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

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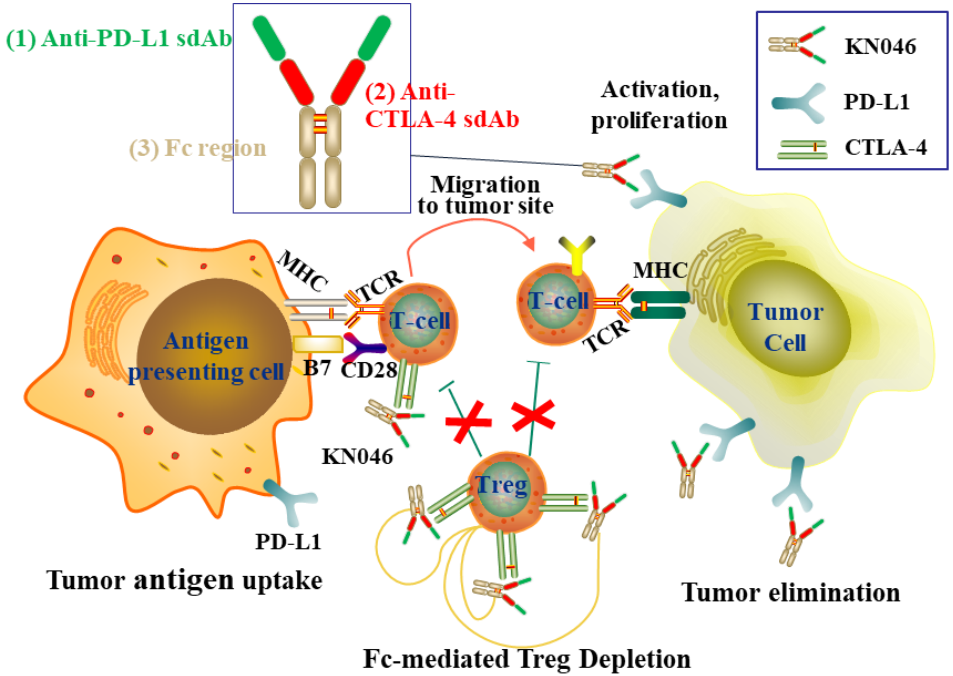
DISCLOSURES

Honoraria as a speaker	Lily China, Sanofi, BI, Roche, MSD, Qilu, Hengrui, Innovent Biologics, C-stone, LUYE Pharma, TopAlliance Biosciences Inc, Amoy Diagnositics
Advisor	Innovent Biologics, Hengrui, Qilu, TopAlliance Biosciences Inc.



Mechanism of action of KN046

- ☑ Blocking CTLA-4 with B7 and PD-L1 with PD-1.
- ☑ Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity.
- ☑ IgG1 Fc domain, CTLA-4 blocking-mediated Treg cells deletion.

Study Design

- Stage IV NSCLC
- Fail 1st line platinum-doublets
- No prior PD-(L)1 therapy
- ECOG PS 0 or 1

→ 3 mg/kg Q2W IV, n~30
→ 5 mg/kg Q2W IV, n~30

→ To progressive disease, unacceptable toxicity, and withdraw consent.

Primary endpoint
- ORR

Secondary endpoints
- PFS, OS
- Safety and tolerability

Baseline characteristics

Parameters	Total (N =64)
Gender, n (%)	
Male	52 (81.3%)
Female	12 (18.8%)
Age (years)	
Mean (SD)	58.2(9.85)
Median (Min, Max)	61.0 (29, 72)
ECOG, n (%)	
0	9 (14.1%)
1	55(85.9%)
Primary Tumor Type	
Squamous Carcinoma	23 (35.9%)
Non-Squamous Carcinoma	41 (64.1%)
Primary prior Therapies	
Surgery	15 (23.4%)
Chemotheraphy	64(100%)
Radiotherapy	8 (12.5%)

