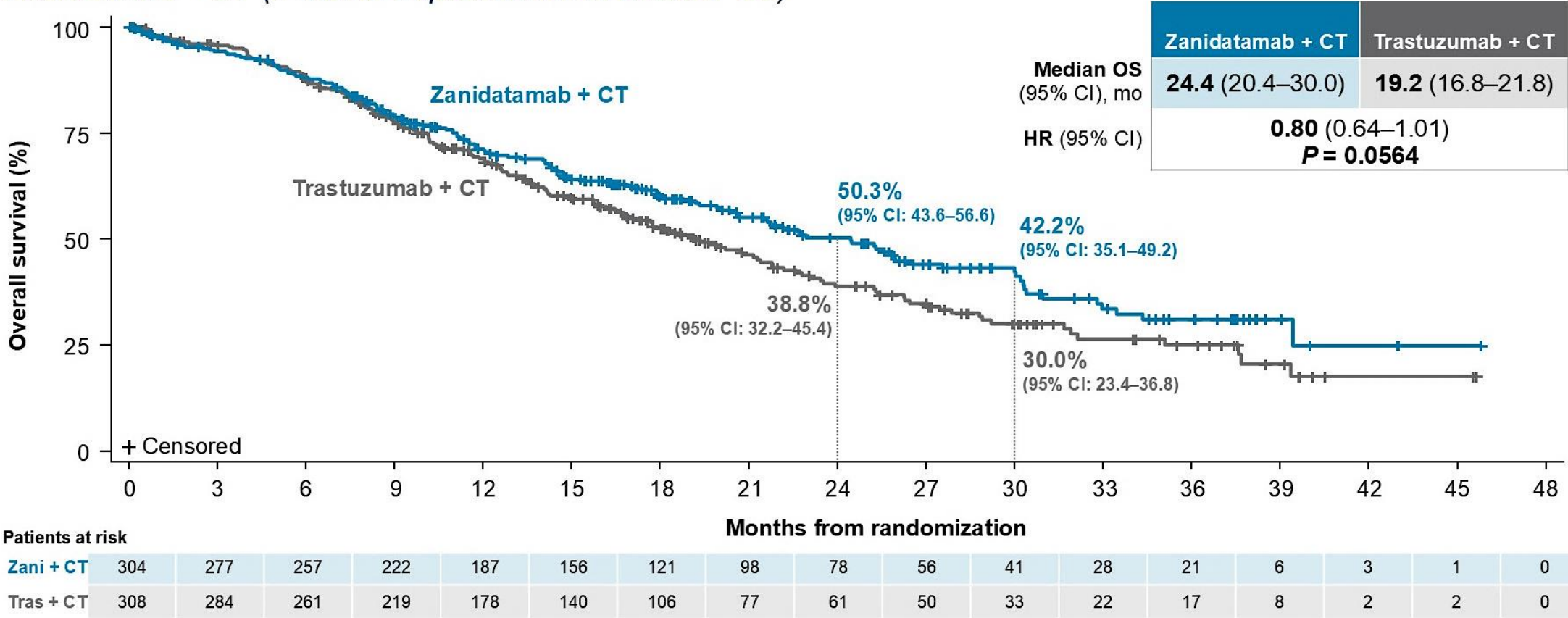
Zanidatamab + tislelizumab + CT demonstrated a statistically significant and clinically meaningful OS benefit with a >7-month improvement in median OS vs trastuzumab + CT



CT, chemotherapy; HR, hazard ratio; OS, overall survival; TIS, tislelizumab; Tras, trastuzumab; Zani, zanidatamab.

HERIZON-GEA-01: Interim OS Analysis with Zanidatamab and Chemotherapy

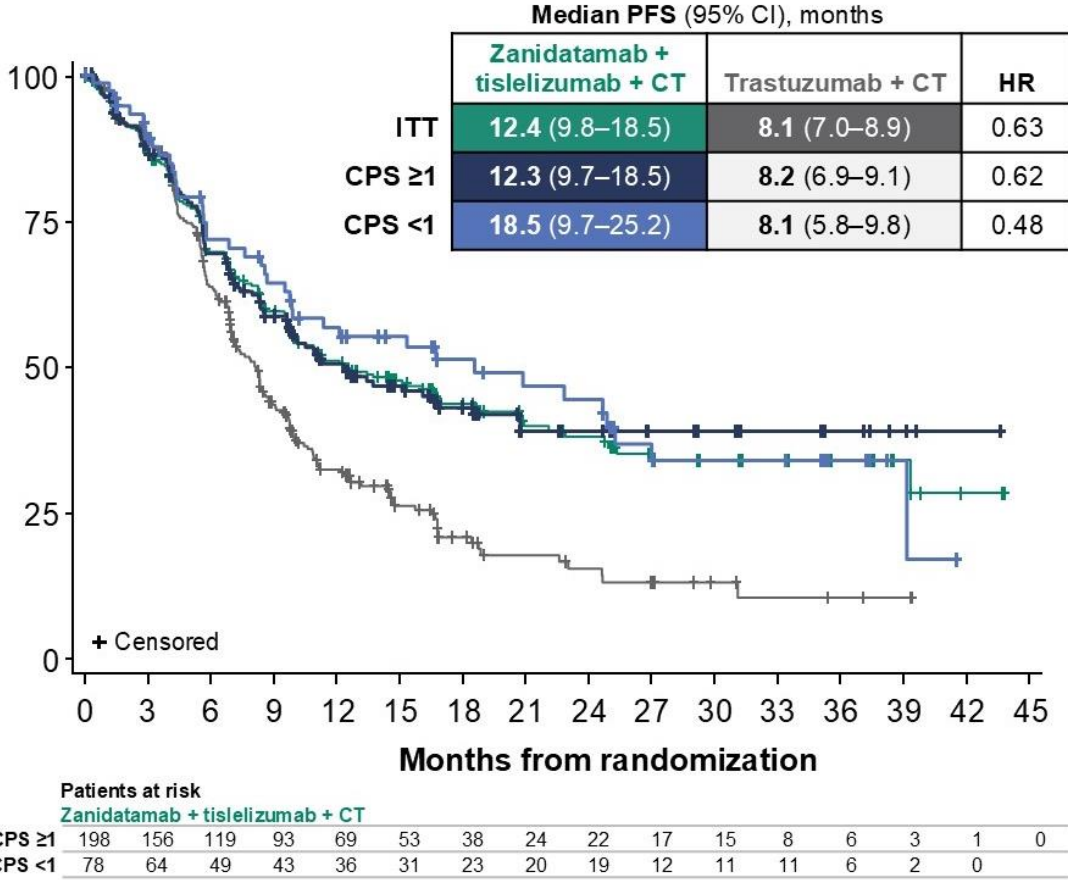
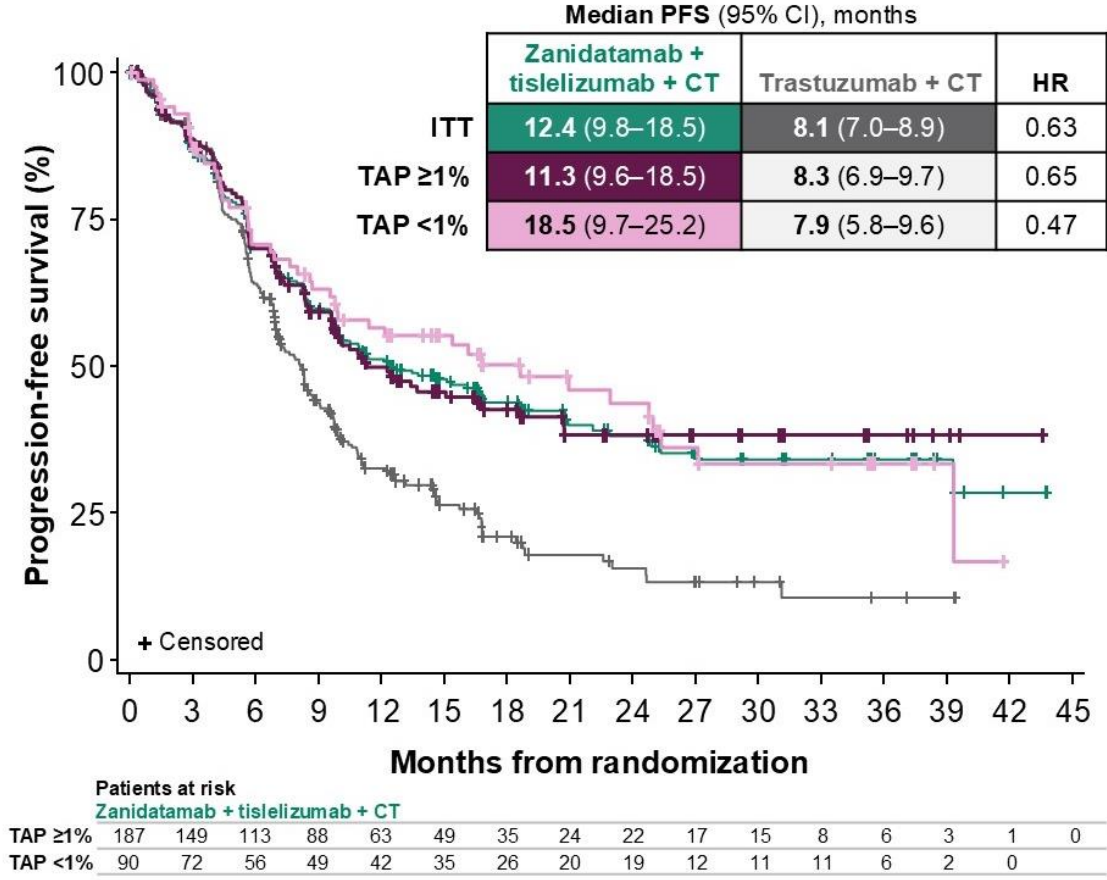
At this interim analysis, there was a strong trend toward significance for OS favoring zanidatamab + CT vs trastuzumab + CT (5-month improvement in median OS)



CT, chemotherapy; HR, hazard ratio; OS, overall survival; Tras, trastuzumab; Zani, zanidatamab.

HERIZON-GEA-01 Subgroup Analysis: PFS per BICR by PD-L1 Subgroups

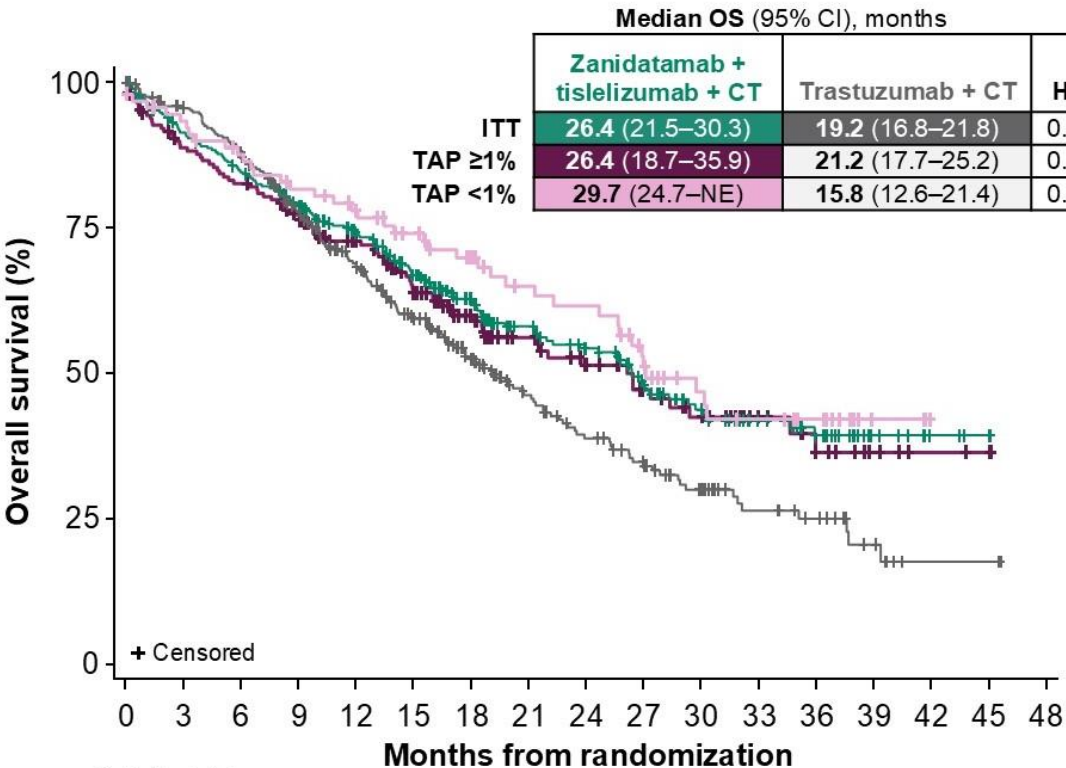
PFS improvements with zanidatamab + tislelizumab + CT vs trastuzumab + CT were independent of PD-L1 status



Data cutoff: October 1, 2025. The widths of the confidence intervals for the PD-L1 subgroups were not adjusted for multiplicity and cannot be used to infer treatment effects.
BICR, blinded independent central review; CPS, combined positive score; CT, chemotherapy; ITT, intent-to-treat; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TAP, tumor area positivity.

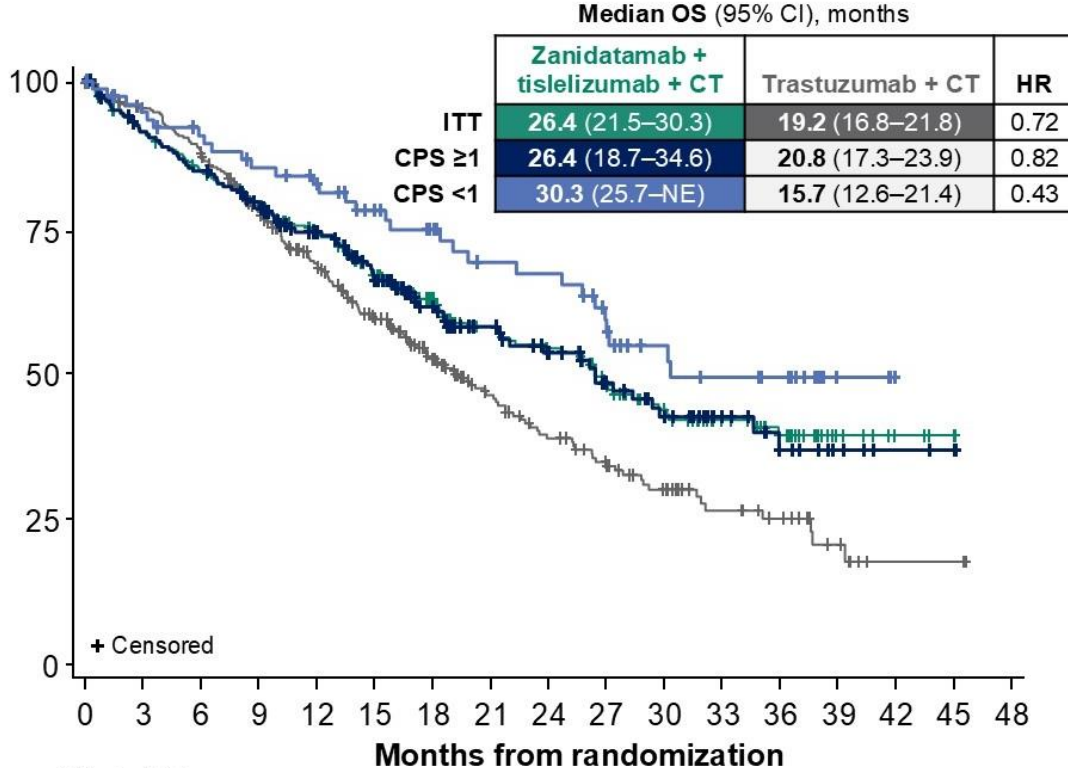
HERIZON-GEA-01 Subgroup Analysis: OS by PD-L1 Subgroups

OS improvements with zanidatamab + tislelizumab + CT vs trastuzumab + CT were independent of PD-L1 status



Patients at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Zanidatamab + tislelizumab + CT	187	163	152	137	114	92	69	53	41	33	27	17	11	6	3	2	0
TAP ≥1%	90	83	76	70	64	56	48	40	38	29	21	18	15	3	0		
TAP <1%	97	80	76	67	50	36	21	13	3	4	6	0	0	0	0	0	0



Patients at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Zanidatamab + tislelizumab + CT	198	174	161	145	120	99	73	56	44	35	28	18	11	6	3	2	0
CPS ≥1	78	71	66	61	57	48	43	36	35	27	20	17	15	3	0		
CPS <1	120	103	95	84	63	51	30	20	9	8	8	1	0	0	0	0	0

Data cutoff: October 1, 2025. The widths of the confidence intervals for the PD-L1 subgroups were not adjusted for multiplicity and cannot be used to infer treatment effects. CPS, combined positive score; CT, chemotherapy; ITT, intent-to-treat; NE, not estimable; OS, overall survival; PD-L1, programmed death-ligand 1; TAP, tumor area positivity.

