# KN046 (an anti-PD-L1/CTLA-4 Bispecific Antibody) in combination with Lenvatinib in the treatment for advanced unresectable or metastatic hepatocellular carcinoma (HCC): preliminary efficacy and safety results of a prospective phase II trial

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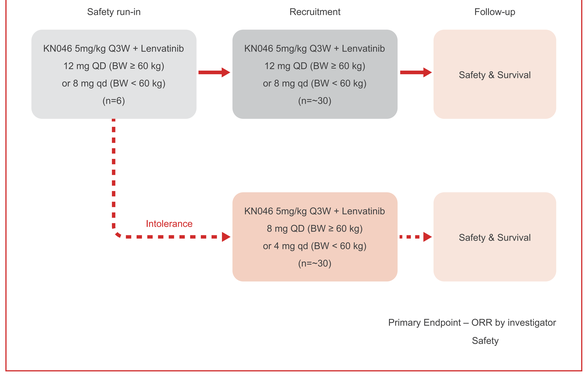
## BACKGROUND

- The combination of anti-angiogenic therapy and immune checkpoint inhibitor therapy creates a positive feedback loop between vascular normalization and immune remodeling in the treatment of hepatocellular carcinoma (HCC) [1].
- Though demonstrated longer OS (19.2m) in IMbrave150 study, the ORR(29.8%) is unmet clinical need to further improve ORR in conversion treatment for unresectable HCC [2].
- Here we assessed the safety and efficacy of KN046 in combination with Lenvatinib in 1st line HCC treatment.

## STUDY DESIGN




## RESULTS

- 25 pts enrolled with unresectable BCLC stage B or stage C and Child-Pugh score ≤7 had received Lenvatinib 12 mg/day (bodyweight [BW] ≥60 kg) or 8 mg/day (BW<60 kg) orally and KN046 5 mg IV on Day 1 of a 21-day cycle until disease progression or intolerable toxicity or 2 years.
- The median duration of combination treatment was 10 weeks. As of cutoff date, only two pts discontinued treatments, one for disease progression and one for pneumonitis.
- For 21 evaluable pts, ORR was 57% (95% CI 34.0%-78.2%) and DCR was 95% (95% CI 76.2%-99.9%) by RECIST v1.1 and imRECIST criteria. When evaluated by mRECIST, ORR and DCR improved to 76.2% (95% CI 52.8%-91.8%) and 95% (95% CI 76.2%-99.9%), respectively.
- Treatment-emergent adverse events (TEAEs) occurred in 64% (16/25) of pts, 20% (5/25) was ≥grade 3. The incidence of ≥grade 3 TEAE related with KN046 was 8%, including pneumonitis (n=1, 4.0%) and platelet count decreased (n=1, 4.0%).

### Baseline characteristics

| | KN046 5 mg/kg Q3W + Lenvatinib 12 mg QD (N=15) | KN046 5 mg/kg Q3W + Lenvatinib 8 mg QD (N=10) | Total (N=25) |
|---|---|---|---|
| ECOG | | | |
| 0 | 14(93.3%) | 10(100%) | 24(96.0%) |
| 1 | 1(6.7%) | 0 | 1(4.0%) |
| BCLC | | | |
| B | 2(13.3%) | 2(20.0%) | 4(16.0%) |
| C | 13(86.7%) | 8(80.0%) | 21(84.0%) |
| PVTT | | | |
| No | 10(66.7%) | 7(70.0%) | 17(68.0%) |
| Yes | 5(33.3%) | 3(30.0%) | 8(32.0%) |
| EHS | | | |
| No | 9(60.0%) | 7(70.0%) | 16(64.0%) |
| Yes | 6(40.0%) | 3(30.0%) | 9(36.0%) |
| Prior treatment | | | |
| Surgery | 2(13.3%) | 2(20.0%) | 4(16.0%) |
| Radiation | 2(13.3%) | 0 | 2(8.0%) |
| Intervention | 2(13.3%) | 1(10.0%) | 3(12.0%) |
| Others | 2(13.3%) | 0 | 2(8.0%) |
| HBV | | | |
| No | 3(20%) | 0(0%) | 3(12.0%) |
| Yes | 12(80%) | 10(100.0%) | 22(88.0%) |

