2026 ESMO GASTROINTESTINAL CANCERS
Annual Congress

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HERIZON-GEA-01: Exploratory Analysis of Response Characteristics and PFS2 in Advanced or Metastatic Gastroesophageal Adenocarcinoma

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Declaration of Interests: Filippo Pietrantonio, MD

Consulting or advisory role: BMS, MSD, Amgen, Pierre-Fabre, Johnson&Johnson, Servier, Bayer, Takeda, Astellas, GSK, Daiichi-Sankyo, Pfizer, BeOne Medicines, Ltd, Jazz Pharmaceuticals, Incyte, Rottapharm, Merck-Serono, Italfarmaco, Gilead, AstraZeneca, Agenus, Revolution Medicine

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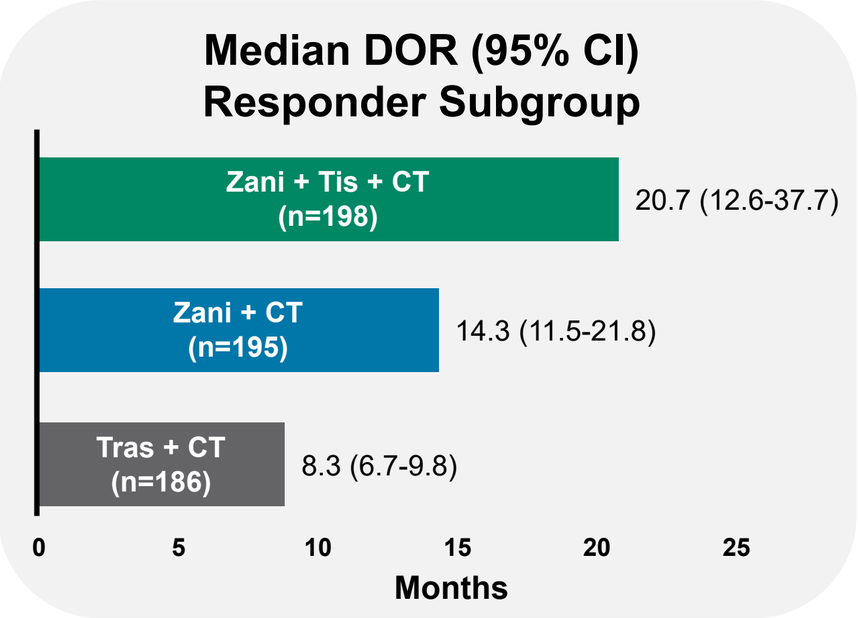
Background

HERIZON
GEA-301

Presenter: Filippo Pietrantonio, MD

- **HERIZON-GEA-01** (NCT05152147) is a global phase 3 trial evaluating **zanidatamab + tislelizumab + CT** and **zanidatamab + CT** vs **trastuzumab + CT** in treatment-naive patients with **HER2+ mGEA**[1]
  - Treatment with **zani + tis + CT** and **zani + CT** significantly prolonged PFS, and **zani + tis + CT** yielded a statistically **significant OS benefit** vs tras + CT[1]
- **Confirmed ORR** was 70.7% in the **zani + tis + CT** arm and 69.6% in the **zani + CT** arm vs 65.7% in the trastuzumab + CT arm
- **Median DOR** was longest in the **zani + tis + CT** arm



Here we present a post hoc analysis of outcomes in patients who responded to treatment

CT, chemotherapy; DOR, duration of response; HER2, human epidermal growth factor receptor 2; mGEA, advanced or metastatic gastroesophageal adenocarcinoma; mo, months; OS, overall survival; PFS, progression-free survival, tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