HERIZON-GEA-01: Common Treatment-Related Adverse Events

Event	Zanidatamab + Tislelizumab + Chemotherapy (N= 294)†	Zanidatamab + Chemotherapy (N= 305)†	Trastuzumab + Chemotherapy (N= 302)
	<i>number of patients with event (percent)</i>		
Diarrhea	244 (83.0)	241 (79.0)	161 (53.3)
Nausea	164 (55.8)	166 (54.4)	144 (47.7)
Anemia	139 (47.3)	135 (44.3)	147 (48.7)
Decreased appetite	135 (45.9)	123 (40.3)	109 (36.1)
Vomiting	126 (42.9)	133 (43.6)	100 (33.1)
Hypokalemia	114 (38.8)	100 (32.8)	65 (21.5)
Weight decreased	104 (35.4)	109 (35.7)	65 (21.5)
Neutrophil count decreased	79 (26.9)	71 (23.3)	93 (30.8)
Peripheral sensory neuropathy	78 (26.5)	98 (32.1)	98 (32.5)
Infusion-related reaction	74 (25.2)	77 (25.2)	40 (13.2)
Platelet count decreased	68 (23.1)	63 (20.7)	94 (31.1)
Aspartate aminotransferase increased	63 (21.4)	61 (20.0)	64 (21.2)
Hypoalbuminemia	61 (20.7)	45 (14.8)	58 (19.2)
Fatigue	60 (20.4)	56 (18.4)	45 (14.9)
White-cell count decreased	60 (20.4)	50 (16.4)	62 (20.5)
Palmar–plantar erythrodysesthesia syndrome	54 (18.4)	51 (16.7)	64 (21.2)

FDA Approves Zanidatamab and Tislelizumab for HER2-Positive Gastric, Gastroesophageal Junction or Esophageal Adenocarcinoma

Press Release: August 25, 2026

“...the Food and Drug Administration approved zanidatamab-hrii:

- In combination with fluoropyrimidine- and platinum-containing chemotherapy and tislelizumab-jsgr, as first-line treatment for adults with HER2-positive (IHC 3+ or IHC 2+/ISH+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-approved test, and
- in combination with fluoropyrimidine-, and platinum-containing chemotherapy, as first-line treatment for adults with HER2-positive (IHC 3+) unresectable locally advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma, as detected by an FDA-approved test.”

The approval is based on data from HERIZON-GEA-01, the global Phase III clinical trial evaluating zanidatamab with chemotherapy, with and without tislelizumab, compared to trastuzumab with chemotherapy as first-line treatment for advanced or metastatic HER2-positive gastroesophageal adenocarcinoma.

Positive Top-Line Results Announced from the Second Interim Analysis of Phase III HERIZON-GEA-01 Trial

Press Release: August 31, 2026

Positive top-line results were announced from the second interim analysis (IA2) of the Phase III HERIZON-GEA-01 trial evaluating zanidatamab, in combination with chemotherapy, with and without tislelizumab, as first-line treatment for HER2-positive locally advanced or metastatic gastroesophageal adenocarcinoma.

“At IA2, zanidatamab plus chemotherapy demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) compared with trastuzumab plus chemotherapy, meeting the remaining primary endpoint analysis of the study.

IA2 also provided longer follow-up data for the tislelizumab plus zanidatamab and chemotherapy regimen, demonstrating an improved OS hazard ratio, continued durable outcomes, and a generally manageable safety profile. These results reinforce findings from IA1, in which the regimen met the progression-free survival (PFS) and OS endpoints, with the overall survival benefit observed across PD-L1 and HER2+ expression levels.

The safety profile of zanidatamab plus chemotherapy and tislelizumab plus zanidatamab and chemotherapy at IA2 was generally consistent with that of IA1 and the known safety profiles of the individual treatment components, with no new safety signals identified.

The results from IA2 have been submitted for presentation at a major medical meeting in the fourth quarter of 2026.”

Phase Ib/II DESTINY-Gastric03 Study Design

Part 1 **ENROLLMENT COMPLETE**

(1A and 1B published)¹²

Dose escalation (3 + 3)*

1A: T-DXd IV q3w + 5-FU IV on Days 1–5, q3w

1D(a): T-DXd IV q3w +
5-FU IV on Days 1–5 q3w
+ oxaliplatin IV q3w

1B: T-DXd IV q3w + cap (oral) BID on Days 1–14

1D(b): T-DXd IV q3w +
cap (oral) BID on Days 1–14
+ oxaliplatin IV q3w

1C: T-DXd IV q3w + 5-FU IV on Days 1–5, q3w

1E(a): T-DXd IV q3w +
5-FU IV on Days 1–5
+ durvalumab IV q3w

1E(b): T-DXd IV q3w +
cap (oral) BID on Days 1–14
+ durvalumab IV q3w

Parts 2A–2E Dose expansion

ENROLLMENT COMPLETE

N≈40 participants per arm;

2F RECRUITING: N≈30 participants^{†‡}

2A: Trastuzumab + fluoropyrimidine
+ platinum-based chemotherapy

2B: T-DXd monotherapy IV q3w

2C:[§] T-DXd IV q3w + fluoropyrimidine
± oxaliplatin IV q3w

2D:^{†||} T-DXd IV q3w + fluoropyrimidine
+ pembrolizumab IV q3w

2E:^{||} T-DXd IV q3w +
pembrolizumab IV q3w

2F:^{||**††} T-DXd IV q3w + fluoropyrimidine
+ pembrolizumab IV q3w

Part 3 **RECRUITING**

Volrustomig safety cohort

N=6 per dose^{‡‡}

T-DXd IV q3w + fluoropyrimidine +
volrustomig IV q3w^{**}



Part 3 **RECRUITING**

Volrustomig main cohort

N≈18–30[†]

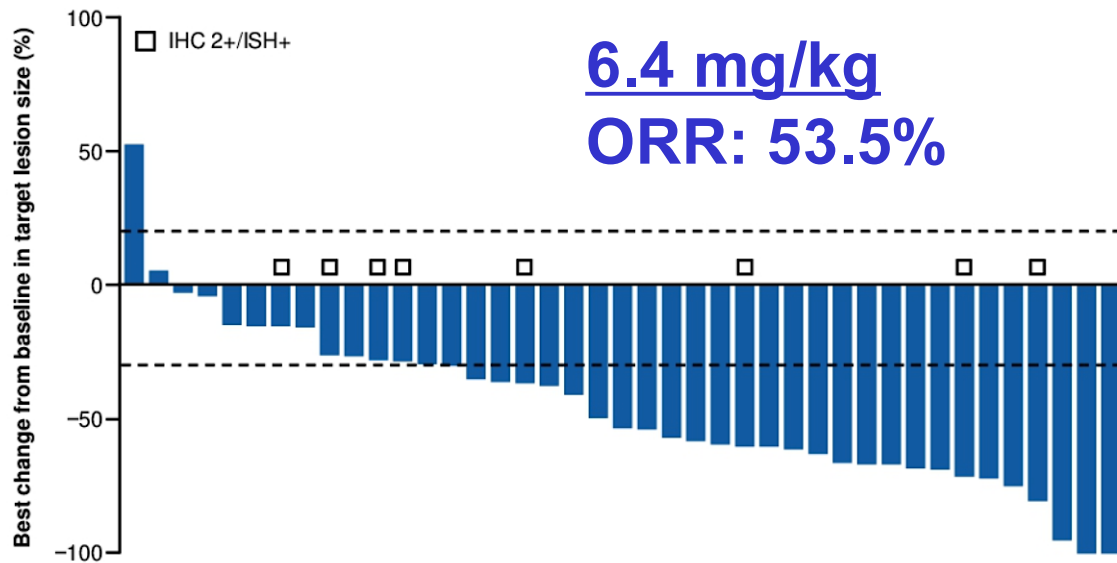
3A: HER2+
T-DXd IV q3w + fluoropyrimidine +
volrustomig IV q3w^{**§§}

3B: HER2-low
T-DXd IV q3w + fluoropyrimidine +
volrustomig IV q3w^{**§§}

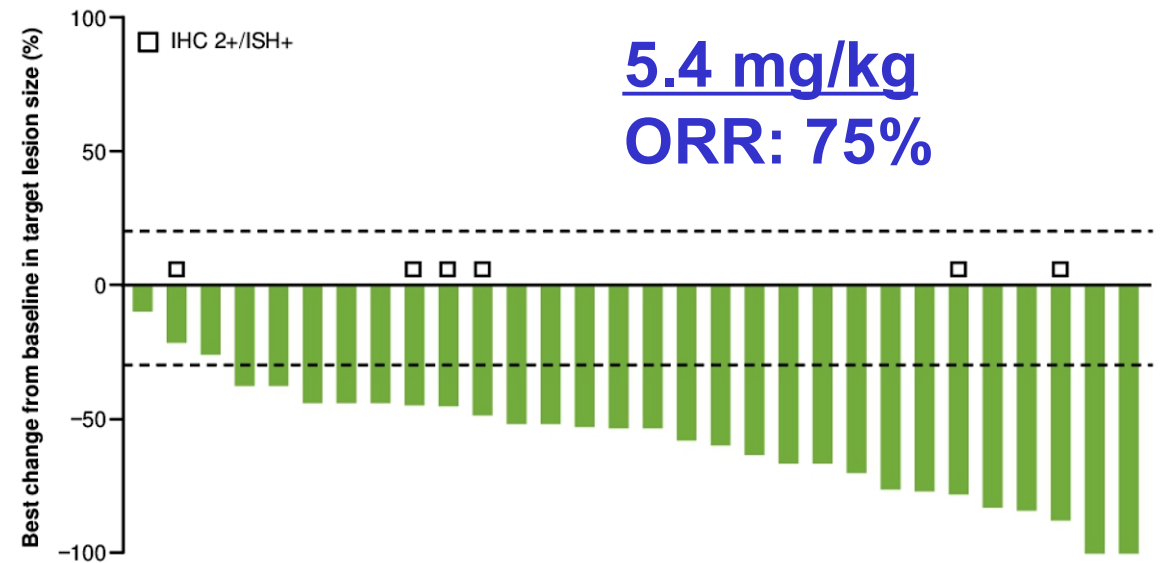
During Part 1 of the study, the FDA granted accelerated approval for first-line pembrolizumab plus trastuzumab and chemotherapy for HER2+ gastric cancer in patients whose tumors express PD-L1.¹¹ Therefore, the study sponsor amended the study design to include Arm 2F, and terminated Arm 2A early as this was a control arm using the standard of care

DESTINY-Gastric03: Phase Ib/II Study of First-Line T-DXd with Pembrolizumab and Fluoropyrimidine for HER2-Positive GEJ Cancer (Arms D and F) – Response

A Arm D: T-DXd 6.4 mg/kg 5-FU/capecitabine 1000 mg/m² + pembrolizumab



B Arm F: T-DXd 5.4 mg/kg + 5-FU/capecitabine 750 mg/m² + pembrolizumab

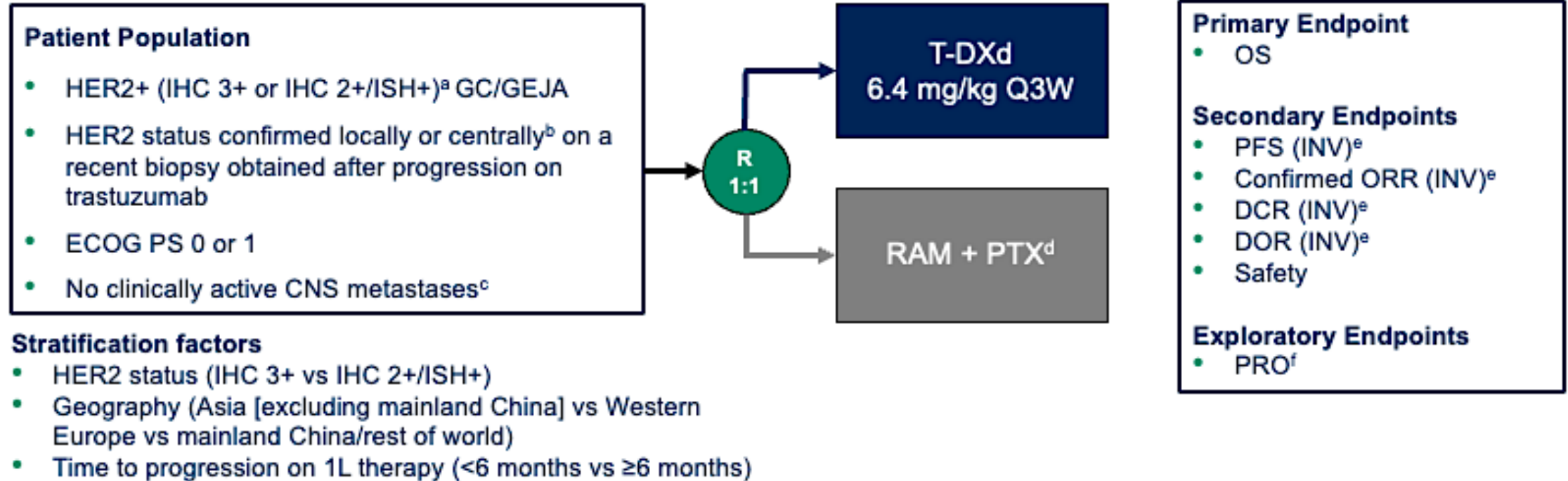


- At similar periods of follow up, the confirmed ORR by investigator assessment was 53.5% in the T-DXd 6.4 mg/kg triplet combination arm (**Figure 2A**) and 75.0% in the 5.4 mg/kg triplet combination arm (**Figure 2B**)
 - In the T-DXd 6.4 mg/kg triplet combination arm, the ORR (n/N) was 55.9% (19/34) in patients with IHC 3+ and 44.4% (4/9) in patients with IHC 2+/ISH+
 - In the T-DXd 5.4 mg/kg triplet combination arm, the ORR (n/N) was 73.1% (19/26) in patients with IHC 3+ and 83.3% (5/6) in patients with IHC 2+/ISH+

Select Ongoing Phase III Trials of First-Line Therapy for Advanced HER2-Positive Gastroesophageal Adenocarcinoma

Trial identifier	Estimated N	Setting	Treatment arms	Estimated completion date
DESTINY-Gastric05 (NCT06731478)	726	Main cohort: Unresectable, locally advanced or metastatic gastric or GEJ cancer, PD-L1 CPS ≥ 1 Exploratory cohort: Gastric or GEJ cancer, PD-L1 CPS < 1	- T-DXd + fluoropyrimidine $\pm$ pembrolizumab - Standard chemotherapy + trastuzumab $\pm$ pembrolizumab	February 2030
ARTEMIDE-Gastric01 (NCT06764875)	840	Locally advanced or metastatic gastric or GEJ adenocarcinoma with tumor PD-L1 CPS ≥ 1	- T-DXd + rilvegostomig + fluoropyrimidine - Pembrolizumab + trastuzumab + FP (5-FU + cisplatin) or CAPOX - Rilvegostomig + trastuzumab + FP or CAPOX	December 2030

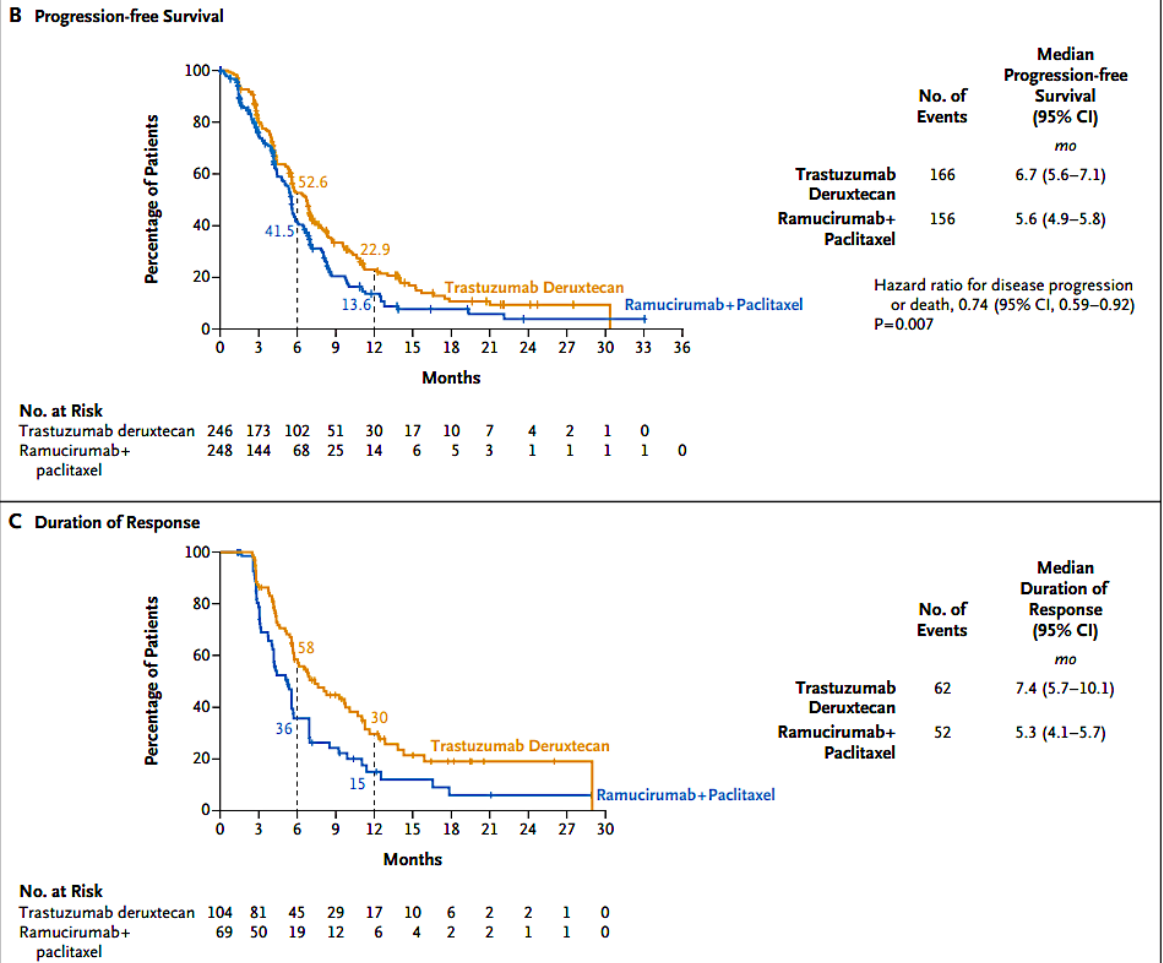
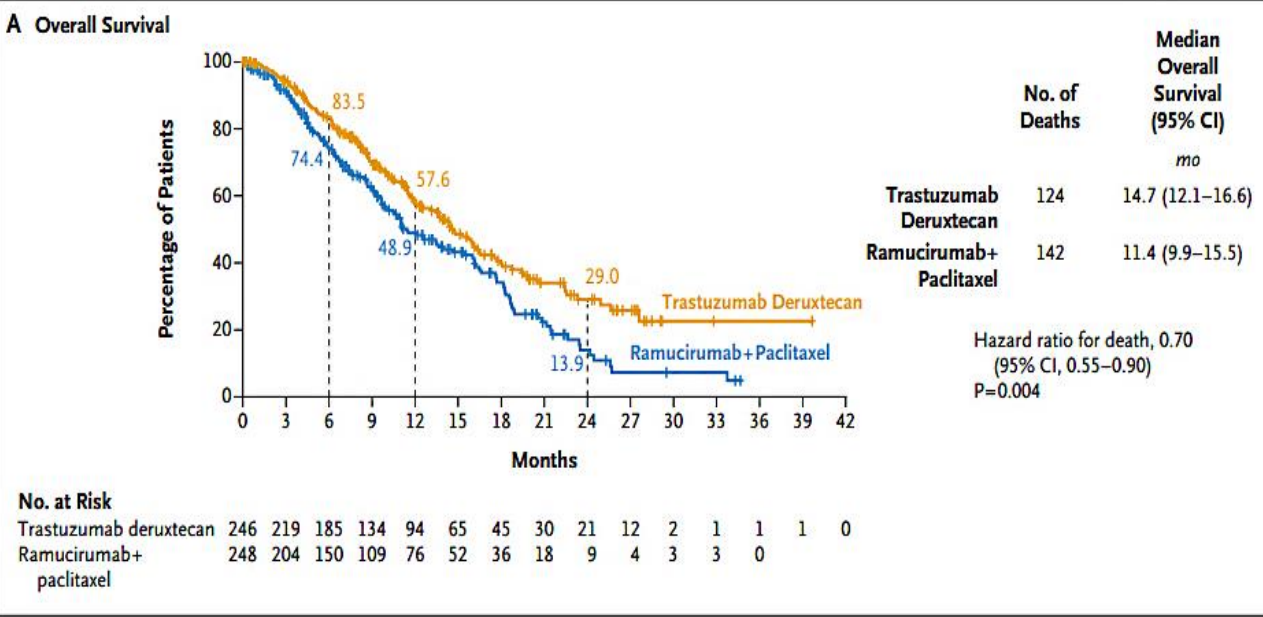
DESTINY-Gastric04 Phase III Trial of Trastuzumab Deruxtecan (T-DXd) Compared to Ramucirumab/Paclitaxel for Gastric Cancer



