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Sintilimab plus chemotherapy (chemo) versus chemo as first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16): First results of a randomized, double-blind, phase III study

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Background

ORIENT-16 is a randomized, double-blind, phase 3 trial to evaluate the efficacy and safety of sintilimab in combination with chemo (S+C) vs chemo (C) as the first-line treatment for patients (pts) with advanced G/GEJ adenocarcinoma. We report the first results from a pre-specified interim analysis.

Methods

Eligible pts were adults (≥18 years) with untreated, unresectable locally advanced or metastatic G/GEJ adenocarcinoma, regardless of PD-L1 expression. Pts were randomized 1:1 to receive sintilimab (3mg/kg and 200 mg, respectively, for body weights <60kg and ≥60kg, IV Q3W) or placebo plus chemo (CapeOX: oxaliplatin 130 mg/m^2 IV Q3W, up to 6 cycles, capecitabine 1000 mg/m^2 PO Bid d1-14 Q3W) for up to 24 months. The primary endpoints were OS in the pts with CPS ≥5 and all randomized pts. Data cutoff date for interim analysis was June 20, 2021.

Results

As of the cutoff date, 650 pts were randomized (327 in S+C and 323 in C), including 397 (61.1%) pts with CPS≥5. Median follow-up was 18.8 months (range 0.0-29.1). S+C showed a significant improvement in OS vs C in pts with CPS≥5 (median 18.4 vs 12.9 mo; HR 0.660; 95%CI 0.505-0.864; P =0.0023) and all pts (median 15.2 vs 12.3 mo; HR 0.766; 95%CI 0.626-0.936; P =0.0090). OS benefits were consistently observed at all pre-specified CPS cutoffs (CPS ≥1, 5, and 10). PFS was superior with S+C vs C in pts with CPS≥5 (HR 0.628; 95%CI 0.489-0.805; P =0.0002) and all pts (HR 0.636; 95%CI 0.525-0.771; p<0.0001). Unconfirmed ORR were 72.8% vs 59.6% in pts with CPS≥5 and 65.1% vs 58.7% in all pts with measurable disease, with a median DOR of 8.4 vs 5.5 and 8.6 vs 5.5 months, respectively. Among all treated pts, 196 (59.8%) of 328 in S+C and 168 (52.5%) of 320 in C experienced grade ≥3 treatment-related adverse events (TRAEs). TRAE leading to death were occurred in 6 (1.8%) pts in S+C and 2 (0.6%) in C.

Conclusions

Sintilimab is the first PD-1 inhibitor that demonstrated superior OS and PFS with an acceptable safety profile, in combination with chemo, in Chinese pts with G/GEJ cancer regardless of PD-L1 expressions. Sintilimab plus chemo provides a new standard first-line treatment option for these pts.

Clinical trial identification

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Legal entity responsible for the study

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Disclosure

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