Preliminary Safety and Efficacy Results of KN046 in combination with KN026 in Patients with Locally Advanced Unresectable or Metastatic HER2-positive other solid tumors

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Abstract# CT542

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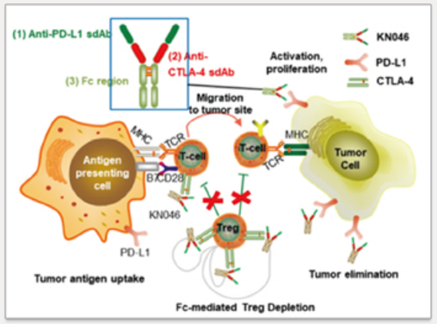
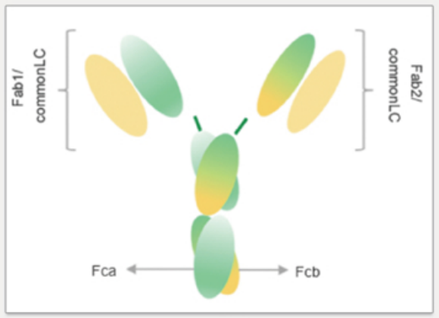
Background

Besides breast cancer and gastric cancer, HER2 gene amplification or overexpression is also expressed in other solid tumors, including but not limited to colorectal cancer (CRC), non-small cell lung cancer (NSCLC), gallbladder cancer, renal pelvis cancer and pancreatic cancer. The reports of immunotherapy combined with HER2-targeted therapy are limited. KN046 is a novel bispecific antibody that blocks both PD-L1 interaction with PD-1 and CTLA4 interaction with CD80/CD86. KN026 is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes. Here the preliminary safety and efficacy results of KN046 in combination KN026 were reported in patients with locally advanced unresectable or metastatic other solid tumors who received ⩾ 1 line prior systemic therapy.



KN046



KN026

Study Design

Methods: HER2-positive locally advanced unresectable or metastatic other solid tumors with progression after ⩾ 1 line of prior systemic therapy were recruited, including 14 CRC patients, 4 NSCLC patients, 4 gallbladder cancer patients, 1 renal pelvis cancer patient and 1 pancreatic cancer patient. These patients were treated by KN046 (iv. 5 mg/kg Q3W) plus KN026 (iv. 30 mg/kg Q3W, loading on C1D1, D8) until progression, unacceptable toxicity, or patient withdrawal. The primary endpoint was objective response rate (ORR) according to RECIST 1.1 Q6W by investigator.

Results

As of the August 10th, 2021, 24 non-breast or non-gastric cancer patients with the median age of 56 years (range: 37-66) were enrolled. 20 and 24 patients were evaluable for overall response and safety, respectively.

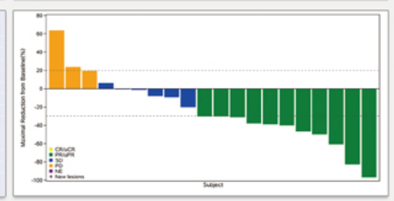
The ORR was 55.0% (11 of 20, 95% CI: 31.5-76.9). And the disease control rate (DCR) was 85.0% (17 of 20, 95% CI 62.1-96.8). The 6-month progression-free survival (PFS) rate was 84.1%. Out of 11 evaluable CRC patients, the ORR and DCR in CRC was 45.5% (5 of 11, 95% CI: 16.7-76.6) and 90.9% (10 of 11, 95% CI: 58.7-99.8), respectively.

Efficacy

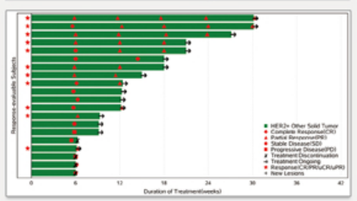
	HER2+ Other Solid Tumor Cancer (N = 20)	HER2+ Colorectal (N=11)
Best of response		
Complete response (CR)	0	0
Partial response (PR)	7 (35.0%)	3 (27.3%)
Unconfirmed complete response (uCR)	0	0
Unconfirmed partial response (uPR)	4 (20.0%)	2 (18.2%)
Stable disease (SD)	6 (30.0%)	5 (45.5%)
Progressive Disease (PD)	3 (15.0%)	1 (9.1%)
Not evaluable (NE)	0	0
Objective response rate (ORR)	11 (55.0%)	5 (45.5%)
95% CI	31.5, 76.9	16.7,76.6
Disease control rate (DCR)	17 (85.0%)	10 (90.9%)
95% CI	62.1, 96.8	58.7,99.8

