Two-year follow-up from KN046 in combination with Platinum doublet chemotherapy as first-line（1L）treatment for NSCLC: an open-label, multi-center phase 2 trial

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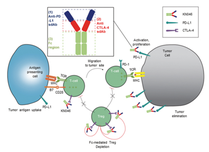
BACKGROUND

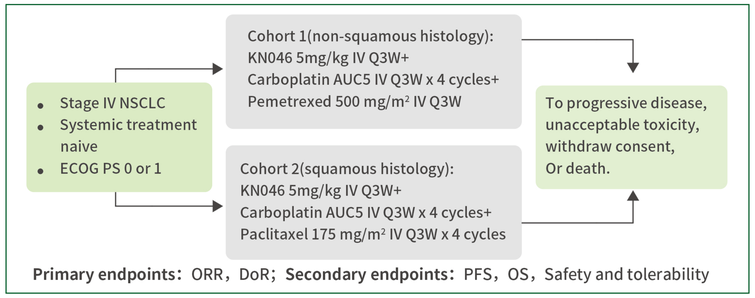
- KN046 is a novel bispecific domain antibody, which blocks both PD-L1 and CTLA-4.
- Primary analysis[1] of this phase 2 trial (data as of January 19, 2021) showed promising efficacy and well tolerated safety in advanced NSCLC. Herein, we present an updated analysis(data as of Mar 15, 2022).

Figure 1 Mechanism of action of KN046



Methods

- Tumor response evaluation was performed per RECIST 1.1 by investigators.
- Safety and tolerability were assessed per NCI-CTCAE v5.0.



Primary endpoints：ORR，DoR；**Secondary endpoints**：PFS，OS，Safety and tolerability

RESULTS

- At data cut-off date (Mar 15, 2022), the median follow-up was 23.1 month (Interquartile Range [IQR]20.7,26.9). 87 patients were enrolled (cohort 1 n = 51, cohort 2 n = 36)(Table 1).
- In 87 efficacy evaluable patients, confirmed ORR was 46% (95% CI: 35.2, 57.0)(Figure 2). DoR of cohort 1 and cohort 2 were 9.7 months (95% CI:4.01, 20.73) and 7.3 months (95% CI:3.52, -)(Figure 3).
- Median PFS in cohort 1 and cohort 2 were 5.8 months (95% CI: 4.80, 7.16) and 5.7 months (95% CI: 4.17, 8.71) (Figure 4), and median OS were 27.2 months (95% CI: 15.18, -) and 26.6 months (95% CI: 12.19, -) respectively (Figure 5).
- The most common KN046 related TEAEs (≥Grade 3) were Diarrhea (n=6, 6.9%), Alanine aminotransferase increase (n=4, 4.6%) and Rash (n=4, 4.6%)(Table 2).
- The incidence of ≥Grade 3 Immune-related AEs was 12.6%(n=11)(Table 3).

Table 1 Baseline characteristics

Parameters	Cohort1 (N=51)	Cohort2 (N=36)	Total (N =87)
Gender，n (%)			
Male	34 (66.7)	32(88.9)	66 (75.9)
Female	17 (33.3)	4(11.1)	21 (24.1)
Age（years）			
Median (Min, Max)	59.0(41,74)	64.5 (32,76)	61.0 (32,76)
ECOG, n (%)			
0	11(21.6)	4(11.1)	15 (17.2)
1	40 (78.4)	32(88.9)	72 (82.8)
Primary Tumor Type			
Squamous Carcinoma	0(0)	36 (100)	36 (41.4)
Non-Squamous Carcinoma	51 (100)	0(0)	51 (58.6)
Tumor PD-L1 expression			
TC≥1%	30 (58.8)	16 (44.4)	46 (52.9)
TC<1%	18(35.3)	19(52.8)	37 (42.5)
Unknown	3 (5.9)	1 (2.8)	4 (4.6)