1. Shitara K, et al. *N Engl J Med.* 2026;394(20):2002-2014.

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HERIZON-GEA-01 Study Design

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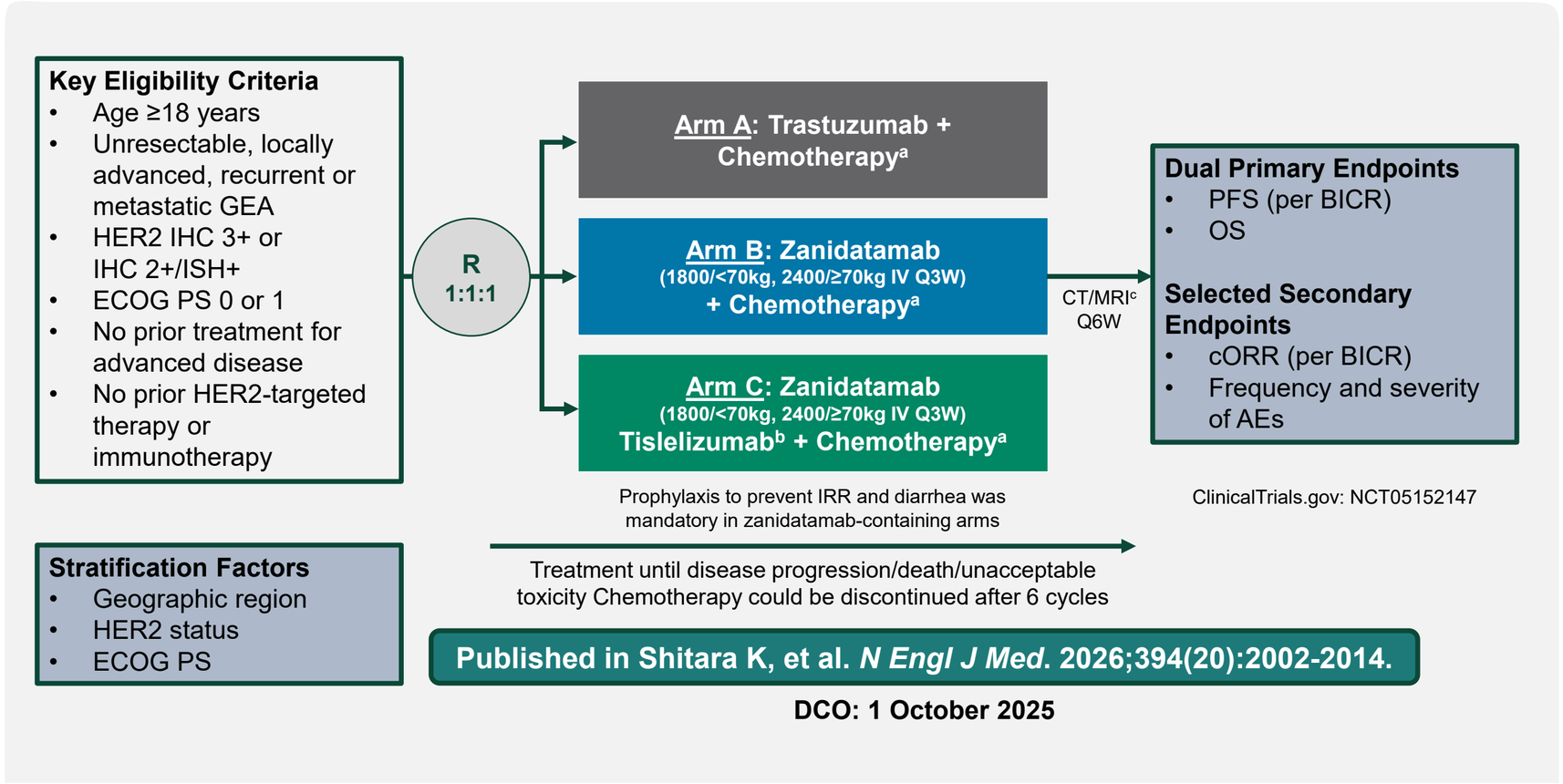
Global phase 3 trial of zanidatamab + tislelizumab + CT and zanidatamab + CT vs trastuzumab + CT in previously untreated patients with HER2+ mGEA



Post Hoc Analysis – Responder Subgroup

Analysis Inclusion Criteria

- Patients with measurable disease at baseline and confirmed response (by BICR per RECIST v1.1)[d]

Outcomes

- Time to response
- DOR
- Depth of response (DpR)[e]
- PFS
- PFS2[f]
- Frequency and severity of AEs

[a]Physician's choice of capecitabine plus oxaliplatin or 5-fluorouracil plus cisplatin. CT 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 wks for the first 54 wks, then every 9 wks. [d]The percentage of patients in each arm is based on the ITT patients assigned to each arm. [e]Maximum percent shrinkage of the tumor sum of diameters from baseline. [f]Time from randomization to disease progression after subsequent anti-cancer therapy or death.
AE, adverse event; BICR, blinded independent central review; cORR, confirmed objective response rate; CT, chemotherapy/computed tomography; DCO, data cut-off; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GEA, gastroesophageal adenocarcinoma; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; 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.

