

Safety, Anti-Tumor Activity, and Biomarker Results of the HER2-Targeted Bispecific Antibody ZW25 in HER2-Expressing Solid Tumors

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Disclosure Information

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ZW25, A HER2-Targeted Bispecific Antibody in HER2-expressing Cancers

- ZW25 is a novel HER2-targeted bispecific antibody that binds to the ECD4 and ECD2 domains of HER2
- The unique biparatopic binding configuration of ZW25 leads to multiple MOAs, including increased receptor binding, clustering and internalization relative to trastuzumab, potent activation of ADCC, and inhibition of ligand-dependent and independent growth
- Phase 1 dose-escalation study of single-agent ZW25 identified 10 mg/kg weekly or 20 mg/kg every other week as recommended doses (RDs)
- Safety and anti-tumor activity at RDs in HER2-expressing cancers excluding breast cancer are presented here



Patient Characteristics

Median of 3 prior systemic regimens, including HER2-targeted therapies

	BTC (N=11)	CRC (N=14)	GEA (N=28)	Other (N=16)	Total (N=69)
Baseline ECOG					
0 (n, [%])	2 (18)	5 (36)	2 (7)	2 (13)	11 (16)
1 (n, [%])	9 (82)	9 (64)	26 (93)	14 (88)	58 (84)
Median prior systemic regimens (range)	4.5 (1–8)	5.5 (3–10)	3.0 (1–7)	3.0 (1–7)	3.0 (1–10)
HER2 status per central assessment (IHC 3+ or IHC 2+/FISH+) (n, [%])	11 (100)	14 (100)	24 (86)	16 (100)	65 (94)
Prior HER2 therapy (n, [%])	2 (18)	4 (29)	26 (93)	9 (56)	41 (59)
Prior HER2 agents received (n, [%])					
Trastuzumab	2 (18)	4 (29)	26 (93)	9 (56)	41 (59)
Pertuzumab	0	2 (14)	0	5 (31)	7 (10)
T-DM1	0	1 (7)	1 (4)	3 (19)	5 (7)
Lapatinib	0	1 (7)	0	1 (6)	2 (3)
Neratinib	0	0	1 (4)	0	1 (1)