Note: 1. calculate the percentage using the number of efficacy subjects in each group as the denominator; 2. ORR = CR + PR + uCR + uPR; 3. DCR = CR + PR + uCR + uPR + SD ⩾6 weeks.

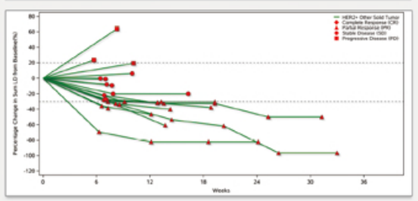
Waterfall plot



Swimming lane



Spider plot



Baseline Disease Characteristics

	HER2-positive other solid tumor(N=24)
Sex	
F	13 (54.2%)
M	11 (45.8%)
Age Group	
< 60 years	18 (75.0%)
⩾60 years	6(25.0%)
ECOG score	
Not collected	1(4.2%)
0	7(29.2%)
1	16 (66.7%)
Distant metastasis	
Yes	22 (91.7%)
No	2 (8.3%)
Number of metastatic sites	
< 3	13(54.2%)
⩾3	9(37.5%)
Prior anticancer Therapy	
Radiation	9 (37.5%)
Surgery	15 (62.5%)
Chemotherapy	24 (100%)
Number of previous treatment lines	
1st-line treatment	3(12.5%)
2nd-line treatment	13(54.2%)
3rd-line treatment	2(8.3%)
>3rd-line treatment	6(25.0%)

Twenty of 24(83.3%) patients suffered from treatment-related adverse events (TRAEs) of any grade. Total 4 of 24 (16.7%) patients had experienced ⩾grade 3 TRAEs, including 4 cases related to KN046 and 3 cases related to KN026. The most common (⩾10%) TRAEs were infusion related reaction (29.2%), diarrhea (19.4%), alanine aminotransferase increased (16.7%), aspartate aminotransferase increased (16.7%), vomiting(12.5%) and decreased appetite (12.5%). No treatment-related deaths were observed.

Safety overview

	HER2+ Other Solid Tumor (N =24)	
	Grade⩾3	All
Subjects with at least 1 TEAE	5 (20.8%)	21 (87.5%)
Related to KN046	4 (16.7%)	19 (79.2%)
Related to KN026	3 (12.5%)	19 (79.2%)
Related to KN046 or KN026	4 (16.7%)	20 (83.3%)
Subjects with at least 1 IRR	1 (4.2%)	7 (29.2%)
Related to KN046	1 (4.2%)	2 (8.3%)
Related to KN026	0	7 (29.2%)
Subjects with at least 1 irAE	2 (8.3%)	10 (41.7%)
Related to KN046	2 (8.3%)	10 (41.7%)
Subjects with at least 1 SAE during treatment	4 (16.7%)	6 (25.0%)
Related to KN046	3 (12.5%)	5 (20.8%)
Related to KN026	2 (8.3%)	3 (12.5%)
Subjects with at least 1 TEAE Leading to KN046 Withdrawn	2 (8.3%)	4 (16.7%)
Related to KN046	2 (8.3%)	4 (16.7%)
Related to KN026	0	0
Subjects with at least 1 TEAE Leading to KN026 Withdrawn	0	0
Related to KN046	0	0
Related to KN026	0	0
Subjects with at least 1 TEAE Leading to Death	0	0
Related to KN046	0	0
Related to KN026	0	0

Conclusion

This chemotherapy-free regimen of KN046 in combination with KN026 has shown promising clinical efficacy and manageable toxicity in HER2-positive non-breast and non-gastric solid tumors with ⩾ 1 line prior systemic therapy. The trial is currently ongoing.

ClinicalTrials.gov Number, NCT04521179

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