Zanidatamab (zani), a HER2-targeted bispecific antibody, in combination with chemotherapy (chemo) and tislelizumab (TIS) as first line (1L) therapy for patients (pts) with advanced HER2-positive gastric/gastroesophageal junction adenocarcinoma (G/GEJC): Preliminary results from a Phase 1b/2 study

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Abstract:

Background: Zani, also known as ZW25, is a novel HER2-targeted bispecific antibody that targets two distinct extracellular domains of HER2. Zani has shown preliminary antitumor activity and tolerability in pts with HER2+ gastroesophageal adenocarcinoma as monotherapy/with chemo in Phase 1/2 studies (NCT02892123, NCT03929666). TIS, an anti-PD-1 antibody, has demonstrated antitumor activity in pts with advanced solid tumors. Combining anti-HER2 therapy with anti-PD-1 therapy and chemo increased tumor response in G/GEJC in a Phase 3 clinical trial.

Methods: Cohort 2 of this ongoing open-label, Phase 1b/2 study was in pts with untreated locally advanced/metastatic HER2+ G/GEJC (NCT04276493). Cohort A received zani 30 mg/kg IV, Cohort B received zani 1800 mg IV (weight < 70 kg) or 2400 mg IV (weight ≥ 70 kg), both with TIS 200 mg IV and capecitabine/oxaliplatin (CAPOX) Q3W. Primary endpoints were safety and investigator (INV)-assessed objective response rate (ORR) per RECIST v1.1. Secondary endpoints included INV-assessed duration of response (DoR), disease control rate (DCR) and progression-free survival (PFS).

Results: As of Nov 26, 2021, 33 pts with a median age of 64.0 years (range: 29.0–80.0) were assigned to Cohort A (n=19) or B (n=14). Median study follow-up was 7.7 months (range: 2.1–19.0) and the median number of treatment cycles was 10 (range: 1–28), 20 (60.6%) pts remained on treatment. All pts were efficacy evaluable ([EE], n=33),

confirmed ORR was 72.7% (95% CI: 54.5, 86.7). Median PFS was 10.9 months (95% CI: 6.9, NE). Efficacy data are summarized in Table 1. All pts experienced ≥ 1 treatment emergent adverse event (TEAE), and 24 (72.7%) pts experienced ≥ Grade 3 TEAEs. All pts experienced treatment related TEAEs (trTEAEs), 20 (60.6%) pts experienced ≥ Grade 3 trTEAEs and trTEAEs leading to death occurred in two (6.1%) pts. Immune-mediated AEs (imAEs) occurred in nine (27.3%) pts, of which seven (21.2%) pts experienced ≥ Grade 3 imAEs.

Conclusions: Zani, TIS and CAPOX combination demonstrated a manageable safety profile and antitumor activity as 1L therapy for pts with HER2+ G/GEJC.

Table 1. Summary of efficacy results (EE analysis set)

	Cohort A (n=19)	**Cohort B (n=14)**	**Total (n=33)**
Confirmed best overall response, n (%)			
Complete response	1 (5.3)	0 (0)	1 (3.0)
Partial response	13 (68.4)	10 (71.4)	23 (69.7)
Stable disease*	5 (26.3)	4 (28.6)	9 (27.3)
Progressive disease	0 (0)	0 (0)	0 (0)
Confirmed ORR, n (%)	14 (73.7)	10 (71.4)	24 (72.7)
95% CI	48.8, 90.9	41.9, 91.6	54.5, 86.7
Confirmed DCR, n (%)	19 (100.0)	14 (100.0)	33 (100.0)
95% CI	82.4, 100.0	76.8, 100.0	89.4, 100.0
Confirmed DoR, range	2.4–15.3	2.8–7.2	2.4–15.3
*One pt's partial response is to be confirmed Data cut off: Nov 26, 2021			