January 9, 2026

Zanidatamab: Pivotal Phase 3 HERIZON-GEA-01 Trial Results in Gastroesophageal Adenocarcinoma (GEA)

Innovating to Transform the Lives of Patients and Their Families

Jazz Pharmaceuticals

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Caution Concerning Forward-Looking Statements

This presentation contains forward-looking statements and financial targets, including, but not limited to, statements related to: the Company's development, regulatory and commercialization strategy; the advancement of pipeline programs and the timing of development activities, regulatory activities and submissions related thereto; the Company's expectations with respect to its products and product candidates and the potential of the Company's products and product candidates, including the potential therapeutic benefits of zanidatamab and of combination therapies with zanidatamab, zanidatamab's potential as a new standard of care in HER2+ first-line GEA and other HER2-expressing cancers, the potential of zanidatamab to be more than a two billion dollar peak potential and to become the therapy of choice for multiple HER2+ tumors, expected timing of interim OS data from the pivotal Phase 3 HERIZON-GEA-01 trial, plans to submit an sBLA in first half of 2026; the Company's ability to realize the commercial potential of its products including the commercial plans with respect to zanidatamab in 1L GEA, if approved; potential regulatory approvals; and other statements that are not historical facts. These forward-looking statements are based on the Company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties.

Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the successful completion of development and regulatory activities with respect to the Company's product candidates including zanidatamab in multiple HER2+ tumors; obtaining and maintaining adequate coverage and reimbursement for the Company's products; the time-consuming and uncertain regulatory approval process, including the risk that the Company's current and/or planned regulatory submissions may not be submitted, accepted or approved by applicable regulatory authorities in a timely manner or at all, including the risk that the Company's supplemental biologics license application for zanidatamab's use in combination with chemotherapy, with or without the PD-1 inhibitor tislelizumab, as first-line treatment for HER2-positive (HER2+) locally advanced or metastatic GEA may not be approved in a timely manner or at all, the costly and time-consuming pharmaceutical product development and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients; global economic, financial, and healthcare system disruptions and the current and potential future negative impacts to the Company's business operations and financial results; protecting and enhancing the Company's intellectual property rights and the Company's commercial success being dependent upon the Company obtaining, maintaining and defending intellectual property protection and exclusivity for its products and product candidates; delays or problems in the supply or manufacture of the Company's products and product candidates; complying with applicable U.S. and non-U.S. regulatory requirements, including those governing the research, development, manufacturing and distribution; government investigations, legal proceedings and other actions; the sufficiency of the Company's cash flows and capital resources; and other risks and uncertainties affecting the Company, including those described from time to time under the caption "Risk Factors" and elsewhere in the Company's Securities and Exchange Commission filings and reports, including the Company's Annual Report on Form 10-K for the year ended December 31, 2024, as supplemented by the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, and future filings and reports by the Company. Other risks and uncertainties of which the Company is not currently aware may also affect the Company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated.

Agenda

Introduction and Overview

Renee Gala

President and Chief Executive Officer

Results from the Phase 3 HERIZON-GEA-01 Trial and Clinical Perspective

Geoffrey Ku, M.D.

Associate Attending Physician on the Gastrointestinal Oncology Service in the Department of Medicine at Memorial Sloan Kettering Cancer Center

Zanidatamab: Shifting Treatment Paradigm

Rob Iannone, M.D., M.S.C.E.

Executive Vice President, Global Head of Research and Development and Chief Medical Officer

Zanidatamab: Commercial Perspective

Sam Pearce

Executive Vice President, Chief Commercial Officer

Introduction and Overview

Renee Gala

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Phase 3 HERIZON-GEA-01 Data Presented at ASCO GI

ASCO® Gastrointestinal Cancers Symposium

Zanidatamab + chemotherapy ± tislelizumab for first-line HER2-positive locally advanced, unresectable, or metastatic gastroesophageal adenocarcinoma: Primary analysis from HERIZON-GEA-01

Geoffrey Y. Ku, M.D.

Memorial Sloan Kettering Cancer Center™

Associate Attending Physician on the Gastrointestinal Oncology Service in the Department of Medicine at Memorial Sloan Kettering Cancer Center

Geoffrey Ku, MD is a Medical Oncologist who specializes in the treatment of malignancies of the gastrointestinal tract at Memorial Sloan Kettering Cancer Center in New York, New York. He is an Associate Attending physician and Head of the Esophagogastric Section on the Gastrointestinal Oncology Service and a Member of the Cellular Therapy Service, both in the Department of Medicine. His research focuses on the evaluation of novel therapies, including cellular therapies, and combined modality treatments for esophagogastric cancer. He is a member of the Esophagogastric Task Force of the National Cancer Institute and of the Gastrointestinal (non-Colorectal Cancer) Committee of the NRG Cooperative Group.

He graduated from the University of Pennsylvania School of Medicine and completed his Internal Medicine Residency in New York Presbyterian Hospital, Weill Cornell Campus, prior to his Medical Oncology Fellowship at MSKCC. Post-fellowship, he spent one year at the Immune Monitoring Facility at MSKCC, which is part of the Ludwig Center for Cancer Immunotherapy.

Zanidatamab + chemotherapy ± tislelizumab for first-line HER2-positive locally advanced, unresectable, or metastatic gastroesophageal adenocarcinoma: Primary analysis from HERIZON-GEA-01

Elena Elimova[1], Sun Young Rha[2], Kohei Shitara[3], Tianshu Liu[4], Josep Tabernero[5], Keun-Wook Lee[6], Michael Schenker[7], Niall Tebbutt[8], Jaffer Ajani[9], Norhidayu Bt Salimin[10], Geoffrey Ku[11], Jong Gwang Kim[12], Inmaculada Ales Diaz[13], Jingdong Zhang[14], Filippo Pietrantonio[15], Li-Yuan Bai[16], Samuel Le Sourd[17], Ye Chen[18], Jonathan Grim[19], Lin Shen[20]

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Key Takeaway Points

HERIZON-GEA-01 supports zanidatamab as a new standard in HER2-targeting agents, potentially replacing trastuzumab, as well as the use of tislelizumab in 1L HER2+ mGEA

Progression-Free Survival and Overall Survival

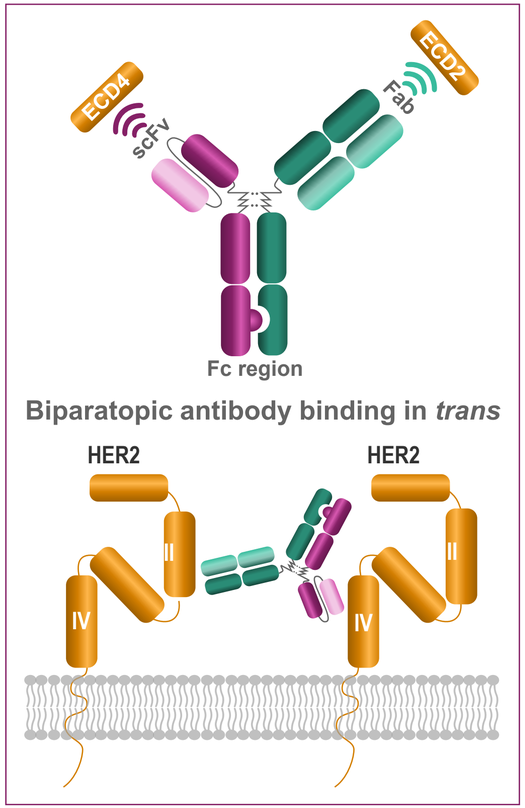
- **Statistically significant ~35% reduction** in the risk of disease progression or death for **both zanidatamab + CT** and **zanidatamab + tislelizumab + CT** vs trastuzumab + CT (**>4-month improvement in median PFS**)
- There was **a strong trend toward statistical significance for OS favoring zanidatamab + CT** vs trastuzumab + CT (**5-month improvement in median OS**)
- **Statistically significant 28% reduction** in the risk of death for **zanidatamab + tislelizumab + CT** vs trastuzumab + CT (**>7-month improvement in median OS**)
- The PFS and OS benefits were generally observed across key prespecified subgroups, including in patients with **PD-L1 TAP scores <1% and ≥1%**

Safety Profile

- The safety profile was consistent with the known profiles of each individual treatment

Background

- Outcomes with current SoC for 1L HER2+ mGEA remain modest, with an mPFS of <1 year and mOS of <2 years[1-7]
- **Zanidatamab** is a **dual HER2-targeted bispecific** IgG1-like antibody that binds to **extracellular domains 2 and 4 on HER2** in a **trans configuration**[8]
  - This **biparatopic binding** enables zanidatamab to **crosslink neighboring HER2 proteins, leading to receptor clustering**
  - In preclinical studies, zanidatamab **enhanced HER2 internalization**, **reduced downstream signaling,** and promoted **immune-mediated cytotoxicity (CDC, ADCC, ADCP)**
- **Tislelizumab** is a **high-affinity immune checkpoint inhibitor targeting PD-1** and is specifically engineered to minimize Fcγ receptor binding on macrophages[9,10]
- **Promising efficacy and a tolerable safety profile** were observed with zanidatamab + chemotherapy ± tislelizumab across **independent phase 2 trials in 1L HER2+ mGEA**[11,12]



1. Bartley AN, et al. J Clin Oncol. 2017;35(4):446-64. 2. Lordick F, et al. Ann Oncol. 2022;33(10):1005-20. 3. US Food and Drug Administration. FDA approved pembrolizumab for HER2 positive gastric or gastroesophageal junction adenocarcinoma expressing PD-L1 (CPS ≥1). Accessed October 14, 2025. http://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-her2-positive-gastric-or-gastroesophageal-junction-adenocarcinoma. 4. Bang YJ, et al. Lancet. 2010;376(9742):687-97. 5. Janjigian YY, et al. N Engl J Med. 2024;391(14):1360-2. 6. Janjigian YY, et al. Lancet. 2023;402(10418):2197-208. 7. Meric-Bernstam F, et al. Nat Commun. 2025;16(1):4293. 8. Weisser NE, et al. Nat Commun. 2023;14(1):1394. 9. Hong Y, et al. FEBS Open Bio. 2021;11(3):782-92. 10. Zhang T, et al. Cancer Immunol Immunother. 2018;67(7):1079-90. 11. Elimova E, et al. Lancet Oncol. 2025;26(7):847-59. 12. Lee KW, et al. Clin Cancer Res. 2025. http://doi.org/10.1158/1078-0432.CCR-24-4295.

