Abstract #299429

The preliminary efficacy and safety data of KN046 in patients failed on prior immune checkpoint inhibitors therapy

Hongyun Zhao, Yuxiang Ma, Yang Zhang, Shaodong Hong, Yunpeng Yang, Wenfeng Fang, June Xu, Hardy Van, Paul Kong, Fei Yang, Jingying Li, Yao Lu, Li Zhang; Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Sun Yat-sen University, Guangzhou, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; Alphamab Oncology, Suzhou, China

Background:
KN046 is a bispecific antibody that blocks PD-L1 and CTLA-4 by interaction with PD1 and CD80/CD86. KN046-CHN-001 (NCT03529526) is a, dose escalation and expansion phase Ia/Ib clinical trial in China. Here we reported safety, tolerability and preliminary efficacy in patients failed on prior immune checkpoint inhibiters (ICIs) treatment.

Methods:
Patients progressed on ICIs (including but not limited to antibodies targeting PD-1, PD-L1, OX40, et al) with pathologically confirmed solid tumor, ECOG 0-1, measurable lesion per RECIST v1.1, no immune-related adverse events (IRAEs) led to ICIs discontinuation, were enrolled and received intravenous KN046 treatment across four dose levels including 3.0 mg/kg (n = 3) and 5.0 mg/kg (n = 20) Q2W; and 5.0 mg/kg (n = 4), 300.0 mg flat dose (n = 2) Q3W. Safety and tolerability were assessed per NCI-CTCAE v5.0. Treatment-emergent AEs (TEAEs) and IRAEs were decided by investigators. Efficacy was evaluated by investigators per RECIST 1.1 every 6 weeks.

Results:
Twenty-nine who progressed on prior ICIs therapy were enrolled (25anti-PD-1 antibody; 3 anti-OX40 antibody; and 1 anti-CD137 antibody) and were included in the current analysis. Among 29 patients, 19 were nasopharyngeal cancer (NPC) and 9 were non-small cell lung cancer (NSCLC). The median duration of the exposure of KN046 was 12 weeks (range 2 to 40). Eleven patients remained on the treatment and 18 discontinued due to disease progression (n = 13), AE (n = 1), death (n = 1) and others (n = 3). Twenty-six (89.7%) patients experienced TRAEs of all grades and 2 (6.9%) experienced grade≥3 TRAEs (1 grade 3 anemia and 1 grade 3 infusion-related reaction). The most common (≥10%) TRAEs were pruritus (8, 27.6%), rash (8, 27.6%), asthenia (6, 20.7%), fatigue (6, 20.7%), pyrexia (5, 17.2%), infusion related reaction (4, 13.8%), alanine aminotransferase elevation (3, 10.3%) and white blood cell count elevation (3, 10.3%). Eleven (37.9%) patients experienced irAEs (with no grade≥3). Objective responses were occurred in 3 (12.0%, 25 evaluable) patients, disease control rate was 52.0% (10 stable disease). Median progression free survival was 2.69 (95%CI 1.31,5.52) months. Median overall survival was not reached. PFS rates for 3 and 6 Months were 41.0% (95%CI 18.5, 62.5) and 21.9% (95%CI 4.6, 47.3). OS rates for 6 and 9 months were88% (95%CI 57.2, 97.1) and 58.7% (95%CI 8.3, 89.2), respectively.

Conclusions:
Overall, KN046 showed a favorable safety profile and promising clinical benefit in advanced solid tumor patients who failed on prior ICIs therapy.