^aAs classified by 2018 ASCO/CAP guidelines. ^bStudy protocol originally mandated HER2 status be determined centrally but was later amended to allow local determination. ^cClinically active CNS metastases were defined as being untreated and symptomatic or requiring therapy with corticosteroids or anticonvulsants. Patients with clinically inactive CNS metastases could be enrolled. ^dRAM administered as 8 mg/kg on days 1 and 15 of each 28-day cycle and PTX administered as 80 mg/m² on days 1, 8, and 15 of each 28-day cycle. ^eDetermined by investigator-based assessment on RECIST v1.1. ^fBased on EORTC EQ-5D-5L VAS and FACT-Ga subscales.

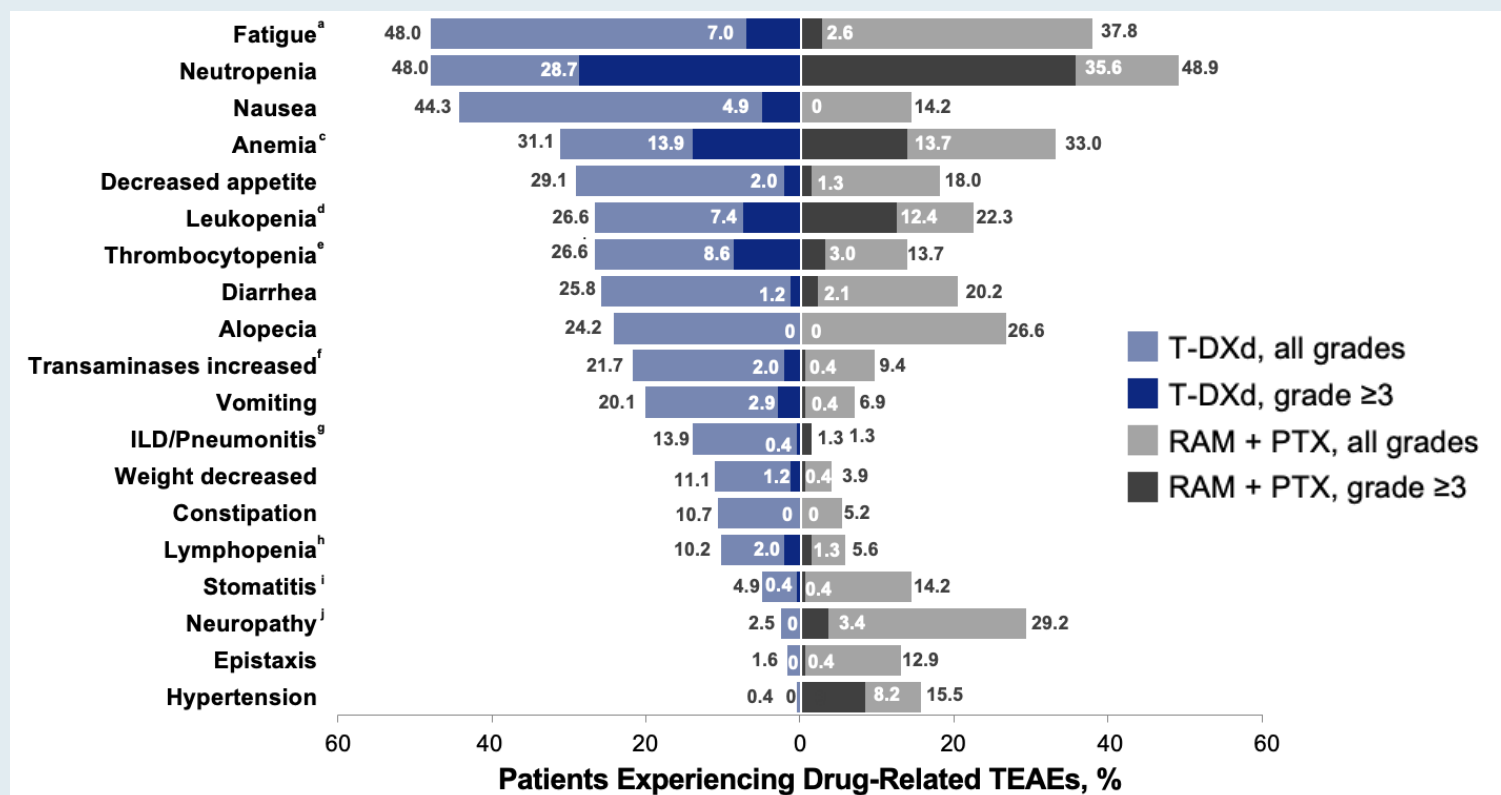
GC = gastric cancer; GEJA = gastroesophageal junction adenocarcinoma; RAM = ramucirumab; PTX = paclitaxel

DESTINY-Gastric04: Survival and Duration of Response with T-DXd for Gastric Cancer



DESTINY-Gastric04: Safety with T-DXd for Gastric Cancer

Drug-related TEAEs in
≥10% of patients



Adjudicated drug-related ILD/pneumonitis

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 244)	7 (2.9)	26 (10.7)	1 (0.4)	0	0	34 (13.9)
RAM + PTX (n = 233)	0	0	2 (0.9)	0	1 (0.4)	3 (1.3)

Left ventricular dysfunction^a

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 244)	0	3 (1.2)	3 (1.2)	0	0	6 (2.5)
RAM + PTX (n = 233)	2 (0.9)	2 (0.9)	0	0	0	4 (1.7)

TEAEs = treatment-emergent adverse events; ILD = interstitial lung disease

Shitara K et al. ASCO 2025;Abstract LBA4002; Shitara K et al. *N Engl J Med* 2025;393:336-48.

Agenda

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Module 2: Clinician Survey Results

Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

Module 6: Clinician Survey Results

Regulatory and reimbursement issues aside, which first-line treatment would you most likely recommend for a 65-year-old patient presenting with metastatic CLDN18.2-negative, HER2-positive, microsatellite-stable (MSS) gastric adenocarcinoma with a PD-L1 combined positive score (CPS) of 0?



Dr Ilson

Zanidatamab/chemotherapy/tislelizumab



Dr Janjigian

Zanidatamab/chemotherapy/tislelizumab



Dr Kim

Zanidatamab/chemotherapy/tislelizumab



Dr Klempner

Zanidatamab/chemotherapy/tislelizumab



Dr Mehta

Zanidatamab/chemotherapy/tislelizumab



Dr Shah

Zanidatamab/chemotherapy



Dr Strickler

Zanidatamab/chemotherapy/tislelizumab



Dr Wainberg

Zanidatamab/chemotherapy

Regulatory and reimbursement issues aside, which first-line treatment would you most likely recommend for a 65-year-old patient presenting with metastatic CLDN18.2-negative, HER2-positive, MSS gastric adenocarcinoma with the PD-L1 CPS scores below?

		PD-L1 CPS 1	PD-L1 CPS 10
	Dr Ilson	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Janjigian	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Kim	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Klempner	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Mehta	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Shah	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Strickler	Zanidatamab/chemotherapy/ tisnelizumab	Zanidatamab/chemotherapy/ tisnelizumab
	Dr Wainberg	Zanidatamab/chemotherapy/tisnelizumab or trastuzumab/chemotherapy/pembrolizumab	Zanidatamab/chemotherapy/tisnelizumab or trastuzumab/chemotherapy/pembrolizumab

For a patient to whom you have elected to administer zanidatamab/chemotherapy in combination with an anti-PD-1 antibody, how will you approach the selection of the anti-PD-1 antibody?



Dr Ilson

I will use tislelizumab according to the trial



Dr Janjigian

I will use tislelizumab according to the trial



Dr Kim

I will use tislelizumab according to the trial



Dr Klempner

I will use any of the anti-PD-1 antibodies



Dr Mehta

I will use tislelizumab according to the trial



Dr Shah

I will use tislelizumab according to the trial



Dr Strickler

I will use any of the anti-PD-1 antibodies



Dr Wainberg

I will use any of the anti-PD-1 antibodies

In general, would you prioritize a CLDN18.2-targeted or a HER2-targeted therapy for a patient with newly diagnosed CLDN18.2-positive, HER2-positive metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma with a PD-L1 CPS of 0?



Dr Ilson

HER2-targeted therapy



Dr Janjigian

HER2-targeted therapy



Dr Kim

HER2-targeted therapy



Dr Klempner

HER2-targeted therapy



Dr Mehta

HER2-targeted therapy



Dr Shah

HER2-targeted therapy



Dr Strickler

HER2-targeted therapy



Dr Wainberg

HER2-targeted therapy

In general, do you order repeat biopsies for your patients with HER2-positive gastroesophageal cancers after disease progression on HER2-targeted therapy?



Dr Ilson

No



Dr Janjigian

Yes



Dr Kim

Yes



Dr Klempner

Yes



Dr Mehta

Yes



Dr Shah

Yes



Dr Strickler

Yes



Dr Wainberg

Yes

What would you most likely recommend as second-line therapy for a patient with metastatic CLDN18.2-negative, HER2-positive, MSS gastric adenocarcinoma with a PD-L1 CPS of ≥ 1 who experienced disease progression (PD) on the first-line regimens below?

		PD on first-line FOLFOX/trastuzumab/pembrolizumab	PD on first-line zanidatamab/ chemotherapy/tislelizumab
	Dr Ilson	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Janjigian	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Kim	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Klempner	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Mehta	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Shah	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Strickler	Trastuzumab deruxtecan	Trastuzumab deruxtecan
	Dr Wainberg	Trastuzumab deruxtecan	Trastuzumab deruxtecan

For a patient with HER2-positive gastric/GEJ adenocarcinoma who experienced PD on first-line FOLFOX/trastuzumab/pembrolizumab and on second-line trastuzumab deruxtecan, would you offer treatment with zanidatamab?

	Dr Ilson	No
	Dr Janjigian	Yes
	Dr Kim	No
	Dr Klempner	Yes
	Dr Mehta	Yes
	Dr Shah	No
	Dr Strickler	No
	Dr Wainberg	No

Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

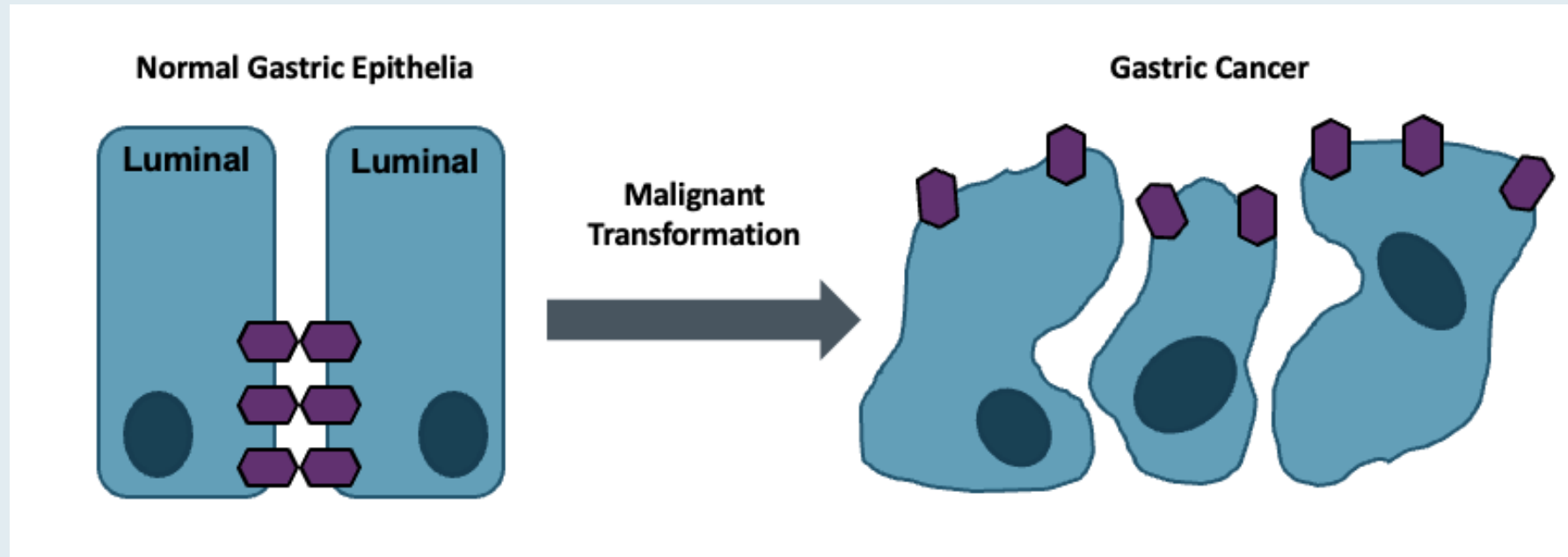
Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

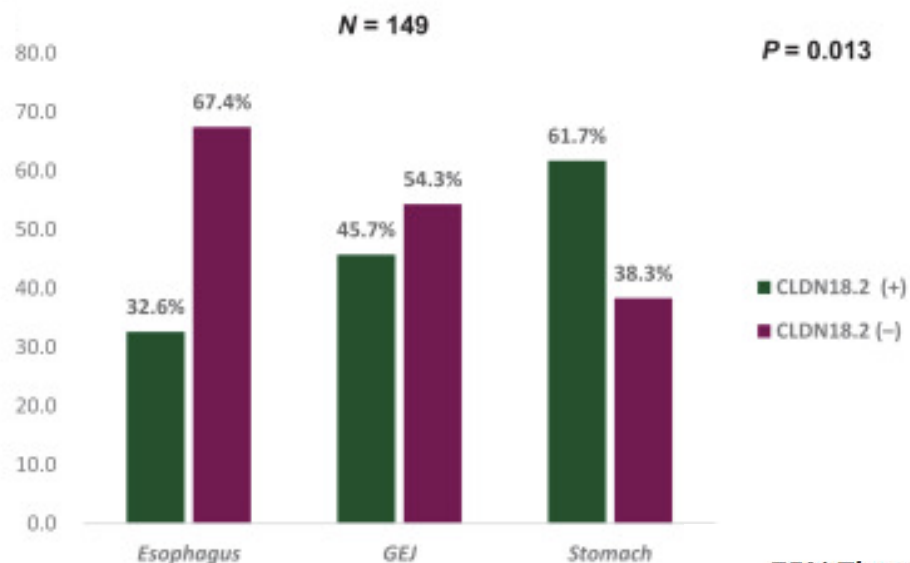
Module 6: Clinician Survey Results

Claudin 18.2: Leveraging Biology



- Claudin 18.2 is a major structural component of intercellular tight junctions
- Not routinely expressed in any normal tissue outside gastric mucosa (cancer-restricted antigen)
- Broadly expressed in several tumor types, including gastric, GEJ, biliary and pancreatic