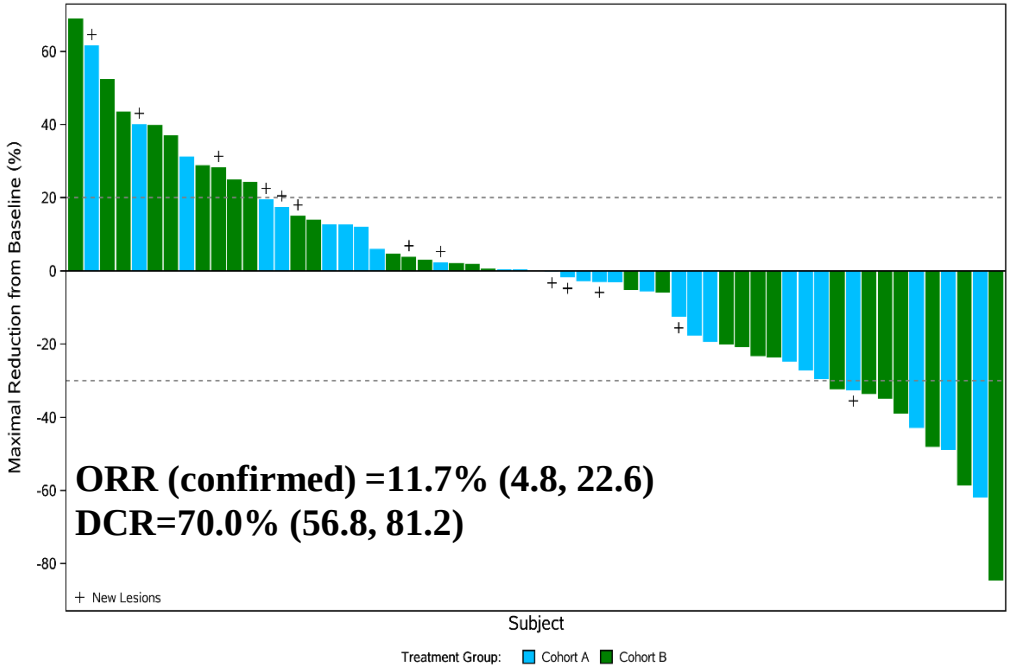
≥ Grade 3 TRAE

Preferred Term	Grade ≥ 3
Subjects with at least 1 KN046 Related CTCAE Grade ≥ 3 TEAE	24 (37.5%)
Infusion related reaction	7 (10.9%)
Anaemia	3 (4.7%)
Drug-induced liver injury	2 (3.1%)
Hepatic function abnormal	2 (3.1%)
Lung infection	2 (3.1%)
Neutrophil count decreased	2 (3.1%)
White blood cell count decreased	2 (3.1%)
Adrenal insufficiency, Gastroenteritis, Herpes zoster, Hyperglycaemia, Hypokalaemia, Hyponatraemia, Hypophysitis, Hypopituitarism, Lymphangitis, Muscular weakness, Myocardial infarction, Papule, Platelet count decreased, Pneumonitis, Rash, Renal failure, Thyroid mass	1 (1.6%)

≥ Grade 3 irAE

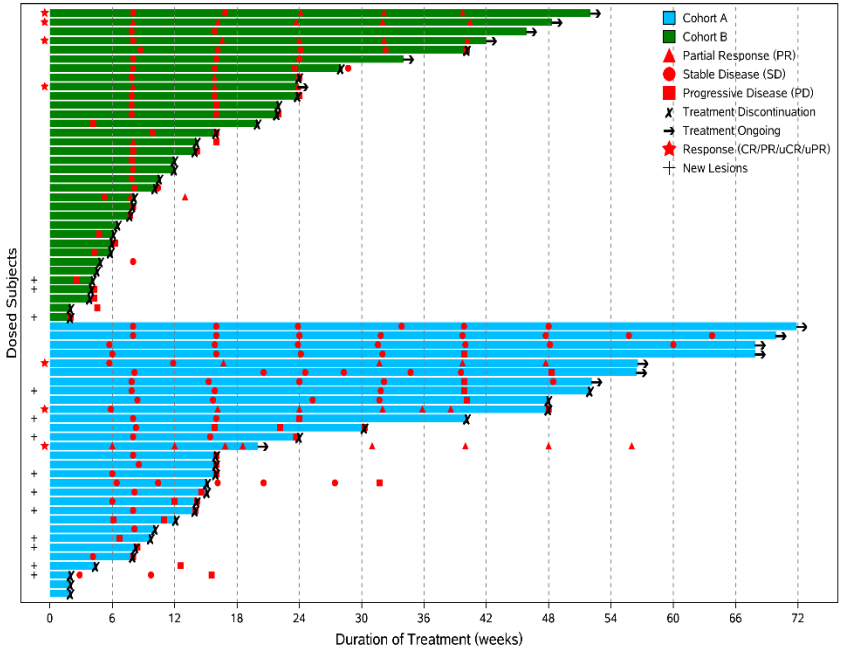
Preferred Term	Grade ≥ 3
Subjects with at least 1 CTCAE Grade ≥ 3 immune related AE	12 (18.8%)
Neutrophil count decreased	2 (3.1%)
White blood cell count decreased	2 (3.1%)
Adrenal insufficiency, Drug-induced liver injury, Gastroenteritis, Hepatic function abnormal, Herpes zoster, Hyperglycaemia, Hyponatraemia, Hypophysitis, Hypopituitarism, Lung infection, Muscular weakness, Myocardial infarction, Papule, Platelet count decreased, Pneumonitis, Rash, Renal failure, Thyroid mass	1 (1.6%)