HERIZON-GEA-01 Study Design

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

Key Eligibility Criteria

- Age ≥18 years
- Unresectable, locally advanced, recurrent or metastatic GEA
- HER2 IHC 3+ or IHC 2+/ISH+ per central testing
- ECOG PS 0 or 1
- No prior treatment for locally advanced or metastatic disease
- No prior HER2-targeted agents or immunotherapy in any setting

Stratification Factors

- Geographic region
- HER2 status
- ECOG PS

R 1:1:1

N = 914

Arm A: Trastuzumab + chemotherapy[a]

Arm B: Zanidatamab 1800 mg (<70 kg)/2400 mg (≥70 kg) IV Q3W + chemotherapy[a]

Arm C: Zanidatamab 1800 mg (<70 kg)/2400 mg (≥70 kg) IV Q3W + tislelizumab[b] + chemotherapy[a]

Prophylaxis to prevent IRR and diarrhea was mandatory in the zanidatamab-containing arms

CT/MRI[c] Q6W

Treatment until disease progression/death/unacceptable toxicity
Chemotherapy could be discontinued after 6 cycles

Dual Primary Endpoints

- PFS (per BICR)
- OS

Select Secondary Endpoints

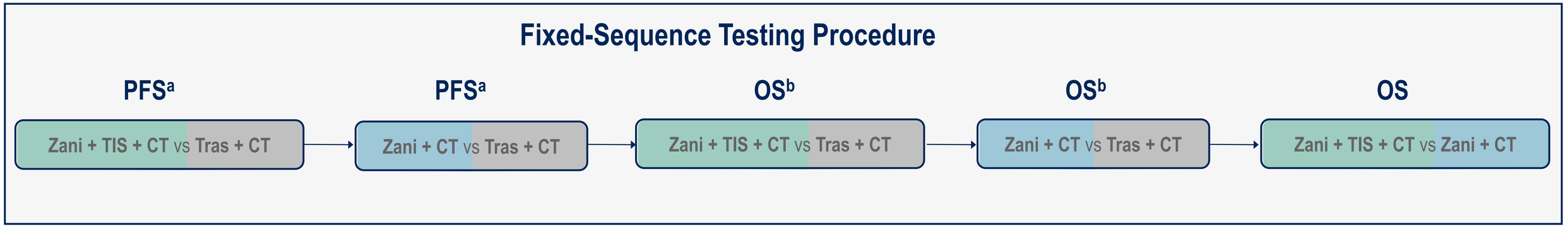
- cORR (per BICR)
- Frequency and severity of AEs

ClinicalTrials.gov: NCT05152147

[a]Physician'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.
[b]Tislelizumab 200 mg was administered IV Q3W. [c]CT/MRI scans were performed every 6 weeks for the first 54 weeks, then every 9 weeks.

Statistical Design

- **Dual primary endpoints (PFS and OS): Analyzed in the intent-to-treat population using log-rank tests with a 2-sided α = 0.05**
  - **Primary PFS analysis**: After target event count was reached and patients had ≥7 months of follow-up
  - **First interim OS analysis:** Performed at the time of data cutoff for the primary PFS analysis



[a]For the primary analysis of PFS, the 2-sided alpha was 0.05. [b]For the first interim analysis of OS, the 2-sided alpha was 0.020.

Patient Disposition

A total of 914 patients were randomized, and median follow-up was >2 years

Randomized
N = 914

Zanidatamab + CT	Zanidatamab + tislelizumab + CT	Trastuzumab + CT
n = 304; 300 patients treated[a]	n = 302; 299 patients treated[a]	n = 308; 302 patients treated
Ongoing treatment, n = 69 (23%)	**Ongoing treatment**, n = 88 (29%)	**Ongoing treatment**, n = 37 (12%)
Discontinued treatment, n = 231 (76%)	**Discontinued treatment**, n = 211 (70%)	**Discontinued treatment**, n = 265 (86%)
• Progressive disease, n = 132	• Progressive disease, n = 117	• Progressive disease, n = 200
• Adverse event, n = 25	• Adverse event, n = 27	• Adverse event, n = 10
• Death, n = 27	• Death, n = 26	• Death, n = 17
• Withdrawal by patient, n = 23	• Withdrawal by patient, n = 26	• Withdrawal by patient, n = 20
• Physician decision, n = 19	• Physician decision, n = 13	• Physician decision, n = 13
• Other, n = 5[b]	• Other, n = 2[b]	• Other, n = 5[b]
Survival follow-up, n = 69 (23%)	**Survival follow-up**, n = 58 (19%)	**Survival follow-up**, n = 81 (26%)
Median (range) follow-up 26.0 (7.6–46.0) months	**Median (range) follow-up** 25.9 (7.9–45.5) months	**Median (range) follow-up** 25.8 (7.5–45.6) months

[a]Treated includes all randomized patients who received any amount of any study treatment and does not necessarily reflect the safety analysis set. Five patients assigned to the zanidatamab-tislelizumab-chemotherapy arm did not receive tislelizumab and are included in the safety analysis set for the zanidatamab-chemotherapy arm. [b]Includes protocol violations and "other" reasons.

Baseline Demographics and Disease Characteristics

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Demographics and clinical characteristics were balanced across all 3 treatment arms

	Zanidatamab + CT (n = 304)	Zanidatamab + tislelizumab + CT (n = 302)	Trastuzumab + CT (n = 308)
Age, median (range), years	62.5 (25–87)	63.0 (22–81)	64.0 (21–84)
Male sex	244 (80.3)	244 (80.8)	238 (77.3)
Geographic region			
Asia	163 (53.6)	159 (52.6)	165 (53.6)
EU/North America	91 (29.9)	95 (31.5)	93 (30.2)
Rest of the world	50 (16.4)	48 (15.9)	50 (16.2)
ECOG PS[a]			
0	134 (44.1)	121 (40.1)	120 (39.0)
1	170 (55.9)	180 (59.6)	188 (61.0)
Disease status			
Metastatic	295 (97.0)	284 (94.0)	299 (97.1)
Unresectable locally advanced	9 (3.0)	18 (6.0)	9 (2.9)

	Zanidatamab + CT (n = 304)	Zanidatamab + tislelizumab + CT (n = 302)	Trastuzumab + CT (n = 308)
Anatomical subtype			
Gastric	204 (67.1)	208 (68.9)	226 (73.4)
GEJ	61 (20.1)	74 (24.5)	60 (19.5)
Esophageal	39 (12.8)	20 (6.6)	22 (7.1)
HER2 IHC 3+	251 (82.6)	251 (83.1)	255 (82.8)
PD-L1 status[b]			
TAP score <1%	108 (35.5)	90 (29.8)	98 (31.8)
TAP score ≥1%	178 (58.6)	187 (61.9)	188 (61.0)
Choice of chemotherapy backbone			
CAPOX	276 (90.8)	273 (90.4)	282 (91.6)
FP	28 (9.2)	29 (9.6)	26 (8.4)

All data are shown as n (%) unless otherwise indicated.
[a]One patient in the zanidatamab-tislelizumab-chemotherapy arm had an ECOG PS score of 2 at baseline. [b]PD-L1 status was missing for 7.1% (n = 65) of patients across arms.

Primary Endpoint: PFS per BICR

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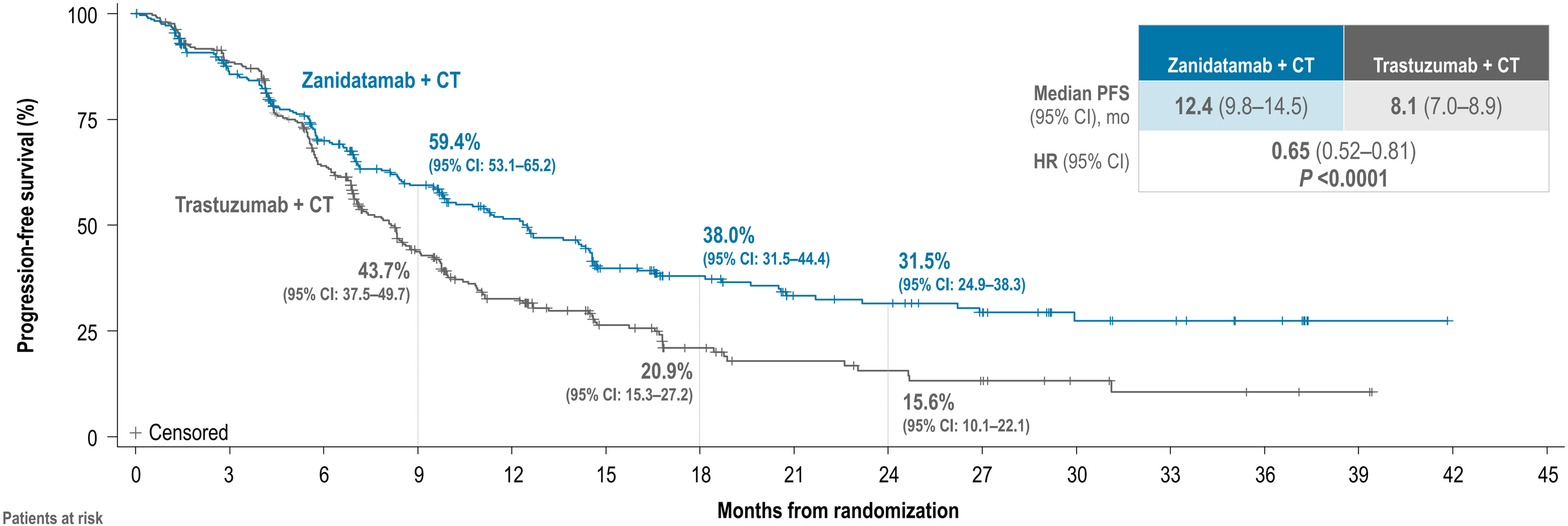
Statistically significant and clinically meaningful improvement in PFS with zanidatamab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



	Zanidatamab + CT	Trastuzumab + CT
Median PFS (95% CI), mo	**12.4** (9.8–14.5)	**8.1** (7.0–8.9)
HR (95% CI)	**0.65** (0.52–0.81)	
	***P* <0.0001**	

Patients at risk

Zani + CT	304	231	175	137	105	70	53	37	34	26	14	12	8	1	0	
Tras + CT	308	247	168	97	63	37	23	16	13	10	6	4	3	2	0	

