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 prior EGFR-TKIs

Poster No. 1034P

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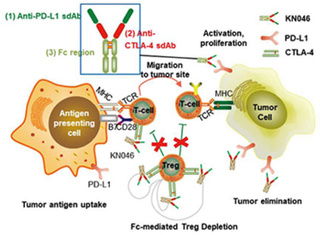
BACKGROUND

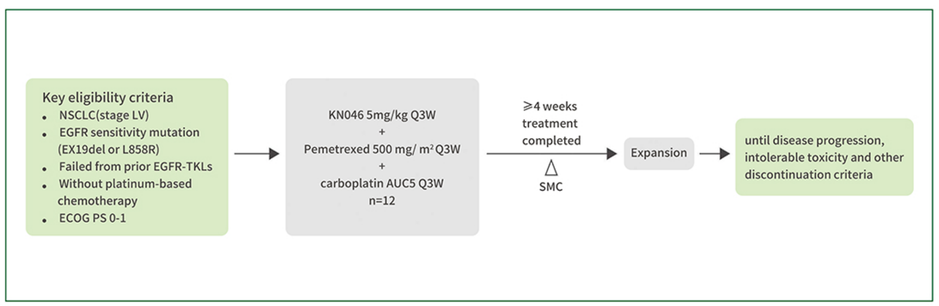
- KN046 is a novel bispecific antibody that blocks both PD-L1 interaction with PD1 and CTLA-4 interaction with CD80/CD86.
- Here, we reported the efficacy and safety results of KN046 combined with chemotherapy in treatment of advanced NSCLC with EGFR sensitivity mutation who failed prior tyrosine kinase inhibitors (TKIs) from Cohort D in this study.

Figure 1 Mechanism of action of KN046



STUDY DESIGN

- This is an open-label, multi-center, multiple cohorts, single arm study to evaluate the efficacy, safety and tolerability of KN046 in NSCLC.
- Primary endpoint was objective response rate (ORR) per RECIST version 1.1.



RESULTS

- Between Jan 7, 2020 and Dec17, 2021, 26 subjects with metastatic NSCLC were enrolled. At the data cutoff of Jan 25, 2022, the median follow-up was 11.56 months (95% CI, 7.66, 12.52). (Table 1)
- Among all 26 subjects, the ORR was 26.9% (95% CI, 11.57， 47.79) , disease control rate (DCR) was 80.8% (95% CI, 60.65, 93.45) with 7 PR and 14 SD. Clinical benefit rate (CBR:CR+PR+SD≥12 weeks) was 65.4% (95% CI, 44.33, 82.79). (Figure2, table 2)
- Median progression-free survival (mPFS) was 5.52 months (95% CI, 4.17, 6.77) and median overall survival (mOS) was 12.68 months (95% CI, 11.4, -). The 12-month OS rate was 71.57%(95% CI,43.59,87.39).(Figure 3, Figure 4)
- In terms of the treatment-related adverse event (TRAE), 14(53.8%) out of the 26 subjects had experienced TRAE at grade 3 or higher levels.The most common (≥10%) TRAEs were anemia (11/26 [42.3%]), AST increased (11/26 [42.3%]), ALT increased (9/26 [34.6%%]), infusion-related reaction (8/26 [30.8%]), etc. (Table 3)

Table 1 Baseline characteristics

Characteristic	n=26
Age (years), median (range)	57 (38-73)
Male, n (%)	13 (50.0%)
ECOG PS score, n (%)	
0	3 (11.5%)
1	23 (88.5%)
Smoking	
Never smoking	16 (61.5%)
Smoking	1 (3.8%)
Quit smoking	9 (34.6%)
Brain metastasis, n (%)	
Yes	10 (38.5%)
No	16 (61.5%)
Pathological type, n (%)	
Non-squamous cell carcinoma	26 (100%)
Clinical stages, n (%)	
IVa	13 (50.0%)
IVb	13 (50.0%)

