A phase II study of KN046 (a bispecific anti-PD-L1/CTLA-4) in patients with metastatic non-small cell lung cancer (NSCLC) who failed first line treatment

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Abstract No. 2973

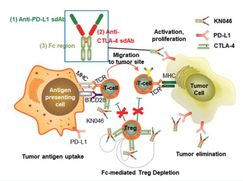
Anwen Xiong[1], Xingya Li[2], Yun Fan[3], Zhiyong Ma[4], Jian Fang[5], Qiang Xie[6], Wu Zhuang[7], Mafei Kang[8], Ting Xu[9], Mo Xu[9], Qing Liu[9], Ni Wang[9], Xiangyun Yan[9], Caicun Zhou[1]*

[1] Shanghai Pulmonary Hospital, Shanghai, China; [2] The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [3] Zhejiang Cancer Hospital, Hangzhou, China; [4] Henan Cancer Hospital, Zhengzhou, China; [5] Beijing Cancer Hospital, Beijing, China; [6] Fuzhou Pulmonary Hospital of Fujian, Fuzhou, China; [7] Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China; [8] Affiliated Hospital of Guilin Medical University, Guilin, China; [9] Jiangsu Alphamab Biopharmaceuticals Co., Ltd, Suzhou, China.

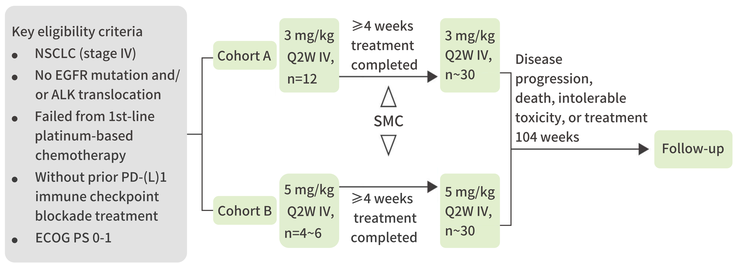
BACKGROUND

- KN046 is a novel bispecific antibody that blocks both PD-L1 interaction with PD1 and CTLA-4 interaction with CD80/CD86.
- Here, we reported the efficacy and safety results of KN046 as second line treatment of advanced NSCLC from Cohort A and B in this study.

Figure 1 Mechanism of action of KN046



STUDY DESIGN



RESULTS

- Between May 16, 2019 and April 30, 2020, 64 subjects with metastatic NSCLC who failed first line treatment were enrolled (Table1). At the data cutoff of August 31, 2021, the median follow-up was 21.6 months (95% CI, 20.3, 23.2).
- For tumor response, 64 subjects (30 in the 3 mg/kg, 34 in the 5 mg/kg) had received at least one tumor assessment. ORR and DCR were 14.1% (95% CI, 6.64, 25.02) and 65.6% (95% CI, 52.70, 77.05) respectively. (Table 2, Figure 2)
- Median progression-free survival (mPFS) was 3.68 months (95% CI, 2.89, 5.52). Median PFS were 3.68 months (95%CI: 3.22-7.29) in 3 mg/kg and 3.68 months (95%CI: 1.81-7.39) in 5 mg/kg respectively. (Figure 3)
- Median overall survival (mOS) was 18.40 months (95% CI, 12.88, 21.29). Median OS were 19.70 months (95%CI: 15.44-NE) in 3 mg/kg and 13.04 months (95%CI: 9.86-NE) in 5 mg/kg respectively. (Figure 4)
- Furthermore, the ORR was 10.0% (95% CI, 1.23, 31.70), mPFS was 7.43 months (95% CI, 1.81, 14.39) and mOS was 12.88months (95% CI, 8.97, -) in squamous NSCLC (n=20). And in non-squamous NSCLC (n=41), the ORR was 17.1% (95% CI, 7.15, 32.06), mPFS was 3.68 months (95% CI, 2.76, 5.45) and mOS was 19.81 months (95% CI, 13.04, 23.36). (Table 3)
- In terms of the treatment-related adverse event (TRAE), 27(42.2%) out of the 64 subjects had experienced TRAE at grade 3 or higher levels. The most common(⩾10%) TRAEs were anemia (18/64 [28.1%]), hyperglycemia (17/64 [26.6%]), infusion-related reaction (17/64 [26.6%]), rash (13/64 [20.3%]), etc. (Table 4)