Primary Endpoint: PFS per BICR

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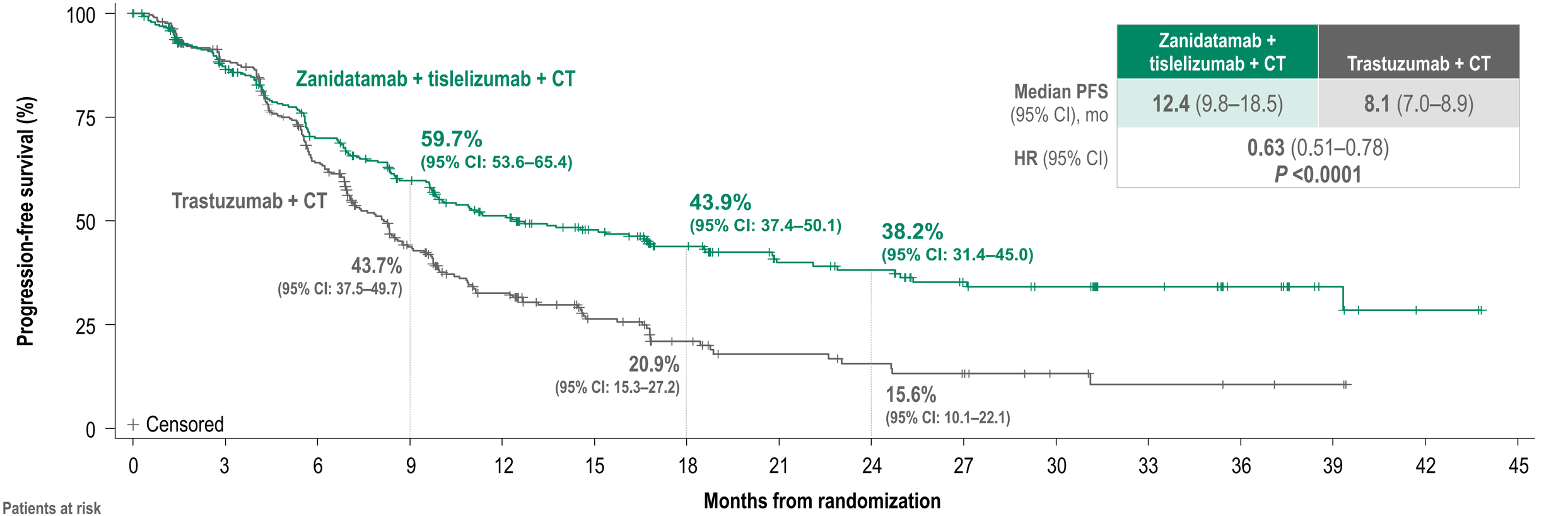
Statistically significant and clinically meaningful improvement in PFS with zanidatamab + tislelizumab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



	Zanidatamab + tislelizumab + CT	Trastuzumab + CT
Median PFS (95% CI), mo	**12.4** (9.8–18.5)	**8.1** (7.0–8.9)
HR (95% CI)	**0.63** (0.51–0.78) ***P* <0.0001**	

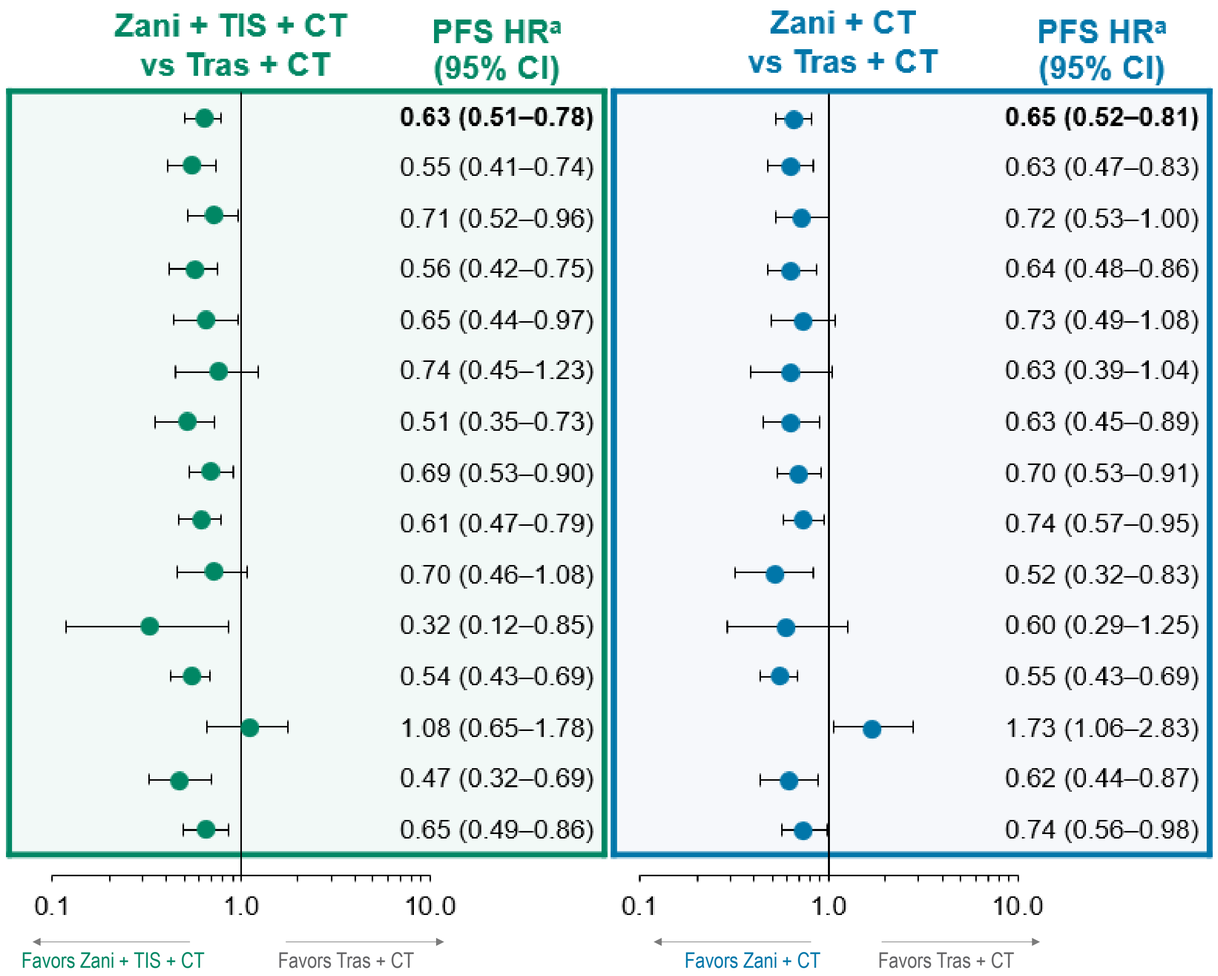
Patients at risk

Zani + TIS + CT	302	240	183	147	113	90	65	46	42	30	27	20	13	6	2	0
Tras + CT	308	247	168	97	63	37	23	16	13	10	6	4	3	2	0	

PFS in Key Prespecified Subgroups

Improvements in PFS were generally consistent across major prespecified subgroups

Subgroup	Category	Events/patients: Zanidatamab + tislelizumab + CT	Zanidatamab + CT	Trastuzumab + CT
All patients		**154/302**	**160/304**	**196/308**
Age, years	<65	79/163	94/174	105/162
	≥65	75/139	66/130	91/146
Geographic region	Asia	78/159	81/163	106/165
	EU/NA	47/95	49/91	55/93
	ROW	29/48	30/50	35/50
ECOG PS	0	51/121	63/134	74/120
	1	103/180	97/170	122/188
Anatomical subtype	Gastric	105/208	112/204	140/226
	GEJ	43/74	29/61	44/60
	Esophageal	6/20	19/39	12/22
HER2 status	IHC 3+	121/251	125/251	167/255
	IHC 2+/ISH+	33/51	35/51	29/52
PD-L1 status	TAP <1%	47/90	61/108	71/98
	TAP ≥1%	91/187	94/178	114/188



[a]The widths of the confidence intervals were not adjusted for multiplicity and cannot be used to infer treatment effects.

Primary Endpoint: Overall Survival

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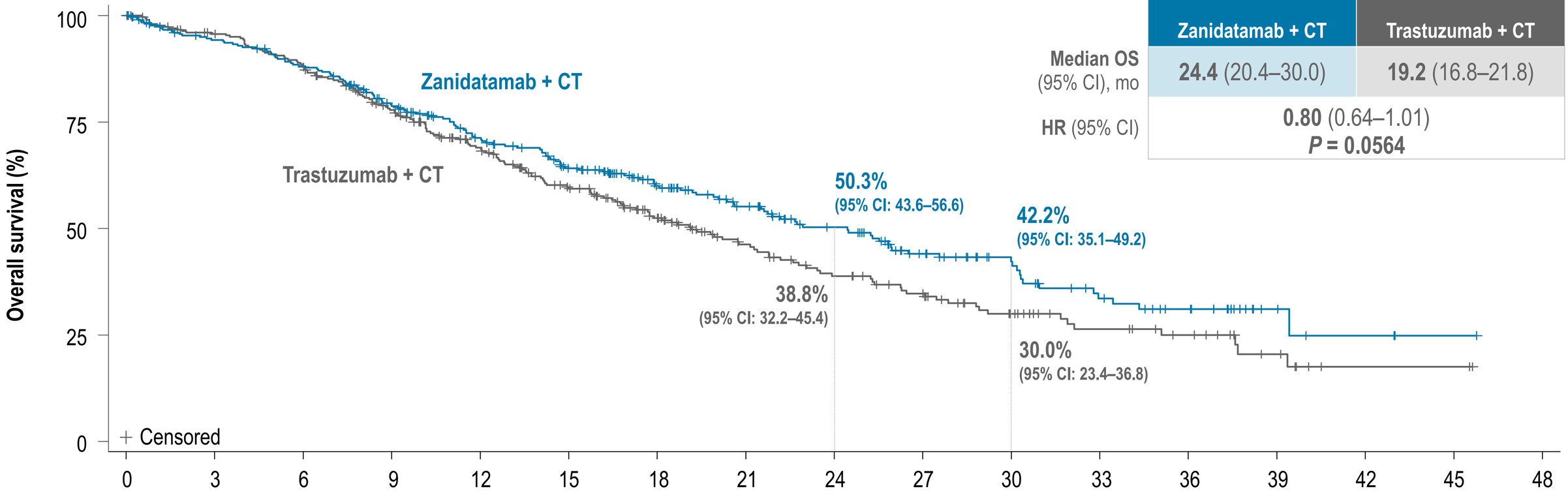
At this interim analysis, there was a strong trend toward significance for OS favoring zanidatamab + CT vs trastuzumab + CT (5-month improvement in median OS)

