Two and a half years follow-up data of HER2-targeted bispecific antibody KN026 combined with docetaxel as first-line treatment for HER2-positive recurrent/metastatic breast cancer

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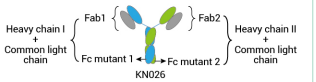
Background

- KN026 is a novel bispecific HER2-targeted antibody.
  - Fully humanized, IgG1-like antibody binds to two distinct HER2 epitopes, the same domains as trastuzumab and pertuzumab.
- Preliminary efficacy and safety results (cut off date: Aug 18, 2022) were presented at SABCs 2022(PD18-08)[1], showed promising efficacy and tolerability.
- 2-year follow-up of efficacy and safety data (cut off date: Aug 4, 2023), published in ESMO 2023(FPN:418P)[2].
- Herein, we update the 2.5-year follow-up results.

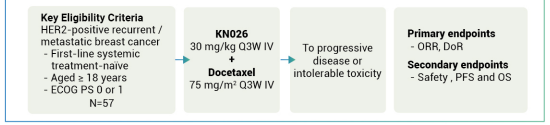
Figure 1 Structure of KN026



Methods

- Study design is shown in Figure 2.
- Eligible subjects with recurrent/metastatic breast cancer, HER2 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.

Figure 2 Study Design



Results

- As of data cut off date (Sep 15, 2023), 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)

Table 1 Baseline Characteristics - Intent to Treat Analysis Set

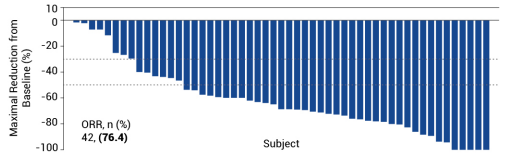
	N=57, n (%)		N=57, n (%)
Age (Year)		Baseline ECOG score, n (%)	
Mean	52.0	0	22 (38.6)
Median	52.0	1	35 (61.4)
Min, Max	30, 67	Clinical staging at screening, n (%)	
Gender, n (%)		IIIa	1 (1.8)
Male	0	IIIb	2 (3.5)
Female	57 (100)	IIIc	2 (3.5)
Whether they are fertile, n (%)		IV	52 (91.2)
Yes	20 (35.1)	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) (95% CI: 62.98, 86.77) (Table2, Figure 3). The DoR was not reached (95% CI: 20.73, NE) with a median follow-up of 28.1 mos (95% CI: 26.28, 29.08). (Figure 4).
- The median follow-up was 30.6 mos (95% CI: 29.11, 31.77). The mPFS was 27.7 mos (95% CI: 17.97, NE) (Figure 5) and the mOS was not reached.

Table 2 Summary of Response-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)

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



The maximal reduction from baseline of 01-040 and 14-002 was 0.

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

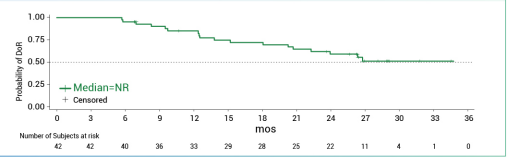
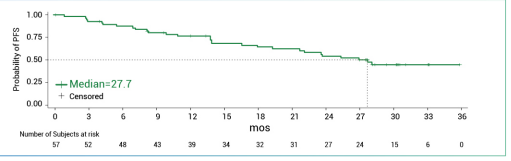
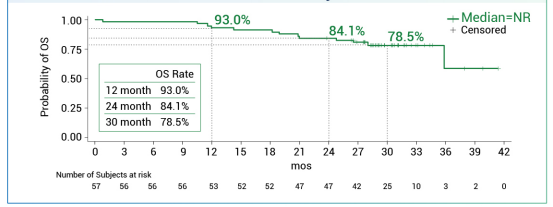


Figure 5 Kaplan - Meier Curve for Progression Free Survival-Intent to Treat Analysis Set



- The OS rates at 12m, 24m and 30m were 93.0% (95% CI: 82.37, 97.31), 84.1% (95% CI: 71.73, 91.41) and 78.5% (95% CI: 65.16, 87.17), respectively. (Figure 6)

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



- The mPFS of subjects with or without visceral metastasis were 23.6 mos and not reached. The mPFS of subjects with or without brain metastasis were 13.7 mos and 28.1 mos, respectively. The mPFS of 48 subjects with high HER2 expression (3+) was 28.1 mos. (Figure7-9)

