1293P: KN046 (an anti-PD-L1/CTLA-4 Bispecific Antibody) in combination with Platinum doublet chemotherapy as first-line(1L) treatment in patients with advanced NSCLC harboring resistant oncogenic driver alterations

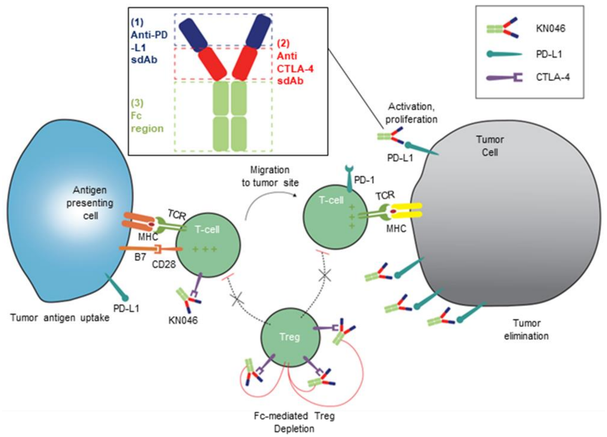
*Wenfeng Fang[1#], Yunpeng Yang[1#], Yan Huang[1], Xingya Li[3], Siyuan Huang[3], Jingxun Wu[4], Yibin Li[4], Baoping Chang[5], Sheng Hu[6], Shujun Yang[7], June Xu[2], Hardy Van[2], Lihua Zhi[2], Yue Xia[2], Lily Li[2], Fei Yang[2], Yi Xia[2], Ting Xu[2], Li Zhang[1]**

Author Affiliations: 1. Sun Yat-sen University Cancer Center, guangzhou, guangdong, China; 2. Jiangsu Alphamab Biopharmaceuticals Co.,Ltd., Suzhou, China; 3. The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan, China; 4. The First Affiliated Hospital of Xiamen University, Xiamen, Fujian, China; 5. First Affiliated Hospital of Henan University of Science and Technology, Luoyang, Henan, China; 6. Hubei Cancer Hospital, Wuhan, Hubei, China; 7. The AffiliatedCancer Hospital of Zhengzhou University &Henan Cancer Hospital, Zhengzhou, Henan, China

*Contact: zhangli@sysucc.org.cn #: co-first author The first author has no conflicts of interest.

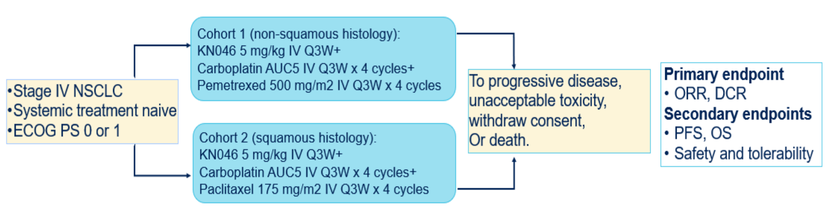
BACKGROUND

- KN046 bifunctionally targets CTLA-4 and PD-L1.
- Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity.
- IgG1 Fc domain, CTLA-4 blocking-mediated Treg cells depletion.
- KN046 in combination with platinum doublet chemotherapy as 1L therapy showed promising efficacy and acceptable safety in stage IV NSCLC patients.



STUDY DESIGN

- Efficacy evaluation was performed by investigators per RECIST 1.1.
- Safety and tolerability were assessed per NCI-CTCAE v5.0.
- Patients from the two cohorts with systemic treatment naive, stage IV NSCLC harboring a driver oncogenic alteration were enrolled.



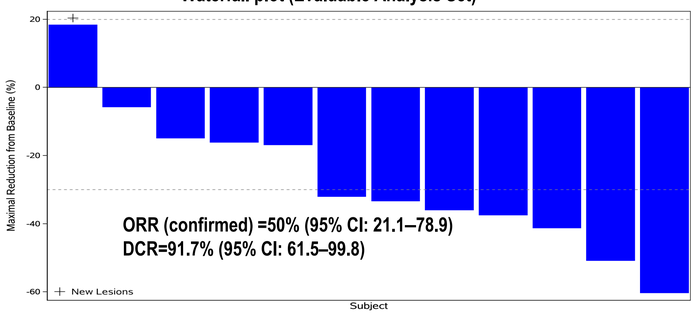
Demographics & Baseline characteristics

Parameters	Total (N =12)
Gender, n (%)	
Male	4 (33.3%)
Female	8 (66.7%)
Age (years)	
Mean (SD)	55.3 (8.03)
Median (Min, Max)	53.0 (44, 69)
ECOG, n (%)	
0	2 (16.7%)
1	10 (83.3%)
Primary Tumor Type	
Squamous Carcinoma	1 (8.3%)
Non-Squamous Carcinoma	11 (91.7%)
Mutation	
EGFR exon 20 insertion mutation	8 (66.7%)
HER2 exon 20 insertion mutation	1 (8.3%)
EGFR amplification	2 (16.7%)
RET fusion	1 (8.3%)