	Zanidatamab + CT	Trastuzumab + CT
Median OS (95% CI), mo	**24.4** (20.4–30.0)	**19.2** (16.8–21.8)
HR (95% CI)	**0.80** (0.64–1.01) ***P* = 0.0564**	



Patients at risk

Zani + CT	304	277	257	222	187	156	121	98	78	56	41	28	21	6	3	1	0
Tras + CT	308	284	261	219	178	140	106	77	61	50	33	22	17	8	2	2	0

Primary Endpoint: Overall Survival

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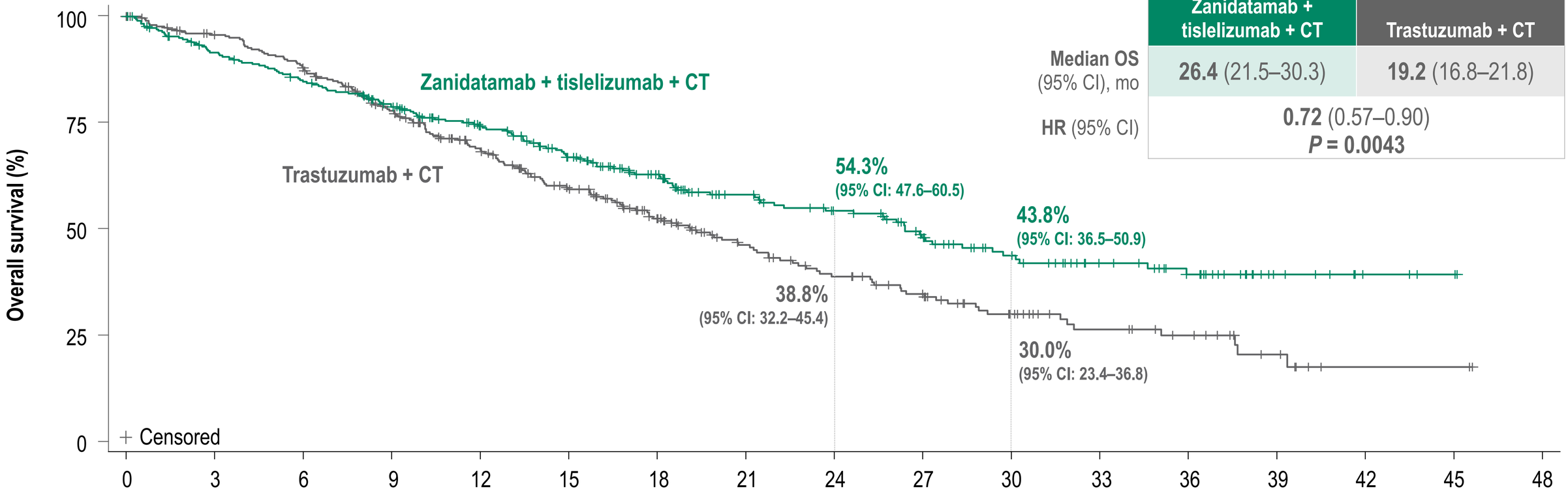
Zanidatamab + tislelizumab + CT demonstrated a statistically significant and clinically meaningful OS benefit with a >7-month improvement in median OS vs trastuzumab + CT



	Zanidatamab + tislelizumab + CT	Trastuzumab + CT
Median OS (95% CI), mo	**26.4** (21.5–30.3)	**19.2** (16.8–21.8)
HR (95% CI)	**0.72** (0.57–0.90) ***P* = 0.0043**	

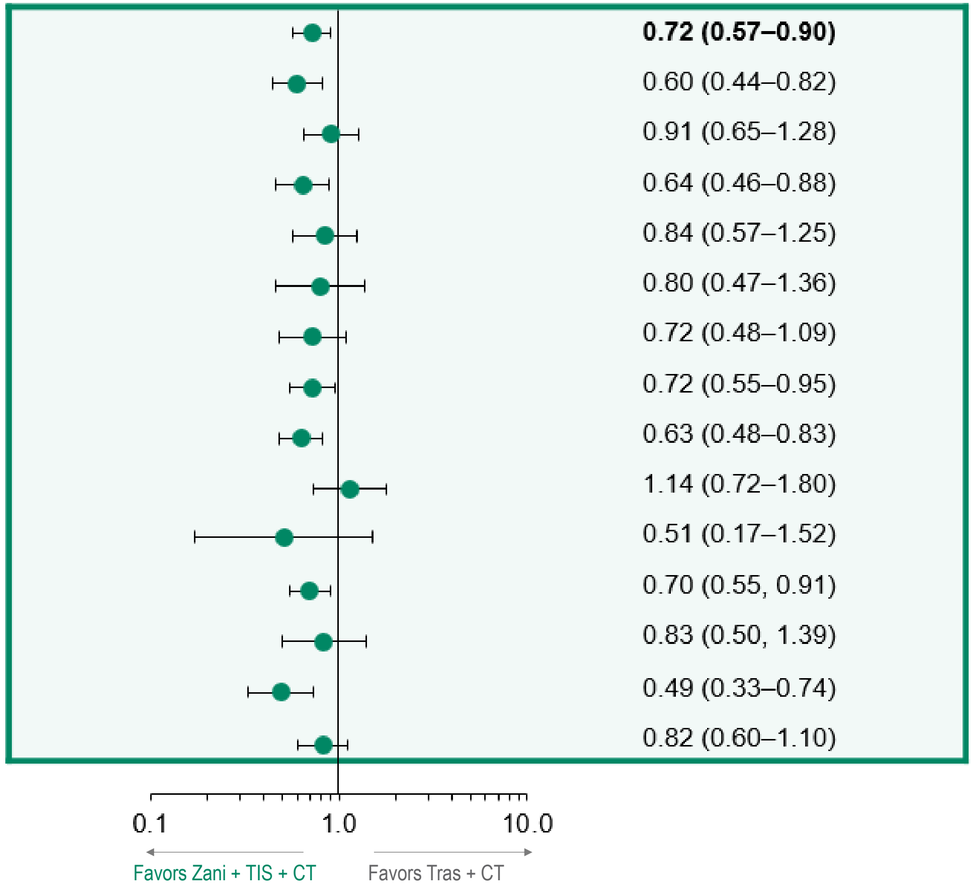
Patients at risk

Zani + TIS + CT	302	267	246	222	190	157	125	96	82	64	49	36	27	10	4	2	0
Tras + CT	308	284	261	219	178	140	106	77	61	50	33	22	17	8	2	2	0

OS in Key Prespecified Subgroups

Improvements in OS occurred across major prespecified subgroups, including regions and PD-L1 TAP scores

Subgroup	Category	Events/patients: Zanidatamab + tislelizumab + CT	Events/patients: Trastuzumab + CT	Zani + TIS + CT vs Tras + CT: OS HR[a] (95% CI)
All patients		**134/302**	**170/308**	**0.72 (0.57–0.90)**
Age, years	<65	68/163	99/162	0.60 (0.44–0.82)
	≥65	66/139	71/146	0.91 (0.65–1.28)
Geographic region	Asia	63/159	89/165	0.64 (0.46–0.88)
	EU/NA	46/95	52/93	0.84 (0.57–1.25)
	ROW	25/48	29/50	0.80 (0.47–1.36)
ECOG PS	0	41/121	52/120	0.72 (0.48–1.09)
	1	92/180	118/188	0.72 (0.55–0.95)
Anatomical subtype	Gastric	87/208	127/226	0.63 (0.48–0.83)
	GEJ	42/74	33/60	1.14 (0.72–1.80)
	Esophageal	5/20	10/22	0.51 (0.17–1.52)
HER2 status	IHC 3+	106/251	138/255	0.70 (0.55, 0.91)
	IHC 2+/ISH+	28/51	31/52	0.83 (0.50, 1.39)
PD-L1 status	TAP <1%	38/90	65/98	0.49 (0.33–0.74)
	TAP ≥1%	79/187	92/188	0.82 (0.60–1.10)



[a]The widths of the confidence intervals were not adjusted for multiplicity and cannot be used to infer treatment effects.