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RESULTS: Demographics — Responders Subgroup

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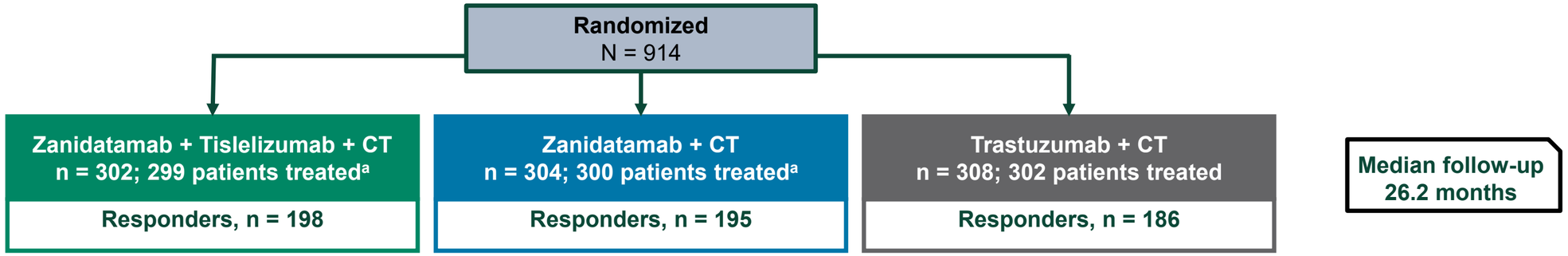
The 3 arms were generally balanced and consistent with the overall study population



Parameter	Zani + Tis + CT (n = 198)	Zani + CT (n = 195)	Tras + CT (n = 186)
Median age (IQR), y	63 (55-69)	62 (55-69)	64 (56-70
≥65 y, n (%)	91 (46.0)	82 (42.1)	90 (48.4)
Male, n (%)	163 (82.3)	155 (79.5)	147 (79.0)
Region, n (%)			
Asia	115 (58.1)	108 (55.4)	103 (55.4)
EU/North America	57 (28.8)	56 (28.7)	57 (30.8)
Rest of world	26 (13.1)	31 (15.9)	26 (14.0)
ECOG PS 0, n (%)	85 (42.9)[b]	87 (44.6)	77 (41.4)

Parameter	Zani + Tis + CT (n = 198)	Zani + CT (n = 195)	Tras + CT (n = 186)
Anatomical subtype, n (%)			
Gastric	140 (70.7)	129 (66.2)	138 (74.2)
GEJ	42 (21.2)	42 (21.5)	37 (19.9)
Esophageal	16 (8.1)	24 (12.3)	11 (5.9)
HER2 IHC 3+, n (%)	167 (84.3)	172 (88.2)	156 (83.9)
PD-L1 status[c], n (%)			
PD-L1 TAP <1%	61 (30.8)	67 (34.4)	61 (32.8)
PD-L1 TAP ≥1%	122 (61.6)	115 (59.0)	112 (60.2)

[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]One patient in the zanidatamab-tislelizumab-chemotherapy arm had an ECOG PS score of 2 at baseline. [c]PD-L1 status was missing for 7.1% (n = 41) of patients across arms.

CT, chemotherapy; DCO, data cut-off; ECOG PS, Eastern Cooperative Oncology Group performance status; EU, European Union; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IQR, interquartile range; PD-L1, programmed death-ligand 1; TAP, tumor area positivity; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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RESULTS: Time to, Duration, and Depth of Response