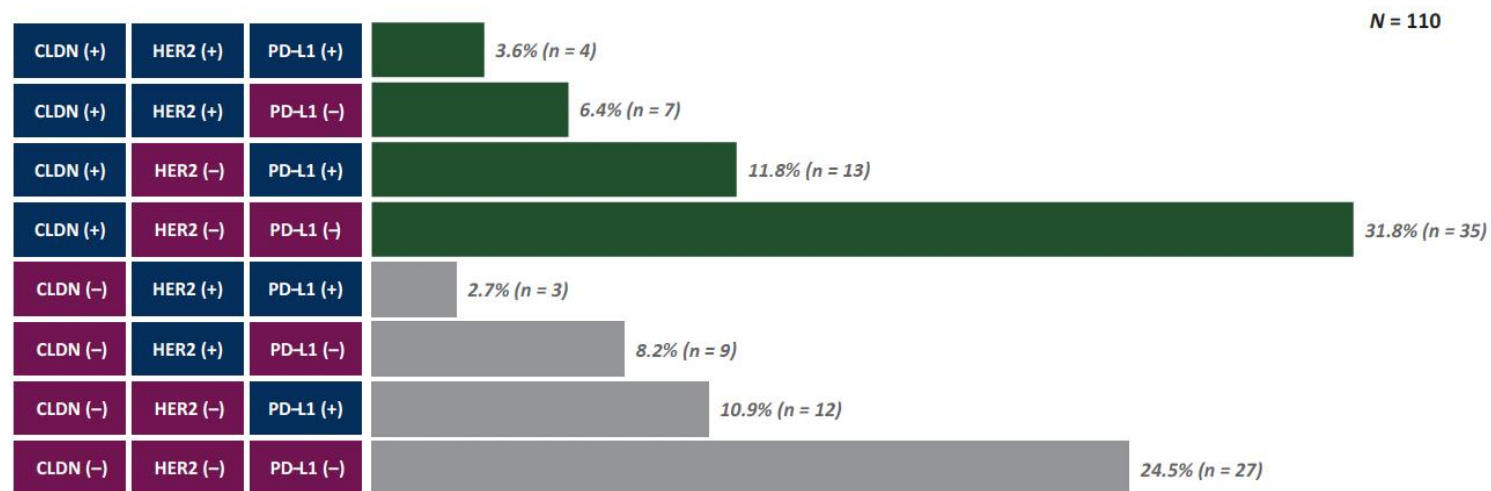
Claudin 18.2 (CLDN18.2): Characteristics and Overlap



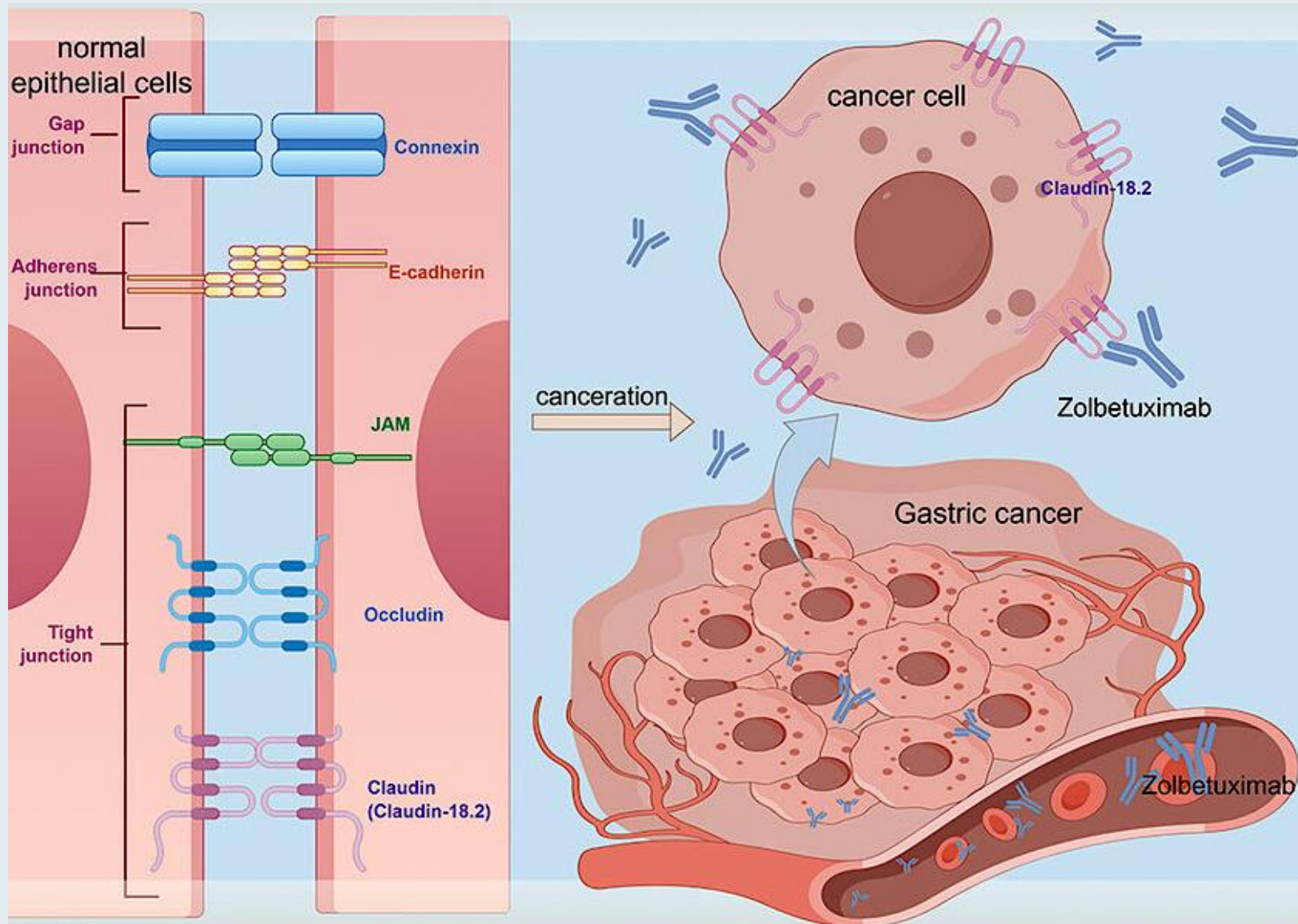
- **CLDN18.2 positivity rates:**
 - Highest in gastric followed by GEJ and esophagus
 - **48.3% (75% threshold: $\geq 75\%$ of tumor cells with 2-3+ staining)**
 - 71.1% (H-score 25; $\geq 1+$ intensity in $\geq 25\%$ of cells)
 - 73.8% (H-score 10; $\geq 1+$ intensity in $\geq 10\%$ of cells)

- No significant association with HER2, PD-L1 CPS or mismatch repair
- ~30% sole biomarker

75% Threshold

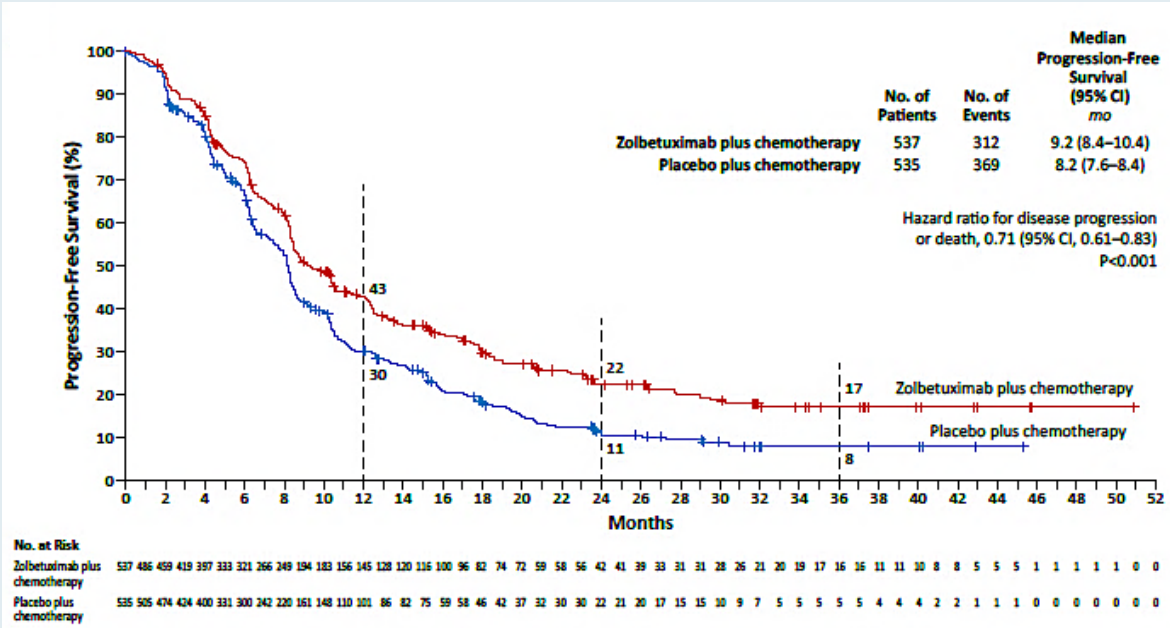


Zolbetuximab Mechanism of Action

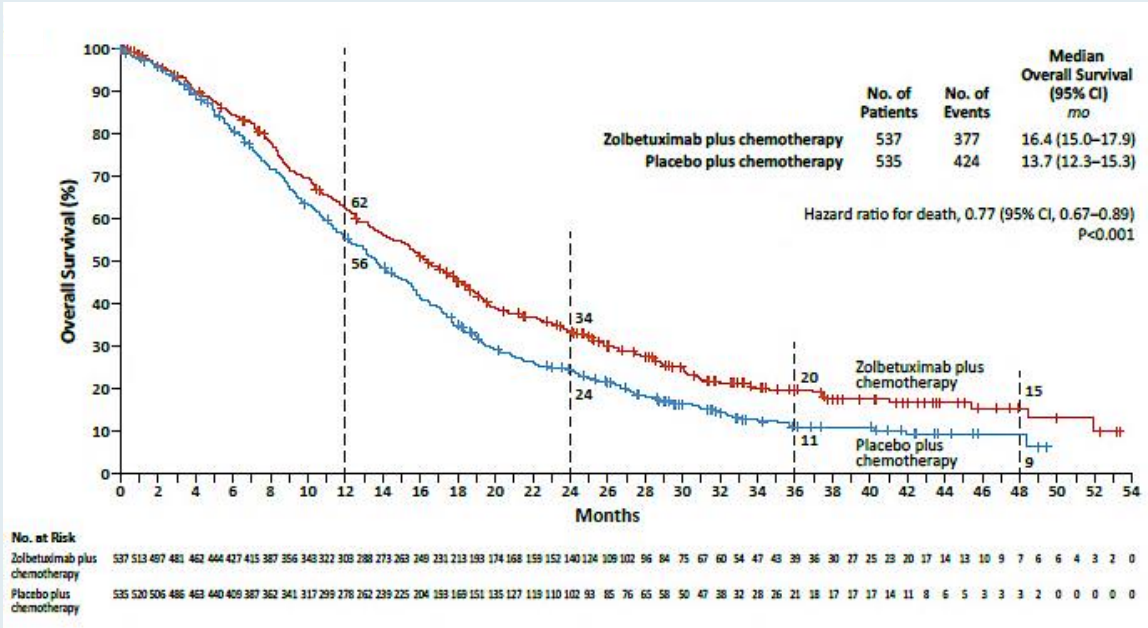


SPOTLIGHT and GLOW Trials Combined Analysis: Survival with First-Line Zolbetuximab and Chemotherapy for Gastric or GEJ Adenocarcinoma

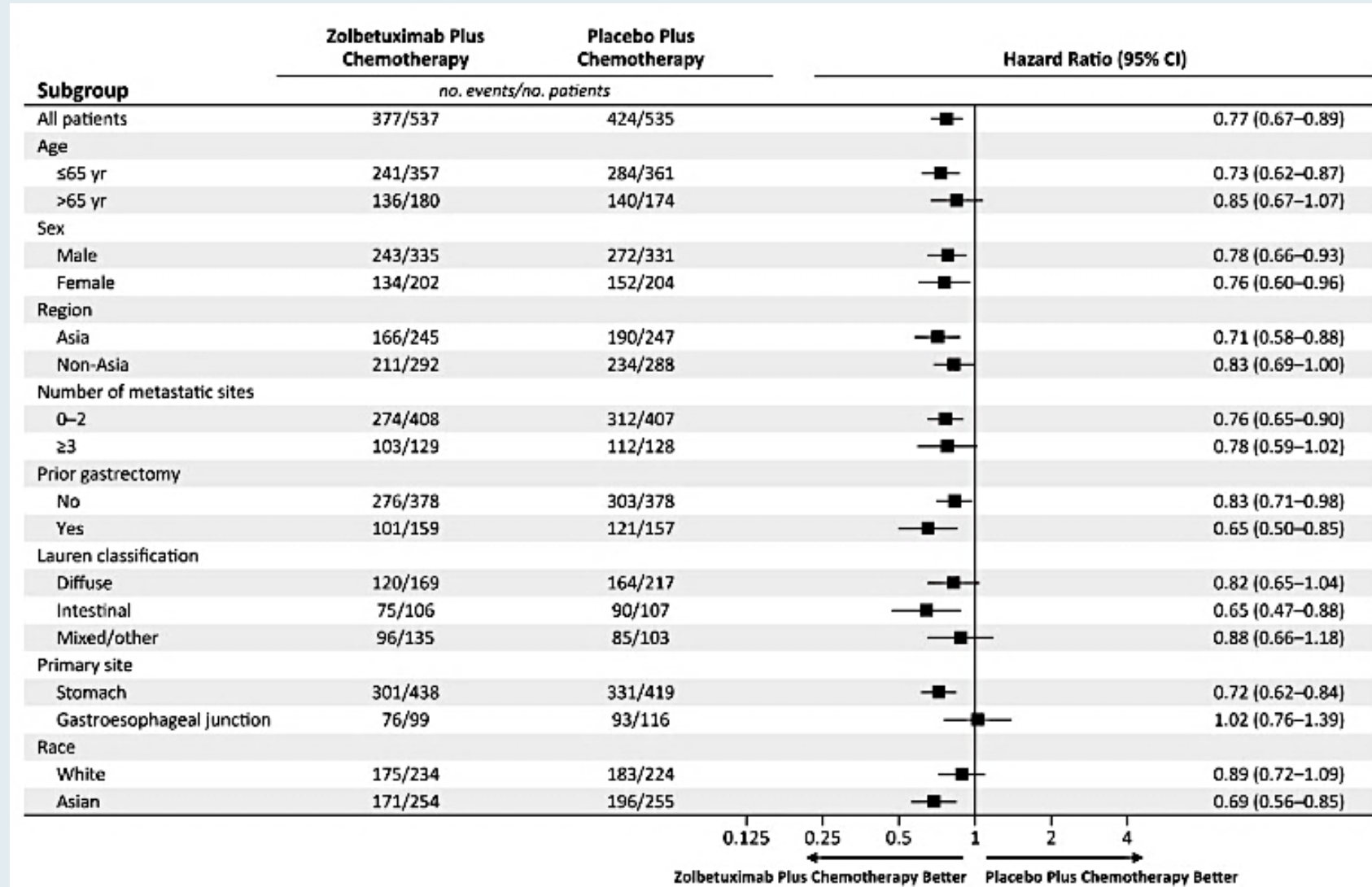
Updated PFS



Final OS Analysis



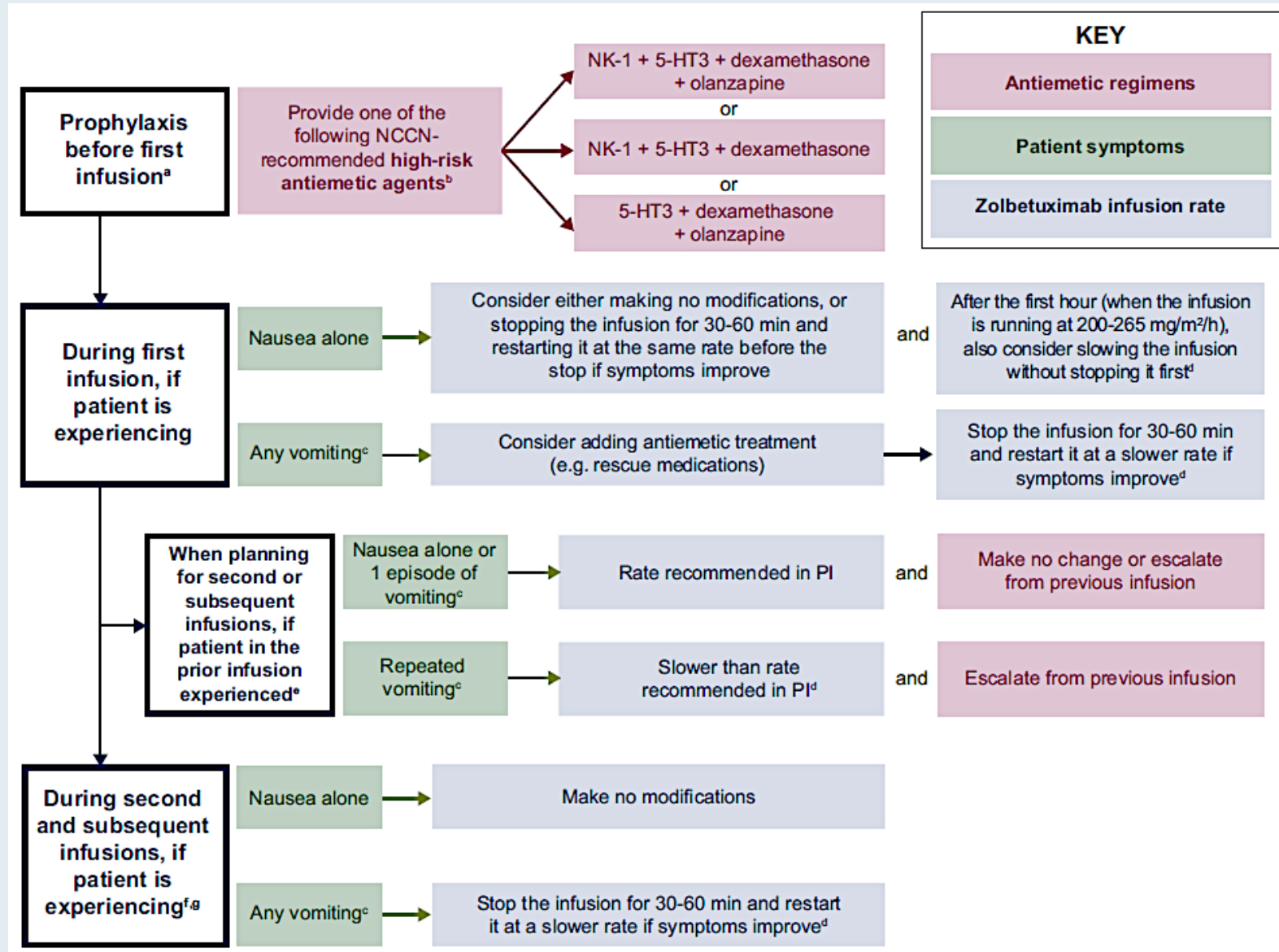
SPOTLIGHT and GLOW Combined Analysis: Overall Survival with First-Line Zolbetuximab and Chemotherapy for Gastric or GEJ Adenocarcinoma