Key Secondary Endpoint: Antitumor Activity

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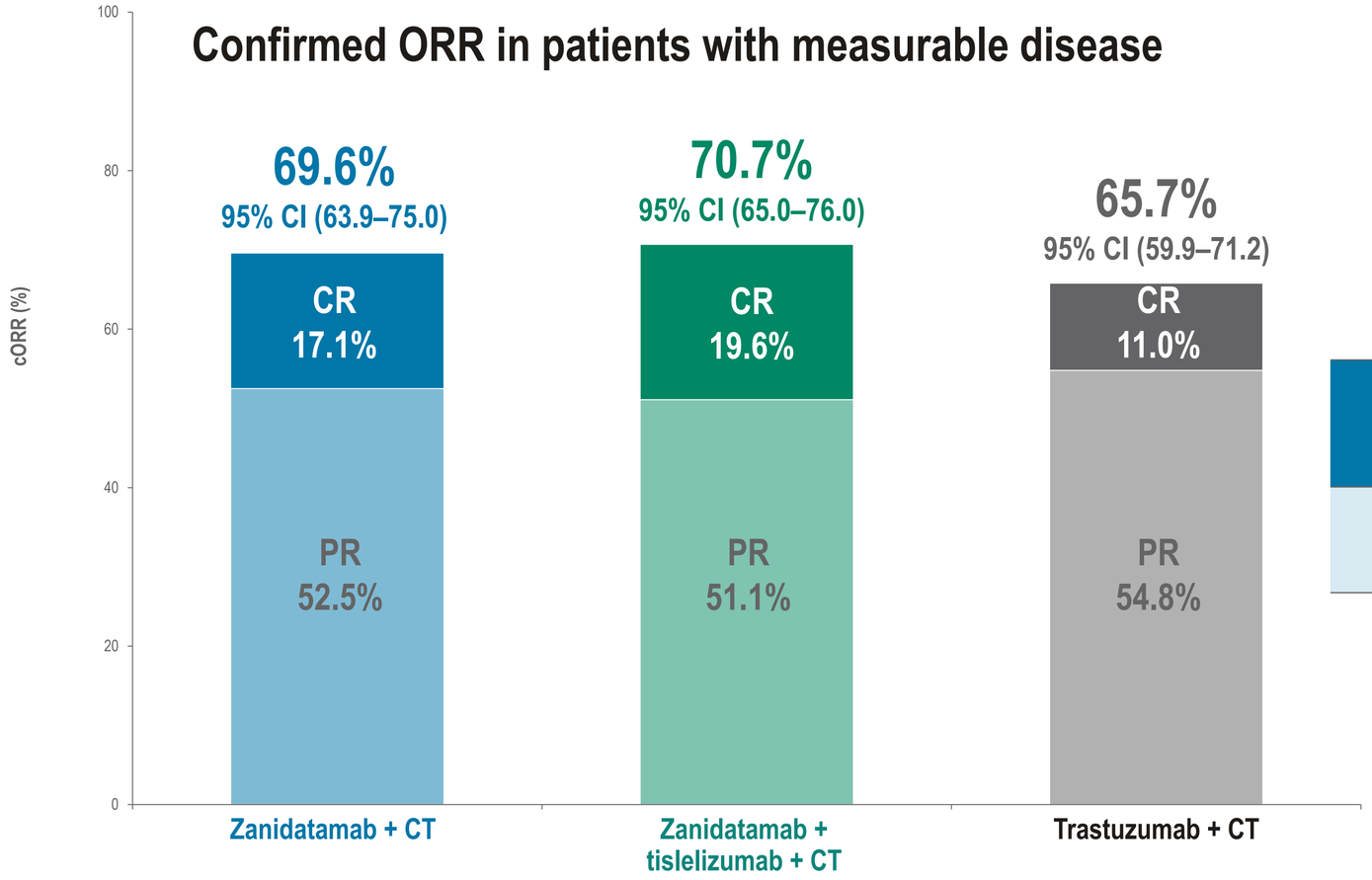
Responses were deeper and more durable in the zanidatamab-containing arms vs the trastuzumab + CT arm



Median DOR (95% CI), mo

Zanidatamab + CT (n = 186)	Zanidatamab + tislelizumab + CT (n = 195)	Trastuzumab + CT (n = 198)
14.3 (11.5–21.9)	20.7 (12.6–37.7)	8.3 (6.7–9.8)

cORR was defined as the proportion of patients achieving a best overall response of CR or PR, as determined by BICR using RECIST v1.1, with the response confirmed at a subsequent visit ≥28 days after the initial assessment. DOR was assessed among patients with measurable disease at baseline who achieved a confirmed objective response by BICR per RECIST v1.1. The widths of the confidence intervals were not adjusted for multiplicity and cannot be used to infer treatment effects.

Safety Summary

HERIZON GEA-301

The safety profile was generally manageable, and no unexpected safety signals were identified

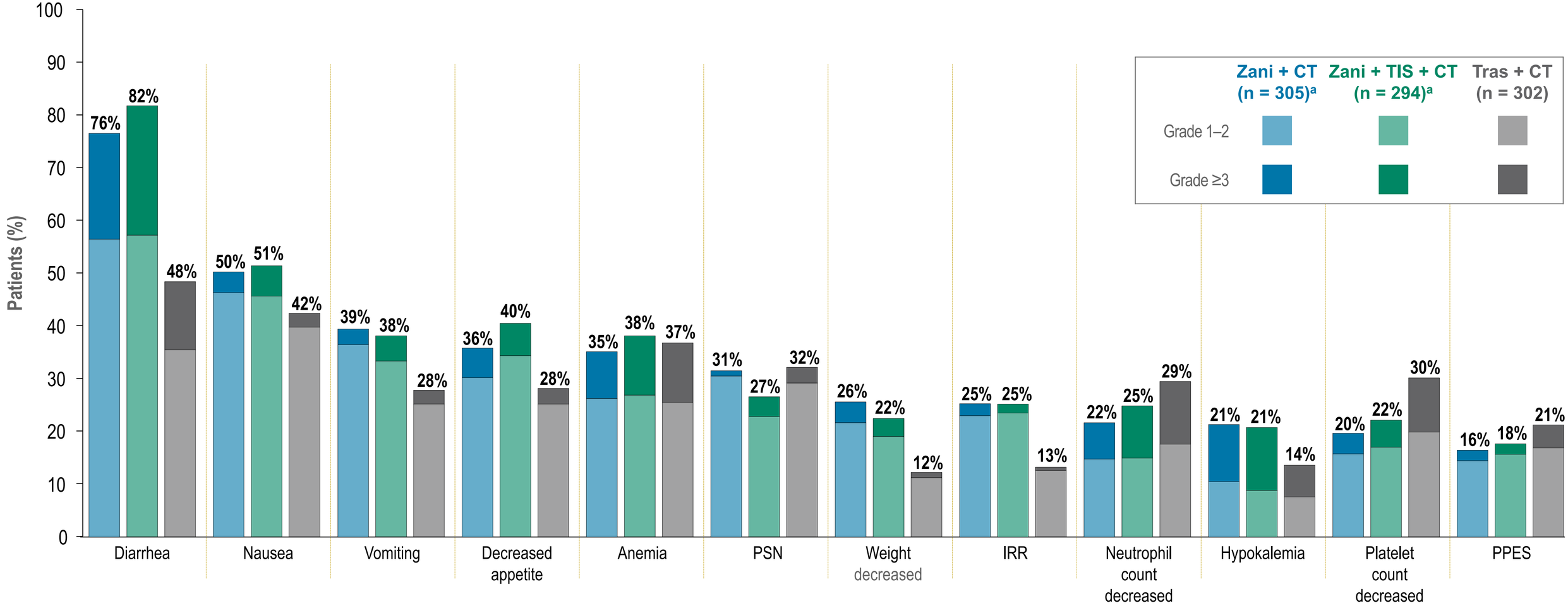
	Zanidatamab + CT (n = 305)[a]	Zanidatamab + tislelizumab + CT (n = 294)[a]	Trastuzumab + CT (n = 302)
Duration of treatment, median (IQR), weeks	31.0 (53.8)	43.1 (56.7)	30.0 (32.2)
Any-grade TEAE, n (%)	301 (98.7)	293 (99.7)	297 (98.3)
TRAE, n (%)	296 (97.0)	289 (98.3)	291 (96.4)
Grade ≥3	180 (59.0)	211 (71.8)	180 (59.6)
Serious TEAEs, n (%)	150 (49.2)	172 (58.5)	128 (42.4)
Treatment-related	86 (28.2)	121 (41.2)	61 (20.2)
TEAEs leading to death, n (%)	25 (8.2)	28 (9.5)	22 (7.3)
Treatment-related	1 (0.3)	7 (2.4)	4 (1.3)
Discontinuation due to TRAEs, n (%)			
Any component	105 (34.4)	125 (42.5)	88 (29.1)
Zanidatamab or trastuzumab	26 (8.5)	35 (11.9)	7 (2.3)
Tislelizumab	—	42 (14.3)	—
AESIs[b], n (%)	93 (30.5)	102 (34.7)	56 (18.5)
IRRs	77 (25.2)	74 (25.2)	40 (13.2)
Noninfectious pulmonary toxicities	4 (1.3)	20 (6.8)	3 (1.0)
Left ventricular dysfunction	19 (6.2)	26 (8.8)	13 (4.3)
Immune-mediated AEs[b], n (%)	38 (12.5)	111 (37.8)	31 (10.3)

[a]Five patients who were assigned to the zanidatamab-tislelizumab-chemotherapy arm did not receive tislelizumab. Data from these patients are summarized in the zanidatamab-chemotherapy arm. [b]AESIs for zanidatamab were IRRs, noninfectious pulmonary toxicities, and left ventricular dysfunction; AESIs for tislelizumab were IRRs and immune-mediated AEs. AESIs for zanidatamab and tislelizumab were reported in all treatment groups, even if the study agent was not administered in that group.

Common TRAEs (≥20% of Patients in Any Arm)

HERIZON GEA-301

Diarrhea was the most common TRAE in all treatment arms



[a]Five patients who were assigned to the zanidatamab-tislelizumab-chemotherapy arm did not receive tislelizumab. Data from these patients are summarized in the zanidatamab-chemotherapy arm. .

Treatment-Emergent Diarrhea

HERIZON GEA-301

Treatment-emergent diarrhea generally occurred early in treatment and resolved within 3 weeks, and few patients discontinued zanidatamab due to diarrhea

	Zanidatamab + CT (n = 305)[a]	Zanidatamab + tislelizumab + CT (n = 294)[a]	Trastuzumab + CT (n = 302)
Treatment-related diarrhea, n (%)			
Any grade	233 (76.4)	240 (81.6)	146 (48.3)
Grade ≥3	61 (20.0)	72 (24.5)	39 (12.9)
Treatment-related diarrhea leading to discontinuation, n (%)			
Any component	15 (4.9)	22 (7.5)	5 (1.7)
Zanidatamab or trastuzumab	4 (1.3)	12 (4.1)	0
Tislelizumab	—	6 (2.0)	—
Time to first onset of diarrhea, median (IQR), days			
Any grade	6.0 (12.0)	7.0 (14.5)	10.0 (30.0)
Grade 3/4	11.0 (23.0)	16.0 (43.0)	37.0 (56.0)
Duration of first diarrhea event, median (95% CI), days			
Any grade	17.0 (13.0–20.0)	14.0 (11.0–18.0)	10.0 (7.0–15.0)
Grade 3/4	9.0 (6.0–11.0)	8.0 (7.0–9.0)	9.0 (6.0–12.0)

Mandatory diarrhea prophylaxis for patients in the zanidatamab-containing arms
Loperamide (4 mg BID) for the first 7 days of cycle 1 only

[a]Five patients who were assigned to the zanidatamab-tislelizumab-chemotherapy arm did not receive tislelizumab. Data from these patients are summarized in the zanidatamab-chemotherapy arm.