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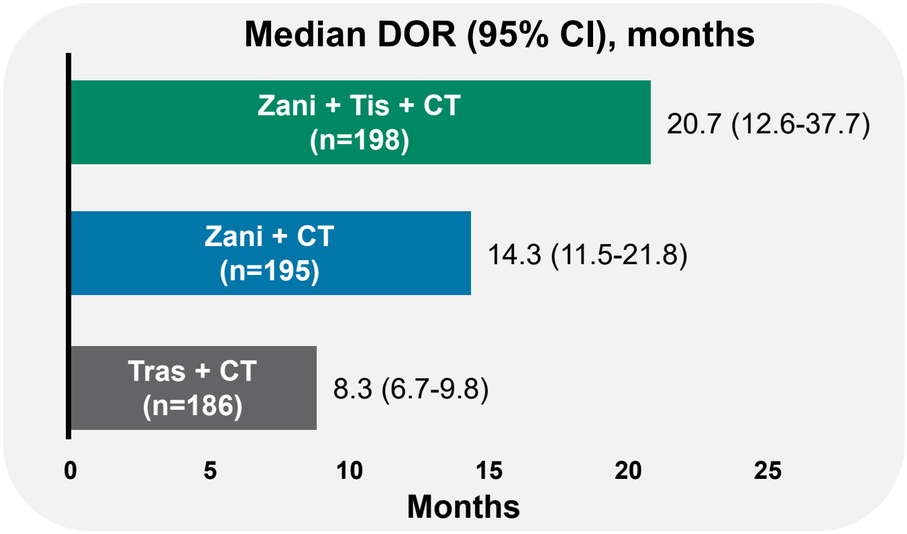
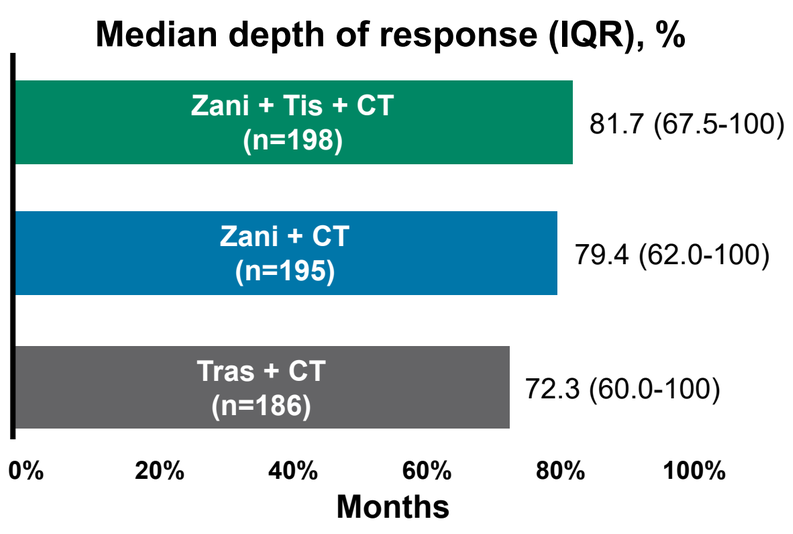
- In the ITT population, ORR was greatest in the zanidatamab + tislelizumab + CT arm; response by PD-L1 TAP score ≥1% and <1% were similar

ITT Population	Zani + Tis + CT (n = 280)	Zani + CT (n = 280)	Tras + CT (n = 283)
ORR, % (95% CI) [n]	70.7 (65.0-76.0) [198]	69.6 (63.9-75.0) [195]	65.7 (59.9-71.2) [186]
PD-L1 TAP score ≥1%, % (95% CI) [n]	71.8 (64.4-78.4) [122]	68.5 (60.8-75.4) [115]	65.1 (57.5-72.2) [112]
PD-L1 TAP score <1%, % (95% CI) [n]	70.9 (60.1-80.2) [61][a]	70.5 (60.3-79.4) [67][a]	65.6 (55.0-75.1) [61][a]

Treatment Responder Subgroup

- Among the responders subgroup, the median time to response was 1.4 months across all treatment arms; the median DOR and depth of response was greatest in the zanidatamab + tislelizumab + CT arm





[a]Missing data: zani + tis +CT (n=15); zani + CT (n=13); tras + CT (n=13).

CT, chemotherapy; DCO, data cut-off; DOR, duration of response; IQR, interquartile range; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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RESULTS: Probability of Durability of Response