Table 1. Baseline characteristics

Characteristic	3 mg/kg (n=30)	5 mg/kg (n=34)	Total (n=64)
Age, years, median (range)	59 (34-72)	61 (29-72)	61 (29-72)
Male, n (%)	23 (76.7%)	29 (85.3%)	52 (81.3%)
ECOG PS score, n (%)			
0	7 (23.3%)	2 (5.9%)	9 (14.1%)
1	23 (76.7%)	32 (94.1%)	55 (85.9%)
Smoking			
Never smoking	9 (30.0%)	10 (29.4%)	19 (29.7%)
Smoking	0	1 (2.9%)	1 (1.6%)
Quit smoking	21 (70.0%)	23 (67.6%)	44 (68.8%)
Brain metastasis, n (%)			
Yes	1 (3.3%)	2 (5.9%)	3 (4.7%)
No	29 (96.7%)	32 (94.1%)	61 (95.3%)
Pathological type, n (%)			
Non-squamous cell carcinoma	22 (73.3%)	19 (55.9%)	41 (64.1%)
Squamous cell carcinoma	8 (26.7%)	12 (35.3%)	20 (31.3%)
Poorly differentiated carcinoma	0	3 (8.8%)	3 (4.7%)
Clinical stages, n (%)			
IVa	27 (90.0%)	21 (61.8%)	48 (75.0%)
IVb	3 (10.0%)	13 (38.2%)	16 (25.0%)
History of antitumor therapy, n (%)			
Surgery	7 (23.3%)	8 (23.5%)	15 (23.4%)
Radiotherapy	6 (20.0%)	4 (11.8%)	10 (15.6%)
Medications	30(100%)	34(100%)	64(100%)
Other treatment	2 (6.7%)	4 (11.8%)	6 (9.4%)
PD-L1 expression level, n (%)			
TC < 1%	16 (53.3%)	20 (58.8%)	36 (56.3%)
TC ⩾ 1%	14 (46.7%)	12 (35.3%)	26 (40.6%)
Missing	0	2 (5.9%)	2 (3.1%)

Figure 2. Waterfall plots of best tumor diameter changes from baseline.

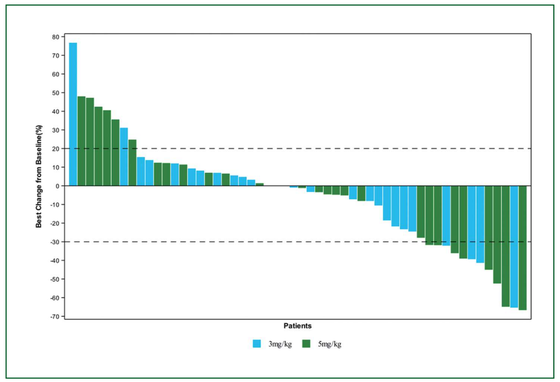


Figure 3. Kaplan-Meier curve analysis of Progression-free survival.

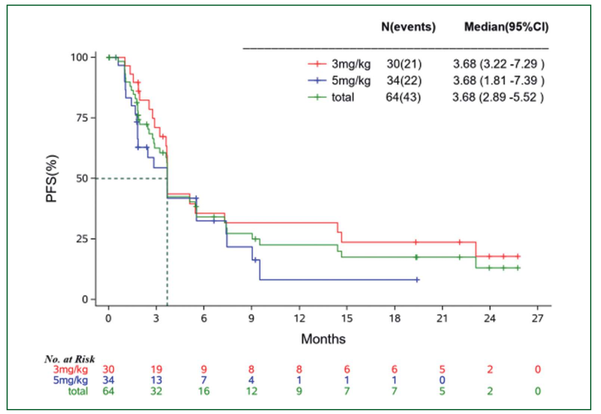


Figure 4. Kaplan-Meier curve analysis of Overall survival.

