

# Efficacy and Safety of KN026 in combination with KN046 in Patients with Locally Advanced Unresectable or Metastatic HER2-positive Other Solid Tumors (Abstract 3621)

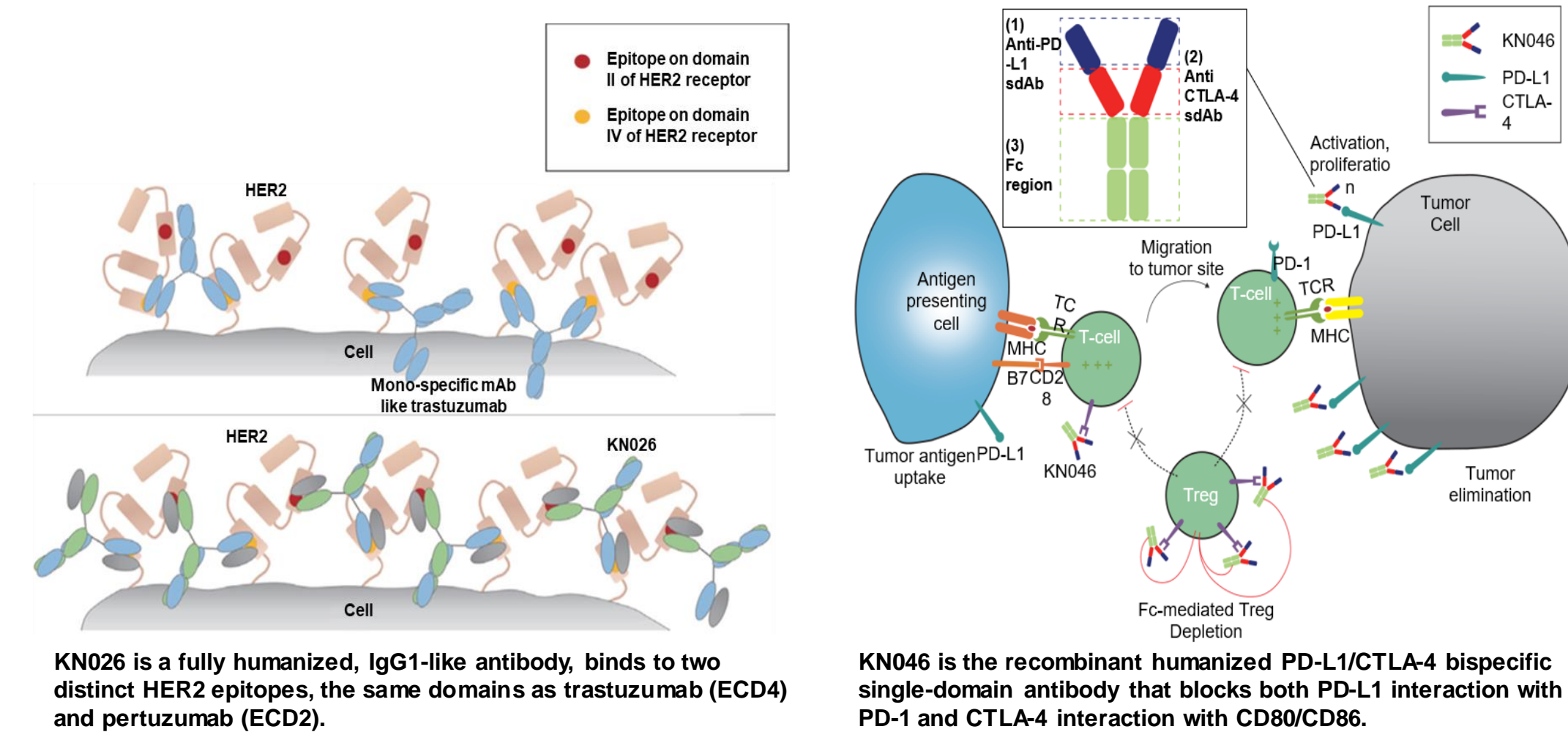
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## BACKGROUND