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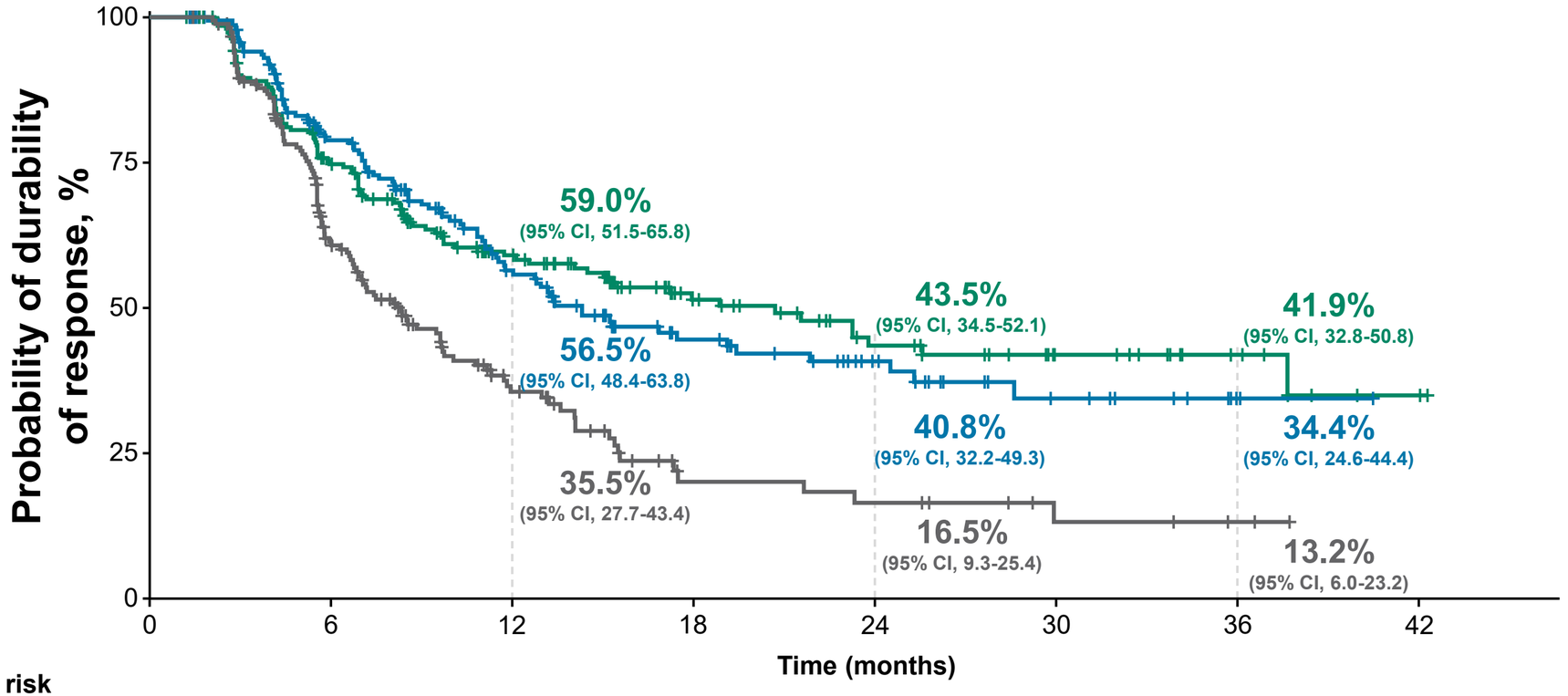
Among the responders subgroup, the probability of maintaining a response at 1, 2, and 3 years was higher in the zanidatamab + tislelizumab + CT arm



Number at risk

Zani + Tis +CT	198	139	84	46	30	18	8	2
Zani + CT	195	131	77	39	24	11	2	0
Tras +CT	186	96	37	11	9	4	2	0

CT, chemotherapy; DCO, data cut-off; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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RESULTS: PFS and PFS2 in ITT Population

