

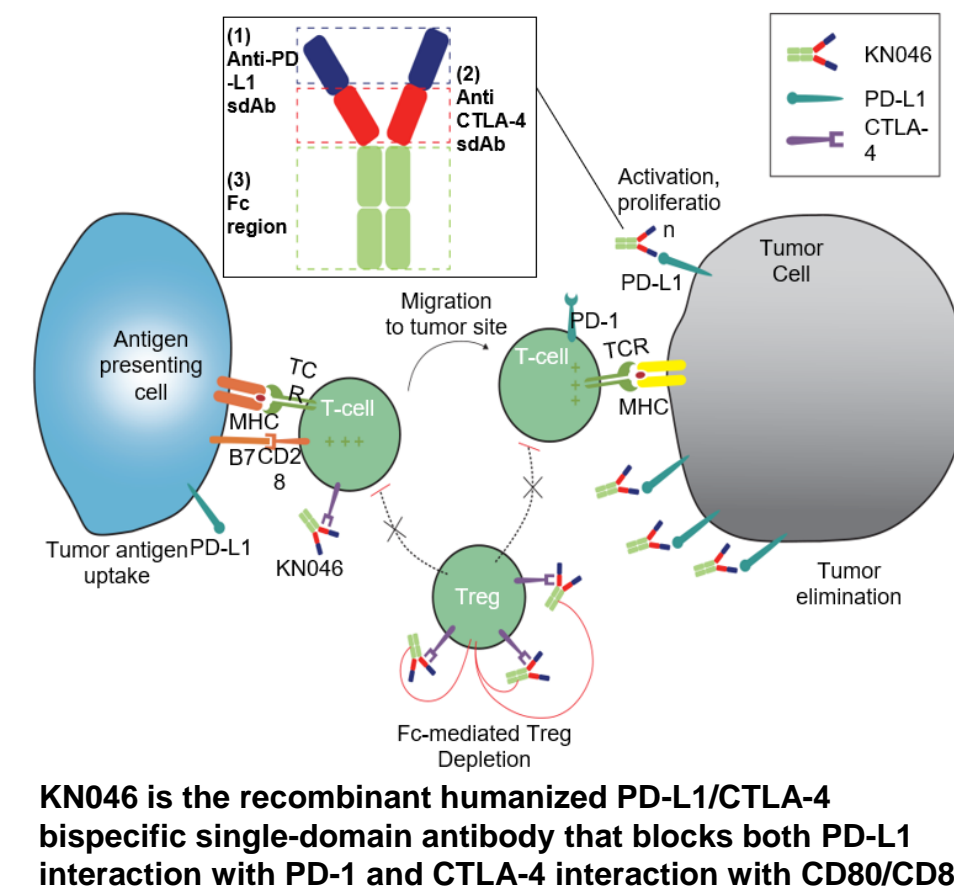
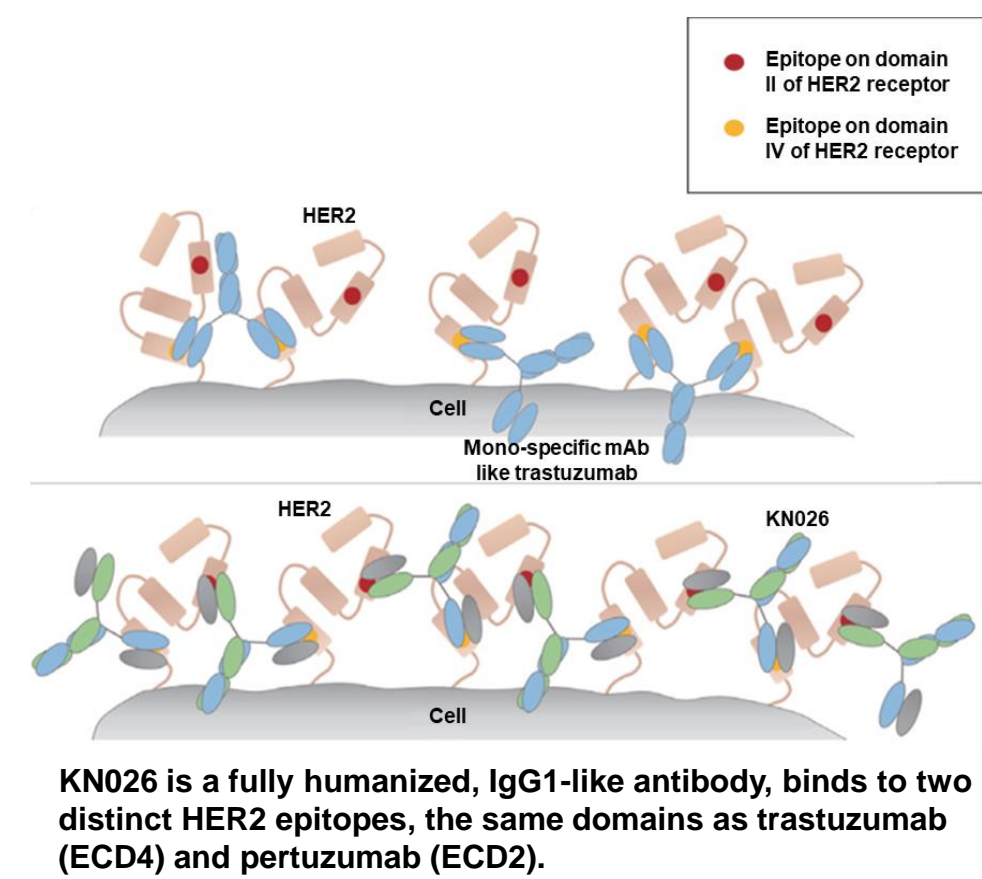
# The preliminary efficacy and safety of KN026 combined with KN046 treatment in HER2-positive locally advanced unresectable or metastatic gastric/gastroesophageal junction cancer without prior systemic treatment in a phase II study