Cutoff date 2021/4/8

### Safety-Summary of AEs observed in SS

| | KN046 5 mg/kg Q3W + Lenvatinib 12 mg QD (N=15) | | KN046 5 mg/kg Q3W + Lenvatinib 8 mg QD (N=10) | | Total (N=25) | |
|---|---|---|---|---|---|---|
| | ≥ Gr 3 | total | ≥Gr 3 | total | ≥Gr 3 | total |
| TEAE | 3(20.0%) | 9(60.0%) | 2(20.0%) | 7(70.0%) | 5(20.0%) | 16(64.0%) |
| KN046 related | 1(6.7%) | 8(53.3%) | 1(10.0%) | 7(70.0%) | 2(8.0%) | 15(60.0%) |
| Lenvatinib related | 3(20.0%) | 7(46.7%) | 2(20.0%) | 7(70.0%) | 5(20.0%) | 14(56.0%) |
| IRR | 0 | 3(20.0%) | 0 | 3(30.0%) | 0 | 6(24.0%) |
| irAE | 0 | 1(6.7%) | 1(10.0%) | 1(10.0%) | 1(4.0%) | 2(8.0%) |
| SAE | 0 | 0 | 1(10.0%) | 2(20.0%) | 1(4.0%) | 2(8.0%) |
| KN046 related | 0 | 0 | 1(10.0%) | 1(10.0%) | 1(4.0%) | 1(4.0%) |
| Lenvatinib related | 0 | 0 | 1(10.0%) | 2(20.0%) | 1(4.0%) | 2(8.0%) |
| TEAE led to discontinuation | 0 | 0 | 1(10.0%) | 1(10.0%) | 1(4.0%) | 1(4.0%) |
| KN046 related | 0 | 0 | 1(10.0%) | 1(10.0%) | 1(4.0%) | 1(4.0%) |
| Lenvatinib related | 0 | 0 | 1(10.0%) | 1(10.0%) | 1(4.0%) | 1(4.0%) |

Cutoff date 2021/4/8

### Safety-Summary of ≥Gr3 TEAEs

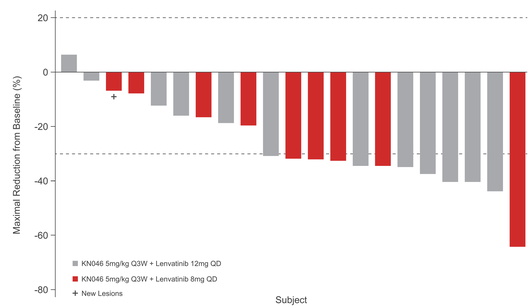
| | KN046 5 mg/kg Q3W + Lenvatinib 12 mg QD (N=15) | KN046 5 mg/kg Q3W + Lenvatinib 8 mg QD (N=10) | Total (N=25) |
|---|---|---|---|
| | total | total | total |
| N (%) | 3(20.0%) | 2(20.0%) | 5(20.0%) |
| Hypertension | 1(6.7%) | 1(10.0%) | 2(8.0%) |
| Hypercholesterolaemia | 0 | 1(10.0%) | 1(4.0%) |
| Pneumonitis* | 0 | 1(10.0%) | 1(4.0%) |
| Blood potassium decreased | 1(6.7%) | 0 | 1(4.0%) |
| Platelet count decreased* | 1(6.7%) | 0 | 1(4.0%) |
| Blood pressure increased | 1(6.7%) | 0 | 1(4.0%) |

* Pneumonitis and Platelet count decreased were KN046 related TEAE.

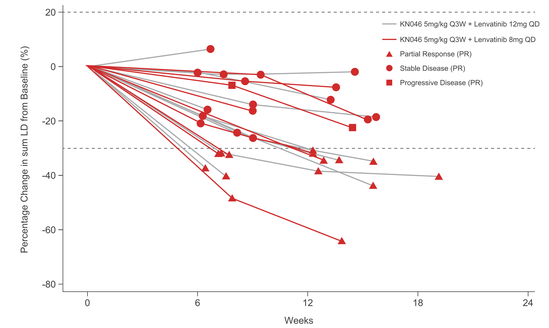
### Efficacy-Overall response

| | RECIST1.1 | mRECIST | imRECIST |
|---|---|---|---|
| ORR, n(%) | 12(57.1%) | 16(76.2%) | 12(57.1%) |
| 95%CI | 34.0%, 78.2% | 52.8%, 91.8% | 34.0%, 78.2% |
| CR | 0 | 1(4.8%) | 0 |
| PR | 2(9.5%) | 7(33.3%) | 2(9.5%) |
| uPR | 10(47.6%) | 8(38.1%) | 10(47.6%) |
| DCR, n(%) | 20(95.2%) | 20(95.2%) | 20(95.2%) |
| 95%CI | 76.2%, 99.9% | 76.2%, 99.9% | 76.2%, 99.9% |

### Efficacy-waterfall plot




### Efficacy-spider plot




## CONCLUSION

- The combination of KN046+Lenvatinib in HCC is tolerable and has an acceptable safety profile.
- KN046+Lenvatinib in 1st line HCC treatment showed promising antitumor activity with high ORR evaluated by RECIST 1.1, that provide chances for conversion treatment.
- Clinical trial information: NCT04542837.

## REFERENCE

1 Fukumura D, et al. Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges. Nat. Rev. Clin. Oncol. 15(5), 325–340 (2018)

2 Finn RS, et al. . IMbrave150: Updated overall survival (OS) data from a global, randomized, open-label phase III study of atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC). 2021ASCO GI，abs267.

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- All authors contributed to and approved the presentation

## DISCLOSURES

All authors declare no conflict of interest.

Please address any questions or comments regarding this poster to xingbaocai88@sina.com