Abstract #300841

Preliminary safety, efficacy and pharmacokinetics (PK) results of KN026, a HER2 bispecific antibody in patients (pts) with HER2-positive metastatic breast cancer

Dongmei Ji, Jian Zhang, Weina Shen, Yiqun Du, June Xu, Jing Yang, Xin Luo, Paul Kong, Fei Yang, Xi-Chun Hu; Fudan University Shanghai Cancer Center, Shanghai, China; Alphamab Oncology, Suzhou, China; Fudan University Cancer Hospital, Shanghai, China

Background:
KN026 is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes, the same domains as trastuzumab (ECD4) and pertuzumab (ECD2). It blocks ligand-dependent and independent tumor growth and enhances HER2 receptor internalization. In preclinical studies, KN026 showed activity in trastuzumab plus pertuzumab resistant tumor cell lines. This first-in-human study evaluated the safety/tolerability, pharmacokinetics (PK), and preliminary efficacy of KN026 monotherapy.

Methods:
This dose-escalation and expansion study enrolled Chinese patients (pts) with metastatic breast cancer who have failed prior anti-HER2 therapy. All pts intravenously received KN026 monotherapy at ascending dose of 5 mg/kg (QW), 10 mg/kg (QW), 20 mg/kg (Q2W) or 30 mg/kg (Q3W). Dose limiting toxicity (DLT) evaluation period was 28 days for QW and Q2W, and 21 days for Q3W. Efficacy evaluation was performed by RECIST 1.1 every 6 weeks and safety assessment according to CTCAE v 4.03.

Results:
As of the Jan 22, 2020, 63 pts [median age: 54 years (31~69)] enrolled and 62 pts were included in the efficacy analysis. 41 pts remained on treatment and 22 pts discontinued treatment due to disease progression (n = 21) and adverse events (n = 1). The median treatment duration was 12 weeks (range: 4~62 weeks). Median prior lines of therapies are 3 (range: 1~15), and median prior lines of HER2 target therapies are 2 (range: 1~12). No DLTs were observed. Treatment-related AEs (TRAEs) occurred in 49 pts and 4 pts experienced 4 grade 3 TRAE (hypertension, infusion related reaction, transaminases increased and ventricular arrhythmia). The common (≥ 10%) TRAE were pyrexia (23.8%), diarrhea (19.0%), aspartate aminotransferase increased (15.9%), neutrophil count decreased (11.1%) and white blood cell count decreased (11.1%). The objective response rate at recommended Phase 2 dose levels (n = 56) was 32.1% (95% CI 20.3, 46.0) and disease control rate 76.8% (95% CI 63.6, 87.0). Pharmacokinetic analysis showed exposure (C_{max} and AUC_{0-t}) of KN026 increased by dose. The recommended Phase 2 dose (RP2D) were 20 mg/kg Q2W and 30 mg/kg Q3W.

Conclusions:
KN026 is well tolerated and has demonstrated encouraging anti-tumor activity in HER2-positive breast cancer patients who have failed standard anti-HER2 therapies. The recommended Phase 2 dose (RP2D) of KN026 were 20 mg/kg Q2W and 30 mg/kg Q3W. Phase II trials in various HER2-positive and HER2-low/intermediate solid tumors are currently ongoing.