Preliminary data from a single-arm, open-label, multicenter phase 2 clinical trial: KN046 combined with axitinib as first-line (1L) treatment for NSCLC

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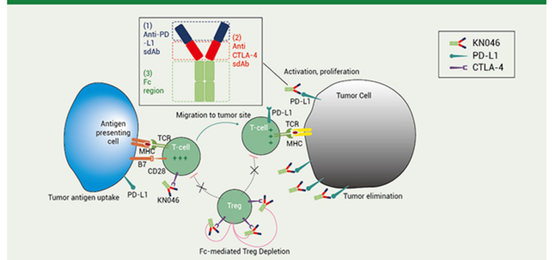
Background

- KN046 is a novel bispecific domain antibody, which blocks both PD-L1 and CTLA-4. (Figure 1)
- KN046 combined with platinum doublet chemotherapy as 1L treatment for metastatic NSCLC had shown promising efficacy and tolerability in the previous clinical trial[1].
- Herein, we present the promising preliminary data of KN046 combination with axitinib as 1L treatment for NSCLC.

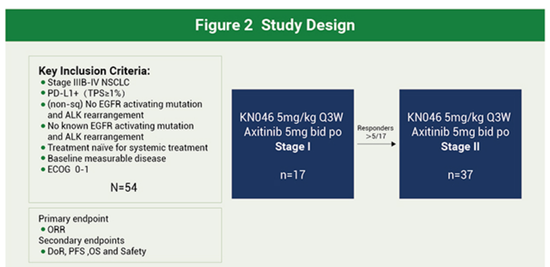
Figure 1 Structure of KN046



Methods

- Study design is shown in Figure 2.
- Eligible subjects with recurrent/metastatic NSCLC, systemic treatment- naïve and PD-L1 expression ≥1% will be enrolled.
- This study adopts a Simon's optimal two-stage design. In the 1st stage, 17 subjects were enrolled, and the 2nd stage enrollment would be discontinued if objective response (CR or PR) observed in less than 6 subjects. Otherwise, 37 subjects will be enrolled in the 2nd stage.
- The primary endpoint is ORR. The secondary endpoints include DoR, safety, PFS and OS.
- The data cut-off date was Aug 8, 2023

Figure 2 Study Design



Results

- 38 subjects were enrolled. 86.8% were male. 86.8% (33/38) were stage IVa or IVb. The proportion of subjects with PD-L1 expression ≥50% was lower (26.3%) than previously reported (about 40%)[2]. (Table 1)

Table 1 Baseline Characteristics

	N=38, n (%)
Age (Year)	
Mean	61.6
Median	64.0
Min, Max	35, 73
Gender, n (%)	
Male	33 (86.8)
Female	5 (13.2)
Chinese, n (%)	
Yes	38 (100)
No	0
Height (cm)	
Mean	165.93
Median	165.50
Min, Max	150.0, 178.0
Weight (kg)	
Mean	61.01
Median	61.10
Min, Max	41.9, 86.0
Baseline ECOG score, n (%)	
0	2 (5.3)
1	36 (94.7)
Pathological types, n (%)	
Squamous	16 (42.1)
Adenocarcinoma	20 (52.6)
Other#	2 (5.3)
Clinical stage at screening, n (%)	
IIIB	4 (10.5)
IIIC	1(2.6)
IVA	15 (39.5)
IVB	18 (47.4)
PD-L1 Expression-Central Laboratory (TPS)	
≥ 50%	10 (26.3%)
1-49%	25 (65.8%)
<1%	2 (5.3%)
Other*	1 (2.6%)

#: The pathological type was unknown.
*: The quality control failed

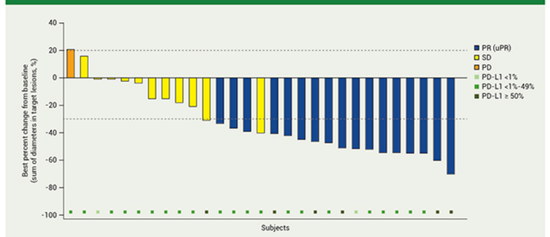
- In the efficacy analysis set, the ORR was 58.6% (17/29, 95% CI: 38.936, 76.476). (Table 2 / Figure 3)

Table 2 Objective Response Rate-Efficacy Analysis Set

	Efficacy Analysis Set (N=29), n (%)
Best of response, BOR	
CR	0
uCR	0
PR	13 (44.8)
uPR	4 (13.8)
SD	11 (37.9)
PD	1 (3.4)
ORR[1] (95%CI)	**17 (58.6)** (38.936, 76.476)
DCR[2] (95%CI)	**28 (96.6)** (82.236, 99.913)

[1] Objective response rate (ORR) : the proportion of patients with the best overall response of CR (uCR) or PR (uPR).
[2] Disease control rate (DCR) : the proportion of subjects who achieved CR/PR/SD ≥ 6 weeks between the first dose and disease progression or death from any cause, as assessed by RECIST v1.1.

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



- Subjects with higher PD-L1 expression had a higher objective response rate. (Table 3)
- The median PFS follow-up was 4.172 mons (1.413, 6.867). The mPFS was 8.345 mons (95% CI: 5.454, NE) (Figure 5). The mPFS was 9.199 mons for non-sq (95% CI: 5.585, NE) (Figure 6). The mOS was not reached.