Waterfall plot



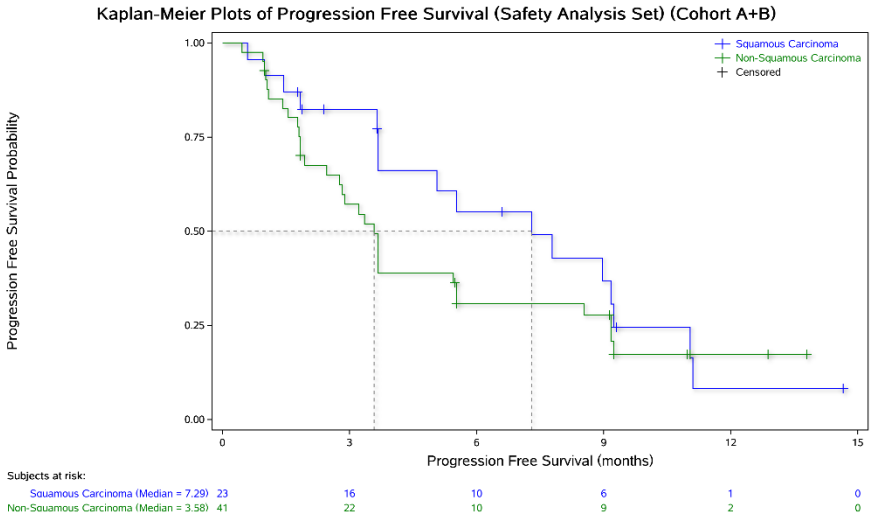
ORR (confirmed) =11.7% (4.8, 22.6)
DCR=70.0% (56.8, 81.2)

Swimming lane plot



DOR not reached.

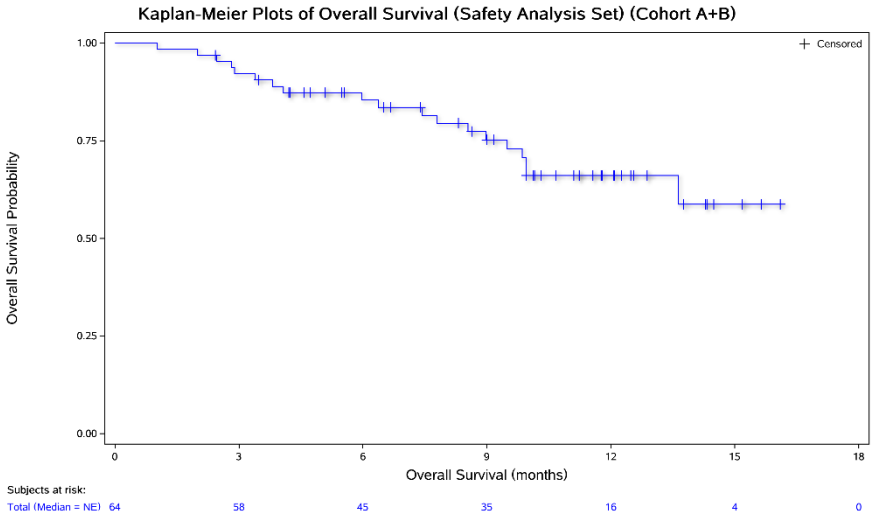
PFS



mPFS was 3.68 months (95%CI 3.35, 7.29)

- non-sq NSCLC, 3.58 months (2.46,5.52)
- **sq-NSCLC 7.29 months (3.68,9.23)**

OS



Median overall survival was not reached.

- 6-month OS rate 85.6%
- 12-month OS rates 69.7%

Summary

The bispecific antibody, KN046 was well tolerated and effective as 2nd line treatment of advanced NSCLC. KN046 showed promising PFS and OS benefit in squamous NSCLC

- ✓ Grade ≥3 related TRAEs were experienced in 24 out of 64 patients (37.5%).
- ✓ Confirmed objective responses rate was 11.7%. Disease control rate is 70 %.
- ✓ With a median follow up of 13 months, median progression free survival was 3.68 months (95%CI 3.35, 7.29): 7.29 months (3.68,9.23) and 3.58 months (2.46,5.52) for sq-NSCLC and non-sq NSCLC, respectively.
- ✓ Median overall survival was not reached. 6 and 12-month OS rates were 85.6% and 69.7%, respectively.