- KN026 is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes. KN046 is a novel bispecific antibody that blocks both PD-L1 interaction with PD-1 and CTLA-4 interaction with CD80/CD86.
- Both preclinical and clinical studies have showed synergistic effect with the combination of an anti-HER2 antibody and an immune checkpoint blockade.
- Besides breast cancer (BC) and gastric cancer, HER2 is also widely expressed in other solid tumors, such as colorectal cancer (CRC), NSCLC, gallbladder cancer (GBC), renal pelvis cancer (RPC), pancreatic ductal adenocarcinoma (PDAC), etc. The reports of immunotherapy combined with HER2-targeted therapy are limited. Here we reported the efficacy and safety of KN026 combined with KN046 in patients with HER2-positive other solid tumors (non-GC/GEJ and non-BC).



## Demographics & Baseline Characteristics

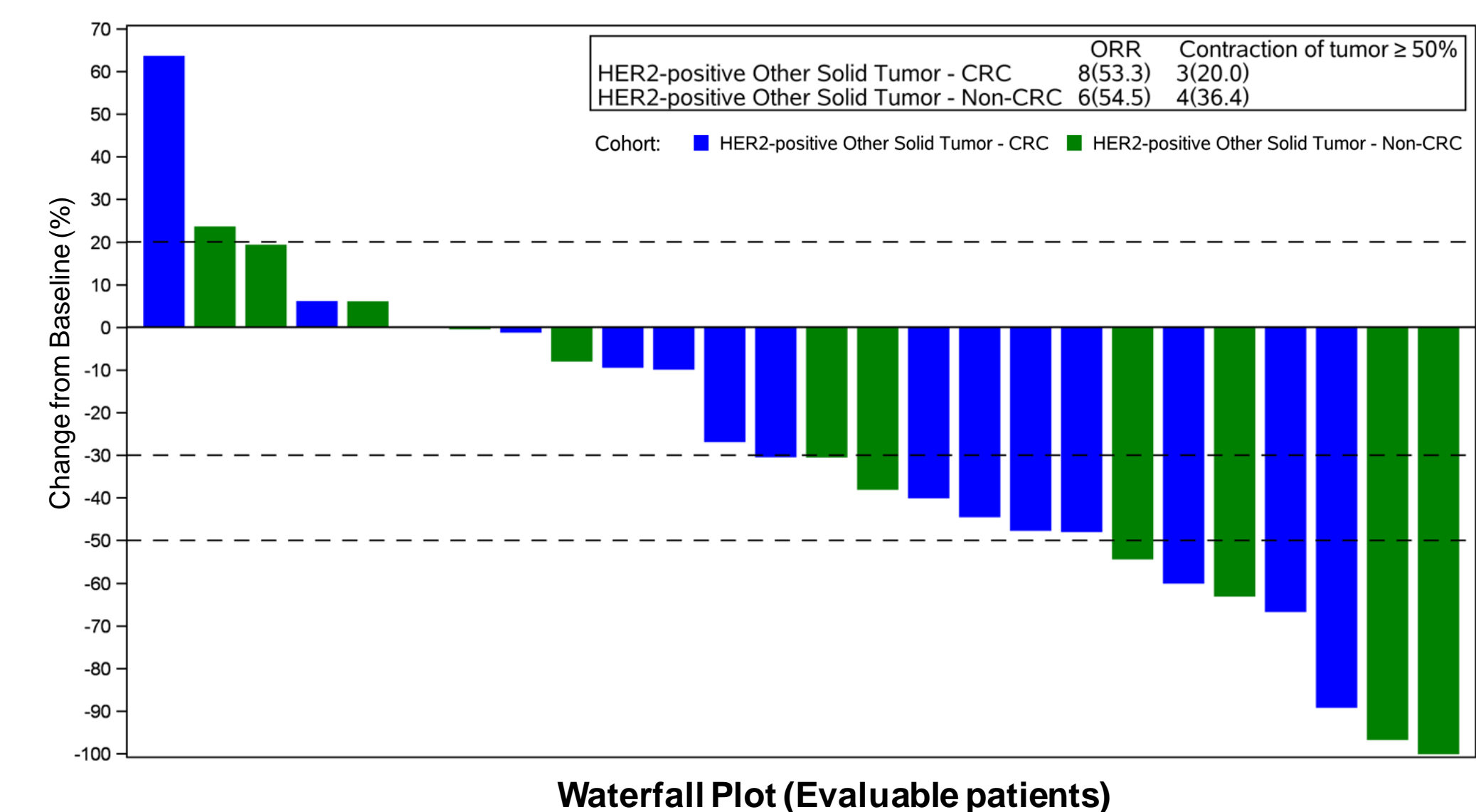
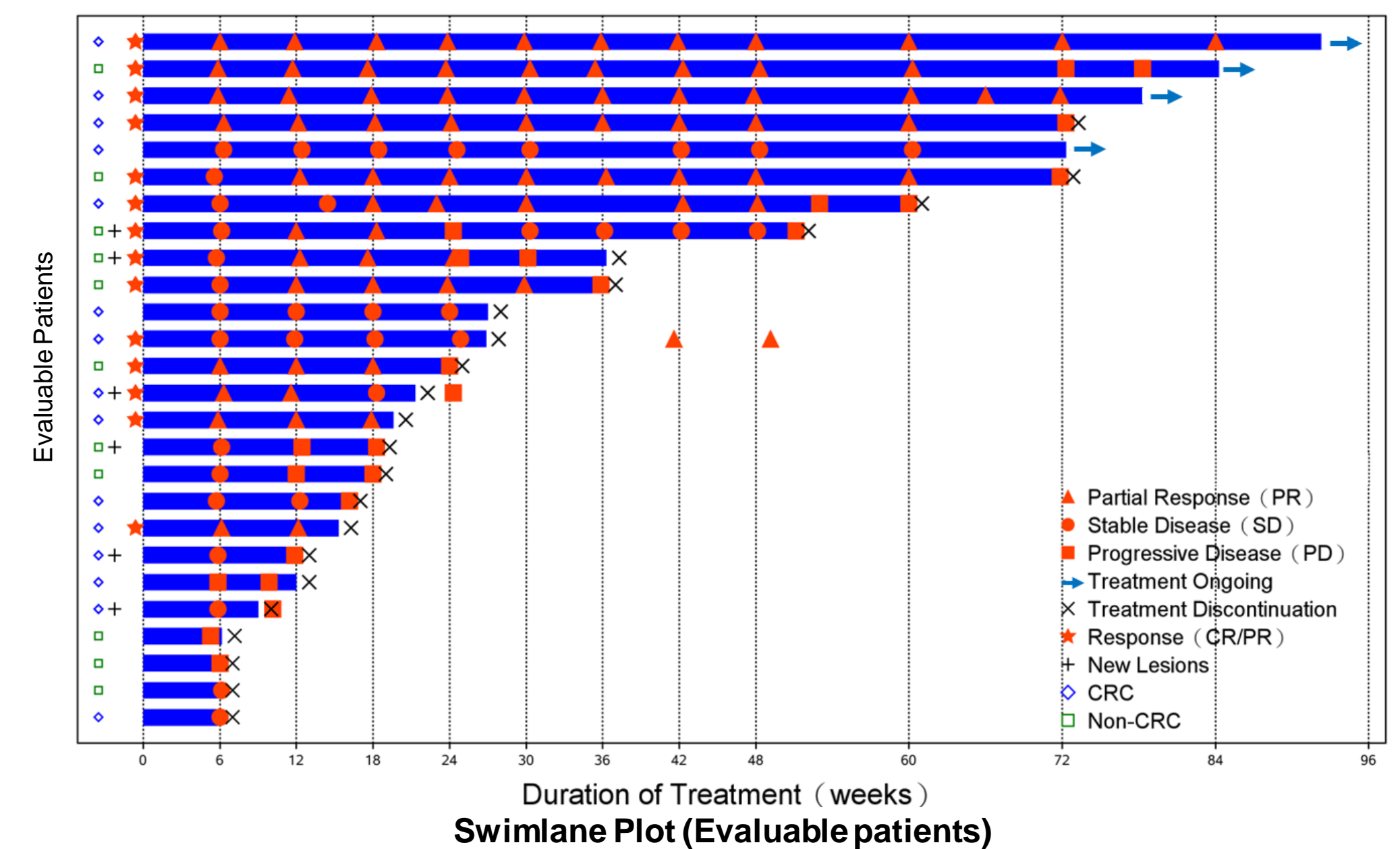
Characteristics	N=26	
Sex	Male (n, %)	12 (46.2)
	Female (n, %)	14 (53.8)
Age (years)	Median (min, max)	56.0 (37, 67)
ECOG	0 (n, %)	9 (34.6)
	1 (n, %)	16 (61.5)
Primary tumor site	CRC (n, %)	15 (57.7)
	NSCLC (n, %)	5 (19.2)
	BTC (n, %)	4 (15.4)
	RPC (n, %)	1 (3.8)
	PADC (n, %)	1 (3.8)
Prior treatment line	1 (n, %)	2 (7.7)
	2 (n, %)	16 (61.5)
	3 (n, %)	8 (30.8)
Prior anti-cancer therapy	anti-HER2 (n, %)	5 (19.2)
	anti-PD-(L)1 (n, %)	6 (23.1)
Distant metastasis	liver (n, %)	15 (57.7)
	lung (n, %)	16 (61.5)