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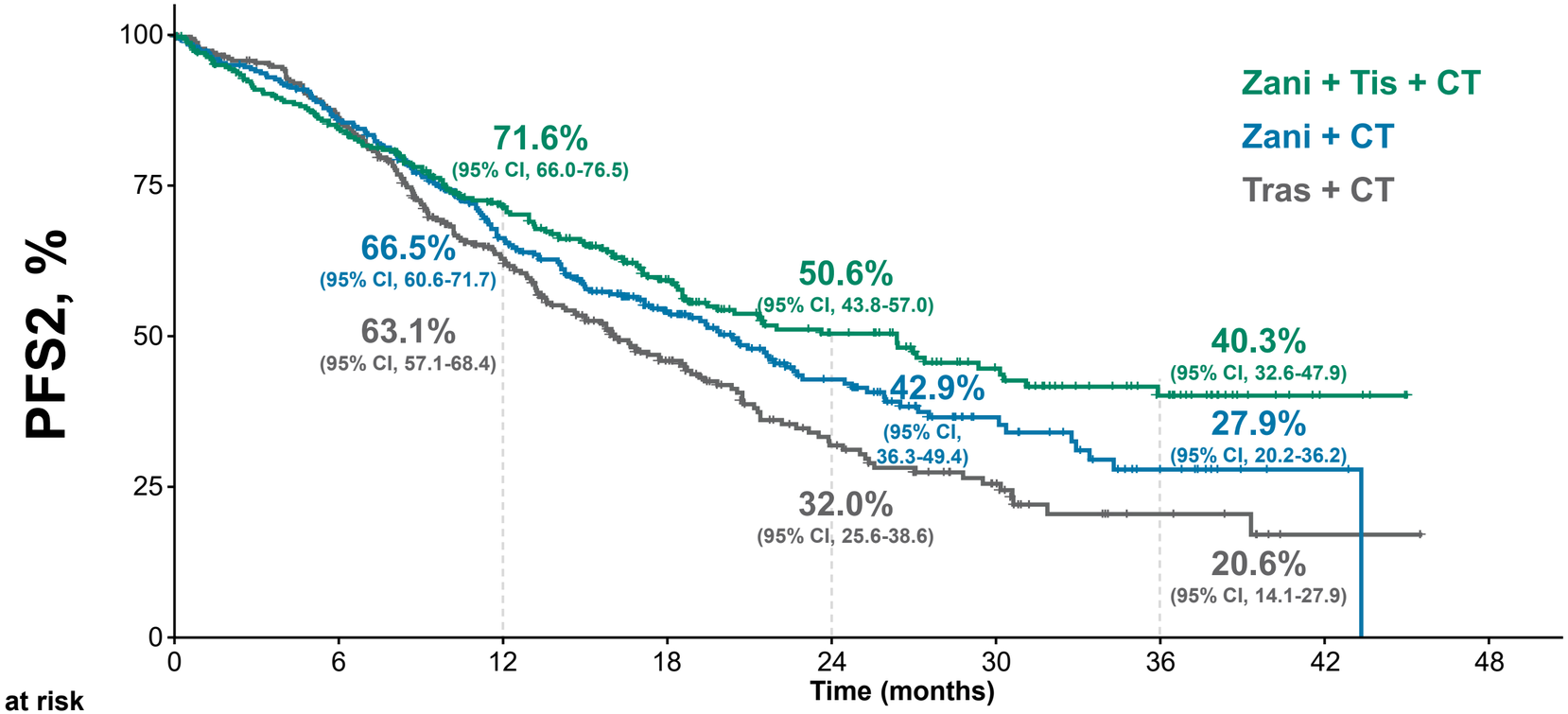
In the ITT population, PFS2 is the longest in the zanidatamab + tislelizumab + CT arm



Number at risk

Zani + Tis +CT	302	244	181	115	71	46	26	4	0
Zani + CT	304	250	172	106	62	29	13	2	0
Tras +CT	308	253	159	90	45	25	8	1	0

PFS[a] and PFS2[a]

Median (95% CI)	Zani + Tis + CT (n = 302)	Zani + CT (n = 304)	Tras + CT (n = 308)
PFS, months	12.6 (11.2-16.6)	12.5 (9.9-14.7)	8.3 (7.2-9.5)
PFS2, months	26.4 (18.6-30.3)	20.4 (17.1-22.9)	16.1 (13.6-18.9)
Subsequent treatment, n (%)			
Any treatment	101 (34.4)	133 (43.8)	174 (56.5)
HER2-targeted	39 (12.9)	70 (23.0)	90 (29.2)

[a] Investigator assessed.

CT, chemotherapy; DCO, data cut-off; PFS, progression-free survival; PFS2, time from randomization to disease progression after subsequent anti-cancer therapy or death; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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RESULTS: PFS and PFS2 in Responder Subgroup