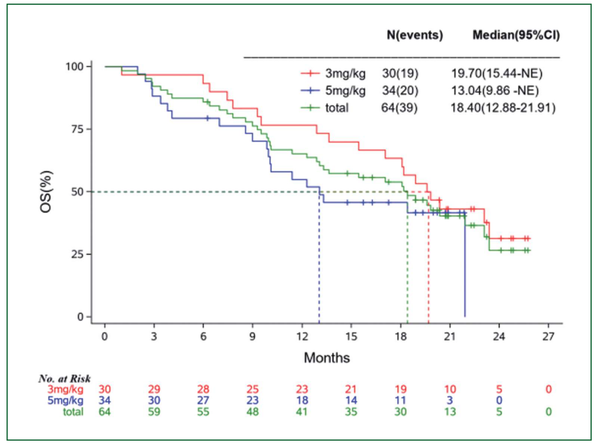


Table 2. Treatment responses

	3 mg/kg (n=30)	5 mg/kg (n=34)	Total (n=64)
CR	0	0	0
PR	4 (13.3%)	5 (14.7%)	9 (14.1%)
SD	19 (63.3%)	14 (41.2%)	33 (51.6%)
PD	5 (16.7%)	11 (32.4%)	16 (25.0%)
NE	2 (6.7%)	4 (11.8%)	6 (9.4%)
ORR	4 (13.3%)	5 (14.7%)	9 (14.1%)
95% CI	3.76, 30.72	4.95, 31.06	6.64, 25.02
DCR	23 (76.7%)	19 (55.9%)	42 (65.6%)
95% CI	57.72, 90.07	37.89, 72.81	52.70, 77.05

Table 3. Efficacy of KN046 in the squamous and non-squamous NSCLC

Variables	Squamous NSCLC (n=20)	Non-squamous NSCLC (n=41)
ORR, n (%)	2 (10.0%)	7 (17.1%)
DCR, n (%)	13 (65.0%)	28 (68.3%)
PFS, months, median (95% CI)	7.43 (1.81-14.39)	3.68 (2.76-5.45)
OS, months, median (95% CI)	12.88 (8.97, -)	19.81 (13.04, 23.36)

Table 4. Treatment-related adverse events

Events	3 mg/kg (n=30)	5 mg/kg (n=34)	Total (n=64)
TRAEs	28 (93.3%)	31 (91.2%)	59 (92.2%)
grade ⩾ 3	10 (33.3%)	17 (50.0%)	27 (42.2%)
TRAEs with incidence ⩾ 10% during the treatment			
Anemia	10 (33.3%)	8 (23.5%)	18 (28.1%)
Hyperglycemia	9 (30.0%)	8 (23.5%)	17 (26.6%)
Infusion-related reaction	5 (16.7%)	12 (35.3%)	17 (26.6%)
Rash	6 (20.0%)	7 (20.6%)	13 (20.3%)
Abnormal liver function	7 (23.3%)	6 (17.6%)	13 (20.3%)
Fatigue	8 (26.7%)	3 (8.8%)	11 (17.2%)
Weight decreased	5 (16.7%)	5 (14.7%)	10 (15.6%)
Hypothyroidism	7 (23.3%)	3 (8.8%)	10 (15.6%)
ALT increased	5 (16.7%)	4 (11.8%)	9 (14.1%)
AST increased	4 (13.3%)	5 (14.7%)	9 (14.1%)
Pruritus	6 (20.0%)	1 (2.9%)	7 (10.9%)
Pyrexia	2 (6.7%)	5 (14.7%)	7 (10.9%)

CONCLUSION

- The bispecific antibody, KN046 was well tolerated and effective as second line treatment of advanced NSCLC.
- KN046 showed promising OS benefit in both squamous and non-squamous NSCLC.

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DISCLOSURES

- Caicun Zhou have received honoraria as a speaker from Lily China, Sanofi, BI, Roche, MSD, Qilu, Hengrui, Innovent Biologics, C-Stone, LUYE Pharma, TopAlliance Biosciences Inc and Amoy Diagnositics. Caicun Zhou is an advisor in Innovent Biologics, Hengrui, Qilu and To pAlliance Biosci ences Inc.
- The remaining authors have no conflicts of interest to declare.