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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.
- This phase II study was to assess the efficacy and safety of KN026 (30mg/kg, Q3W, C1D1 & C1D8 loading) in combination with KN046 (5mg/kg, Q3W) treatment in patients with HER2-positive (IHC 3+ or HER2 gene amplification) solid tumors. Here we reported the efficacy and safety in patients with HER2-positive gastric/gastroesophageal junction cancer (GC/GEJ) without prior systemic treatment (NCT04521179).



Demographics & Baseline Characteristics		
N=31		
Sex	Male (n, %)	21 (67.7)
	Female (n, %)	10 (32.3)
Age (years)	≥ 65 (n, %)	14 (45.2)
	< 65 (n, %)	17 (54.8)
ECOG	0 (n, %)	6 (19.4)
	1 (n, %)	25 (80.6)
HER2	IHC 3+ (n, %)	26 (83.9)
	IHC 2+ & FISH + (n, %)	5 (16.1)
Distant Metastasis	liver (n, %)	19 (61.3)
	lung (n, %)	4 (12.9)

Safety (TRAE ≥ 10%)		
Preferred Term	Any grade (N = 31)	≥Gr3 (N=31)
Subjects with TRAE	25 (80.6%)	5 (16.1%)
Diarrhea	10 (32.3%)	2 (6.5%)
Pyrexia	10 (32.3%)	1 (3.2%)
Leukopenia	7 (22.6%)	0
Neutropenia	5 (16.1%)	0
Infusion related reaction	5 (16.1%)	0
Hypothyroidism	5 (16.1%)	0
ALT increased	4 (12.9%)	0
Direct bilirubin increased	4 (12.9%)	0
Rash	4 (12.9%)	0