Discussion

HERIZON
GEA-301

- HERIZON-GEA-01 is the first phase 3 study in mGEA to demonstrate a median PFS >1 year and a median OS >2 years

- These findings support zanidatamab as a promising new standard in HER2-targeting agents, with potential to replace trastuzumab in first-line treatments for HER2+ mGEA

- The clinically meaningful survival benefit further supports zanidatamab plus tislelizumab and CT as an important new treatment option for this patient population

- **Treatment with zanidatamab-containing regimens** led to a **clinically meaningful prolongation of PFS** that was **statistically superior** to trastuzumab + CT **(>4-month prolongation of median PFS)**
- At this interim analysis, there was a **strong trend** toward statistical significance for OS **favoring zanidatamab + CT** vs trastuzumab + CT (**5-month improvement in median OS**)
    - The trial is ongoing with additional OS analyses planned for zanidatamab + CT
- **Zanidatamab + tislelizumab + CT** demonstrated **a clinically meaningful and statistically superior prolongation of OS** vs trastuzumab + CT (**>7-month prolongation of median OS**)
- The OS and PFS benefits were generally observed across key prespecified subgroups, **including in patients with PD-L1 TAP scores <1% and ≥1%**
- The safety profile was **consistent with the known profiles of each individual treatment**
    - For patients who experienced diarrhea, events generally occurred **early in treatment and resolved within 3 weeks**

Acknowledgments

The authors would like to thank all the patients and their families as well as all the investigators, clinical trial researchers, personnel, and staff who contributed to or participated in the trial

- Clinical research was funded by Jazz Pharmaceuticals in collaboration with BeOne Medicines and Zymeworks
- Under the direction of the authors, Charlotte Pettigrew, PhD, CMPP, of Red Nucleus, Yardley, PA, USA, provided medical writing support, which was funded by Jazz Pharmaceuticals in accordance with Good Publication Practice (GPP 2022) guidelines (https://www.ismpp.org/gpp-2022)

Zanidatamab: Shifting Treatment Paradigm

Rob Iannone, M.D., M.S.C.E.
Executive Vice President,
Global Head of Research & Development,
Chief Medical Officer

Jazz Pharmaceuticals

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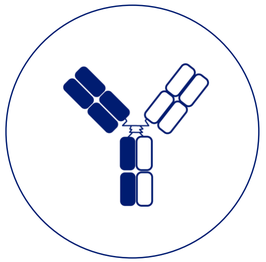
Zanidatamab: Unique MOA Drives Compelling Clinical Profile and Patient Outcomes



Unique dual-targeting HER2 bispecific antibody provides differentiated treatment

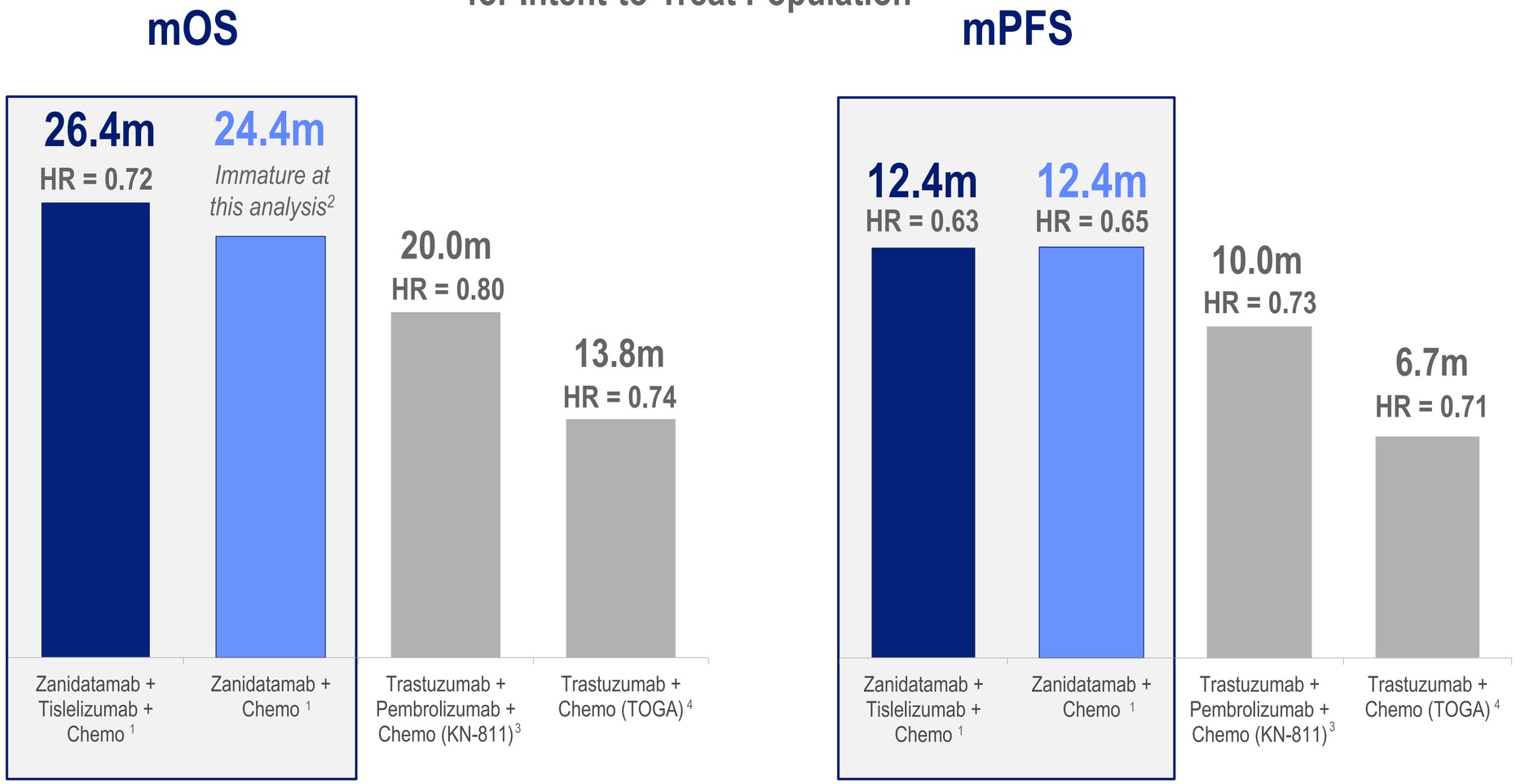
Compelling and durable responses help drive **improved patient outcomes** in HER2+ patients

Favorable tolerability with manageable AE profile

Combination data supports **ability to combine with other agents** in multiple HER2+ indications

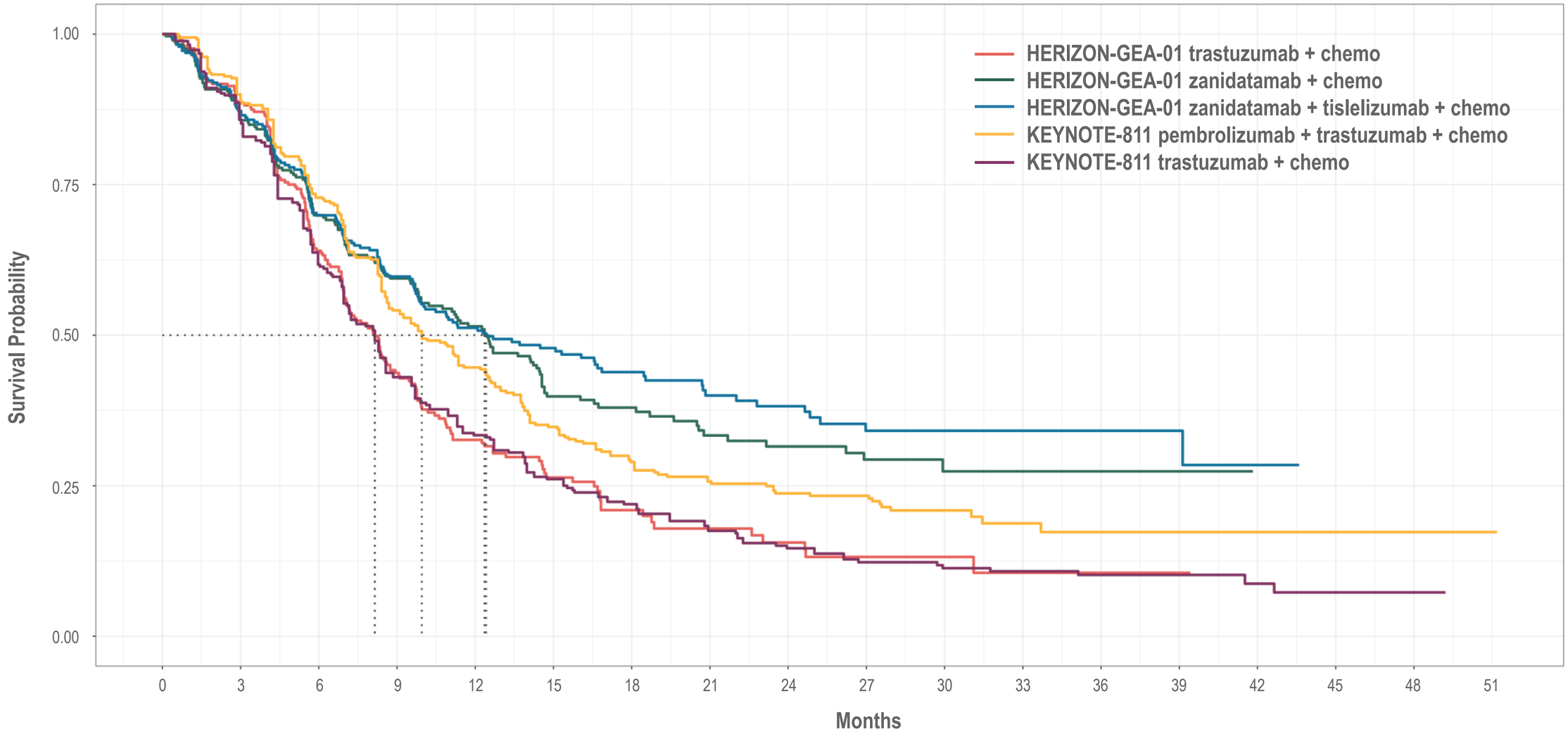
Zanidatamab + Tislelizumab + Chemo in 1L HER2+ GEA: Clinical Benchmarks

