

Exposure-Adjusted (Exp-Adj) Analyses of Safety Patterns in HERIZON-GEA-01: Zanidatamab (Zani) With and Without Tislelizumab (Tis) and Chemotherapy (CT) in 1L HER2+ Metastatic Gastroesophageal Adenocarcinoma (mGEA)

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Background

HERIZON-GEA-01 (NCT05152147) is an ongoing phase 3 trial evaluating zani + CT $\pm$ tis vs trastuzumab (tras) + CT (CT could be discontinued after 6 cycles) in treatment (tx)-naive patients (pts) with HER2+ mGEA. Statistically significant, clinically meaningful prolongation of PFS in both zani arms and OS (interim analysis 1) in the zani + tis + CT arm vs tras + CT were observed (Elimova ASCO GI 2026). The safety profile of zani + CT $\pm$ tis was generally manageable. Median tx duration: zani + tis + CT (9.9 mo); zani + CT (7.1 mo); tras + CT (6.9 mo). This exploratory post hoc analysis was performed to determine if longer tx duration was associated with incidence of AEs.

Methods

Pts who received ≥ 1 dose of any tx were included in the analysis. Overlapping TEAEs with the same preferred term in a given pt were reported as one unique event at the highest grade (G). Primary objective: assess TEAEs using exp-adj measures to normalize for tx duration. Secondary objective: explore incidence of TEAEs by cycle.

Results

The data cutoff date for this analysis was 1 Oct 2025; 901 pts received ≥ 1 dose of any tx and were included in the safety set: zani + tis + CT (n = 294), zani + CT (n = 305), tras + CT (n = 302). The number of TEAEs and the pt-mo of tx exp is shown in the **Table**. The exp-adj event rates (EAER) per 100 pt-mo for any G and G ≥ 3 TEAEs were similar for all arms. EAER/100 pt-mo rates were similar for any G and G ≥ 3 TEAE of diarrhea in the zani-containing arms; rates were also similar for tx-related diarrhea. Within each tx arm, the incidence of TEAEs decreased from cycles 1-3, 4-6, and 7-9.

Conclusions

When normalized by tx exp, overall any G and G ≥ 3 TEAE profiles of zani + tis + CT arm were comparable with the zani + CT arm and the tras + CT arm for pts with mGEA. The exp-adj incidence of diarrhea in the zani + tis + CT arm was similar to the zani + CT arm. A temporal analysis showed the rate of TEAEs decreased after CT reduction or discontinuation.

Table

	Zani + tis + CT n=294		Zani + CT n=305		Tras + CT n=302	
Median tx duration, mo	9.9		7.1		6.9	
Pt-mo of exp	3633.9		3179.2		2712.0	
TEAEs	Any G	G ≥3	Any G	G ≥3	Any G	G ≥3
Events, n	6823	872	6015	703	5157	653
EAER/100 pt-mo (95% CI)	187.8 (183.3-192.3)	24.0 (22.4-25.6)	189.2 (184.5-194.0)	22.1 (20.5-23.8)	190.2 (185.0-195.4)	24.1 (22.3-26.0)
Diarrhea						
Events, n	830	95	745	82	379	46
EAER/100 pt-mo (95% CI)	22.8 (21.3-24.5)	2.6 (2.1-3.2)	23.4 (21.8-25.2)	2.6 (2.1-3.2)	14.0 (12.6-15.5)	1.7 (1.2-2.7)
EAER/100 pt-mo = (total events / pt-mo of exp) × 100 Pts with >1 event occurrence will be counted multiple times in the numerator. Exp time = tx (any) duration for all pts with/without the event. 95% CI calculated using exact Poisson method.						