Table 2 Treatment responses

	n=26
Best overall response, n (%)	
Complete response	0
Partial response	7 (26.9%)
Stable disease	14 (53.8%)
Progressive disease	4 (15.4%)
Not evaluable	1(3.8%)
Objective response rate, n (%)	7 (26.9%)
95% CI	11.57, 47.79
Disease control rate, n (%)	21 (80.8%)
95% CI	60.65, 93.45
Clinical benefit rate#, n (%)	17 (65.4%)
95% CI	44.33, 82.79

Note: #Clinical benefit rate: CR+PR+SD≥12 weeks

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

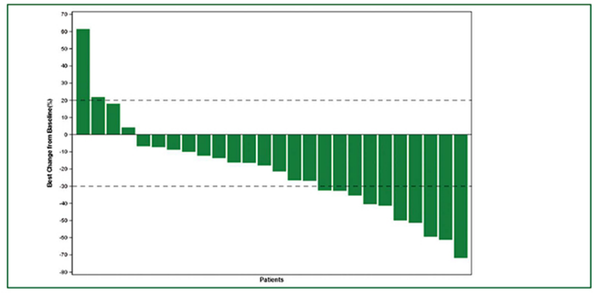


Figure 3. Kaplan-Meier curve analysis of Progression-free survival.

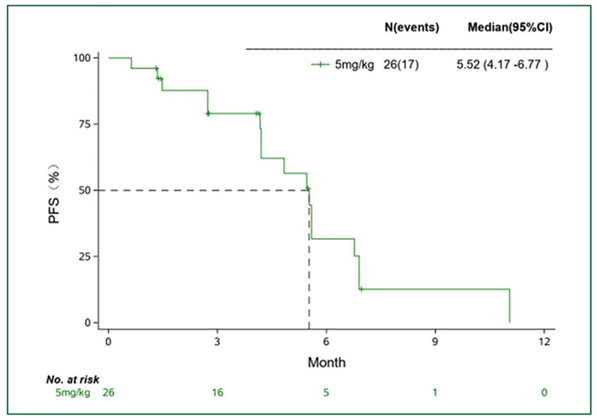


Figure 4. Kaplan-Meier curve analysis of Overall survival.

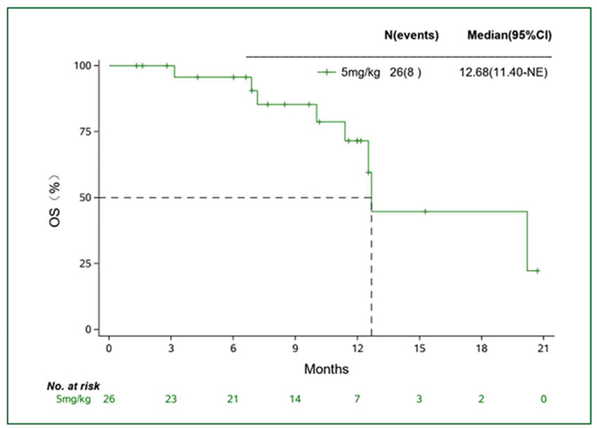


Table 3 Treatment-related adverse events

Events	n=26
TRAEs	18(69.2%)
Grade ⩾ 3	14 (53.8%)
TRAEs with incidence ⩾ 10% during the treatment	
Anemia	11 (42.3%)
AST increased	11 (42.3%)
ALT increased	9 (34.6%)
Platelet count decreased	8 (30.8%)
Neutrophil counts decreased	8 (30.8%)
White blood cell count decreased	8 (30.8%)
Infusion-related reaction	8 (30.8%)
Fatigue	6 (23.1%)
Nausea	5 (19.2%)
Abnormal liver function	4 (15.4%)
Elevated glucose	4 (15.4%)
Elevated bilirubin	3 (11.5%)
Hyperglycemia	3 (11.5%)
Hypokalemia	3 (11.5%)
Hyponatremia	3 (11.5%)
Rash	3 (11.5%)

CONCLUSION

- KN046 showed well tolerated and promising efficacy in treatment of advanced NSCLC with EGFR sensitivity mutation who failed prior EGFR-TKIs.
- Large scale study is needed to further validate the clinical outcome.

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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 TopAlliance Biosciences Inc. The remaining authors have no conflicts of interest to declare.
- All other authors have declared no conflicts of interest.