Figure 2 Waterfall plots of best tumor diameter changes from baseline

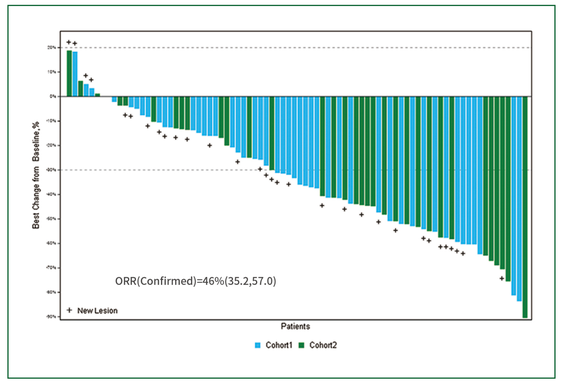


Figure 3 Kaplan-Meier curve analysis of Duration of response

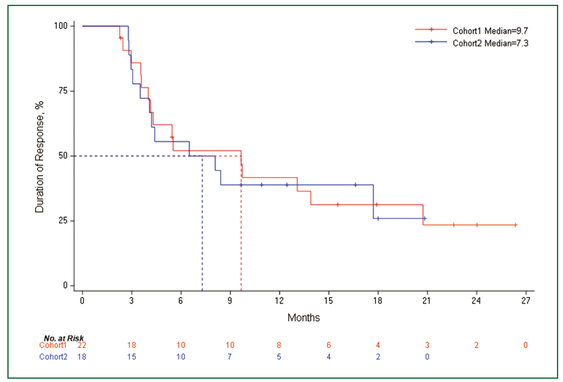


Figure 4 Kaplan-Meier curve analysis of Progression-free survival

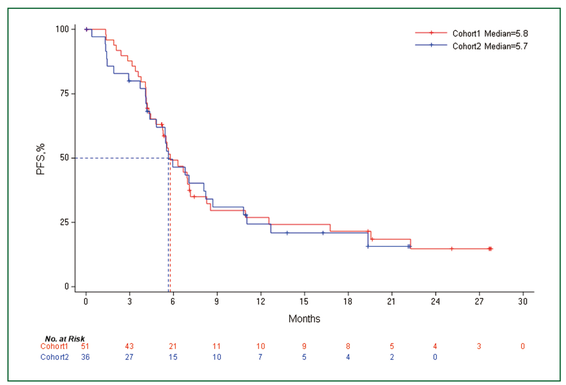


Figure 5 Kaplan-Meier curve analysis of Overall survival

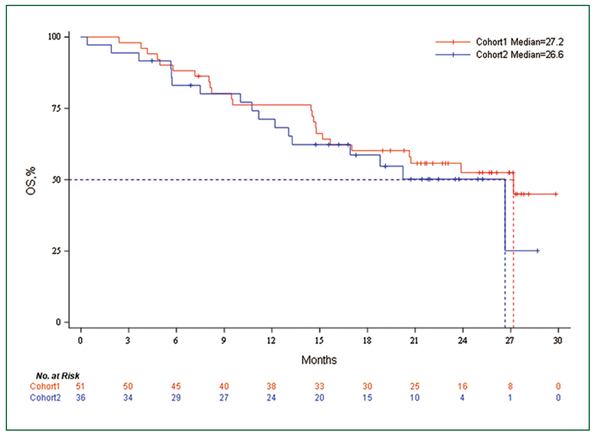


Table 2 TEAE (Grade ≥ 3)

Preferred Term (CTCAE v5.0)	Grade ≥ 3 N=87
Subjects with at least 1 KN046 Related CTCAE Grade ≥ 3 TEAE	30 (34.5%)
Diarrhea	6 (6.9%)
Alanine aminotransferase increase	4 (4.6%)
Rash	4 (4.6%)
Infusion related reaction	3 (3.4%)
Thrombocytopenia	3 (3.4%)
Immune-mediated pneumonitis	3 (3.4%)
Dermatitis allergic	3 (3.4%)
Leucopenia	2 (2.3%)
Pneumonia	1 (1.1%)
Infectious pneumonia	1 (1.1%)
Aspartate aminotransferase increase	1 (1.1%)
Neutropenia	1 (1.1%)
Anaphylactoid reaction	1 (1.1%)
Autoimmune hepatitis	1 (1.1%)
Back pain	1 (1.1%)
Gastrointestinal hemorrhage	1 (1.1%)
Hypopotassemia	1 (1.1%)
Anorexia	1 (1.1%)
Peripheral edema	1 (1.1%)
Hypertension	1 (1.1%)
Febrile neutropenia	1 (1.1%)

Table 3 irAE (Grade ≥ 3)

Preferred Term (CTCAE v5.0)	Grade ≥ 3 N=87
Subjects with at least 1 CTCAE Grade ≥ 3 immune related AE	11 (12.6%)
Diarrhea	3(3.4%)
Dermatitis allergic	2 (2.3%)
Rash	2 (2.3%)
Immune-mediated pneumonitis	2 (2.3%)
Pneumonia	1 (1.1%)
Autoimmune hepatitis	1 (1.1%)
Febrile neutropenia	1 (1.1%)
Neutropenia	1 (1.1%)
Peripheral edema	1 (1.1%)
Immune - mediated dermatitis	1 (1.1%)

CONCLUSION

- KN046 combined with platinum doublet chemotherapy is well tolerated and has shown promising clinical benefit as 1L treatment for NSCLC.
- Median OS in both cohorts were over 2 years, which is very encouraging. Robust efficacy and safety data will be further confirmed in an ongoing large-scale phase 3 clinical trial.

REFERENCE

1. YP Yang et al. A Phase 2, Open-Label, Multi-Center Study to evaluate the efficacy, safety, and tolerability of KN046 in combination with chemotherapy in subjects with advanced non-small cell lung cancer. 2021ASCO, Abstract # 9060

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- All authors participated and approved the presentation

DISCLOSURES

- All authors declare no conflict of interest.
- Please address any questions or comments regarding this poster to zhangli@sysucc.org.cn