**Study Design**

**Key eligibility criteria:**
- Metastatic or inoperable locally advanced gastrointestinal cancer
- HER2-positive, HER2-1/2 negative
- Pretreated or treatment naive

**Primary endpoint:**
- Dose escalation: DLT

**Secondary endpoint:**
- 6-month PFS rate (PFSR-6m), PFSR-12m, CBR
- 6-month OS rate (OSR-6m), OSR-12m
- AE

**Relationship between biomarker and clinical efficacy**

**Results**

- A total of 44 patients were enrolled, and there were 25, 3, 13 and 3 patients in dose level 1 (DL1), DL2, DL3 and DL4 respectively, 34 patients (77.3%) were HER2-positive.
- Out of 34 patients, median DOR was 5.1 months and PFSR-6m was 39.5%.
- The CBR was 85.8% in all 34 HER2-positive patients.

**Conclusions**

- **Kn046** is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes.
- **Kn026** is a novel bispecific antibody that blocks both PD-L1 interaction with PD-1 and CTLA-4/CD80/CD86.
- Both preclinical and clinical studies have suggested a coordination of engagement of innate and adaptive immunity with the combination of an anti-HER2 antibody and an immune checkpoint blockade.

**Efficacy Outcomes (HER2-positive patients)**

**Objective Response Rate (ORR)**

- First line: 71.4 (42.3, 77.1)%
- Late line: 52.4 (28.4, 73.7)%
- Overall: 60.0 (51.8, 68.2)%

**Duration of Response (DOR)**

- First line: 11.2 (4.1, NE) mo
- Late line: 11.2 (9.6, NE) mo
- Overall: 11.2 (4.1, NE) mo

**Overall Survival (OS)**

- First line: 93.3 (61.3, 99.0)%
- Late line: 79.5 (31.7, 95.5)%
- Overall: 85.7 (33.4, 97.9)%

**AEs**

- Anemia: 38.6%, Infusion reaction: 4.2%, Diarrhea: 3.9%

**Discussion**

- There were 34 patients with HER2 positive. 27 patients of them were evaluable, and the ORR was 77.3% for HER2-positive patients.
- The most commonly reported related TEAEs were anemia (38.6%), infusion related reaction (3.4%), AST increased (23.7%), ALT increased (25.0%) and rash (20.5%).

**Declaration: The first and presenting author has no conflicts of interest**