Primary Endpoints of OS and PFS for Intent-to-Treat Population



Zanidatamab + Tislelizumab + Chemo in 1L HER2+ GEA: Clinical Benchmarks

Progression-Free Survival Kaplan-Meier Plot



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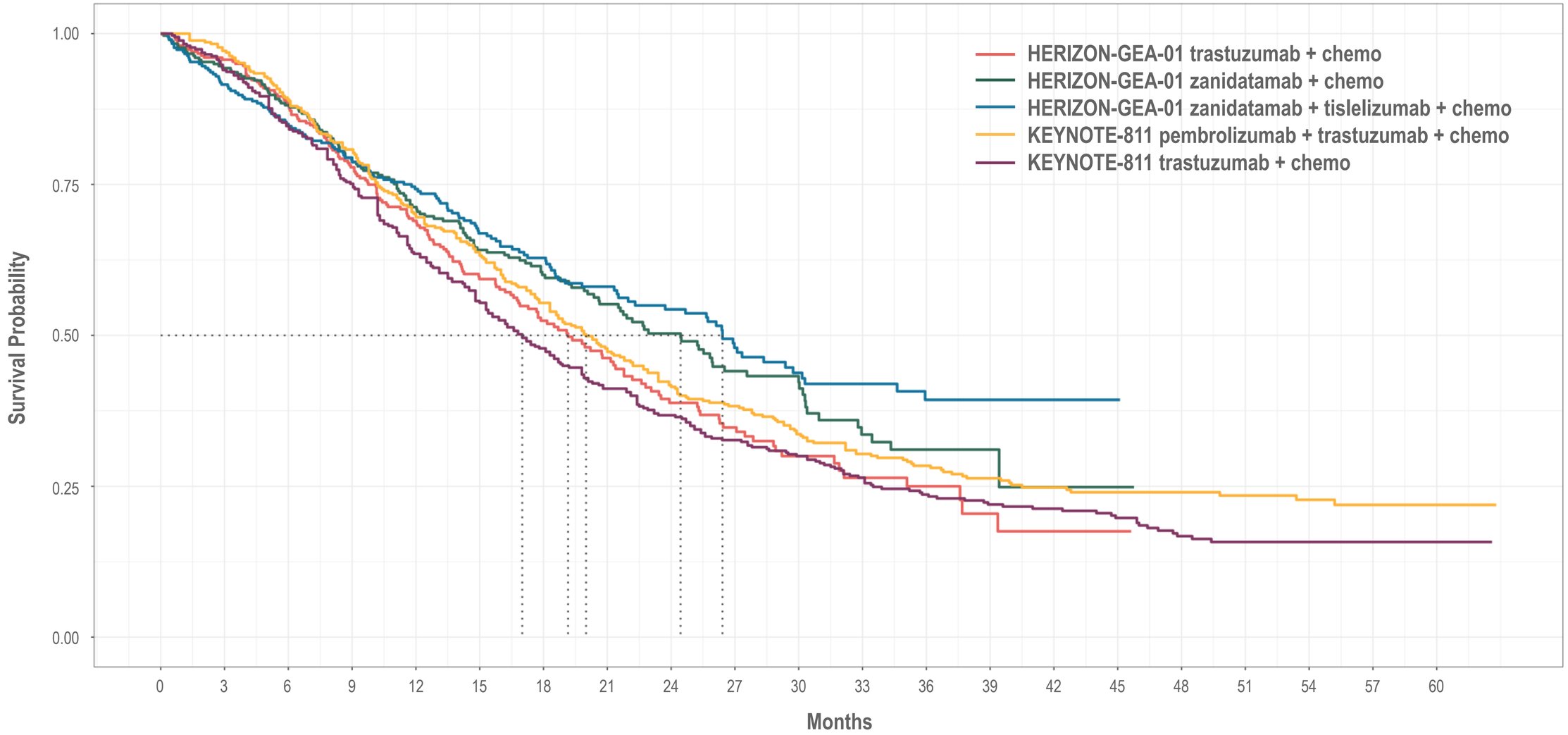
Zanidatamab + Tislelizumab + Chemo in 1L HER2+ GEA: Clinical Benchmarks

Overall Survival Kaplan-Meier Plot



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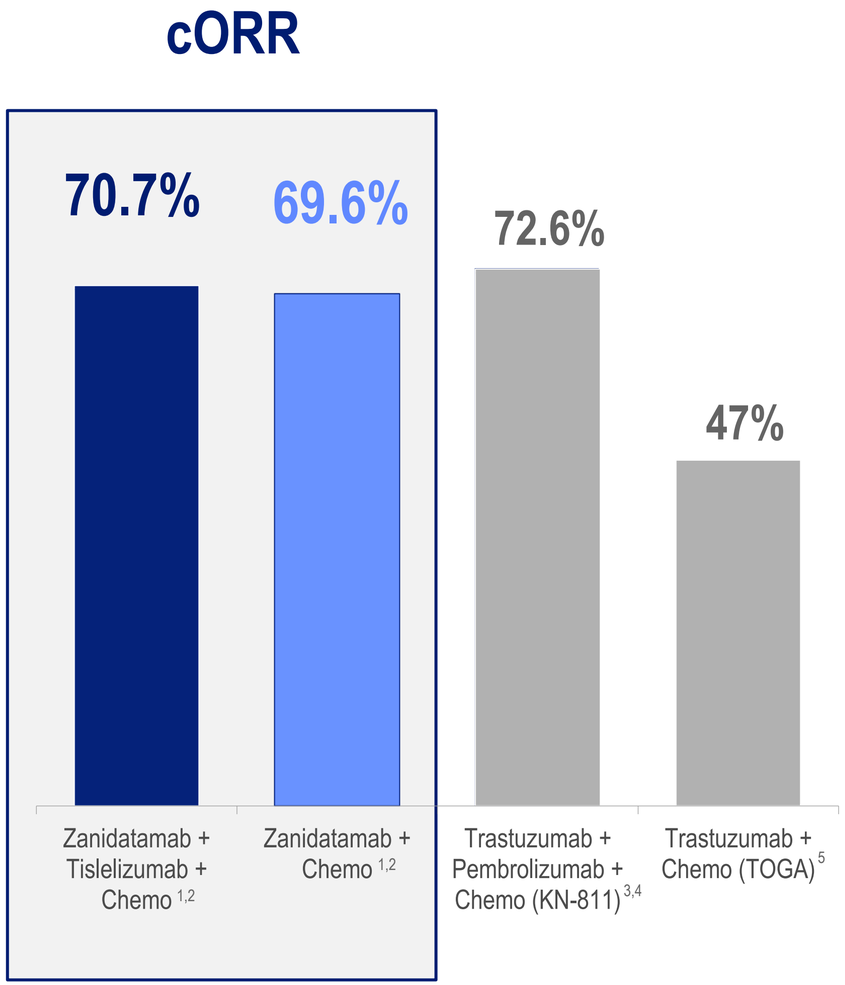
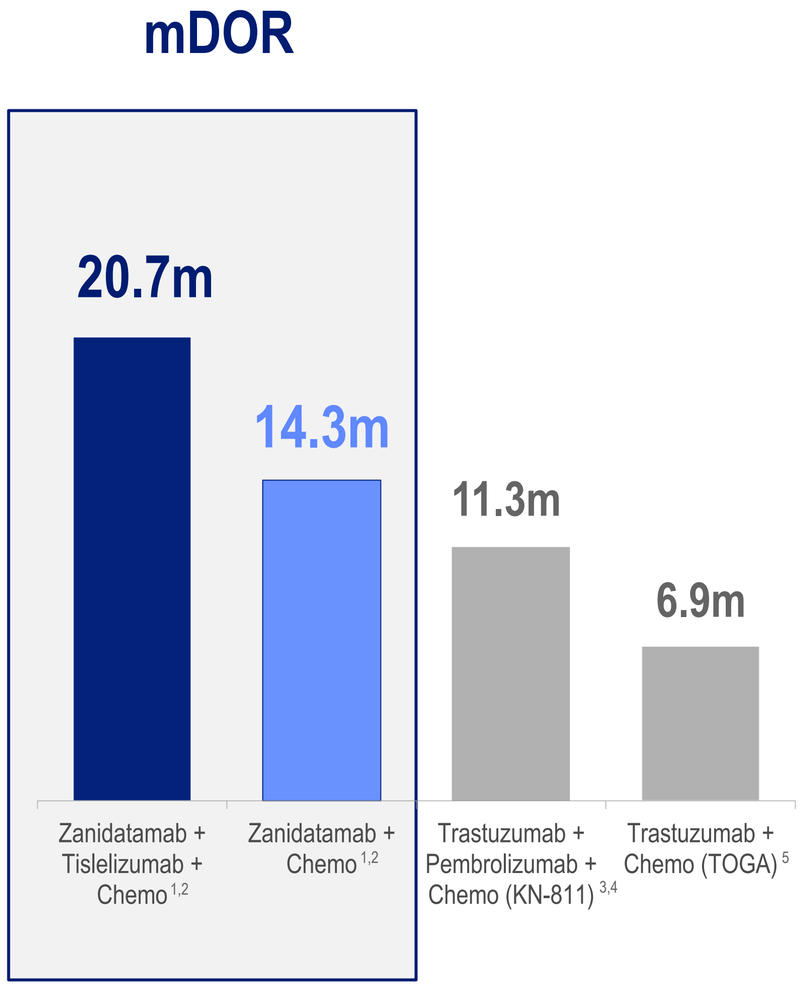
Zanidatamab + Tislelizumab + Chemo in 1L HER2+ GEA: Clinical Benchmarks

Secondary Endpoints of cORR and DOR





Key Ongoing Zanidatamab Clinical Trials

	PHASE 1	PHASE 2	PHASE 3	PHASE 4 / REGULATORY	Recent / Upcoming Milestones
Zanidatamab	Phase 3 1L GEA (pivotal)				**Plan to submit sBLA in 1H26**
	Phase 3 1L BTC				**Phase 3 confirmatory trial** in 1L BTC ongoing
	Phase 3 BC in patients who have progressed on previous T-DXd treatment				**Phase 3 EmpowHER-BC-303 trial** now enrolling
	Phase 2 trial in neoadjuvant and adjuvant breast cancer				**Phase 2 EmpowHER-BC-208 trial** now enrolling
	I-SPY2 Trial: neoadjuvant treatment of locally advanced BC				Novel, collaborative trial for breast cancer
	Phase 2 pan-tumor trial in HER2+ solid tumors				**Phase 2 DiscovHER-Pan-206 trial** now enrolling
	Phase 2 trial + SOC Chemo (1L) in HER2+ solid tumors				
	Open-label trial in early-stage, low-risk, HER2+ breast cancer				In collaboration with the MD Anderson Cancer Center
	Phase 2 trial + paclitaxel and ramucirumab in HER2+ advanced GEA				In collaboration with the Canadian Cancer Trials Group
	Phase 1/1b I-SPY in breast cancer				Novel, collaborative trial for breast cancer