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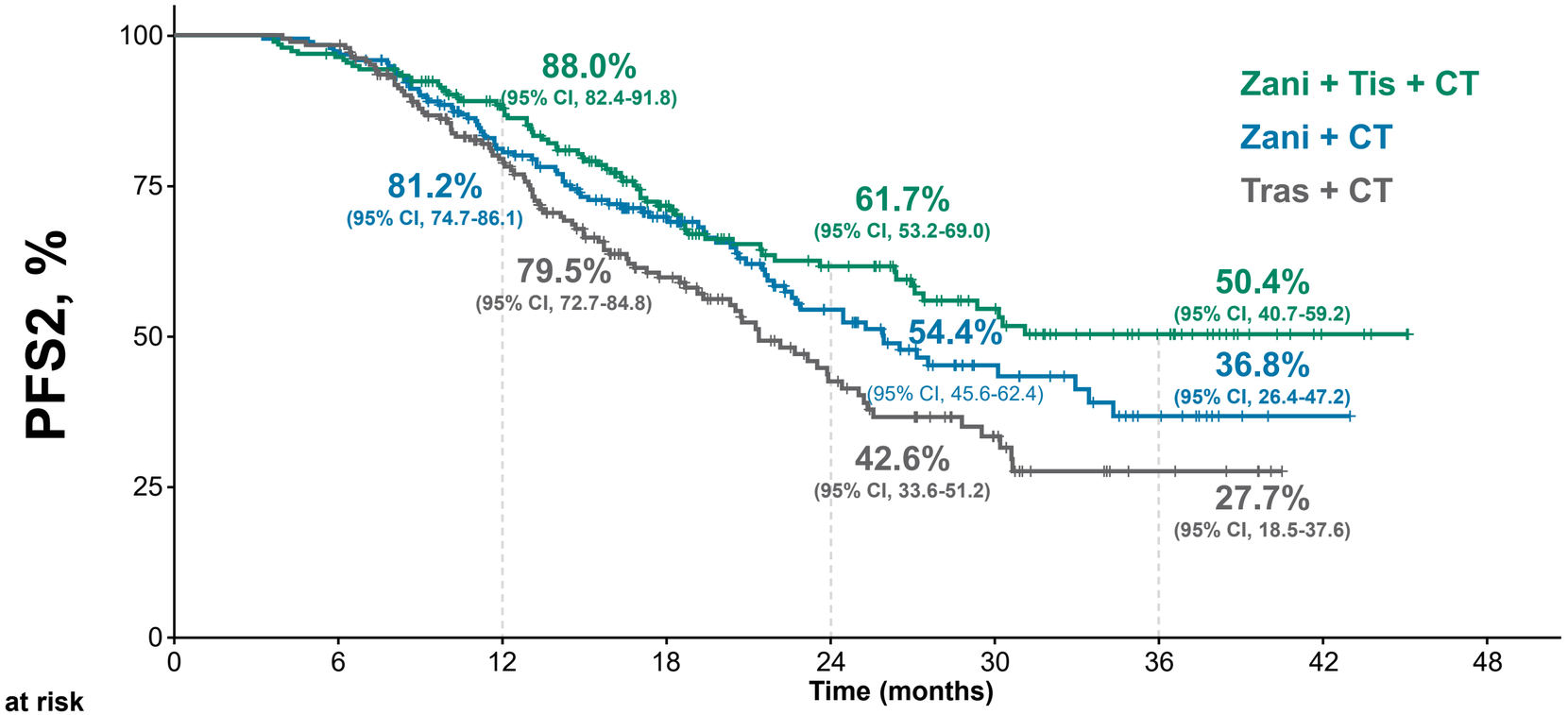
Among the responders subgroup, median PFS was longest and median PFS2 was not reached in the zanidatamab + tislelizumab + CT arm



Number at risk

Zani + Tis +CT	198	190	153	98	63	40	22	4	0
Zani + CT	195	190	141	89	53	25	12	1	0
Tras +CT	186	183	128	74	38	19	6	0	0

PFS and PFS2

Median (95% CI)	Zani + Tis + CT (n = 198)	Zani + CT (n = 195)	Tras + CT (n = 186)
PFS, months	18.7 (14.5-26.9)	16.7 (14.5-18.9)	10.8 (9.5-12.5)
PFS2, months	NR (27.0-NE)	26.0 (21.9-33.4)	21.4 (18.7-25.0)
Subsequent treatment, n (%)			
Any treatment	67 (33.8)	84 (43.1)	115 (61.8)
HER2-targeted	29 (14.6)	46 (23.6)	61 (32.8)

CT, chemotherapy; DCO, data cut-off; PFS, progression-free survival; PFS2, time from randomization to disease progression after subsequent anti-cancer therapy or death; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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RESULTS: Safety Summary

