Efficacy and safety of KN046 plus paclitaxel/cisplatin as first-line treatment for unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC)

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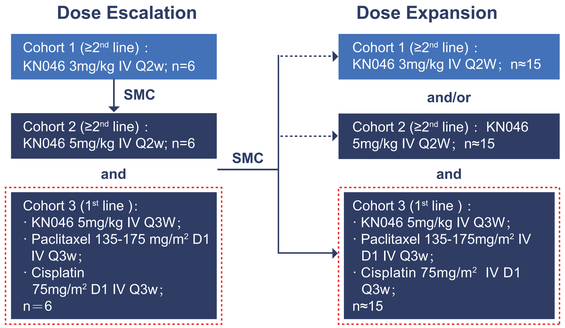
Background

- The prognosis of pts with advanced esophageal squamous cell carcinoma (ESCC) remains dismal clinically.[1-2]
- Paclitaxel and cisplatin were used as the standard first-line regimen in ESCC for almost two decades.[3]
- Recently, the combination of PD-1/PD-L1 pathway blockades with chemotherapy has shown synergistic efficacy in a few clinical trials. [4-6]
- KN046, a novel recombinant humanized bispecific antibody, can simultaneously block PD-1/PD-L1 and CTLA-4 pathways and restore T-cell immune response to tumor.
- The purpose of this ongoing phase II trial was to evaluate the efficacy and safety of KN046 monotherapy or combined with chemotherapy for unresectable locally advanced, recurrent or metastatic ESCC.

Study Design

- The study conducted at 10 sites in China (NCT03925870). Cohort 3 enrolled systemic treatment naïve pts with histologically or cytologically confirmed unresectable locally advanced, recurrent or metastatic ESCC who have ECOG PS of 0-1.



SMC, scientific monitoring committee.

Results

- **Patient characteristics and treatment exposures.**

  As of January 14, 2021, 15 subjects in Cohort 3 received at least one dose of KN046 treatment, and 12 subjects was ongoing. Median KN046 exposure time was 9 wks (range: 4.3-23.0).

Table 1 baseline characteristics

Cohort 3 (N = 15)			
Gender		**ECOG**	
Male	15 (100%)	0	4 (26.7%)
Female	0	1	11 (73.3%)
Age(year)		**Clinical stage**	
Median	63.0	IIIb	3 (20.0%)
Min,Max	51, 77	IV	12 (80.0%)
Ethnic		**Lesions**	
Han	14 (93.3%)	<2	1 (6.7%)
Non-Han	1 (6.7%)	≥2	14 (93.3%)
BMI(kg/m²)		**Previous antitumor therapy**	
Median	20.43	Radiation	1 (6.7%)
Min,Max	17.7, 28.1	Operation	4 (26.7%)
		Chemotherapy	4 (26.7%)

- **Efficacy**

  In Cohort 3, 12 subjects received at least one tumor assessment and entered the evaluable analysis set (EAS). The overall response rate (ORR) and disease control rate (DCR) were 58.3% and 91.7%, respectively. 7 pts (58.3%) had partial response (PR) including one complete response of target lesion. 4 pts (33.3%) had stable disease (SD) with 3 pts showing more than 20% of tumor burden reduction.

Table 2 Summary of efficacy

Cohort 3(N = 12)	
Best overall response	
Partial response (PR)	4 (33.3%)
Unconfirmed partial response (uPR)	3 (25.0%)
Stable disease (SD)	4 (33.3%)
Progressive disease (PD)	1 (8.3%)
Objective response rate (ORR)	7 (58.3%)
95% CI	21.1%, 78.9%
Disease control rate (DCR)	11 (91.7%)
95% CI	61.5%, 99.8%

Notes: 1. ORR = CR + PR + uCR + uPR; 2. DCR = CR + PR + uCR + uPR + SD ≥ 35 days.

Figure 1 Waterfall plot of Cohort 3 (EAS)

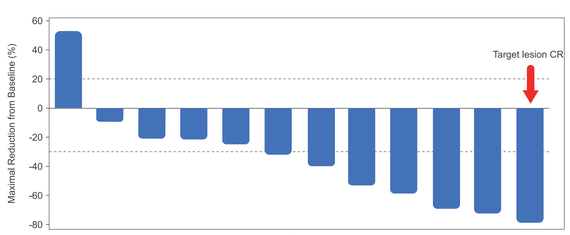


Figure 2 Swimming lane plot of Cohort 3 (EAS)

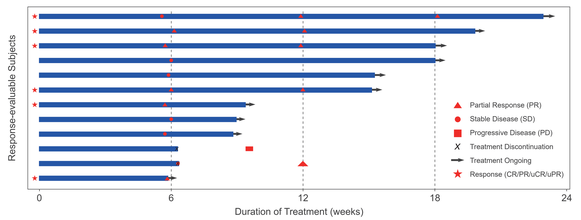
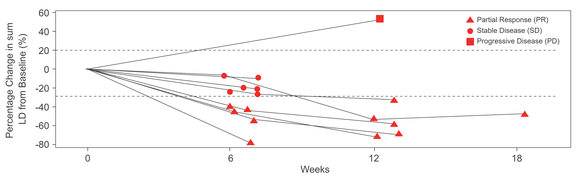


Figure 3 Spider plot of Cohort 3 (EAS)



- **Safety**

  The overall incidence of KN046 related adverse events was 80.0%, with 13.3% Gr 3 or above TRAE. Infusion-related adverse events occurred during 7.8% and most were mild. Immune related adverse events (irAE) were seen in 53.3% and the most common Gr 3 irAE were nausea (n=1, 6.7%) and rash (n=1, 6.7%).

Table 3 Overview of treatment-emergent adverse events

Cohort 3(N = 15)	Grade≥3	Total
Number of TEAE	13	167
Subjects with at least 1 TEAE	10 (66.7%)	15 (100%)
Related to KN046	2 (13.3%)	12 (80.0%)
Subjects with at least 1 CTCAE Grade≥ 3 TEAE	10 (66.7%)	10 (66.7%)
Related to KN046	2 (13.3%)	2 (13.3%)
Subjects with at least 1 IRR	0	3 (20.0%)
Subjects with at least 1 irAE	2 (13.3%)	8 (53.3%)
Subjects with at least 1 CTCAE Grade≥ 3 irAE	2 (13.3%)	2 (13.3%)
Subjects with at least 1 SAE during treatment	5 (33.3%)	5 (33.3%)
Related to KN046	0	1 (6.7%)
Subjects with at least 1 CTCAE Grade ≥3 SAE during treatment	5 (33.3%)	5 (33.3%)
Related to KN046	0	0
Subjects with at least 1 TEAE Leading to Withdrawn	1 (6.7%)	2 (13.3%)
Related to KN046	0	1 (6.7%)
Subjects with at least 1 TEAE Leading to Death	1 (6.7%)	1 (6.7%)
Related to KN046	0	0

Note: Percentages are based on the number of subjects who received at least one dose of KN046.

Conclusion

- KN046 plus paclitaxel/cisplatin demonstrated clinical efficacy and acceptable safety as first-line treatment, and might be a favorable option for pts with advanced ESCC. Clinical trial information: NCT03925870. Research Sponsor: Jiangsu Alphamab Biopharmaceuticals Co., Ltd.

References

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- All authors contributed to and approved the presentation.

Conflicts of interest

- I have no financial relationships to disclose
- Please address any questions or comments regarding this poster to jmxu2003@163.com