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The safety and efficacy of cadonilimab in combination with AK117 (anti-CD47 antibody) plus chemotherapy as first-line treatment for advanced gastric (G) or gastroesophageal junction (GEJ) cancer.

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Background: Despite the approval of anti-PD-1 antibodies plus chemotherapy as first-line (1L) therapy in advanced G/GEJ adenocarcinoma, benefit is very limited for patients (pts) with PD-L1 combined positive scores (CPS)$<$ 5; novel therapeutic approaches are needed. Cadonilimab, a tetrameric bispecific antibody targeting PD-1 and CTLA-4, combined with chemotherapy showed promising activity in untreated pts with advanced G/GEJ adenocarcinoma were presented in ASCO GI 2022 (abstract#308). AK117 is a novel humanized IgG4 anti-CD47 antibody without hemagglutination effect. Blockade of CD47-SIRPα pathway by AK117 leads to a promising therapeutic strategy for cancer treatment with favorable safety features. Here we report the safety and efficacy of Cadonilimab in combination with AK117 and chemotherapy in the 1L treatment of advanced G/GEJ adenocarcinoma. **Methods:** This was an open-label, multi-center phase II study evaluating the safety and efficacy of Cadonilimab +AK117+ XELOX as 1L therapy in advanced HER2(-) G/GEJ adenocarcinoma. Cadonilimab (10 mg/kg, IV, D1, Q3W) plus AK117 (45mg/kg, IV, D1, QW or 45mg/kg, IV, D1, Q3W) and Oxaliplatin (130 mg/m^2, IV, D1, Q3W) and Capecitabine (1000 mg/m^2, po, bid, D1-14, Q3W) were administered until disease progression or unacceptable toxicity. The primary endpoints were safety (CTCAE ver. 5.0) and objective response rate (ORR) by RECIST v1.1. Secondary endpoints included duration of response (DoR), disease control rate (DCR), time-to-response (TTR), progression-free survival (PFS) and overall survival (OS). **Results:** From Aug 4,2022 to Jan 13, 2023, 16 pts with advanced or metastatic G/GEJ adenocarcinoma were enrolled. Median age was 64 years (range 44-71), 75% male, 88% had ECOG 1, 100% with metastases (75% pts with$\geq$2 metastatic organs), and 25% pts with signet ring cell carcinoma component. Median follow-up time was 2.6 months. The incidence of treatment-related adverse events (TRAEs) was 43.8% (7/16), $\geq$grade 3 TRAEs occurred in 25% (4/16) pts including 18.8% (3/16) G3 and 6.3% (1/16) G4, respectively. 6.3% (1/16) pts experienced TRAEs leading to discontinuation. The most common TRAEs (incidence$\geq$10%) were anaemia, pyrexia and vomiting. Of 8 response-evaluable pts (had at least one post-baseline response evaluation) treated with Cadonilimab+AK117 (45mg/kg D1,QW)+XELOX, the ORR by investigator was 75% (6 PRs), tumor shrinkage exceeding 50% was observed in 5 pts (62.5%). The DCR was 100% (8/8), and the median DoR was not reached. The trial is ongoing, and additional data will be presented. **Conclusions:** The study of Cadonilimab combined with AK117 and chemotherapy demonstrated tolerable safety profile and encouraging anti-tumor activities in pts with unresectable locally advanced or metastatic HER2(-) G/GEJ cancer. Clinical trial information: NCT05235542. Research Sponsor: Akeso Biopharma, Inc.