Table 3 Objective Response Rates According to PD-L1 Expression -Efficacy Analysis Set**

	Efficacy Analysis Set (N=29), n(%)
PD-L1 < 1%	2 (6.9)
ORR (%)	1 **(50.0)**
95% CI	(1.258, 98.742)
PD-L1 1-49%	21 (72.4)
ORR (%)	11 **(52.4)**
95% CI	(29.781, 74.287)
PD-L1 ≥ 50%	6 (20.7)
ORR (%)	5 **(83.3)**
95% CI	(35.877, 99.579)

** PD-L1 Expression-Central Laboratory (TPS)

Figure 4 Swimming Plot of Exposure Time - Safety Analysis Set

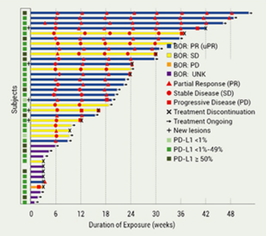


Figure 5 Kaplan - Meier Curve for Progression Free Survival-Intent to Treat Analysis Set

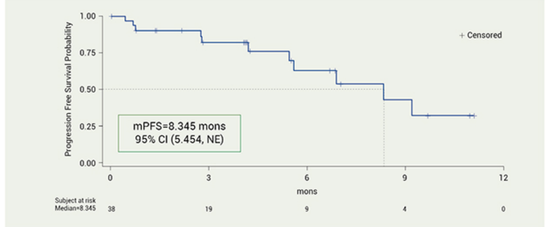
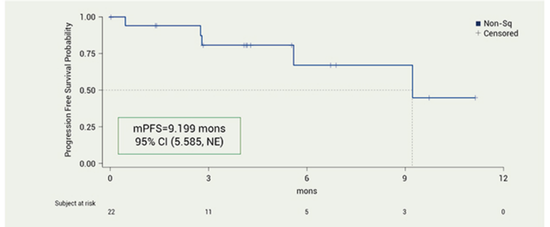


Figure 6 Kaplan - Meier Curve for Progression Free Survival (Non-Sq) -Intent to Treat Analysis Set



- The incidence of TEAE was 92.1% (35/38), of which KN046-related TRAE was 78.9% (30/38). The incidence of KN046-related CTCAE Grade ≥3 TRAE was 23.7% (9/38). There was no KN046-related death. (Table 4).
  The most frequent TRAE was AST increased 7.9% (3/38), ALT increased 5.3% (2/38), diarrhoea 5.3% (2/38) and others less than 3%. (Table 5).
- The incidence of irAE was 15.8% (6/38). Only 2 subjects had Grade ≥3 irAE. (Table 6)

Table 4 Safety Summary - Safety Analysis Set

	(N=38) n (%)
Any TEAE	**35 (92.1)**
TEAE related with any study drug	33 (86.8)
TEAE related with KN046	30 (78.9)
TEAE related with Axitinib	29 (76.3)
TEAE Grade≥ 3	**19 (50.0)**
TEAE Grade≥ 3 relatedwith any study drug	14 (36.8)
TEAE Grade≥ 3 related with KN046	9 (23.7)
TEAE Grade≥ 3 related with Axitinib	13 (34.2)
SAE	
SAE related with any study drug	10 (26.3)
SAE related with KN046	9 (23.7)
SAE related with Axitinib	7 (18.4)
irAE	**6 (15.8)**
irAE Grade≥ 3	2 (5.3)
irAE leading to death	0
TEAE leading to death related with KN046	0
TEAE leading to death related with Axitinib##	1 (2.6)

##: This death was due to hemoptysis, which was judged by the investigator to be related to axitinib

Table 5 Summary of CTCAE Grade ≥ 3 TEAE Related to KN046 - Safety Analysis Set

SOC PT	N=38 n (%)
At least once KN046-related CTCAE ≥ 3 TRAE	**9 (23.7)**
Investigations	**4 (10.5)**
Aspartate aminotransferase increased	3 (7.9)
Alanine aminotransferase increased	2 (5.3)
Platelet count decreased	1 (2.6)
Gastrointestinal disorders	**2 (5.3)**
Diarrhoea	2 (5.3)
Stomatitis	1 (2.6)
Metabolism and nutrition disorders	**2 (5.3)**
Hyperglycaemia	1 (2.6)
Hypochloraemia	1 (2.6)
Hyponatraemia	1 (2.6)
Skin and subcutaneous tissue disorders	**2 (5.3)**
Palmar-plantar erythrodysaesthesia syndrome	1 (2.6)
Rash	1 (2.6)

Table 6 Summary of CTCAE ≥ 3 irAE - Safety Analysis Set

SOC PT	N=38 n (%)
At least once CTCAE ≥3 irAE	**2 (5.3)**
Metabolism and nutrition disorders	**1 (2.6)**
Hyperglycaemia	1 (2.6)
Skin and subcutaneous tissue disorders	**1 (2.6)**
Rash	1 (2.6)

Conclusions

KN046 combined with axitinib is well tolerated and has shown very promising efficacy and safety signal in 1L treatment for advanced NSCLC. The 2nd stage of enrollment is ongoing and a phase 3 RCT for the 1st line NSCLC patient is planned to confirm the combination of KN046 and axitinib as a viable chemo free option.

REFERENCE

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