Clinical efficacy and differentiated mechanism of action supports **continued advancement of zanidatamab development program** focusing on areas where we believe zanidatamab has the potential to be the **preferred HER2-targeted therapy**

Zanidatamab: Commercial Perspective

Sam Pearce
Executive Vice President and
Chief Commercial Officer

Jazz Pharmaceuticals

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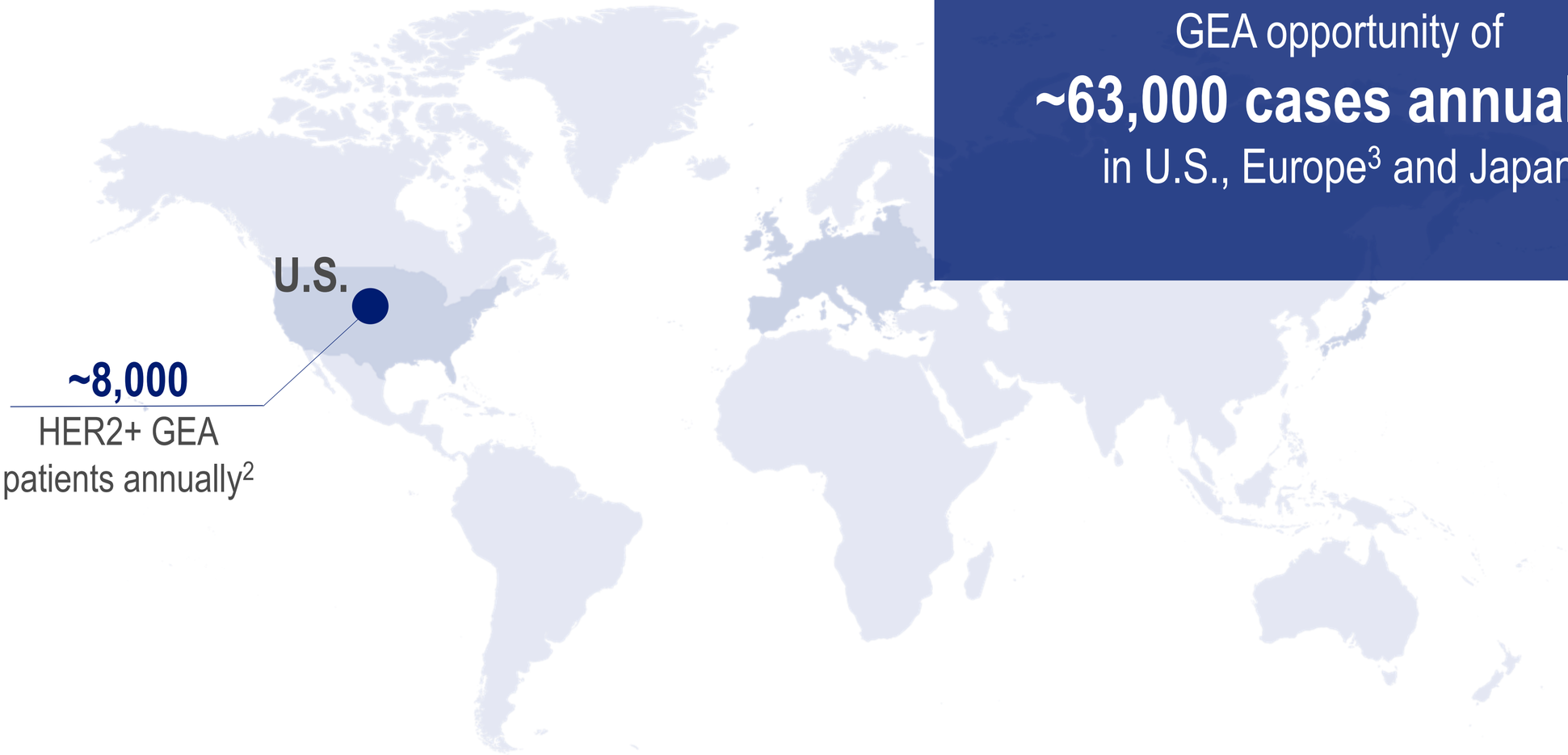
GEA Represents a Significant Unmet Need

<10% five-year survival rate in mGEA[1]



GEA opportunity of
~63,000 cases annually[2]
in U.S., Europe[3] and Japan

Establish Ziihera as the HER2+ Standard of Care Regardless of PDL1 Status

1

Establish Belief in Ziihera Based on Unprecedented Clinical Results

- Practice-changing results supporting Ziihera as the HER2-targeted agent of choice in HER2+ 1L metastatic GEA, replacing trastuzumab as the new standard of care
- The addition of tislelizumab further improved outcomes, regardless of PD-L1 status
- Combination regimens including Ziihera were generally well tolerated

2

Leverage Existing Footprint and Infrastructure to Accelerate Launch

- High physician awareness of Ziihera due to existing approval in 2L BTC and broad development program
- Significant overlap in the customer footprint with GEA and BTC accounts (90+% overlap)

3

Utilize Existing Access Infrastructure

- Existing payer access simplifies reimbursement (Example utilize existing J-code)
- Robust access and reimbursement support for patients; flexible ordering and fulfillment options

Zanidatamab: De-Risked Near-Term Opportunity with $2B+ Peak Potential

Goal to be the HER2-targeted agent of choice

- Data presented at ASCO GI January 8th
- Rapid submission to NCCN Guidelines
- Plan to submit sBLA for 1L HER2+ mGEA in 1H26

Biliary Tract Cancer

Ongoing launch in 2L BTC

1L BTC **confirmatory trial ongoing**

Granted **conditional marketing** authorization by EC in 2L BTC for monotherapy treatment

~12,000
BTC cases annually[1] in U.S., Europe[2] and Japan

Gastroesophageal Adenocarcinoma

Plan to submit **sBLA for 1L GEA** in **1H26**

Potential to become the **new standard of care anti-HER2 therapy** for patients with HER2+ first-line metastatic GEA **regardless of PD-L1 status**[3]

Opportunity to **explore potential in neoadjuvant** populations[3]

~63,000
GEA cases annually[1] in U.S., Europe[2] and Japan

Breast Cancer

Expanded opportunity across lines of therapy[3]:
- Post T-DXd (Ph 3 EmpowHER-BC-303 trial)
- Early lines of therapy (neoadjuvant)
- Novel combinations

Initiated Phase 2 EmpowHER-208 trial:
- Zanidatamab + taxane with or without carboplatin vs TCHP in patients with untreated, histologically confirmed eBC

Potential for **novel chemo-free regimen** for **HER2+/HR+** patients[3]

Ongoing trials in early breast cancer:
- I-SPY2 Trial[4]
- MD Anderson collaboration

~150,000
BC cases annually[5] in U.S., Europe[2] and Japan

Other HER2-Expressing Cancers

Broad potential beyond BTC, GEA and BC in multiple HER2-expressing indications **based on compelling clinical activity from early trials**[6]:
- Colorectal
- NSCLC
- Ovarian
- Endometrial
- Pancreatic
- Bladder
- Salivary Gland
- Ampullary
- Other HER2-expressing solid tumors

Ongoing Phase 2 DiscovHER-Pan-206
- Zanidatamab monotherapy in previously-treated patients with no available treatment options

Broad Potential
Beyond BTC, GEA, and BC

Thank You

… to the numerous patients and their families who participated in our clinical development program.

… to the clinical investigators, physicians, nurses, site coordinators, and countless support staff.

… to the Jazz team continuously working to deliver this important medicine patients.

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Q&A

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Glossary

Acronym	Definition
1H	First half
1L	First-line
2L	Second-line
ADCC	Antibody-dependent cellular cytotoxicity
ADCP	Antibody-dependent cellular phagocytosis
AE	Adverse event
AESI	Adverse event of special interest
BC	Breast cancer
BICR	Blinded-independent central review
BID	Twice daily
BTC	Biliary tract cancer
CAPOX or FP	Capecitabine/oxaliplatin or fluoropyrimidine
CDC	Complement-dependent cytotoxicity
cORR	Confirmed objective response rate
CR	Complete response
CT	Chemotherapy
CT	Computed tomography
DOR	Duration of response
EC	European Commission
ECD	Extracellular domain
ECOG PS	Eastern Cooperative Oncology Group performance status
EU	European Union
Fab	Fragment antigen binding
Fc	Fragment crystallizable
FP	5-fluorouracil (5-FU) plus cisplatin
GEJ	Gastroesophageal junction
HCP	Healthcare provider
HER2	Human epidermal growth factor receptor 2
HR	Hazard ratio
HR+	Hormone receptor-positive

Acronym	Definition
IHC	Immunohistochemistry
IQR	Interquartile range
IRR	Infusion-related reaction
ISH	In situ hybridization
IV	Intravenously
M	Month
mGEA	Metastatic gastroesophageal adenocarcinoma
MOA	Mechanism of action
MRI	Magnetic resonance imaging
NA	North America
NCCN	National Comprehensive Cancer Network
NSCLC	Non-small cell lung cancer
OS	Overall survival
ORR	Objective response rate
PD-1	Programmed cell death protein 1
PD-L1	Programmed death-ligand 1
PFS	Progression-free survival
PPES	Palmar-plantar erythrodysesthesia syndrome
PR	Partial response
PSN	Peripheral sensory neuropathy
Q3W	Every 3 weeks
Q6W	Every 6 weeks
R	Randomization
RECIST v1.1	Response Evaluation Criteria in Solid Tumors version 1.1
ROW	Rest of world
sBLA	Supplemental biologics license application
SoC	Standard of care
scFv	Single-chain variable fragment
T-DXd	Trastuzumab deruxtecan
TAP	Tumor area positivity

Acronym	Definition
TEAE	Treatment-emergent adverse event
TCHP	Docetaxel, Carboplatin, Trastuzumab, and Pertuzumab
TIS	Tislelizumab
Tras	Trastuzumab
Zani	Zanidatamab