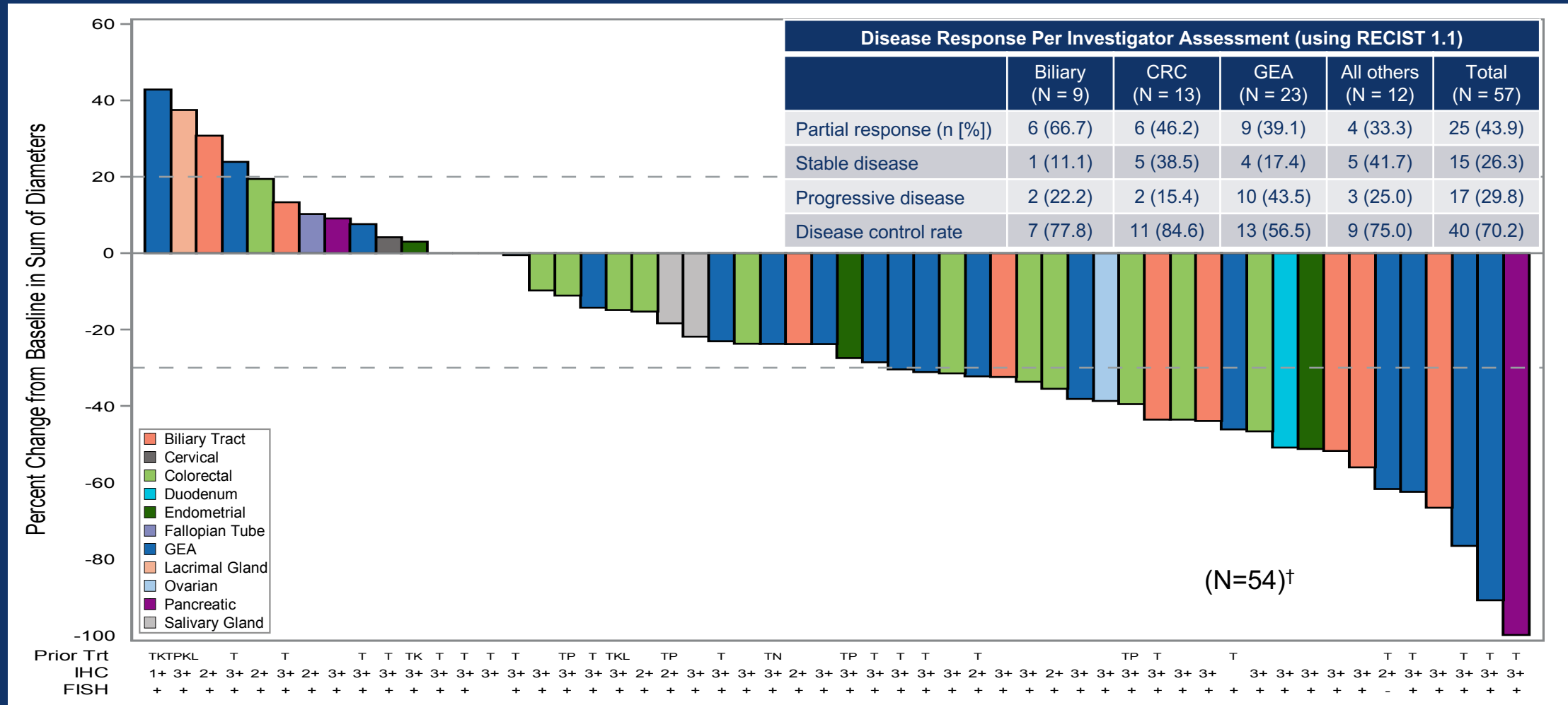
Safety

ZW25 well tolerated as outpatient therapy, all treatment-related AEs Grade 1 or 2

ZW25-related AEs (occurring in ≥ 20% of patients)	BTC (N = 11) n (%)		CRC (N=14) n (%)		GEA (N = 28) n (%)		Other (N = 16) n (%)		Total (N = 69) n (%)	
	Any	≥3	Any	≥3	Any	≥3	Any	≥3	Any	≥3
Diarrhea	5 (45)	0	5 (36)	0	11 (39)	0	9 (56)	0	30 (43)	0
Infusion related reaction	2 (18)	0	4 (29)	0	9 (32)	0	3 (19)	0	18 (26)	0
Nausea	0	0	3 (21)	0	3 (11)	0	3 (19)	0	9 (13)	0

