Background: Pembrolizumab is FDA-approved for the treatment of pts with recurrent locally advanced or metastatic G/GJE adenocarcinoma whose disease has progressed on or after ≥2 prior therapies and whose tumors express PD-L1 (combined positive score ≥1). Combining chemo with pembrolizumab in the neoadjuvant/adjuvant setting may benefit pts with locally advanced, resectable G/GJE cancer. KEYNOTE-585 (NCT03221426) is a phase 3, randomized, double-blind study of chemo + pembrolizumab vs placebo as neoadjuvant/adjuvant treatment for locally advanced resectable G/GJE cancer.

Trial design: Eligibility criteria are age ≥18 years; previously untreated, resectable G/GJE adenocarcinoma (pts with Siewert type 1 tumors are eligible if initial treatment is planned perioperative chemo and resection), with no evidence of metastatic disease; planned surgery after perioperative chemo; adequate organ function; ECOG performance status 0/1; no active autoimmune disease. Pts will be randomly assigned 1:1 to receive cisplatin 80 mg/m² IV every 3 weeks (Q3W) (capped at 6 doses) plus 5-fluorouracil 800 mg/m² continuous IV on days 1-5 Q3W plus pembrolizumab Q3W for 3 cycles followed by surgery, then adjuvant chemo + pembrolizumab Q3W for 3 cycles or chemo + placebo Q3W for 3 cycles followed by surgery, then adjuvant chemo + placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 3 cycles.

Clinical trial identification: NCT03221426. Study start date was October 9, 2017.

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