## Safety (TRAE Occurring in ≥ 15% of patients)

Preferred Term	Any grade N = 26 (n, %)	≥Gr3 N=26 (n, %)
Subjects with TRAE	25 (96.2)	9 (34.6)
Infusion related reaction	10 (38.5)	1 (3.8)
AST increased	9 (34.6)	2 (7.7)
Conjugated bilirubin increased	7 (26.9)	2 (7.7)
ALT increased	7 (26.9)	1 (3.8)
Anemia	7 (26.9)	1 (3.8)
Blood bilirubin increased	7 (26.9)	0
Rash	7 (26.9)	0
Diarrhea	5 (19.2)	0
Leukopenia	5 (19.2)	0
Serum creatinine increased	5 (19.2)	0
Weightloss	4 (15.4)	1 (3.8)
Hyperthyroidism	4 (15.4)	0

## Efficacy Outcomes (Evaluable patients)

	HER2 positive other solid tumor N=26	HER2 positive CRC N=15
Best Overall Response (BOR)		
Confirmed Complete Response (cCR)	0	0
Confirmed Partial Response (cPR)	14 (53.8%)	8 (53.3%)
Stable Disease (SD)	9 (34.6%)	6 (40.0%)
Progression Disease (PD)	3 (11.5%)	1 (6.7%)
Confirmed ORR (95% CI)	53.8% (33.4%, 73.4%)	53.3% (26.6%, 78.7%)
Median DOR (month, 95% CI)	6.8 (2.9, 15.3)	11.7 (3.2, NE)
Median PFS (month, 95% CI)	5.6 (2.9, 16.5)	12.2 (2.7, NE)
12-OS rate (95% CI)	80.4% (59.1%, 91.4%)	80.0% (50.0%, 93.1%)