Anti-Tumor Activity of ZW25

Figure: Percentage Change from Baseline in Sum of Diameters of Target Lesions



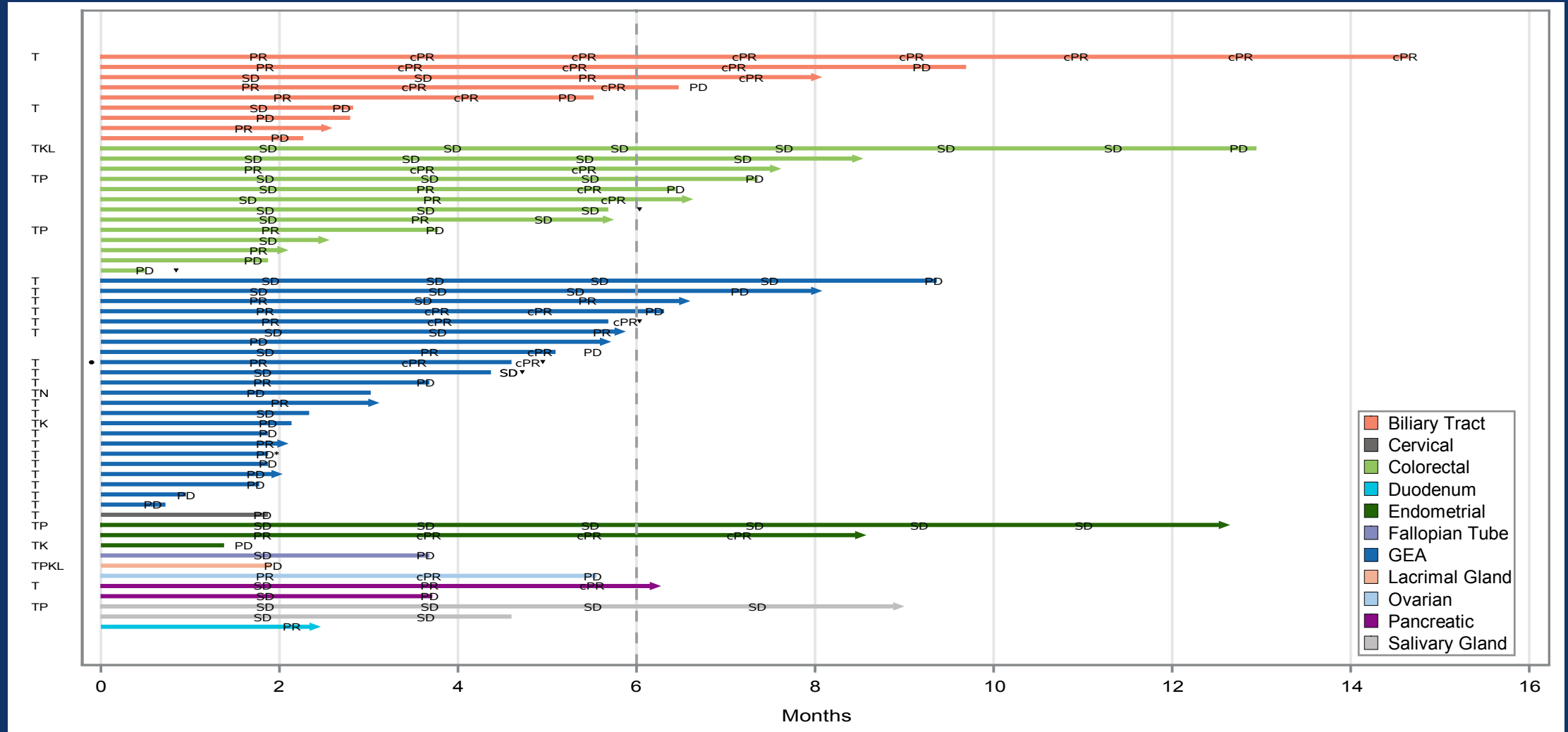
T = Trastuzumab, K = T-DM1, P = Pertuzumab, L = Lapatinib, N = Neratinib

Disease control rate defined as percentage of patients with complete response (CR), partial response (PR), or stable disease (SD) per RECIST 1.1

[†] 3 of the 57 response-evaluable patients had no post-baseline disease assessment of their target lesions and are not included in the waterfall. Response-evaluable includes all patients with measurable disease who had at least one post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment prior to reassessment due to death from any cause or clinical progression (response imputed as PD).

Time on Treatment for Response-evaluable Patients

- Overall median progression-free survival: 5.5 months (95% CI 3.6, 6.4)



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Response-evaluable includes all patients with measurable disease who had at least one post-baseline disease assessment (per RECIST 1.1) or discontinued study treatment prior to reassessment due to death from any cause or clinical progression (response imputed as PD).

▼ Denotes Clinical Progression; ● This patient was FISH- and IHC 2+. All others were FISH+ or IHC3+; *Patient died and did not have any post-baseline tumor assessments.

Conclusions

- ZW25 is well tolerated with promising single-agent anti-tumor activity in patients with advanced HER2-expressing cancers that have progressed after standard of care therapies (median of 3 prior lines of therapy), including HER2-targeted agents
- ZW25 has the potential to provide a cytotoxin-free approach to treatment for patients with high unmet medical need

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