Zanidatamab (zani) Plus Chemotherapy (chemo) and Tislelizumab (TIS) as First-line (1L) Therapy for Patients (pts) With Advanced HER2-positive (+) Gastric/Gastroesophageal Junction Adenocarcinoma (GC/GEJC): Updated Results From a Phase 1b/2 Study

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Background: Zani, an anti-HER2 bispecific antibody, targets two distinct extracellular domains of HER2 and has shown preliminary antitumor activity and tolerability, with chemo, in pts with HER2+ GC/GEJC. These are updated results from the phase 1b/2 study (NCT04276493) for zani plus chemo and TIS, an anti-PD-1 monoclonal antibody. Duration of response is reported for the first time.

Methods: Cohort 2 of this open-label study included pts with untreated, unresectable, locally advanced/metastatic HER2+ GC/GEJC. Cohort 2a received zani 30 mg/kg intravenously (IV), Cohort 2b received zani 1800 mg IV (weight <70 kg) or 2400 mg IV (weight ≥70 kg), each with TIS 200 mg IV every 3 weeks. Both cohorts also received standard capecitabine-oxaliplatin (CAPOX). Primary endpoints were safety and investigator (INV)-assessed objective response rate (ORR) per RECIST v1.1. Secondary endpoints included INV-assessed progression-free survival (PFS), duration of response, and disease control rate.

Results: As of 22 Nov, 2022, 33 pts (median age 64 years [range: 29-80]) were assigned to Cohort 2a (n=19) or 2b (n=14). Overall, 13 (39.4%) pts remained on treatment. Confirmed ORR was 75.8% (95% CI: 57.7, 88.9); median PFS was 16.7 months (95% CI: 8.2, NE). Efficacy data are presented in the **Table**. All pts had ≥1 treatment-related adverse

event (TRAE), and 22 (66.7%) had grade ≥3 TRAEs. Serious TRAEs occurred in 11 (33.3%) pts; TRAEs leading to treatment discontinuation occurred in two (6.1%) pts; and TRAEs leading to death occurred in two (6.1%) pts.

Conclusions: Zani plus TIS and CAPOX produced durable, promising antitumor activity with encouraging PFS as 1L therapy for pts with HER2+ GC/GEJC. Safety was consistent with previous findings. A phase 3 trial (NCT05152147) evaluating this regimen is ongoing.

	Cohort 2a (n=19)	**Cohort 2b (n=14)**	**Overall (N=33)**
Median follow-up, months	19.1	18.0	18.2
Best overall response[a], n (%)			
Complete response	1 (5.3)	0 (0.0)	1 (3.0)
Partial response	14 (73.7)	10 (71.4)	24 (72.7)
Stable disease	4 (21.1)	4 (28.6)	8 (24.2)
ORR[a], n (%)	15 (78.9)	10 (71.4)	25 (75.8)
(95% CI)	(54.4, 93.9)	(41.9, 91.6)	(57.7, 88.9)
DCR[a], n (%)	19 (100.0)	14 (100.0)	33 (100.0)
(95% CI)	(82.4, 100.0)	(76.8, 100.0)	(89.4, 100.0)
Median DoR, months (95% CI)	15.4 (4.9, NE)	NE (7.4, NE)	22.8 (7.4, NE)
Median PFS, months (95% CI)	8.3 (5.6, NE)	NE (8.8, NE)	16.7 (8.2, NE)

[a]Confirmed.

DCR, disease control rate; DoR, duration of response; NE, not estimable; ORR, objective response rate; PFS, progression-free survival.