Two-year follow-up data on the efficacy and safety of KN026, a HER2-targeted bispecific antibody combined with docetaxel as first-line treatment for HER2-positive recurrent/metastatic breast cancer

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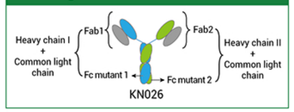
Background

- KN026 is a novel bispecific HER2-targeted antibody. (Figure 1)
  - Fully humanized, IgG1-like antibody binds to two distinct HER2 epitopes, the same domains as trastuzumab and pertuzumab.
- Preliminary safety and efficacy results (data as of Aug 18, 2022) were presented at SABCs 2022 (PD18- 08)[1], showed promising efficacy and tolerability.
- Herein, we update the 2-year follow-up results.

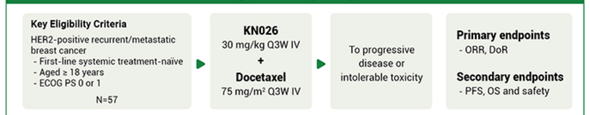
Figure 1 Structure of KN026



Methods

- Study design is shown in Figure 2.
- Eligible subjects with recurrent/metastatic breast cancer, HER-2 positive and treatment-naive were enrolled.
- Subjects received KN026 30 mg/kg combined with docetaxel 75 mg/m² Q3W until disease progression, unacceptable toxicity, or other reasons.
- The primary endpoints were ORR and DoR. The secondary endpoints included safety, PFS and OS.
- The data cut-off date was Aug 4, 2023.

Figure 2 Study Design



Results

- 57 subjects were enrolled, the median age was 52 years (min: 30, max: 67), 100% were female, and 91.2% (52/57) were stage IV. The most common sites of metastasis were lymph nodes, bone, lung, and liver. (Details in Table 1)
- The cut-off date was Aug 4, 2023.

Table 1 Baseline Characteristics

	N=57, n (%)		N=57, n (%)
Age (Year)		**Baseline ECOG score，n (%)**	
Mean	52.0	0	22 (38.6)
Median	52.0	1	35 (61.4)
Min, Max	30, 67	**Clinical staging at screening，n (%)**	
Gender, n (%)		IIIa	1 (1.8)
Male	0	IIIb	2 (3.5)
Female	57 (100)	IIIc	2 (3.5)
Whether they are fertile, n (%)		IV	52 (91.2)
Yes	20 (35.1)	**HER2 immunohistochemical result，n(%)**	
No	37 (64.9)	IHC1+	1 (1.8)
Chinese, n (%)		IHC2+	8 (14.0)
Yes	57 (100)	IHC3+	48 (84.2)
No	0	**Metastatic sites，n (%)**	
Height (cm)		Lymph node	38 (66.7)
Mean	158.17	Bone	24 (42.1)
Median	158.00	Lung	24 (42.1)
Min, Max	145.0, 176.0	Liver	22 (38.6)
Weight (kg)		Pleura	13 (22.8)
Mean	59.37	Brain	6 (10.5)
Median	60.00	Other	14 (24.6)
Min, Max	43.0, 73.0	No metastasis	5 (8.8)

- The confirmed ORR within 55 evaluable subjects was 76.4% (42/55) and DCR was 100% (95% CI 93.51, 100) (Table 2, Figure 3)
- The median DoR follow-up was 26.3 mons (95% CI: 23.92, 28.91) and DoR was 26.8 mons (95% CI 20.73, NE). (Figure 4)

Table 2 Objective response rate-Efficacy Analysis Set

	Efficacy Analysis Set (N=55), n (%)
Best of response, BOR	
CR	3 (5.5)
PR	39 (70.9)
SD	13 (23.6)
PD	0
NE	0
ORR (95%CI)	**42 (76.4)** (62.98, 86.77)
DCR (95%CI)	**55 (100)** (93.51, 100)

Figure 3 Waterfall Plot for Best Percentage Change from Baseline in Sum of Target Lesions Diameters - Efficacy Analysis Set