## RESULTS

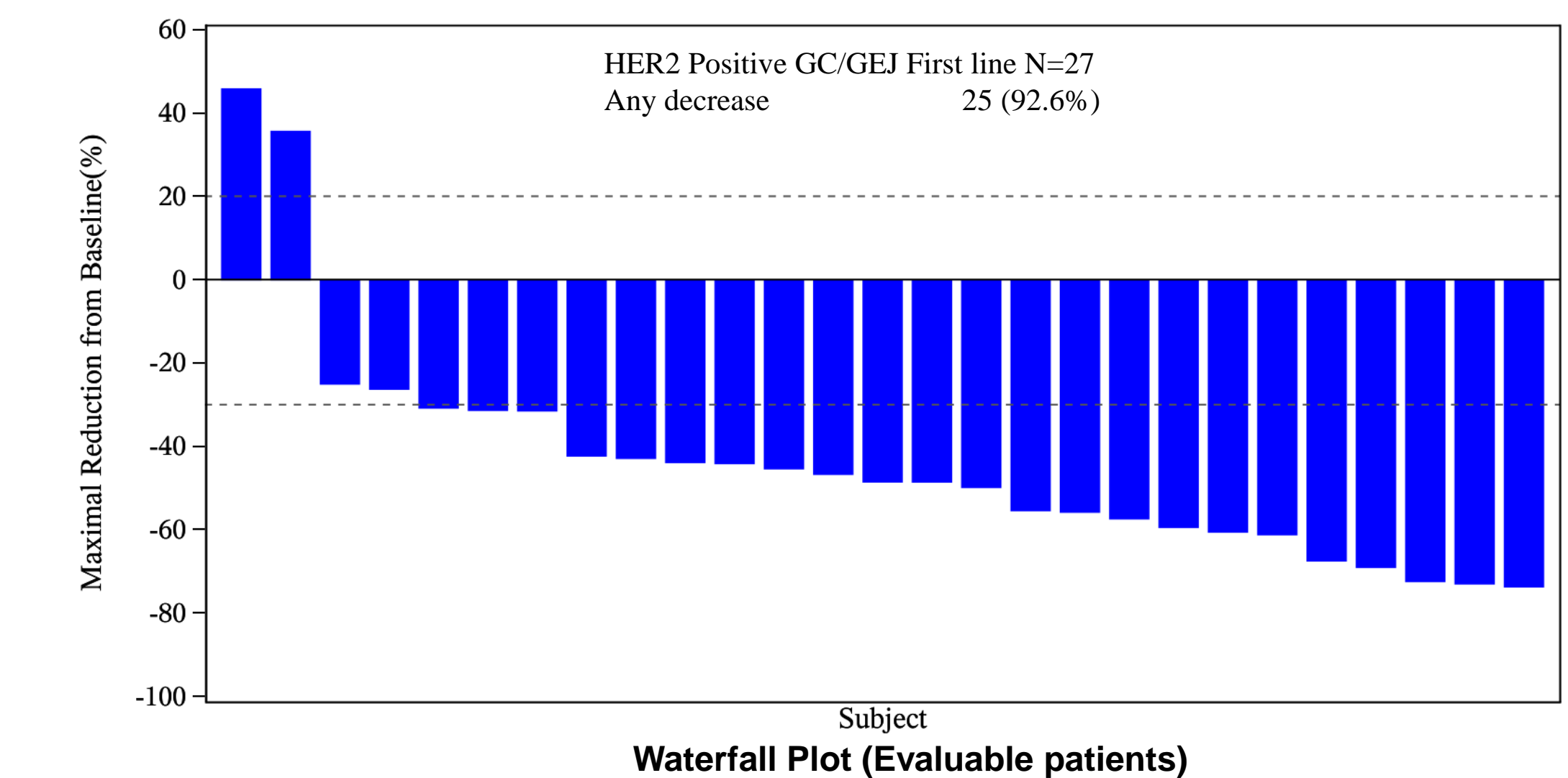
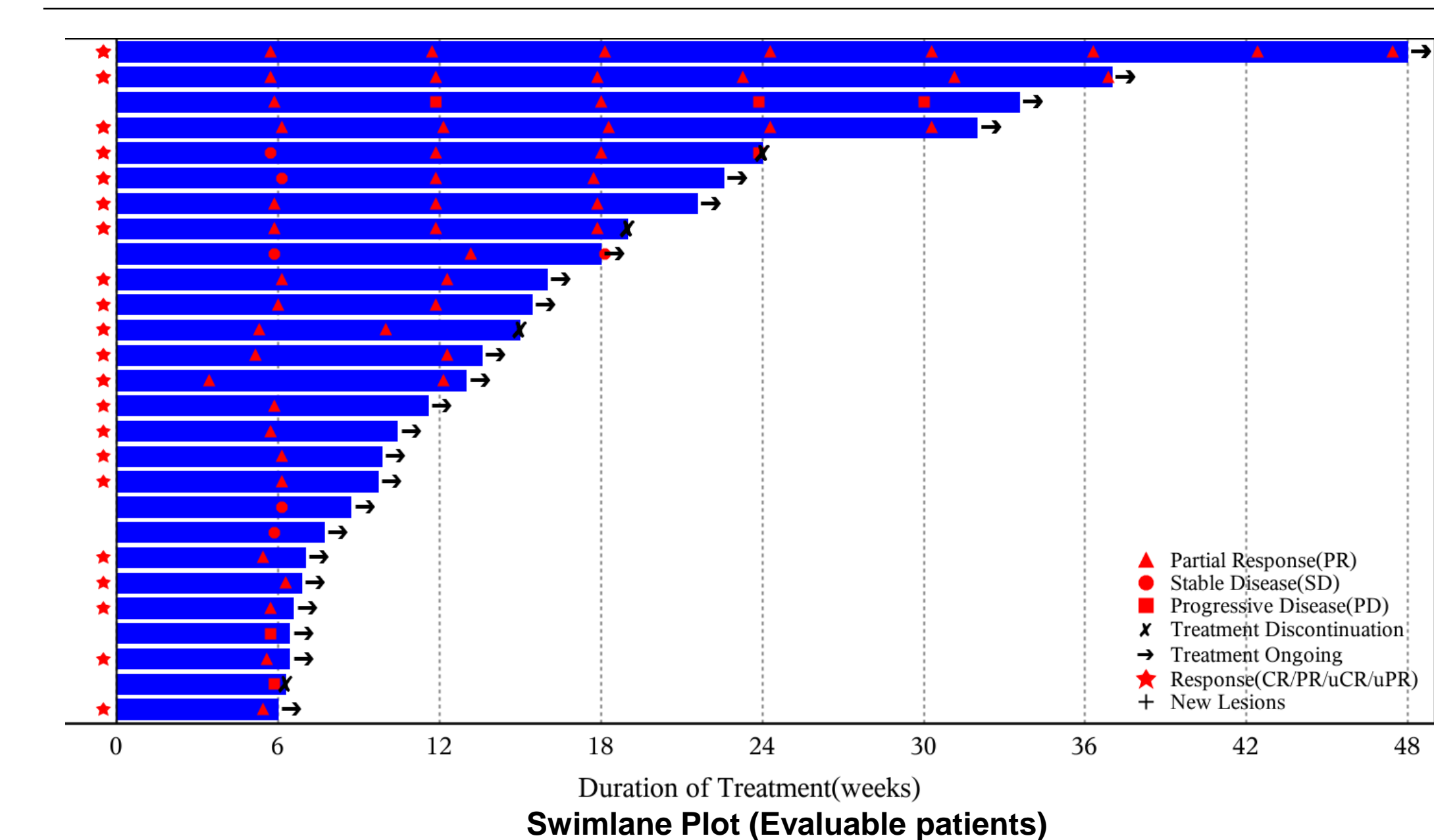
- As of 30 Jan 2022, a total of 31 HER2 positive locally advanced unresectable or metastatic GC/GEJ patients without prior systemic treatment were enrolled, and 26 patients still received study treatment. The median age was 64 years old with 14 patients (45.2%) aged ≥ 65 years. 26 patients (83.9%) were HER2 IHC 3+ and 5 patients (16.1%) were HER2 IHC 2+ with HER2 gene amplification, and 25 patients (80.6%) were ECOG 1. Most patients (61.3%) had liver metastasis.
- As of 30 Jan 2022, 27 patients were evaluable for efficacy with 12 confirmed PRs, 9 unconfirmed PRs, 4 SDs and 2 PDs. The ORR was 77.8% (95% CI: 57.7, 91.4), and the DCR was 92.6% (95% CI: 75.7, 99.1).
- The most common related TEAEs (TRAEs) were diarrhea (32.3%), pyrexia (32.3%), leukopenia (22.6%), neutropenia (16.1%), infusion related reaction (16.1%) and hypothyroidism (16.1%). The majority of the AEs were grade 1 or 2 in severity. Only 5 patients (16.1%) experienced ≥ Gr3 TRAEs and almost all of them had been relieved or recovered. The most common ≥ Gr3 TRAE was diarrhea (6.5%). 3 patients discontinued treatment due to AE of KN046 treatment and no patients discontinued treatment due to AE caused by KN026. There was no treatment related death.