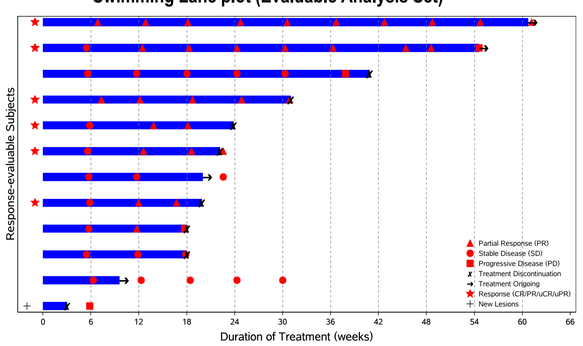
Safety (TEAE ≥ Grade 3)

Preferred Term	Grade ≥ 3
Subjects with at least 1 KN046 Related CTCAE Grade ≥ 3 TEAE	9 (75.0%)
Alanine aminotransferase increased	3 (25.0%)
Anaemia	2 (16.7%)
Aspartate aminotransferase increased	2 (16.7%)
Neutrophil count decreased	4 (33.3%)
White blood cell count decreased	2 (16.7%)
Platelet count decreased.	1 (8.3%)
Epilepsy	1 (8.3%)
Immune-mediated pneumonitis	1 (8.3%)
Hypertension	1 (8.3%)
Infusion related reaction	1 (8.3%)
Back pain	1 (8.3%)

Waterfall plot (Evaluable Analysis Set)



Swimming Lane plot (Evaluable Analysis Set)



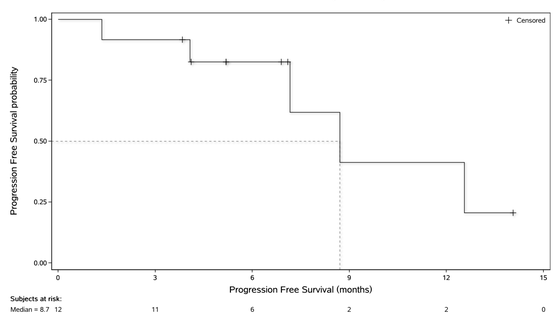
RESULTS

- As of January 19, 2021, 12 pts (EGFR exon 20 insertion mutation, n=8; HER2 exon 20 insertion mutation, n=1; EGFR amplification, n=2; RET fusion, n=1) were enrolled.
- Median age was 53 (range: 44, 69). 66.7% were females. The median treatment duration of KN046 was 21 weeks.
- ORR (confirmed PR) was 50% (6/12; 95% CI: 21.1–78.9). Disease control rate (DCR) was 91.7% (11/12; 95% CI: 61.5–99.8). 5 pts had best response of SD and 1 patient had PD. Median PFS was 8.7 months (95% CI: 4.1, NE). Median overall survival (OS) was not reached, and OS rate was 100% at 6 months.
- The most common TEAEs (≥ Grade 3) were neutrophil count decreased (n=4, 33.3%), alanine aminotransferase increased (n=3, 25.0%), anaemia (n=2, 16.7%), white blood cell count decreased (n=2, 16.7%), aspartate aminotransferase increased (n=2, 16.7%). 5 (41.7%) pts experienced irAEs, all were of Grade 1 or 2.

CONCLUSION

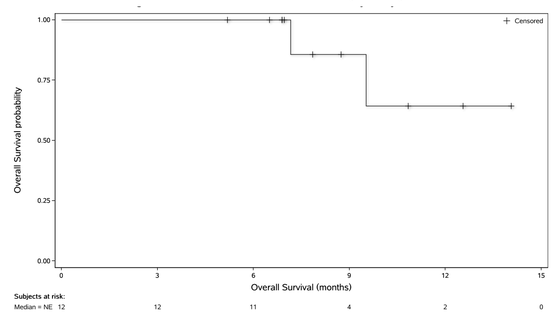
- KN046 combined with platinum-based chemotherapy is well tolerated and has demonstrated promising, albeit preliminary anti-tumor activity as 1L treatment for stage IV NSCLC pts with resistant oncogenic driver alterations.

K-M Plot of PFS Safety Analysis Set



Median PFS was 8.7 months (95% CI: 4.1, NE)

K-M Plot of OS Safety Analysis Set



OS rate was 100% at 6 months