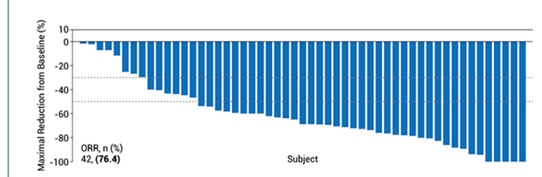
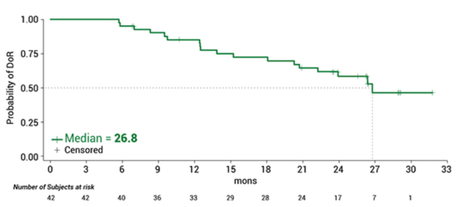
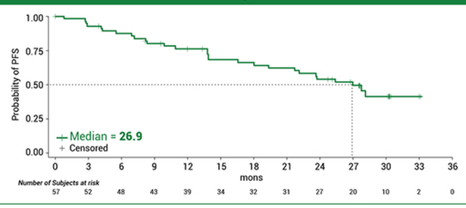


Figure 4 Kaplan - Meier Curve for Duration of Response - Efficacy Analysis Set



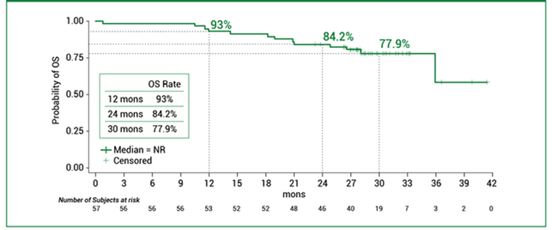
- The median study follow-up was 29.7mons (95%CI: 28.32, 30.59). The mPFS was 26.9 mons (95% CI:17.97, NE) (Figure 5) and the mOS was not reached.

Figure 5 Kaplan - Meier Curve for Progression Free Survival-Intent to Treat Analysis Set



- The OS rates at 12 mons, 24 mons and 30 mons were 93.0% (95% CI: 82.37, 97.31), 84.2% (95% CI: 71.85, 91.45) and 77.9% (95% CI: 64.17, 86.89). (Figure 6)

Figure 6 Kaplan - Meier Curve for Overall Survival-Intent to Treat Analysis Set



- The subjects with no-visceral metastases, no-brain metastases or IHC3+ had a longer PFS. (Figure7-9)

Figure 7 Kaplan - Meier Curve for Subgroup Analysis of Progression Free Survival by Visceral Metastasis

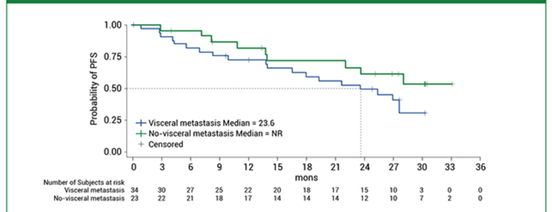


Figure 8 Kaplan - Meier Curve for Subgroup Analysis of Progression Free Survival by Brain Metastasis

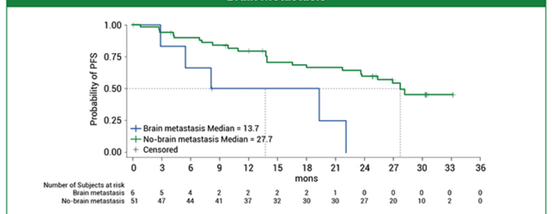
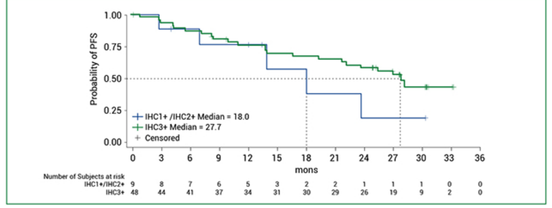


