Efficacy and safety of KN046 plus nab-paclitaxel/gemcitabine as first-line treatment for unresectable locally advanced or metastatic pancreatic ductal adenocarcinoma(PDAC)

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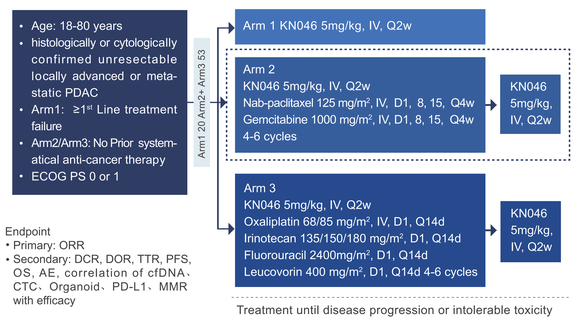
Background

- Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies worldwide and is characterized by extremely poor prognosis.[1-2]
- Nab-paclitaxel plus gemcitabine has been recommended by international guidelines for first-line treatment of advanced PDAC but chemoresistance is difficult to avoid.[3-4]
- Combination of immune checkpoint inhibitors (ICIs) and chemotherapy has demonstrated substantial promise for the treatment of several advanced malignancies. A few recent studies have begun to explore the effect of ICIs monotherapy or combo in advanced PDAC with few meaningful results.[5-6]
- 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 study is to evaluate the efficacy and safety of KN046 plus nab-paclitaxel/gemcitabine as first-line treatment for unresectable locally advanced or metastatic PDAC.

Study Design

- The study conducted at 3 sites in China (NCT04324307)



PDAC, pancreatic ductal adenocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; DCR, disease control rate; TTR, time to response; PFS, progression free survival; OS, overall survival.

Results

- **Patient characteristics and treatment exposures**

  As of January 15, 2021, 17 subjects in Arm 2 received at least one dose of KN046 treatment, and 15 subjects was ongoing. Median KN046 exposure time was 9.5 wks (range: 2.0-23.7).

Table 1 baseline characteristics

Arm 2 (N = 17)			
Gender		**ECOG PS**	
Male	7 (41.2%)	0	8 (47.1%)
Female	10 (58.8%)	1	9 (52.9%)
Age(year)		**Clinical stage**	
Median	56.0	III	9 (52.9%)
Min,Max	36, 75	IV	8 (47.1%)
Ethnic		**Hepatic metastases**	
Han	16 (94.1%)	Yes	7 (41.2%)
Non- Han	1 (5.9%)	No	10 (58.8%)
BMI(kg/m²)		**Lesions**	
Median	22.68	<2	8 (47.1%)
Min,Max	19.0, 29.7	≥2	9 (52.9%)

- **Efficacy**

  In Arm 2, 9 subjects received at least one tumor assessment and entered the evaluable analysis set (EAS). In best overall response assessment, there were 55.6% PR (5/9) and 33.3% SD (3/9). ORR was 55.6% (95% CI: 21.2~86.3), and DCR was 88.9% (95% CI: 51.8~99.7). Table 2.

Table 2 Summary of efficacy

Arm 2 (N = 9)	
Best overall response	
Partial response (PR)	3 (33.3%)
Unconfirmed partial response (uPR)	2 (22.2%)
Stable disease (SD)	3 (33.3%)
Progressive disease (PD)	1 (11.1%)
Objective response rate (ORR)	5 (55.6%)
95% CI	21.2%, 86.3%
Disease control rate (DCR)	8 (88.9%)
95% CI	51.8%, 99.7%

Notes: 1. ORR = CR + PR + uCR + uPR; 2. DCR = CR + PR + uCR + uPR + SD ≥ 42 days.

Figure 1 Waterfall plot of Arm 2 (EAS)

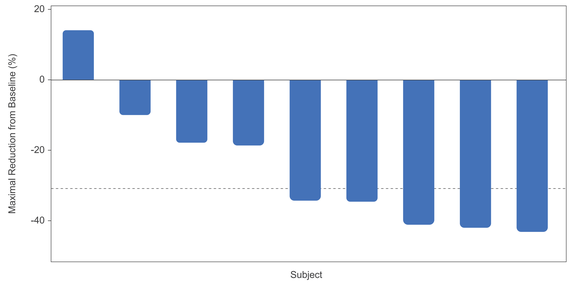


Figure 2 Swimming lane plot of Arm 2 (EAS)

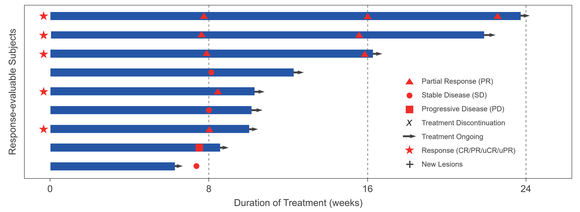
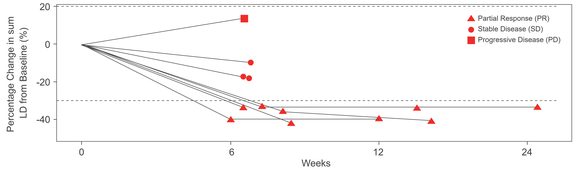


Figure 3 Spider plot of Arm 2 (EAS)



- **Safety**

  The most common KN046 related treatment-emergent adverse events (≥10%) were alanine aminotransferase increased (n=5, 29.4%), nausea (n=3, 17.6%), rash (n=3, 17.6%), aspartate aminotransferase increased (n=2, 11.8%), diarrhoea (n=2, 11.8%), hyperphosphataemia (n=2, 11.8%), pyrexia (n=2, 11.8%), vomiting (n=2, 11.8%).

Table 3 Overview of treatment-emergent adverse events

Arm 2 (N=17)	Grade≥3	Total
Number of TEAE	27	239
Subjects with at least 1 TEAE	11 (64.7%)	16 (94.1%)
Related to KN046	5 (29.4%)	11 (64.7%)
Subjects with at least 1 CTCAE Grade≥ 3 TEAE	11 (64.7%)	11 (64.7%)
Related to KN046	5 (29.4%)	5 (29.4%)
Subjects with at least 1 IRR	0	1 (5.9%)
Related to KN046	0	1 (5.9%)
Subjects with at least 1 irAE	2 (11.8%)	2 (11.8%)
Related to KN046	2 (11.8%)	2 (11.8%)
Subjects with at least 1 CTCAE Grade≥ 3 irAE	2 (11.8%)	2 (11.8%)
Related to KN046	2 (11.8%)	2 (11.8%)
Subjects with at least 1 SAE during treatment	4 (23.5%)	4 (23.5%)
Related to KN046	1 (5.9%)	1 (5.9%)
Subjects with at least 1 CTCAE Grade ≥ 3 SAE during treatment	4 (23.5%)	4 (23.5%)
Related to KN046	1 (5.9%)	1 (5.9%)
Subjects with at least 1 TEAE Leading to Withdrawn	0	0
Related to KN046	0	0
Subjects with at least 1 TEAE Leading to Death	0	0
Related to KN046	0	0

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

Conclusion

- Combining KN046 with nab-paclitaxel and gemcitabine as first-line treatment for unresectable locally advanced or metastatic PDAC patients is safe and feasible, and lays the foundation for subsequent clinical trials.

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Conflicts of interest

- I have no financial relationships to disclose
- Please address any questions or comments regarding this poster to jingang@smmu.edu.cn