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

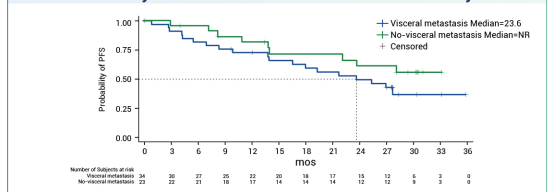


Figure 8 Kaplan - Meier Curve for Subgroup Analysis of Progression Free Survival by Brain Metastasis - Intent to Treat Analysis Set

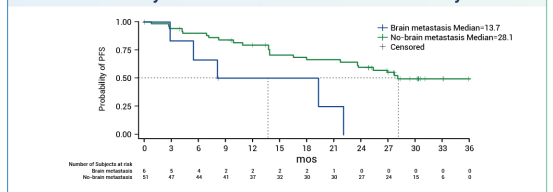
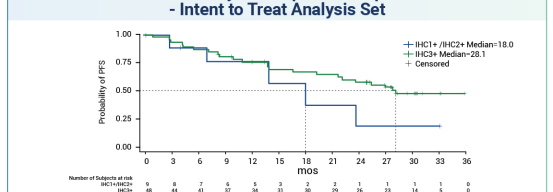


Figure 9 Kaplan - Meier Curve for Subgroup Analysis of Progression Free Survival by HER2- positive Expression - Intent to Treat Analysis Set



- The incidence of TEAE ≥Grade 3 was 63.2% (36/57). There were no deaths due to KN026 related AEs in this study. (Table 3)
- The incidence of KN026-related Grade ≥3 TRAE was 43.9% (25/57) (Table 3), including neutrophil count decreased 24.6% (14/57), white blood cell count decreased 12.3% (7/57), hypokalaemia 7.0% (4/57), diarrhoea 3.5% (2/57) and others less than 2%. (Table 4).
- The incidence of serious adverse events related to KN026 was 12.3% (7/57). (Table 5)

Table 3 Safety Summary (Safety Analysis Set)

	(N=57) n (%)
TEAE	57 (100)
Related to Study Drug	56 (98.2)
Related to KN026	53 (93.0)
Related to Docetaxel	54 (94.7)
CTCAE Grade ≥ 3 TEAE	36 (63.2)
Related to Study Drug	33 (57.9)
Related to KN026	25 (43.9)
Related to Docetaxel	29 (50.9)
SAE during treatment	12 (21.1)
Related to Study Drug	9 (15.8)
Related to KN026	7 (12.3)
Related to Docetaxel	7 (12.3)
TEAE Leading to Death	1 (1.8)##
Related to Study Drug	0
Related to KN026	0
Related to Docetaxel	0

##. Medical records related to the death of this subject could not be obtained, so the death reason was determined to be unknown and unrelated to KN026 and docetaxel, which was determined by the investigator.

Table 4 Summary of CTCAE Grade ≥ 3 TEAE Related to KN026 (Safety Analysis Set)

SOC PT	(N=57) n (%)
CTCAE Grade ≥ 3 TEAE Related to KN026	25 (43.9)
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)
Blood and lymphatic system disorders	2 (3.5)
Anaemia	1 (1.8)
Febrile neutropenia	1 (1.8)
Immune system disorders	2 (3.5)
Hypersensitivity	1 (1.8)
Type I hypersensitivity	1 (1.8)
Ear and labyrinth disorders	1 (1.8)
Vertigo	1 (1.8)
Infections and infestations	1 (1.8)
Upper respiratory tract infection	1 (1.8)

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

SOC PT	(N=57) n (%)
SAE during treatment Related to KN026	7 (12.3)
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)
Infections and infestations	1 (1.8)
Tonsillitis	1 (1.8)
Upper respiratory tract infection	1 (1.8)
Metabolism and nutrition disorders	1 (1.8)
Hypokalaemia	1 (1.8)

Conclusions

- KN026 in combination with docetaxel is well tolerated and has shown promising clinical benefit as 1L treatment for HER2-positive BC. After 2.5 years follow-up, mPFS was 27.7 mos and the 24-mo OS rate was 84.1%, which is very promising. No new safety signals were observed. 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
2. QY Zhang et al. 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. 2023 ESMO, Poster ID: 418P