SPOTLIGHT and GLOW Combined Analysis: Treatment-Emergent Adverse Events

Event – no. (%)	Zolbetuximab + chemotherapy (n = 533)		Placebo + chemotherapy (n = 527)	
	All grade	Grade ≥3	All grade	Grade ≥3
Nausea	405 (76.0)	67 (12.6)	296 (56.2)	25 (4.7)
Vomiting	356 (66.8)	76 (14.3)	180 (34.2)	26 (4.9)
Decreased appetite	241 (45.2)	34 (6.4)	183 (34.7)	13 (2.5)
Anemia	199 (37.3)	53 (9.9)	199 (37.8)	54 (10.2)
Diarrhea	197 (37.0)	27 (5.1)	212 (40.2)	28 (5.3)
Neutrophil count decreased	167 (31.3)	95 (17.8)	150 (28.5)	93 (17.6)
Peripheral sensory neuropathy	164 (30.8)	13 (2.4)	175 (33.2)	21 (4.0)
Neutropenia	152 (28.5)	97 (18.2)	129 (24.5)	72 (13.7)
Constipation	141 (26.5)	3 (0.6)	166 (31.5)	4 (0.8)
Fatigue	118 (22.1)	25 (4.7)	136 (25.8)	24 (4.6)
Aspartate aminotransferase increased	113 (21.2)	10 (1.9)	122 (23.1)	16 (3.0)
Abdominal pain	111 (20.8)	15 (2.8)	143 (27.1)	11 (2.1)
Asthenia	108 (20.3)	28 (5.3)	96 (18.2)	10 (1.9)
Weight decreased	108 (20.3)	7 (1.3)	81 (15.4)	4 (0.8)
Hypoalbuminemia	103 (19.3)	20 (3.8)	53 (10.1)	6 (1.1)
Platelet count decreased	102 (19.1)	22 (4.1)	111 (21.1)	27 (5.1)
White blood cell count decreased	102 (19.1)	13 (2.4)	86 (16.3)	26 (4.9)
Pyrexia	95 (17.8)	2 (0.4)	73 (13.9)	1 (0.2)
Hypokalemia	88 (16.5)	30 (5.6)	80 (15.2)	27 (5.1)
Alanine aminotransferase increased	83 (15.6)	4 (0.8)	103 (19.5)	17 (3.2)

Zolbetuximab: Management of Nausea and Vomiting



Phase II ILUSTRO Study of First-Line Zolbetuximab with mFOLFOX6 and Nivolumab for CLDN18.2-Positive Locally Advanced Unresectable or Metastatic Gastric or GEJ Adenocarcinoma: Cohort 4

Key Eligibility Criteria

- Previously untreated LA unresectable or mG/GEJ adenocarcinoma
- CLDN18.2+ (moderate-to-strong CLDN18 staining in $\geq 50\%$ of tumor cells)^a
 - Intermediate expression: $\geq 50 - < 75\%$ of cells
 - High: $\geq 75\%$ of cells
- HER2^{-b}
- ECOG PS 0–1

Cohort 4A: Safety Lead-In Phase^c (n = 12)

Cycles 1–4 (~5.5 months):

Zolbetuximab^c 600/400 mg/m² + nivolumab 240 mg + mFOLFOX6 Q2W
OR
800/400 mg/m²

Cycles 5+:

Zolbetuximab 400 mg/m² + nivolumab 240 mg + 5-FU/FA^e Q2W

Cohort 4B: Expansion Phase (n = ~65)

Cycles 1–4 (~5.5 months):

Zolbetuximab 800/400^d mg/m² + nivolumab 240 mg + mFOLFOX6 Q2W

Cycles 5+:

Zolbetuximab 400 mg/m² + nivolumab 240 mg + 5-FU/FA^e Q2W

Endpoints and Analyses

PFS, ORR, DCR, DOR, OS, safety and tolerability

Preplanned analyses by CLDN18.2 and ad-hoc analyses by PD-L1 CPS^f

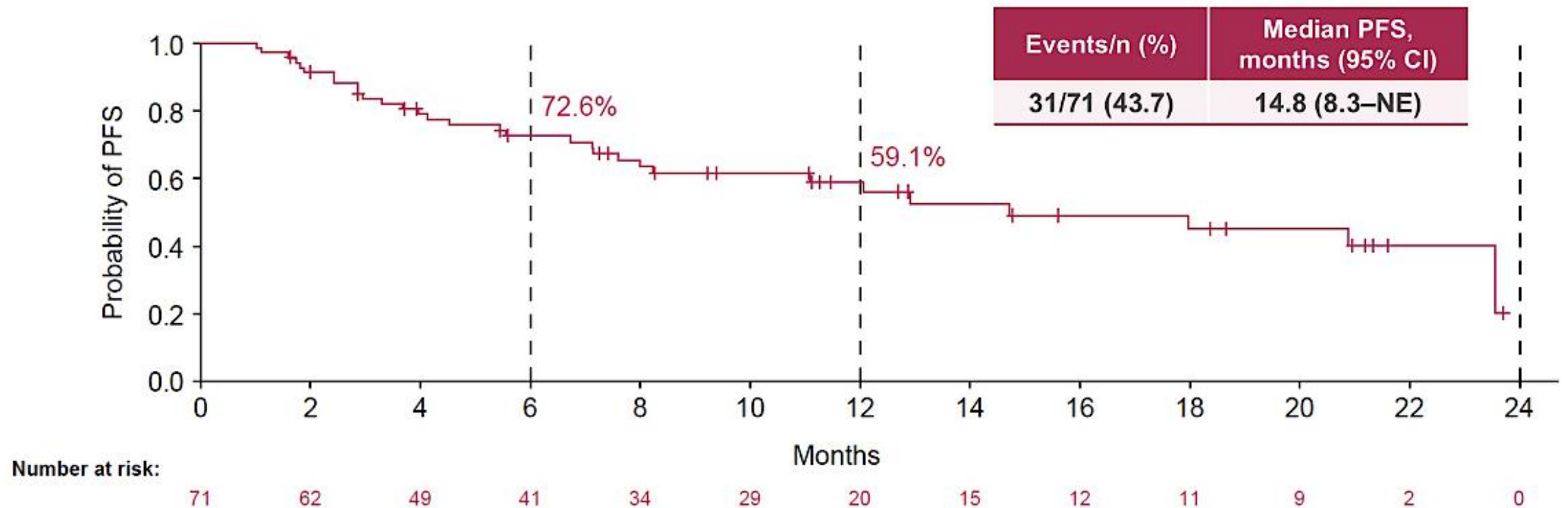
Cycle length was 42 days. Sample sizes shown are approximations based on the expectation to provide safety information and determine tolerability of the dose level of interest (cohort 4A) and the expected number of 50 patients whose tumors had high CLDN18.2 expression, assuming an accrual period of 12 months and a follow-up period of 3–6 months with 20–25 PFS events (cohort 4B).

^aBy central IHC; ^bBy central or local HER2 testing; ^cThe tolerability and safety of zolbetuximab + nivolumab + mFOLFOX6 was evaluated during a 2-week DLT assessment period, cycle 1 day 1 doses of zolbetuximab in Cohort 4A were 600 mg/m² (n = 6) or 800 mg/m² (n = 6), both followed by subsequent doses of 400 mg/m²; ^d800 mg/m² at cycle 1 day 1 followed by subsequent doses of 400 mg/m²; ^eAt the discretion of the investigator; ^fBy the Dako PD-L1 IHC 28-8 pharmDx assay.

mFOLFOX6 = modified FOLFOX-6; LA = locally advanced

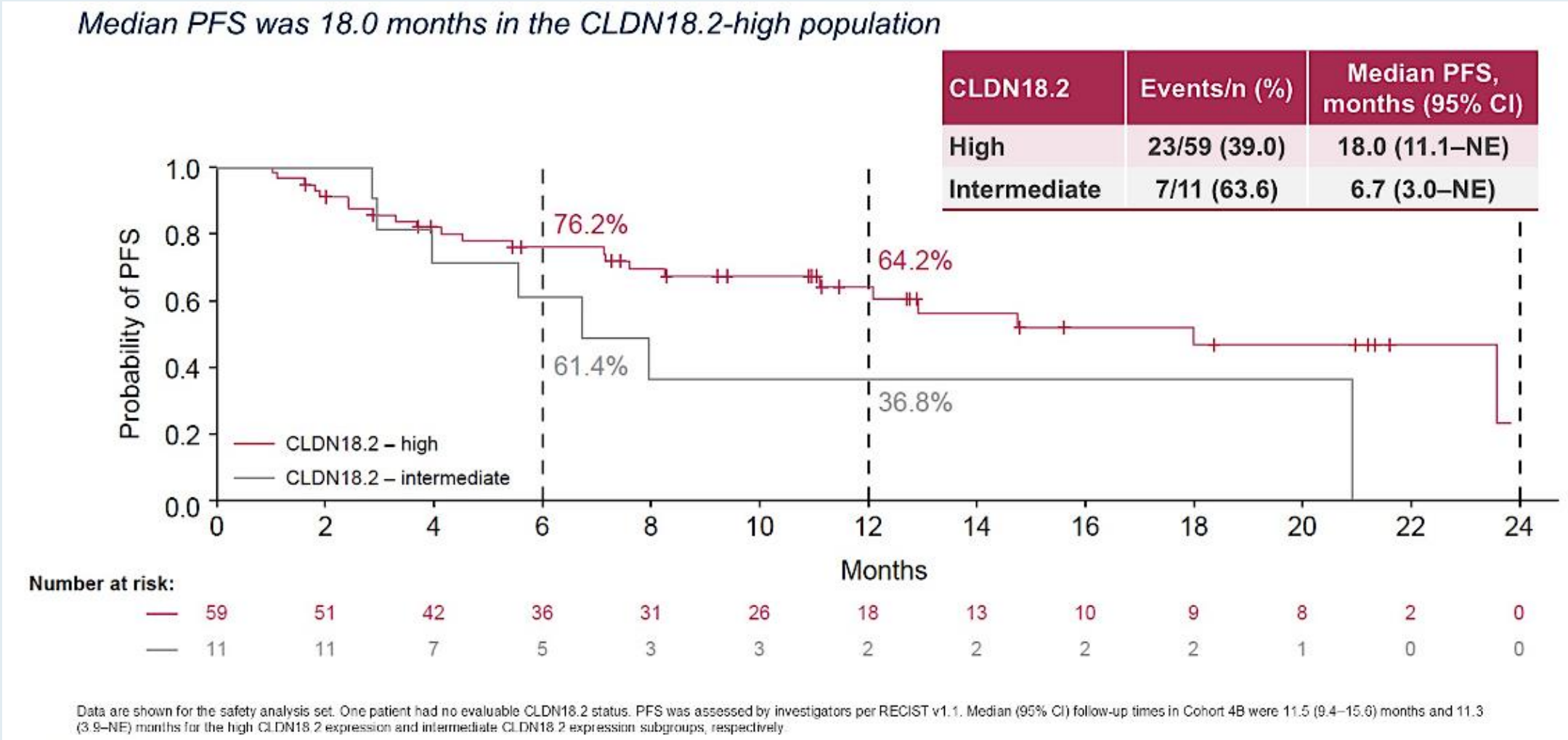
ILUSTRO Cohort 4B: PFS with First-Line Zolbetuximab, Nivolumab and mFOLFOX6

Median PFS was 14.8 months with zolbetuximab + mFOLFOX6 + nivolumab



Data are shown for the safety analysis set. PFS was assessed by investigators per RECIST v1.1. Median (95% CI) follow-up time was 11.5 (10.9–15.6) months for Cohort 4B.

ILUSTRO Cohort 4B: PFS with First-Line Zolbetuximab, Nivolumab and mFOLFOX6, Stratified by CLDN18.2 Expression

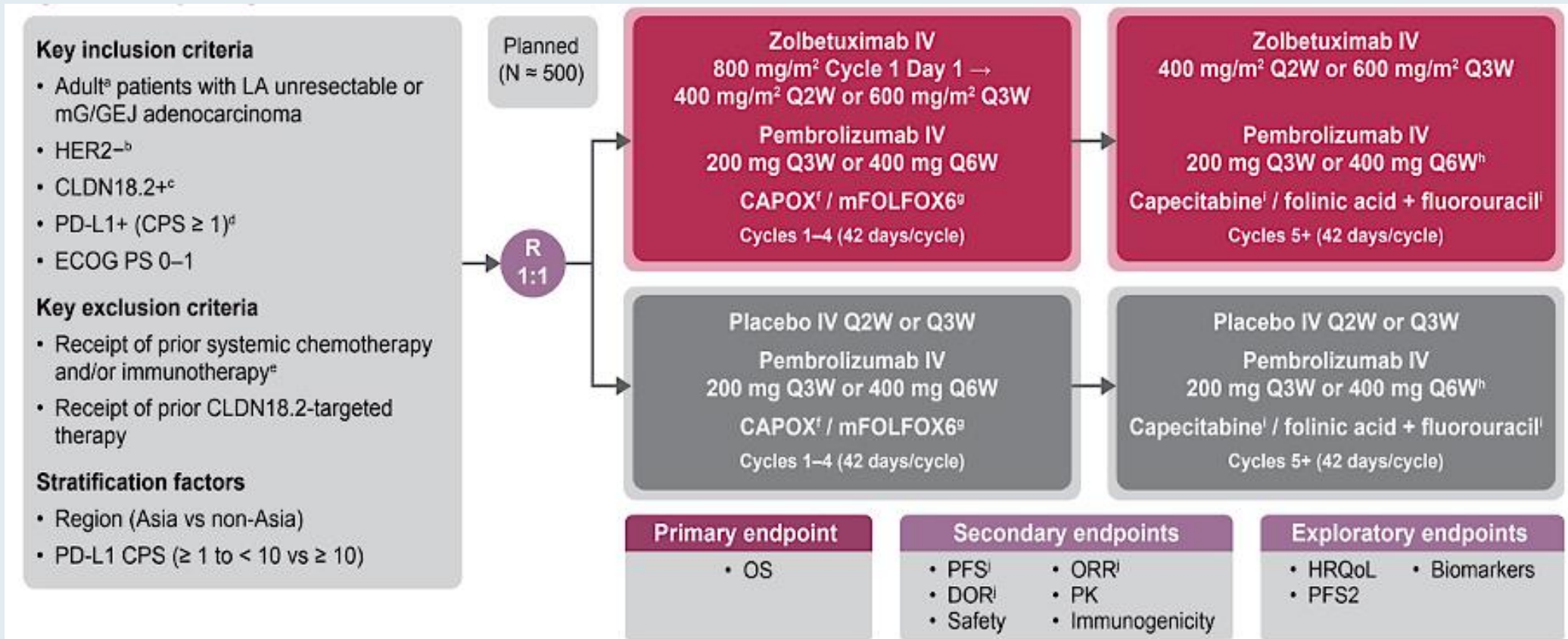


ILUSTRO: Treatment-Emergent Adverse Events with First-Line Zolbetuximab and Nivolumab — Cohorts 4A and 4B

Most common adverse event was nausea; all events were low grade

Event, n (%)	Cohort 4A + 4B (N = 77)	
Any grade	76 (98.7)	
Related to any study drug	76 (98.7)	
Grade ≥ 3	51 (66.2)	
Serious	29 (37.7)	
Related to any study drug	18 (23.4)	
TEAEs in ≥ 20% of patients by preferred terms, n (%)	Any grade	Grade ≥ 3
Nausea	62 (80.5)	0
Decreased appetite	56 (72.7)	6 (7.8)
Neutrophil count decreased	35 (45.5)	25 (32.5)
Peripheral sensory neuropathy	35 (45.5)	2 (2.6)
Vomiting	29 (37.7)	3 (3.9)
Diarrhea	28 (36.4)	1 (1.3)
Pyrexia	24 (31.2)	0
Anemia	19 (24.7)	2 (2.6)
Constipation	17 (22.1)	0

Ongoing Phase III LUCERNA Trial of First-Line Zolbetuximab with Pembrolizumab and Chemotherapy for CLDN18.2-Positive, HER2-Negative, PD-L1-Positive Locally Advanced Unresectable or Metastatic Gastric or GEJ Adenocarcinoma

