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The preliminary efficacy of KN026 (Anti-HER2 BsAb) in advanced gastric and gastroesophageal junction cancer patients with HER2 expression.

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Background:
HER2 overexpression or amplification has been proven to be a validated therapeutic target for HER2-positive gastric and gastroesophageal junction cancer (GC/GEJ) in ToGA trial. However, there is a huge unmet medical need in the HER2-positive GC/GEJ patients who progressed or were refractory to trastuzumab treatment. In HER2 low expression patients, the benefit of novel HER2-targeted therapeutics, eg. Bispecifics, ADC and CAR-T, remain to be explored. Here we report the preliminary results of KN026, a bispecific antibody binds two distinct epitopes of HER2 receptors, in GC/GEJ patients with prior at least one line treatment.

Methods:

GC/GEJ patients who failed to ≥first-line treatment were enrolled into two cohorts according to HER2 overexpression (Cohort 1: IHC3+ or IHC 2+ ISH+) and low expression (Cohort 2: IHC 1+/2+ ISH- or IHC 0/1+ISH+), and treated by KN026 QW10mpkor Q2W(20mpk) or Q3W(30mpk) until progression of disease (PD) or intolerable toxicity or 2 years.

Results:

As of 2020/12/25, a total of 31 pts received KN026 treatment including 20 pts in Cohort 1 and 11 pts in Cohort 2. The median drug exposure period was around 20 wks and 6 wks in two Cohorts, respectively. Among 18 efficacy-evaluable pts in Cohort 1, 11 pts were stilling receiving treatment with 55.6% (10/18) ORR and 72.2% DCR (13/18). The 9-m PFS rate was 60.4% (95%CI: 24.4 to 83.5) in Cohort 1, while the DOR, mPFS and mOS were not reached. Of 9 pts receiving prior-HER2 treatment, the median time from the first dose of KN026 to last prior HER2 treatment was 55 days. The ORR was 44.4% (4/9) with 4.1m DoR, and DCR was 66.7% (6/9). The mPFS and mOS were 5.6m(95%CI: Print E) and 11.0m(95%CI: 1.4 to NE), respectively. In Cohort 2, two partial response was observed out of 9 efficacy-evaluable pts. The ORR and DCR were both 22.2% (2/9) with 1.4 m mPFS (95%CI: 1.0 to 5.9) and 9.6m mOS (95%CI: 3.0 to NE). The overall incidence of KN026 related adverse events was 87.1%, with 9.7% Gr 3 TRAE. The most common KN026-related treatment emergent adverse events (≥10% TRAE) were aspartate aminotransferase increased (n=8,25.8%), rash (n=6,19.4%), anaemia (n=5,16.1%),alanine aminotransferase increased (n=4, 12.9%) and weight decreased(n=4, 12.9%). The ≥Gr 3 TEAE that KN026 related were infusion related reaction(n=1, 3.2%), blood pressure increased (n=1, 3.2%), ureteral stricture with hydronephrosis (n=1, 3.2%).

Conclusions:

KN026 demonstrated promising efficacy in HER2 overexpressing GC/GEJ pts and in anti-HER2 treated GC/GEJ pts with a favorable safety profile. Clinical trial number: NCT03925974. Clinical trial information: NCT03925974