## CONCLUSIONS

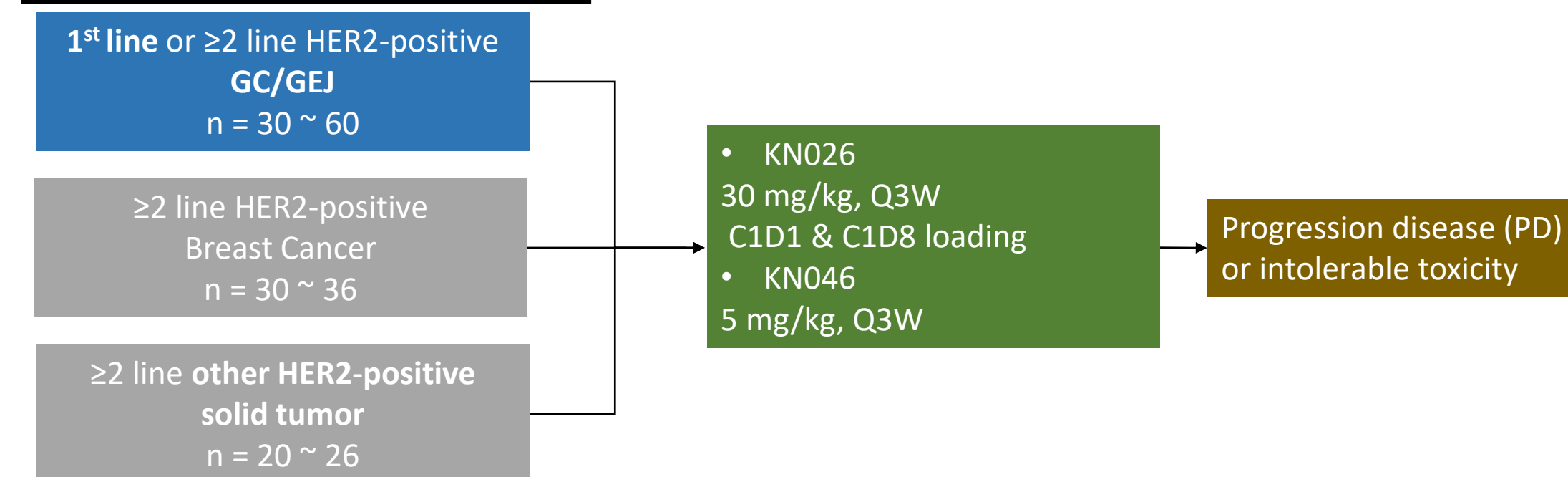
- KN026 combined with KN046 treatment had demonstrated outstanding efficacy and manageable safety in HER2 positive GC/GEJ patients without prior systemic treatment. It is interesting to further test the efficacy and safety in randomized studies or larger sample studies.

## Efficacy Outcomes (Evaluable patients)

N=27	
Best Overall Response (BOR)	
Complete Response (CR)	0
Partial Response (PR)	12 (44.4%)
Unconfirmed Partial Response (uPR)	9 (33.3%)
Stable Disease (SD)	4 (14.8%)
Progression Disease (PD)	2 (7.4%)
Objective Response Rate (ORR)	21 (77.8%)
95% CI	57.7%, 91.4%
Disease Control Rate (DCR)	25 (92.6%)
95% CI	75.7%, 99.1%



## 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