Figure 9 Kaplan - Meier Curve for Subgroup Analysis of Progression Free Survival by HER2- positive Expression



- The incidence of TEAE ≥Grade 3 was 61.4% (35/57). There were no deaths due to KN026 related AEs in this study. (Table 3)
- The incidence of KN026-related Grade≥3 TRAE was 40.4% (23/57), including neutrophil count decreased 24.6% (14/57), white blood cell count decreased 12.3% (7/57) and others less than 10%. (Table 4).
- The incidence of serious adverse events related to KN026 was 10.5% (6/57), including febrile neutropenia 1.8% (1/57), diarrhea 1.8% (1/57), and others. (Table 5)

Table 3 Safety summary

	(N=57) n (%)
Any TEAE	**57 (100)**
TEAE related with any study drug	56 (98.2)
TEAE related with KN026	52 (91.2)
TEAE related with Docetaxel	54 (94.7)
TEAE Grade≥ 3	**35 (61.4)**
TEAE Grade≥ 3 associated with any study drug	31 (54.4)
TEAE Grade≥ 3 associated with KN026	23 (40.4)
TEAE Grade≥ 3 associated with Docetaxel	29 (50.9)
Serious Adverse Event (SAE)	**12 (21.1)**
SAE related with any study drug	9 (15.8)
SAE related with KN026	6 (10.5)
SAE related with Docetaxel	7 (12.3)
TRAE leading to death	**0**

Table 4 Summary of CTCAE Grade ≥ 3 TEAE Related to KN026

SOC PT	(N=57) n (%)
CTCAE Grade ≥ 3 TRAE Related to KN026	23 (40.4)
Investigations	16 (28.1)
Neutrophil count decreased	14 (24.6)
White blood cell count decreased	7 (12.3)
Lymphocyte count decreased	1 (1.8)
Lymphocyte percentage decreased	1 (1.8)
Weight decreased	1 (1.8)
Metabolism and nutrition disorders	4 (7.0)
Hypokalaemia	4 (7.0)
Hypocalcaemia	1 (1.8)
Gastrointestinal disorders	3 (5.3)
Diarrhoea	2 (3.5)
Intestinal obstruction	1 (1.8)
Immune system disorders	2 (3.5)
Hypersensitivity	1 (1.8)
Type I hypersensitivity	1 (1.8)
Blood and lymphatic system disorders	1 (1.8)
Febrile neutropenia	1 (1.8)
Ear and labyrinth disorders	1 (1.8)
Vertigo	1 (1.8)

Note: Percentages are based on Safety Analysis Set. MedDRA Version: 25.1

Table 5 Summary of SAE Related to KN026 (Safety Analysis Set)

SOC PT	(N=57) n (%)
SAE during treatment Related to KN026	6 (10.5)
Gastrointestinal disorders	2 (3.5)
Diarrhoea	1 (1.8)
Intestinal obstruction	1 (1.8)
Blood and lymphatic system disorders	1 (1.8)
Febrile neutropenia	1 (1.8)
Cardiac disorders	1 (1.8)
Arrhythmia	1 (1.8)
Ear and labyrinth disorders	1 (1.8)
Vertigo	1 (1.8)
Metabolism and nutrition disorders	1 (1.8)
Hypokalaemia	1 (1.8)

Note: Percentages are based on Safety Analysis Set. MedDRA Version: 25.1

Conclusions

- KN026 in combination with docetaxel is well tolerated and has shown promising clinical benefit as 1L treatment for HER2-positive BC. After 2 years follow-up, mPFS was 26.9 mons and the 24 mons OS rate was 84.2%, which is very promising. Robustness of efficacy and safety results will be further confirmed in an ongoing randomized phase 3 clinical trial with PTH as control.

REFERENCE

1. QY Zhang et al. Efficacy and safety results of KN026, a HER2-targeted bispecific antibody combined with docetaxel in first-line treatment of HER2-positive recurrent/metastatic breast cancer. 2022 SABCs, Poster ID: PD18-08