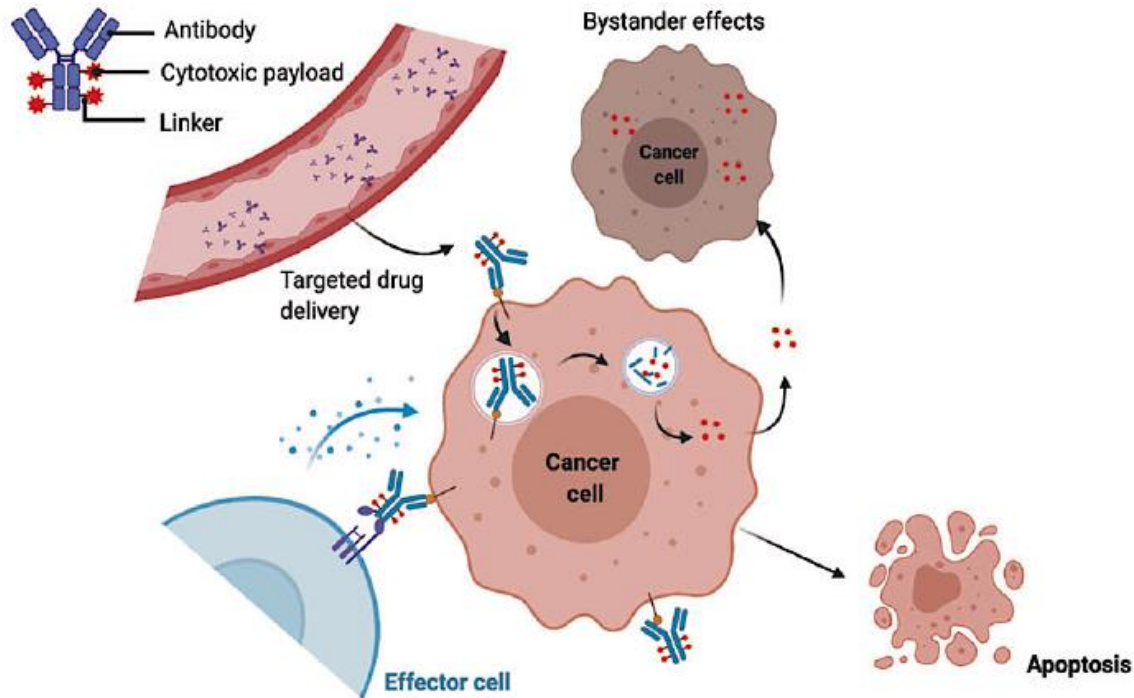


^a≥ 18 years of age; ^bHER2 IHC score of 0+/1+, or HER2 IHC score of 2+ if ISH⁻, per local or central testing; ^c≥ 75% of tumor cells demonstrating moderate-to-strong membranous CLDN18 staining using the VENTANA CLDN18 (43-14A) RxDx Assay per central testing; ^dUsing the Agilent PD-L1 IHC 22C3 pharmDx assay per central testing; ^e1 prior dose of CAPOX or mFOLFOX6, with or without pembrolizumab, is allowed; ^fOral capecitabine 1000 mg/m² twice daily on Days 1–14 and 22–35, and IV oxaliplatin 130 mg/m² Q3W; ^gFolinic acid 400 mg/m², fluorouracil 400 mg/m² bolus followed by 2400 mg/m², and oxaliplatin 85 mg/m², IV Q2W; ^hUp to 24 months; ⁱPer investigator discretion; ^jPer RECIST version 1.1 by investigator assessment.

CAPOX, capecitabine and oxaliplatin regimen; CLDN18, claudin 18; CLDN18.2, claudin 18 isoform 2; CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenous; LA, locally advanced; mFOLFOX6, modified folinic acid, fluorouracil, and oxaliplatin regimen; mG/GEJ, metastatic gastric or gastroesophageal junction; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PK, pharmacokinetics; PFS, progression-free survival; PFS2, progression-free survival after subsequent anticancer therapy; Q2W, every 2 weeks; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomly assigned; RECIST, Response Evaluation Criteria in Solid Tumors.

Expanding Therapy Beyond Zolbetuximab

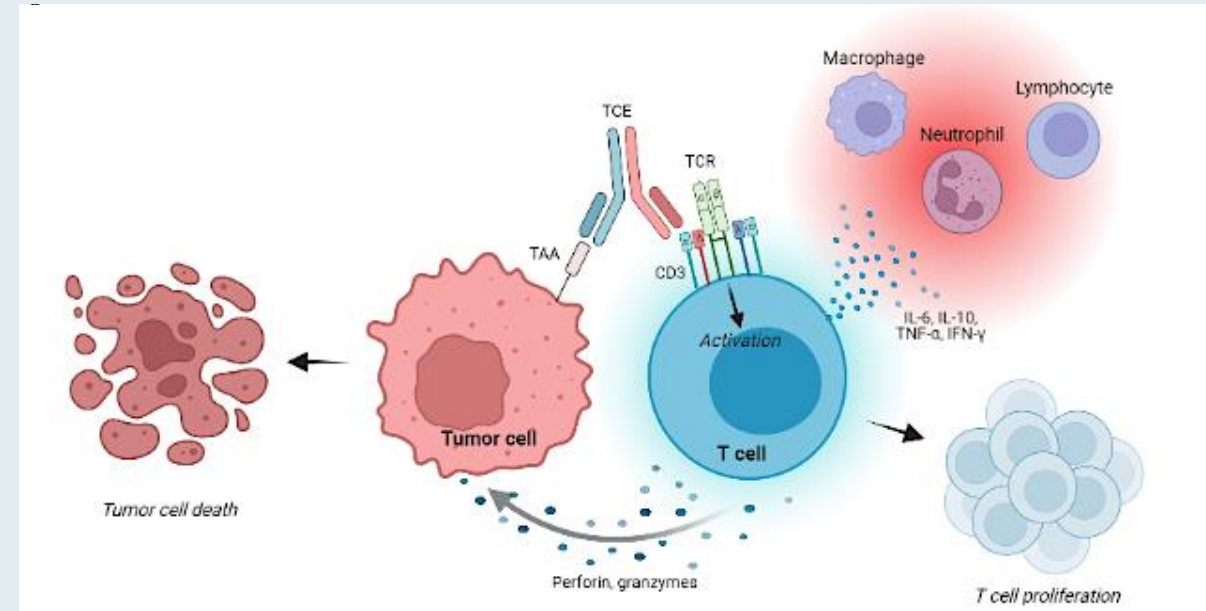
Antibody-drug conjugates (ADCs)



Fu Z et al. *Signal Transduct Target Ther* 2022;7(1):93.

Sonesitug vedotin (AZD0901) – CLDN18.2 ADC with **MMAE** payload
IBI343 – CLDN18.2 ADC with **TOPO I** payload
SHR-A1904 – CLDN18.2 ADC with **TOPO I** payload

Bispecific antibodies and BiTEs

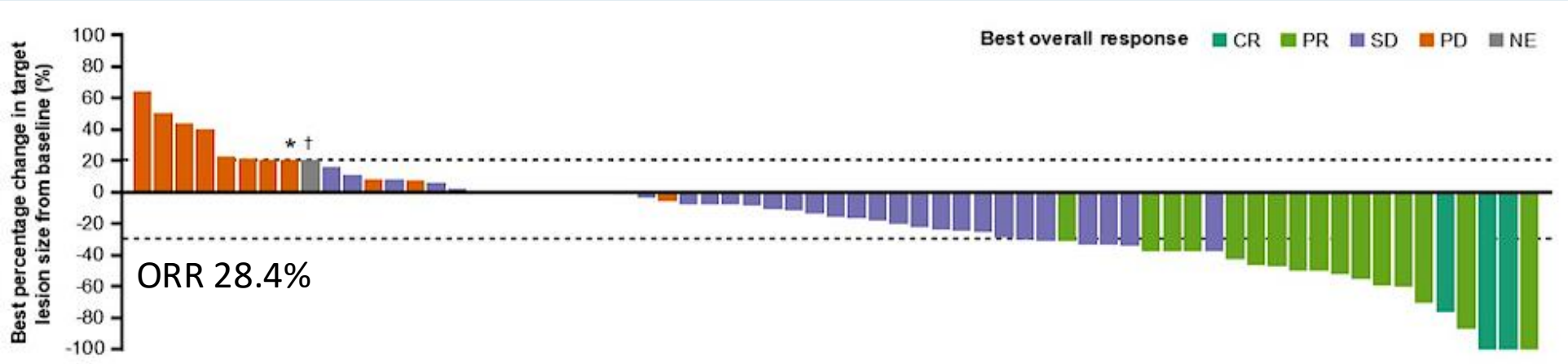


Spinazzola A et al. *Front Immunol* 2025;16:1665838.

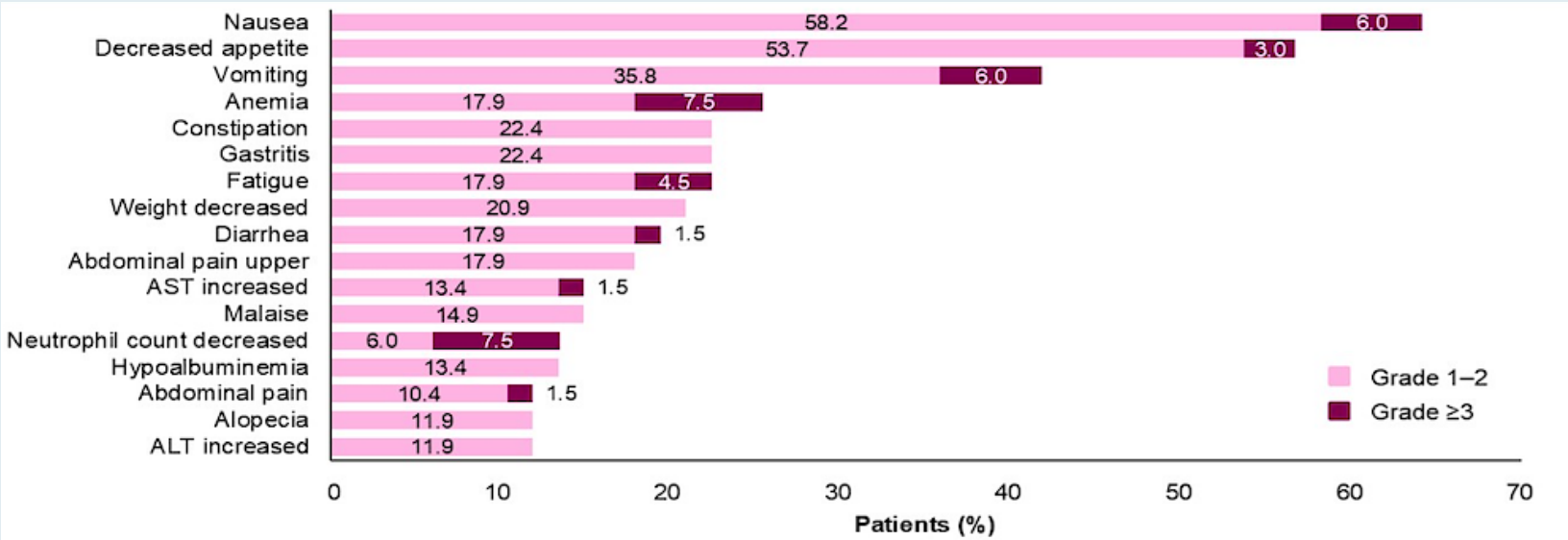
Givastomig – CLDN18.2 x 4-1BB bispecific
Spevatamig – CLDN18.2 x CD47 bispecific
ASP2138 – CLDN18.2 x CD3 BiTE
AZD5863 – CLDN18.2 x CD3 BiTE

BiTE = bispecific T-cell engager

CLARITY-PanTumor01 Substudy 1: Sonesitug Vedotin Activity in Gastric and GEJ Cancer

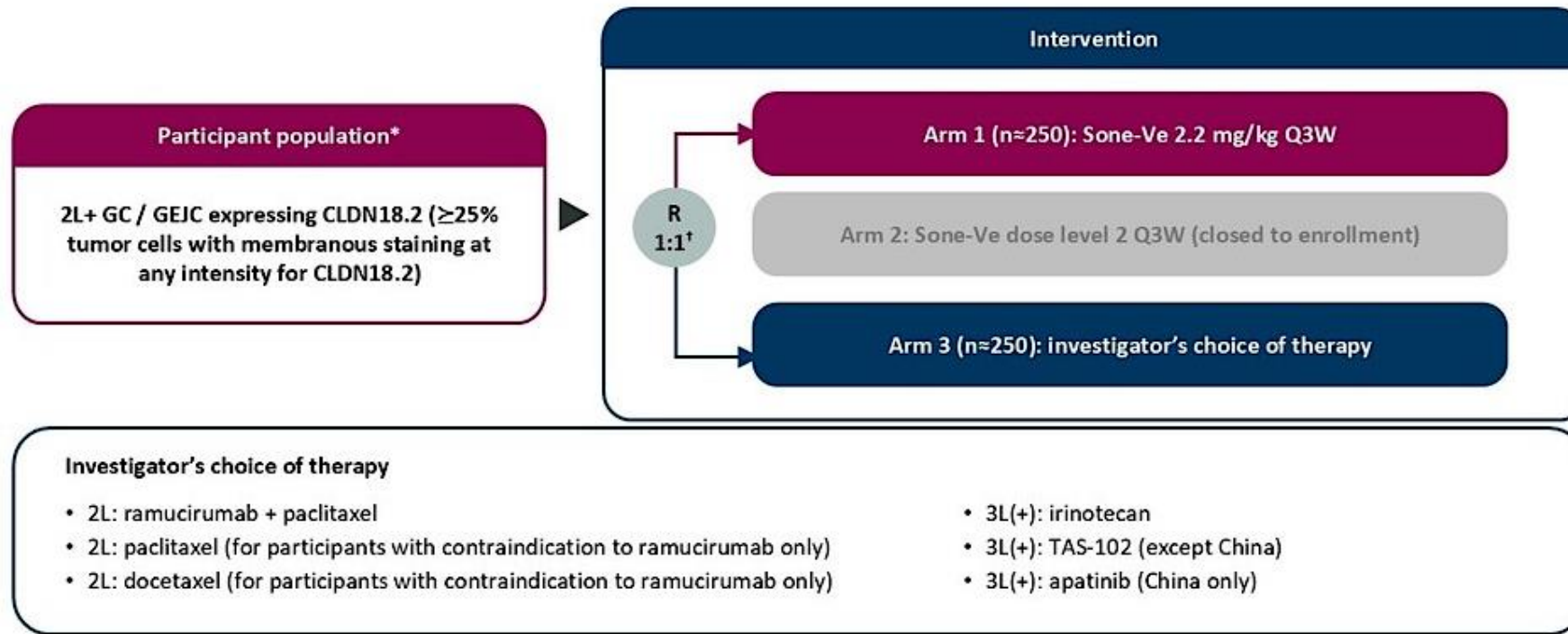


TEAs occurring in ≥10% of patients overall



CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = not evaluable; ORR = objective response rate
Shitara K et al. ASCO 2026;Abstract 4023.

Phase III CLARITY-Gastric 01 Study: Second-or Later-Line Sonesitug Vedotin for Advanced Gastric/GEJ Cancer



*Participants with known HER2-positive status (per local HER2 testing) were excluded. †Patients were randomized 1:1:1 to Sone-Ve dose level 1 IV Q3W (Arm 1), Sone-Ve level 2 IV Q3W (Arm 2) or investigator's choice of therapy (Arm 3). As of January 2025, the optimal Sone-Ve monotherapy dose was determined to be 2.2 mg/kg IV Q3W (Arm 1), and Arm 2 was closed to enrollment. Randomization will continue in a 1:1 ratio to Arm 1 and Arm 3 (Sone-Ve / investigator's choice of therapy) until PD, or any other discontinuation criteria are met. Sone-Ve may continue beyond PD if participant continues to show clinical benefit and provides informed consent. Treatment crossover is not allowed. 2L+, second-line (and later); IV, intravenous; PD, disease progression; Q3W, every 3 weeks; R, randomized.

Primary endpoints: PFS for all patients, OS for patients receiving third-line or later treatment
Estimated completion: October 2026

Sonesitatug Vedotin Demonstrated a Statistically Significant Improvement in Overall Survival in Second- and Later-Line Therapy for CLDN18.2-Positive Advanced Gastric/GEJ Cancers

Press Release: July 27, 2026

“Positive high-level results from the CLARITY-Gastric01 global Phase III trial showed that sonesitatug vedotin (Sone-Ve) demonstrated a statistically significant and highly clinically meaningful improvement in overall survival (OS) in 2nd and later-line Claudin 18.2-positive advanced gastric cancers versus investigator’s choice of therapy. The trial included patients with locally advanced or metastatic gastric cancer, gastroesophageal junction (GEJ) cancer, or esophageal adenocarcinoma (EAC) with Claudin 18.2 (CLDN18.2) expression on at least 25% of tumor cells at any staining intensity.

The trial had dual primary endpoints of OS in 3rd and later-line treatment and progression-free survival (PFS) in the overall trial population. The trial met the dual primary endpoint of OS in 3rd and later-line treatment, and a key secondary endpoint of OS in the overall trial population of patients treated in the 2nd and later-line setting, demonstrating a statistically significant and highly clinically meaningful improvement.

For the other dual primary endpoint of PFS as assessed by blinded independent central review (BICR), results showed a trend toward improved PFS in patients treated in the 2nd and later-line setting but did not reach statistical significance.”