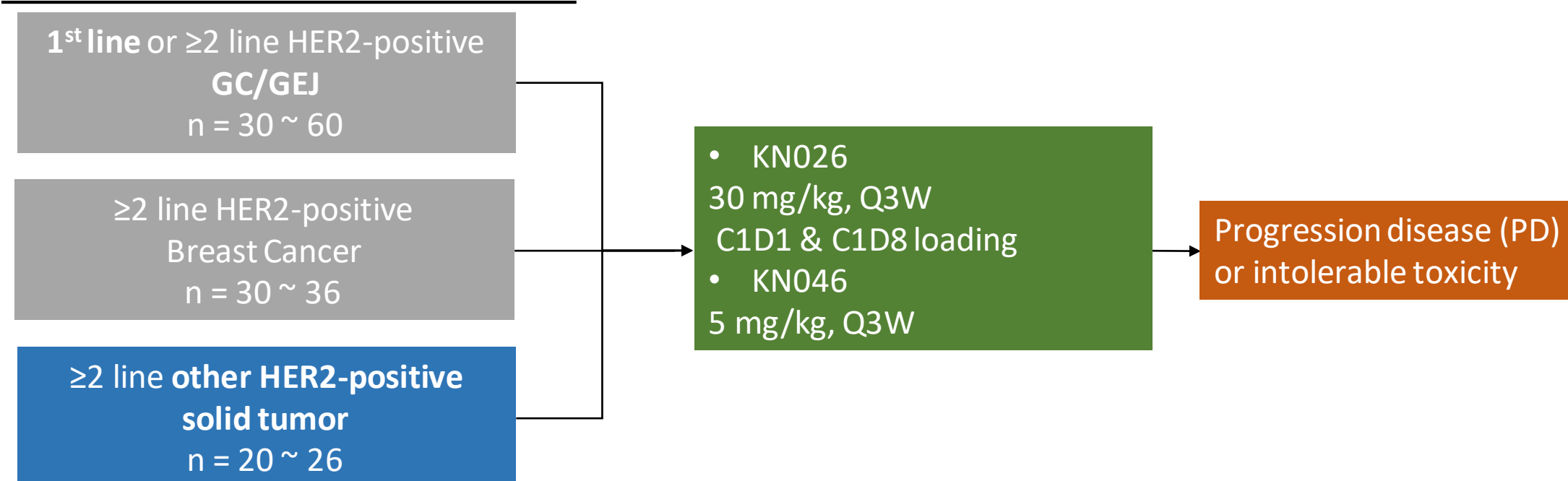
## RESULTS

- As of 10 November 2022, 26 pts with HER2 positive solid tumor other than BC and GC/GEJ were enrolled. The median age was 56 (range 37 ~ 67) years. 15 (57.7%) pts had liver metastasis. 92.3% of pts including all CRC pts had received ≥ 2 lines prior treatment.
- The confirmed ORR was 53.8% (95% CI: 33.4, 73.4) with mDOR 6.8 months (95% CI: 2.9, 15.3). The mPFS was 5.6 months (95% CI: 2.9, 16.5) and 12-month OS rate was 80.4% (95% CI: 59.1, 91.4) with median follow-up time 16.6 months.
- For 15 CRC pts, the confirmed ORR was 53.3% (95% CI: 26.6, 78.7) with mDOR 11.7 months (95% CI: 3.2, NE). The mPFS was 12.2 months (95% CI: 2.7, NE). 12-month OS rate was 80.0% (95% CI: 50.0, 93.1) with median follow-up time 16.0 months.
- Common TRAEs were infusion related reaction (38.5%), AST increased (34.6%), ALT increased (26.9%), conjugated bilirubin increased (26.9%), rash (26.9%), anemia (26.9%) and blood bilirubin increased (26.9%). Most of them were Grade 1 or 2. The most common ≥ Gr3 TRAEs were conjugated bilirubin increased (7.7%) and AST increased (7.7%). There was no treatment related death.

## CONCLUSIONS

- KN026 combined with KN046 treatment had demonstrated favorable efficacy and safety profile in HER2 positive other solid tumors (non-GC/GEJ and non-BC). Especially very promising efficacy were observed in ≥ 3 lines HER2 positive CRC.

## STUDY DESIGN



### Primary endpoint

- ORR and DOR (RECIST v1.1)

### Second endpoint:

- Other efficacy endpoint (PFS, CBR, OS etc.)
- Safety
- Relationship between biomarker and clinical efficacy
- Relationship between KN026/KN046 drug exposure levels and safety/efficacy
- ADA and Nab of KN026/KN046

