Article details

Title of article
KEYNOTE-585: phase III study of perioperative chemotherapy with or without pembrolizumab for gastric cancer

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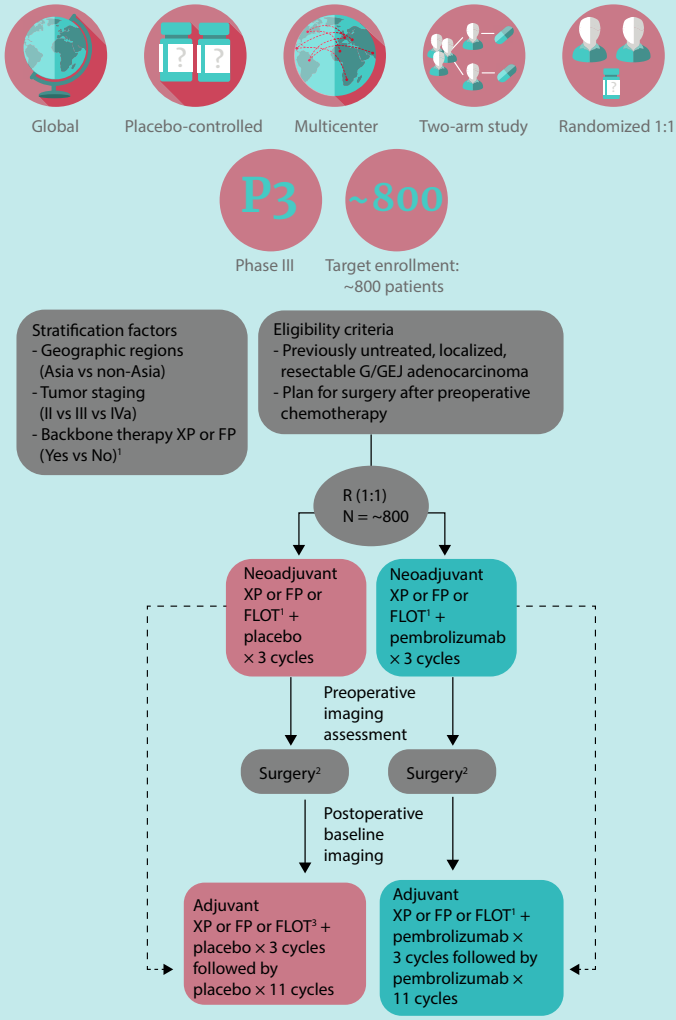
Trial registration number
NCT03221426

Primary objective/rationale

Primary objective
Evaluate OS, EFS, pCR, and safety and tolerability of pembrolizumab plus chemotherapy compared with placebo plus chemotherapy as neoadjuvant and/or adjuvant treatment for localized gastric or gastroesophageal junction adenocarcinoma

Secondary objectives
Evaluate safety and tolerability and DFS of pembrolizumab plus chemotherapy compared with placebo plus chemotherapy as neoadjuvant and/or adjuvant treatment for localized gastric or gastroesophageal junction adenocarcinoma

Study design and treatment including planned sample size, planned study period and study procedures



[1]If adequate safety is demonstrated with FLOT + pembrolizumab in the FLOT safety cohort. [2]Surgery will be performed within 3–6 weeks after the end of the last neoadjuvant cycle. [3]Adjuvant therapy will begin within 4–10 weeks after surgery.

Study design and treatment including planned sample size, planned study period and study procedures (cont)

Receive chemotherapy + pembrolizumab (arm 1) or chemotherapy + placebo (arm 2). Patients will receive neoadjuvant (preoperative) chemotherapy + pembrolizumab Q3W for 3 cycles or chemotherapy + placebo Q3W for 3 cycles followed by surgery, then adjuvant chemotherapy + pembrolizumab Q3W for 3 cycles or chemotherapy + placebo Q3W for 3 cycles, then monotherapy with pembrolizumab or placebo Q3W for 11 cycles. Chemotherapy is cisplatin 80 mg/m² iv. on day 1 + either capecitabine 1000 mg/m² orally twice daily × 14 days or 5-FU 800 mg/m² iv. daily × 5 days (investigator's choice). Pembrolizumab 200 mg iv. is given on day 1. Adjuvant monotherapy is pembrolizumab (arm 1) or placebo (arm 2). In a separate safety cohort, 5-FU 2600 mg/m² iv. + docetaxel 50 mg/m² iv. + oxaliplatin 85 mg/m² iv. + leukovorin 200 mg/m² iv. (FLOT) is being studied as a potential chemotherapy option

Stratified according to geographic region (Asia vs. non-Asia), tumor stage (II vs. III vs. IVa), and chemotherapy backbone (XP/FP versus other [for future additions of novel chemotherapy regimens])

Treatment will continue until confirmed radiographic progression, unacceptable toxicity, investigator or patient decision to withdraw, nonadherence to treatment or trial procedures, or completion of 35 cycles of pembrolizumab or placebo (approximately 2 years)

Key eligibility criteria

Age
≥18 years

Previously untreated localized gastric or gastroesophageal junction adenocarcinoma defined by T3 or greater primary lesion or the presence of any positive clinical nodes without evidence of metastatic disease

For gastroesophageal junction adenocarcinoma, Siewert type 2 or 3 tumors are eligible (eligibility of Siewert type 1 tumors is limited to those for whom planned treatment is perioperative chemotherapy and resection)

Plan to proceed to surgery after preoperative chemotherapy

ECOG performance status 0/1

No active autoimmune disease

Adequate organ function

Willing to provide tumor tissue at baseline and at the time of surgery

Outcome measures/end points

Primary end points

OS, defined as the time from randomization to death from any cause; EFS, defined as the time from randomization to radiographic disease progression per Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1), by blinded independent central review, local or distant recurrence as assessed by computed tomography (CT) or biopsy if indicated (for participants who are disease free after surgery), or death from any cause; and pCR, defined as no invasive disease within an entirely submitted and evaluated gross lesion and histologically negative nodes based on central review; pathologic response will be graded according to Mandard criteria

Secondary end points

Safety and tolerability and DFS, defined as the time from the post-surgery baseline CT until the first documented occurrence of local or distant recurrence per RECIST v1.1 by blinded independent central review or death from any cause among patients who are disease free after surgery

Exploratory end points

Efficacy according to PD-L1 expression, R0 resection rate, HRQOL (assessed using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ] core 30 items [C30] and gastric cancer–specific items [STO22]), utilities (assessed using the EuroQoL 5-dimension, 5-level questionnaire [EQ-5D-5L]) and molecular biomarkers

Glossary

DFS: Disease-free survival; EFS: Event-free survival; G/GEJ: Gastric/gastroesophageal junction; FLOT: 5-fluorouracil + docetaxel + oxaliplatin + leukovorin; FP: 5-fluorouracil + cisplatin; OS: Overall survival; pCR: Pathologic complete response; PD-L1: Programmed death ligand 1; Q3W: Every 3 weeks; R: Randomization; XP: Capecitabine + cisplatin