ESMO 2026 Presidential Symposium II

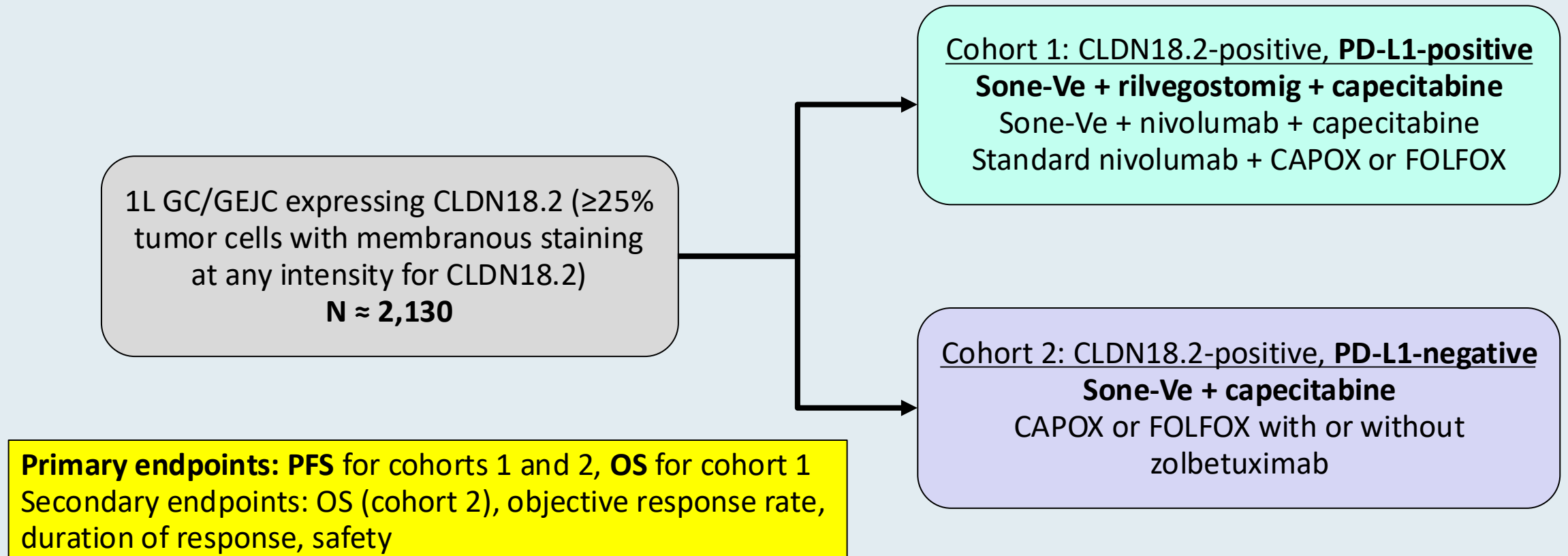
October 25, 2026

Abstract LBA7

CLARITY-Gastric 01 (CG-01): A Phase 3 study of sonesitatug vedotin (Sone-Ve) in second or later-line (2L+) advanced or metastatic claudin 18.2 (CLDN18.2) positive gastroesophageal carcinoma (GEC)

Rui-Hua Xu

Ongoing Phase III CLARITY-Gastric 02 Study: First-Line Sonesitug Vedotin in Combination with Capecitabine with or without Rilvegostomig



Data anticipated: After 2027

Estimated completion: October 2031

Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

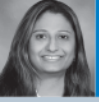
Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

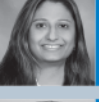
Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

Module 6: Clinician Survey Results

Regulatory and reimbursement issues aside, which first-line treatment would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS gastric adenocarcinoma with a PD-L1 CPS of 0 and the CLDN18.2 status below?

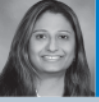
		CLDN18.2 positive	CLDN18.2 negative
	Dr Ilson	Chemotherapy + zolbetuximab	FOLFOX
	Dr Janjigian	Chemotherapy + zolbetuximab	FOLFOX
	Dr Kim	Chemotherapy + zolbetuximab	FOLFOX
	Dr Klempner	Chemotherapy + zolbetuximab	FOLFOX
	Dr Mehta	Chemotherapy + zolbetuximab	FOLFOX
	Dr Shah	Chemotherapy + zolbetuximab	FOLFOX
	Dr Strickler	Chemotherapy + zolbetuximab	FOLFOX
	Dr Wainberg	Chemotherapy + zolbetuximab	FOLFOX

Regulatory and reimbursement issues aside, which first-line treatment would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS gastric adenocarcinoma with a PD-L1 CPS of 1 and the CLDN18.2 status below?

		CLDN18.2 positive	CLDN18.2 negative
	Dr Ilson	Chemotherapy + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Janjigian	Chemotherapy + zolbetuximab	Nivolumab + FOLFOX
	Dr Kim	Chemotherapy + zolbetuximab	Nivolumab + FOLFOX
	Dr Klempner	Chemotherapy + zolbetuximab + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Mehta	Chemotherapy + zolbetuximab	Nivolumab + FOLFOX
	Dr Shah	Chemotherapy + zolbetuximab	IO + FOLFOX
	Dr Strickler	Chemotherapy + zolbetuximab	Nivolumab + FOLFOX
	Dr Wainberg	Chemotherapy + zolbetuximab + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX or pembrolizumab + FOLFOX

IO = immunotherapy

Regulatory and reimbursement issues aside, which first-line treatment would you most likely recommend for a 65-year-old patient presenting with metastatic HER2-negative, MSS gastric adenocarcinoma with a PD-L1 CPS of 10 and the CLDN18.2 status below?

		CLDN18.2 positive	CLDN18.2 negative
	Dr Ilson	Chemotherapy + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Janjigian	Chemotherapy + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Kim	Chemotherapy + anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Klempner	Chemotherapy + anti-PD-1/PD-L1 antibody or chemotherapy + zolbetuximab and an anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Mehta	Chemotherapy + zolbetuximab and an anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Shah	Chemotherapy + anti-PD-1/PD-L1 antibody	IO + FOLFOX
	Dr Strickler	Chemotherapy + zolbetuximab and an anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX
	Dr Wainberg	Chemotherapy + zolbetuximab and an anti-PD-1/PD-L1 antibody	Nivolumab + FOLFOX or pembrolizumab + FOLFOX

How would you indirectly compare the global efficacy of zolbetuximab and chemotherapy to that of an anti-PD-1 antibody and chemotherapy for patients with newly diagnosed gastric/GEJ adenocarcinoma who are eligible for both treatments?



Dr Ilson

An anti-PD-1 antibody with chemotherapy is more efficacious



Dr Janjigian

About the same



Dr Kim

About the same



Dr Klempner

About the same



Dr Mehta

About the same



Dr Shah

About the same



Dr Strickler

About the same



Dr Wainberg

About the same

Outside of a clinical trial, have you administered or would you administer both zolbetuximab and an anti-PD-1/PD-L1 antibody in combination with first-line chemotherapy for a patient with newly diagnosed gastric/GEJ adenocarcinoma?



Dr Ilson

I have not and would not



Dr Janjigian

I have not but would for the right patient



Dr Kim

I have



Dr Klempner

I have



Dr Mehta

I have



Dr Shah

I have not but would for the right patient



Dr Strickler

I have



Dr Wainberg

I have

Based on available information and your own clinical experience, would you currently like to have access to sonositatug vedotin (Sone-V)?



Dr Ilson

Yes, but await presentation of Phase III data and approval status



Dr Janjigian

Yes, for patients with CLDN18.2-positive disease and progression on first-line therapy, including zolbetuximab



Dr Kim

Yes



Dr Klempner

Yes, for CLDN18.2-positive disease (by Sone-V cutoff) in second and third line



Dr Mehta

Yes, for those patients with progression on first-line zolbetuximab



Dr Shah

Yes



Dr Strickler

Yes, possibly in the second-line setting



Dr Wainberg

I'm not sure

If sonositatug vedotin becomes clinically available, in which line of therapy do you think you will administer it?



Dr Ilson

Second line



Dr Janjigian

Second line



Dr Kim

Second line



Dr Klempner

Third line, and second line for some patients



Dr Mehta

Second line



Dr Shah

Second line



Dr Strickler

Second line



Dr Wainberg

Second or third line

Based on available information and your own clinical experience, would you be inclined to administer sonesitug vedotin to a patient who received zolbetuximab/chemotherapy and experienced disease progression?

	Dr Ilson	Maybe
	Dr Janjigian	Yes
	Dr Kim	Maybe
	Dr Klempner	Yes
	Dr Mehta	Yes
	Dr Shah	Maybe
	Dr Strickler	Maybe
	Dr Wainberg	No

Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

Module 4: Clinician Survey Results

Module 5: Integration of Immune Checkpoint Inhibitors into the Care of Patients with Resectable and Unresectable Advanced GE Cancers

Module 6: Clinician Survey Results

FDA Revised Indication for Pembrolizumab for Gastroesophageal Cancers – May 22, 2025

- Pembrolizumab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated as first-line treatment for adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- Pembrolizumab is indicated for patients with locally advanced or metastatic esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation therapy either
 - In combination with platinum- and fluoropyrimidine-based chemotherapy for patients with tumors that express PD-L1 (CPS ≥ 1), or
 - As a single agent after 1 or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

FDA Revised Indication for Nivolumab for Metastatic Gastroesophageal Cancers – May 23, 2025

- Nivolumab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated as first-line treatment for adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) whose tumors express PD-L1 (≥ 1).
- Nivolumab, in combination with ipilimumab, is indicated as first-line treatment for adult patients with unresectable advanced or metastatic ESCC whose tumors express PD-L1 (≥ 1).
- Nivolumab, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated as treatment for adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer or esophageal adenocarcinoma whose tumors express PD-L1 (≥ 1).

Overview of Select Trials of First-Line Immunotherapy for Gastroesophageal Cancers

Parameter	CheckMate-649 ¹	KEYNOTE-859 ²	Rationale-305 ³
Disease location	Gastric, GEJ, esophagus	Gastric, GEJ	Gastric, GEJ
Histology	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
Agent	Nivolumab + chemotherapy vs chemotherapy	Pembrolizumab + chemotherapy vs chemotherapy	Tislelizumab + chemotherapy vs chemo
Setting	First-line advanced	First-line advanced	First-line advanced
ORR, %	60 vs 46 (CPS ≥1)	52 vs 43 (CPS ≥1)	50 vs 43 (TAP ≥5)
PFS HR	0.71 (CPS ≥5), 0.77 (CPS ≥1), 0.79 (all patients)	0.62 (CPS ≥10), 0.72 (CPS ≥1), 0.76 (all patients)	0.67 (TAP ≥5), 0.78 (all patients)
OS Δ, mo	3.3 (CPS ≥5), 2.4 (CPS ≥1), 2.1 (all patients)	4.0 (CPS ≥10), 1.6 (CPS ≥1), 1.4 (all patients)	4.6 (TAP ≥5), 2.1 (all patients)

HR = hazard ratio; CPS = combined positive score; TAP = tumor area positivity

1. Janjigian YY et al. *Ann Oncol* 2026;37(6):787-97. 2. Rha SY et al. ASCO 2025;Abstract 4036. 3. Qiu M-Z et al. *BMJ* 2024;385:e078876.

Microsatellite Instability-High (MSI-H) Gastroesophageal Cancers

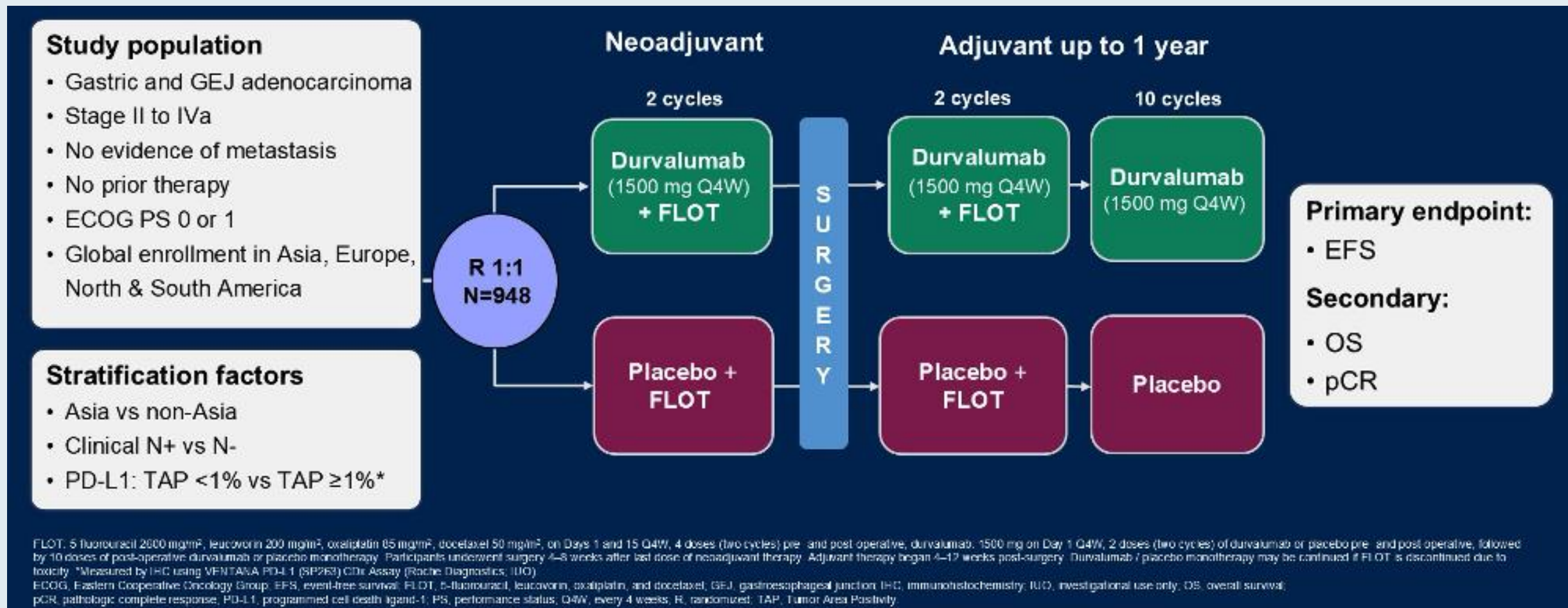
- 4% to 24% of GE cancers are MSI-H
 - ~30% of Stage I to Stage II tumors are MSI-H
 - 4% to 12% of metastatic gastric cancers are MSI-H
- MSI-H GE cancers by anatomical region:
 - 1% esophagus
 - 5% to 12% cardia or fundus
 - 12% to 16% body
 - 15% to 30% antrum

Cancer Genome Atlas Research Network. *Nature* 2014;513(7517):202-9.

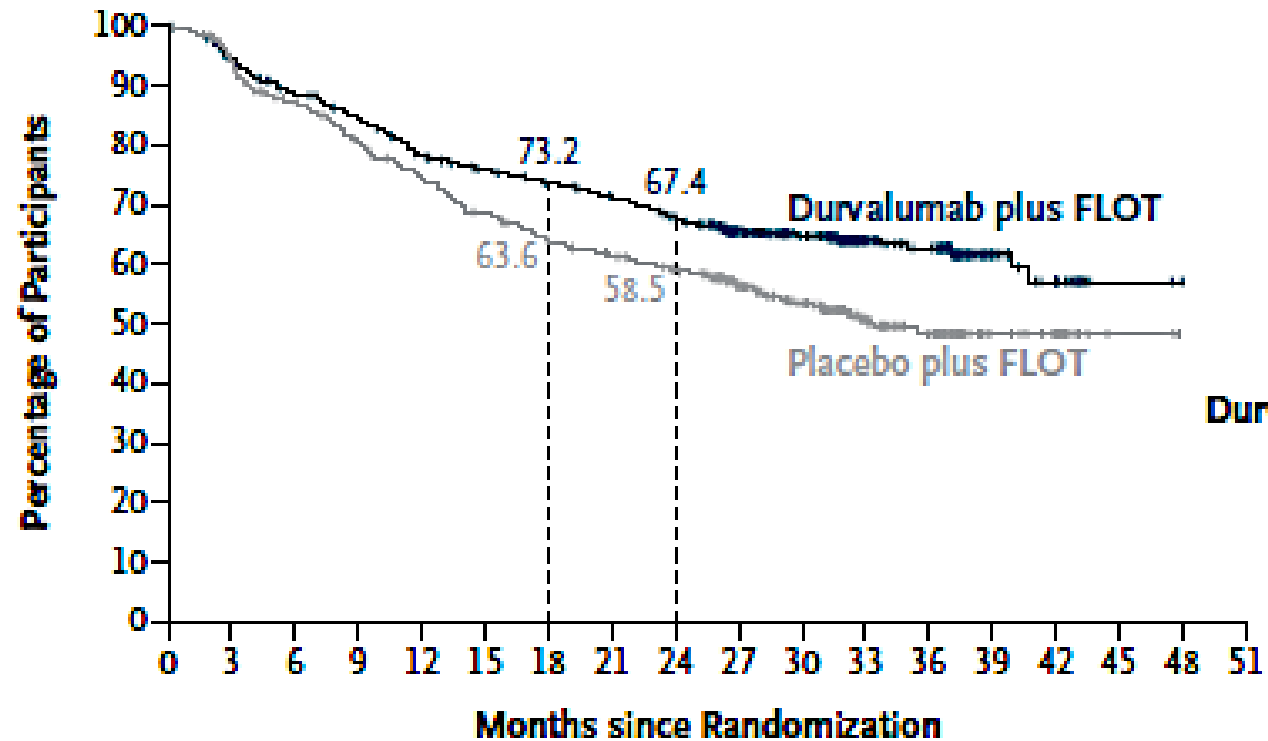
Cristescu R et al. *Nat Med* 2015;21(5):449-56.

