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Efficacy and safety efficacy and safety of KN046 (a bispecific anti-PD-L1/CTLA-4) in patients with metastatic non-small cell lung cancer who previously treated with immune checkpoint inhibitor (s)

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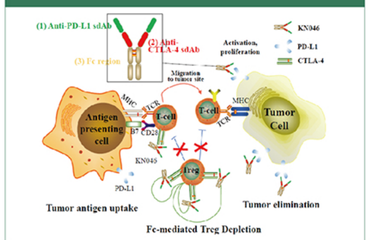
Background

KN046 is a novel bispecific antibody that inhibits both PD-L1/PD1 and CTLA-4/CD80/CD86 pathways. (Figure1) Previous phase I (KN046-CHN-001, NCT03733951) and phase II (KN046 -201, NCT03838848) trials showed promising anti-tumor effects of KN046 in non-small cell lung cancer (NSCLC) patients who had failed prior immune checkpoint inhibitor(s) (ICIs) therapy. We present the efficacy and safety outcomes of KN046 in this population from pooled analysis of KN046-CHN-001 and KN046-201 (cohort C).

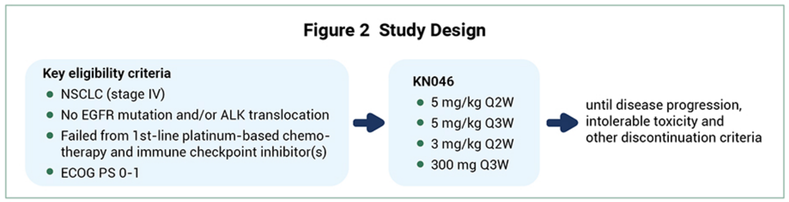
Figure 1 Mechanism of action of KN046



Methods

KN046-CHN-001 and KN046-201 assessed the efficacy, safety and tolerability of KN046 in NSCLC. Eligible patients had NSCLC that progressed after ICI(s) and platinum-based chemotherapy. Patients with EGFR mutation and/or ALK translocation were excluded. All patients received KN046 (26 pts at 5 mg/kg Q2W, 2 pts at 5 mg/kg Q3W, 2 pts at 300mg Q3W and 1 pts at 3 mg/kg Q2W) by IV infusion. The primary endpoints were confirmed ORR by RECIST version 1.1 and safety. (Figure2)

Figure 2 Study Design



Results

Between April 19, 2019 and July 13, 2020, 31 pts with metastatic NSCLC who failed ICI (s) and platinum-based chemotherapy were enrolled. At the data cutoff of July 30, 2022 for KN046-201 and August 31, 2021 for KN046-CHN-001, the median follow-up was 25.0 months (95% CI, 24.4, NE). (Table 1)

Table 1 Baseline characteristics

Characteristic		n=31
Age(years), median (range)		61 (30-74)
Sex, n (%)	Male	23 (74.2%)
	Female	8 (25.8%)
ECOG PS score, n (%)	0	5 (16.1%)
	1	26 (83.9%)
Pathological type, n (%)	Squamous cell carcinoma	17 (54.8%)
	Non-squamous cell carcinoma	14 (45.2%)
Clinical stages, n (%)	IV	31 (100%)
Front line therapy, n (%)	Line 1	6 (19.4%)
	Line 2	9 (29.0%)
	≥ Line 3	16 (51.6%)

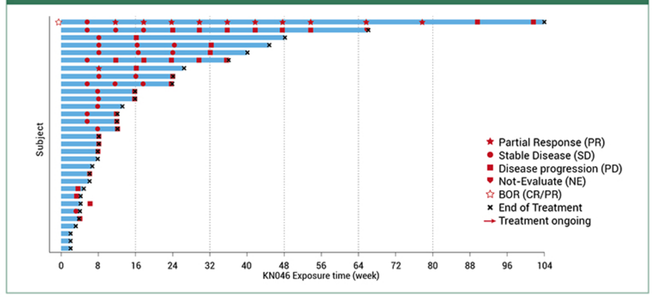
Among all 31 pts, the ORR was 3.2% (1/31, 95% CI, 0.1, 16.7%), disease control rate (DCR) was 38.7% (12/31, 95% CI, 21.8, 57.8%), clinical benefit rate (CBR) was 16.1% (5/31, 95% CI, 5.5, 33.7%). (Table2, Figure 3)

Table 2 Treatment responses

	n=31
Best overall response, n (%)	
Partial response	1 (3.2%)
Stable disease	11 (35.5%)
SD≥12 weeks	4 (12.9%)
Progressive disease	11 (35.5%)
Objective response rate, n (%)	1 (3.2%)
95% CI	0.1, 16.7
Disease control rate, n (%)	12 (38.7%)
95% CI	21.8, 57.8
Clinical benefit rate#, n (%)	5 (16.1%)
95% CI	5.5, 33.7

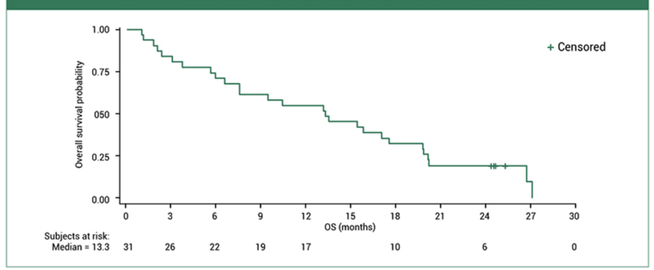
Note: #Clinical benefit rate: CR + PR + SD ≥ 12 weeks

Figure 3 Study therapeutic exposure time swimming map



Median progression-free survival (mPFS) was 2.8 months (95% CI, 1.8, 3.7) and median overall survival (mOS) was 13.3 months (95% CI, 6.5, 17.5). The 12-month OS rate was 54.8% (95% CI, 35.97, 70.26). (Figure 4)

Figure 4 Kaplan-Meier curve analysis of Overall survival



In terms of the treatment-related adverse event (TRAE), 7(22.6%) out of the 31 patients had experienced TRAE at grade 3 or higher levels. Commonly reported TRAEs of grade 3 or higher were anemia (9.7%), febrile neutropenia (3.2%), fatigue (3.2%) etc. (Table 3)

Table 3 Treatment-related adverse events

Events	n=26
TRAEs	25 (80.6%)
Grade ≥ 3	7 (22.6%)
Grade ≥ 3 TRAEs during the treatment	
Anemia	3 (9.7%)
Febrile neutropenia	1 (3.2%)
Fatigue	1 (3.2%)
Decreased feeding	1 (3.2%)
White blood cell count decreased	1 (3.2%)
Infusion-related reaction	1 (3.2%)
Immune-mediated hepatitis	1 (3.2%)

Conclusions

KN046 was well tolerated and showed encouraging efficacy result especially in OS benefit in NSCLC patients who had failed prior ICI(s) therapy. Further study is warranted to confirm the clinical results.

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Disclosure

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