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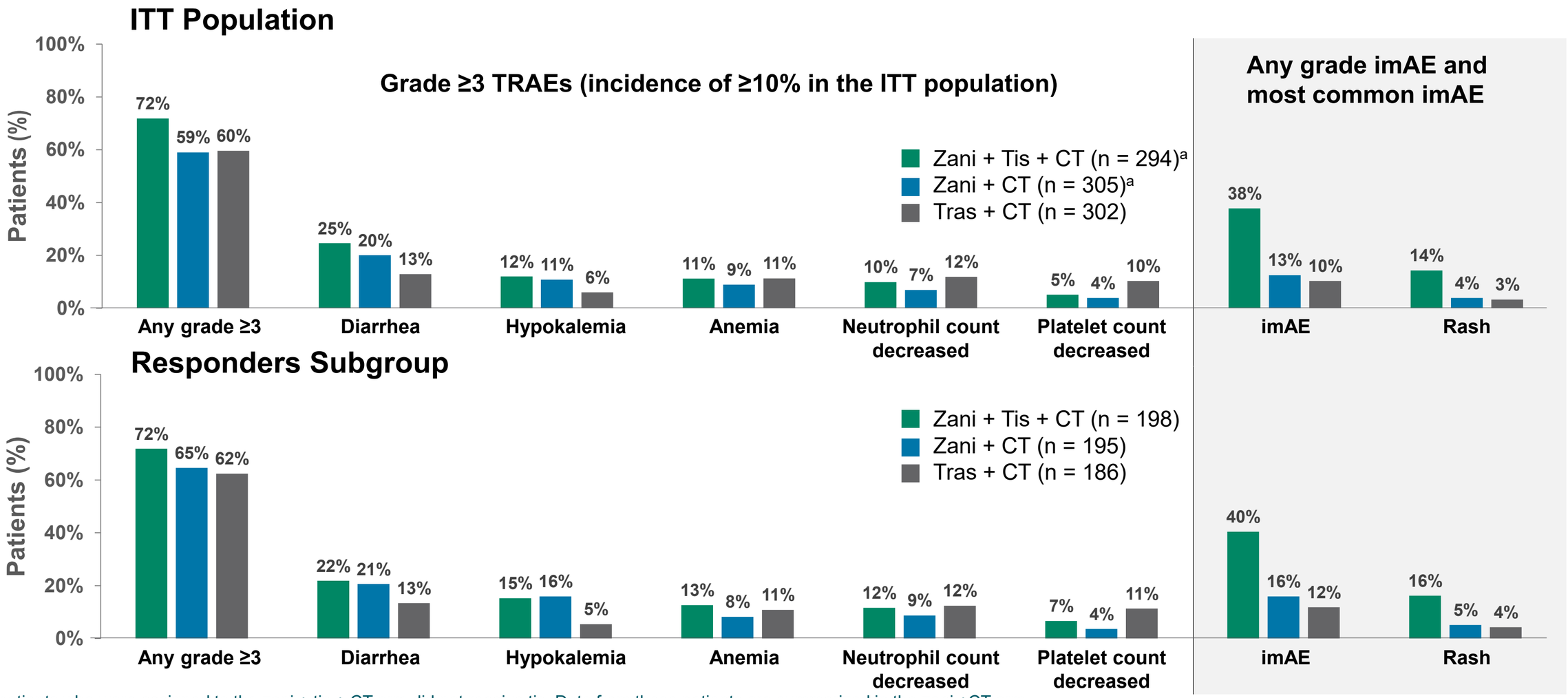
Rates of grade ≥3 TRAEs and any grade imAEs in the responders subgroup were nearly identical with overall safety population



[a]Five patients who were assigned to the zani + tis + CT arm did not receive tis. Data from these patients are summarized in the zani +CT arm.

CT, chemotherapy; imAE, immune-mediated adverse event; TRAE, treatment-related adverse event; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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Conclusions

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- In this responder subgroup analysis, **zani + tis + CT** demonstrated substantial depth and durability of response, while maintaining a safety profile consistent with the ITT population
  - Median DOR was 20.7 months with **zani + tis + CT**, 14.3 months with **zani + CT**, and 8.3 months with **tras + CT**
  - Patients treated with **zani + tis + CT** had the greatest probability of maintaining a response at 3 annual landmarks, with the greatest difference seen at 36 months
- **Zani + tis + CT** had the greatest median PFS and median PFS2 was prolonged in this responder subgroup analysis

CT, chemotherapy; DOR, duration of response; PFS, progression-free survival; PFS2, time from randomization to disease progression after subsequent anti-cancer therapy or death; tis, tislelizumab; tras, trastuzumab; zani, zanidatamab.

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