Zhou KI et al. *J Gastrointest Cancer* 2024;55(2):483-96.

Phase III MATTERHORN Trial of Perioperative Durvalumab for Gastric and Gastroesophageal Junction Cancer



MATTERHORN: Event-Free Survival in the Full-Analysis Population



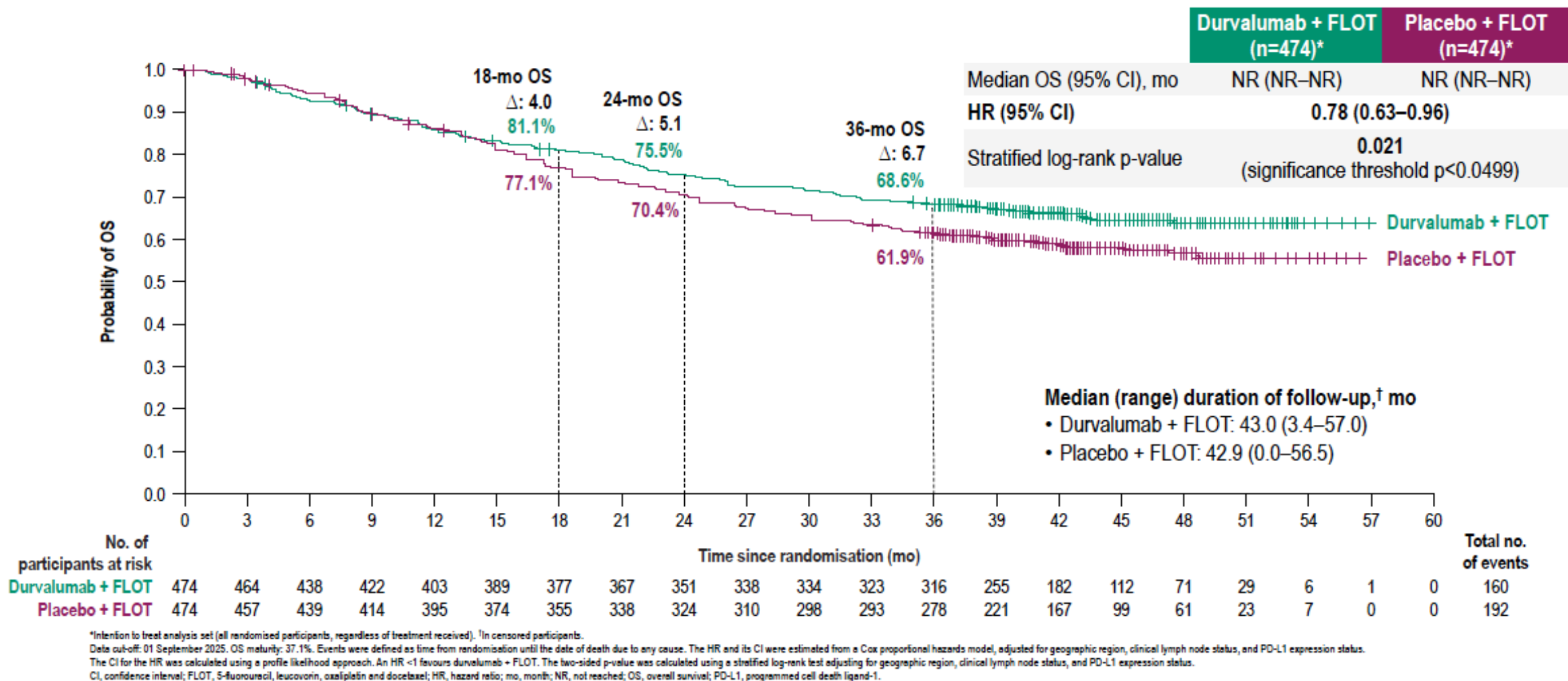
	No. of Participants with Event/ Total No. of Participants (%)	Median Event-free Survival (95% CI) mo
Durvalumab plus FLOT	167/474 (35.2)	NR (40.74–NR)
Placebo plus FLOT	218/474 (46.0)	32.8 (27.86–NR)

Stratified hazard ratio for event or death,
0.71 (95% CI, 0.58–0.86)
P<0.001 by stratified log-rank test

No. at Risk

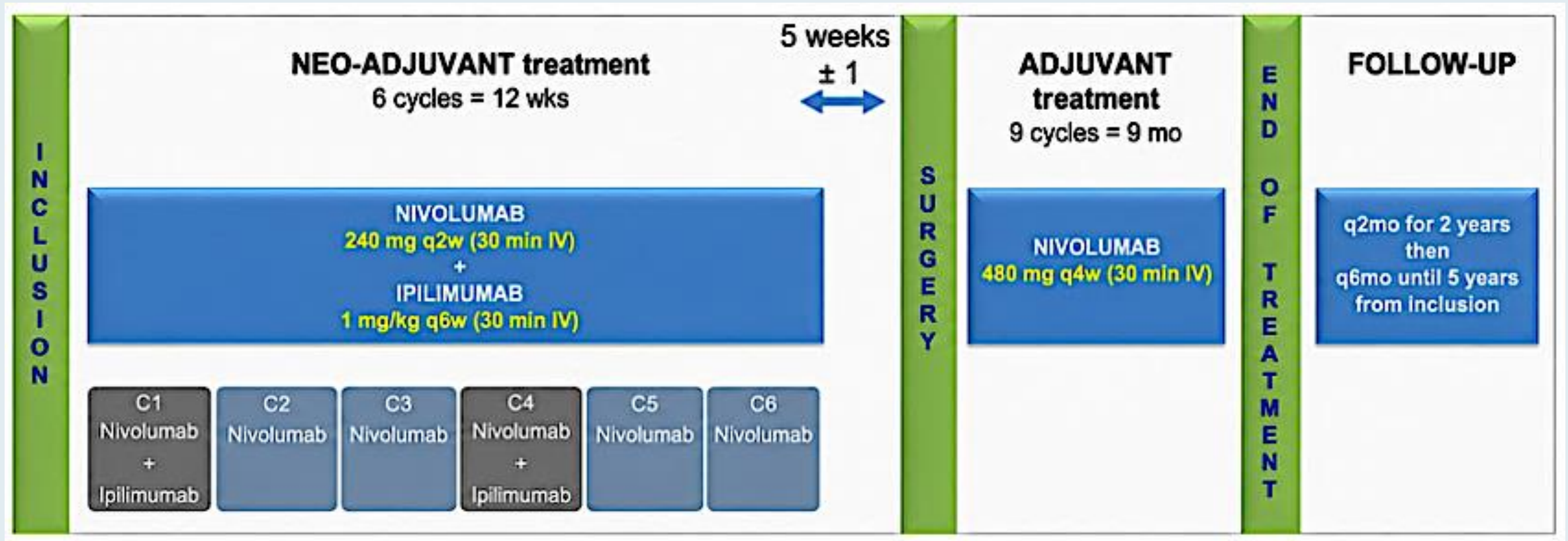
Durvalumab plus FLOT	474	436	404	381	351	334	320	307	288	234	187	107	88	33	20	2	1	0
Placebo plus FLOT	474	429	392	360	329	302	278	264	249	202	160	89	65	26	21	2	1	0

MATTERHORN: Final Overall Survival Analysis



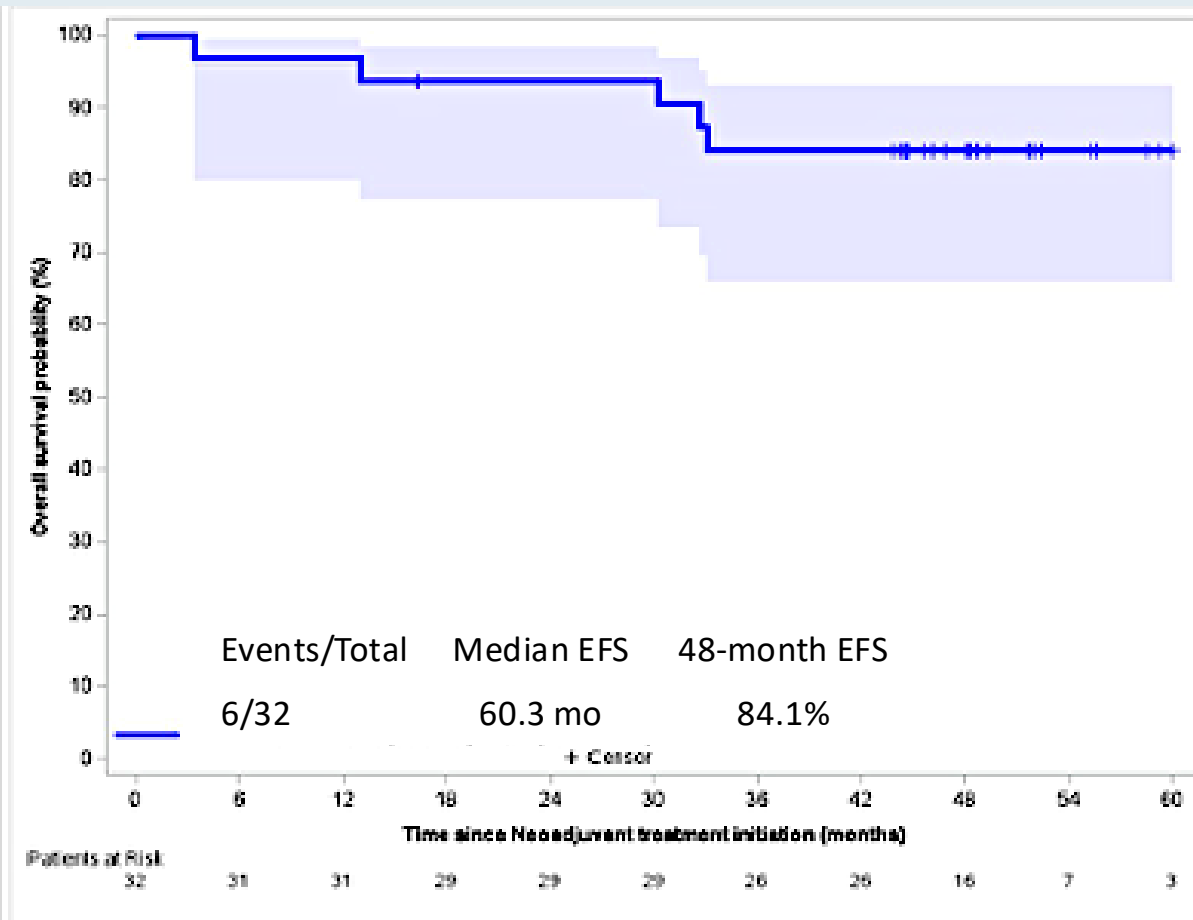
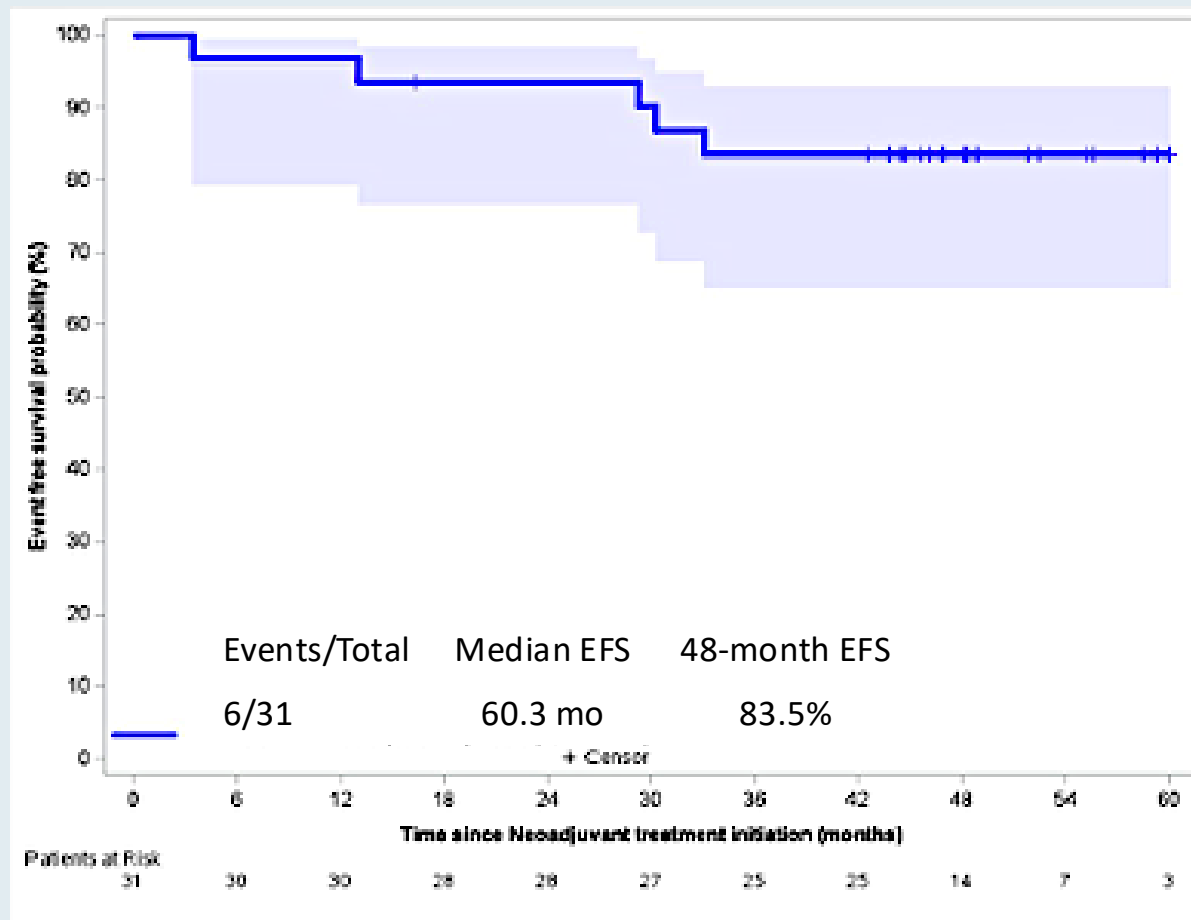
Phase II NEONIPIGA Study of Neoadjuvant Nivolumab with Ipilimumab and Adjuvant Nivolumab for MSI-High/dMMR Esophagogastric Adenocarcinoma

Inclusion criteria: Histologically proven resectable MSI-H/dMMR gastric or esophagogastric adenocarcinoma, cT-T4NxM0



MSI = microsatellite instability; dMMR = mismatch repair deficient

NEONIPIGA Long-Term Follow-Up: Event-Free and Overall Survival



Median follow-up 48.3 months

Agenda

Module 1: Optimizing the Management of HER2-Positive Advanced Gastroesophageal (GE) Cancers

Module 2: Clinician Survey Results

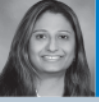
Module 3: Current and Future Strategies to Target CLAUDIN18.2 in Advanced GE Cancers

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Module 6: Clinician Survey Results

Which primary treatment would you most likely recommend for a 65-year-old patient (PS 0) with MSI-high/mismatch repair-deficient, HER2-negative gastric adenocarcinoma, PD-L1 CPS ≥ 1 , that appeared to be amenable to surgical resection, if the patient had T2N1 disease? Would your treatment recommendations change if the patient had node-negative disease?

		Tx if T2N1	Tx if node-negative
	Dr Ilson	Neoadjuvant ipi/nivo followed by adjuvant nivo or neoadjuvant durvalumab + tremelimumab	No change
	Dr Janjigian	Neoadjuvant ipi/nivo followed by adjuvant nivo	No change
	Dr Kim	Neoadjuvant ipi/nivo followed by adjuvant nivo	No change
	Dr Klempner	Neoadjuvant ipi/nivo followed by adjuvant nivo	No significant change
	Dr Mehta	Ipi/nivo followed by nivo and if ctDNA clears at 6 wk, would consider NOM	Surgery alone vs definitive pembrolizumab monotherapy
	Dr Shah	Neoadjuvant ipi/nivo followed by adjuvant nivo	No change
	Dr Strickler	Neoadjuvant ipi/nivo followed by adjuvant nivo	No change; may consider organ preservation if cCR
	Dr Wainberg	Neoadjuvant dostarlimab	No change

Given that durvalumab in combination with perioperative FLOT has received regulatory approval, for which patients with resectable gastric adenocarcinoma are you prioritizing this strategy?

	Dr Ilson	All patients with T3 or higher or node-positive disease
	Dr Janjigian	Fit patients with resectable Stage II to IV disease who resemble the MATTERHORN population, particularly those with clinically higher-risk T-stage and/or node-positive disease
	Dr Kim	Nearly all patients who are fit for FLOT-based therapy and surgery
	Dr Klempner	Most patients, unless disease is MSI-H
	Dr Mehta	All patients with T2 or higher or node-positive disease and no contraindications to immunotherapy
	Dr Shah	CPS >1
	Dr Strickler	Patients with resectable gastric or GEJ adenocarcinoma (Stage II to IVa), medically fit, good/excellent PS, and are candidates for surgical resection
	Dr Wainberg	Most patients, unless disease is MSI-H

PS = performance status; MSI-H = microsatellite instability high

Which perioperative chemotherapy regimen do you typically use for your patients with resectable gastric/GEJ adenocarcinoma who are unable to tolerate FLOT?

	Dr Ilson	FOLFOX
	Dr Janjigian	FOLFOX
	Dr Kim	I will first dose-reduce all drugs in FLOT before going to FOLFOX
	Dr Klempner	I first tend to start with empiric dose reduction. If patient truly not a FLOT candidate, I will consider FOLFOX for select patients
	Dr Mehta	FOLFOX
	Dr Shah	Reduced FLOT
	Dr Strickler	FOLFOX + durvalumab could be considered
	Dr Wainberg	Dose-modified FLOT

Questions?