GEMINI-PeriOp Gastric: A phase 2 study of novel agent-based combinations as perioperative therapy for previously untreated, locally advanced resectable gastric, gastroesophageal junction, or esophageal adenocarcinoma

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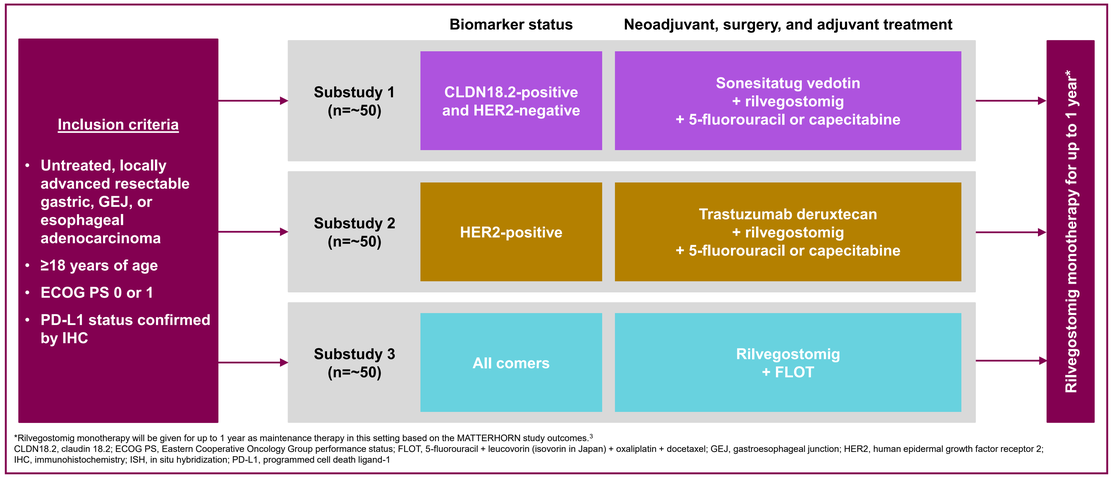
Background

- The addition of perioperative chemotherapy to radical surgery has improved outcomes for patients with resectable gastric cancer, but rates of relapse remain high in the first few years following treatment.[1,2]
- FLOT (5-fluorouracil + leucovorin [isovorin in Japan] + oxaliplatin + docetaxel) is a widely accepted perioperative regimen for patients with resectable gastric cancer and a high risk of relapse who are suitable for intensive chemotherapy, based on the survival benefits observed in the FLOT4 trial.[2]
- The phase 3 MATTERHORN trial demonstrated improved event-free survival and overall survival with perioperative durvalumab + FLOT versus FLOT alone, establishing a role for immunotherapy-based treatment combinations in this setting.[3]
- Rilvegostomig is a monovalent, Fc-reduced, bispecific, humanized immunoglobulin G1 monoclonal antibody targeting programmed cell death-1 (PD-1) and T cell immunoreceptor with immunoglobulin and ITIM domain (TIGIT), which are both highly expressed in gastric cancers.[4]
  - Rilvegostomig + chemotherapy demonstrated manageable safety and promising efficacy when given as first-line therapy for human epidermal growth factor receptor 2 (HER2)-negative, locally advanced unresectable or metastatic gastric cancers in substudy 2 of the phase 2 GEMINI-Gastric study.[5]
- The antibody-drug conjugates sonesitatug vedotin (AZD0901; anti-claudin 18.2 [CLDN18.2]) and trastuzumab deruxtecan (anti-HER2) may also provide benefit for patients with resectable gastric cancers when given with additional agents in the perioperative setting.
  - Sonesitatug vedotin is being evaluated in the phase 3 CLARITY-Gastric 01 study of patients with advanced gastric or gastroesophageal junction (GEJ) cancer who have received at least one line of previous therapy.[6]
  - Trastuzumab deruxtecan is approved as second-line therapy for patients with HER2-positive gastric or GEJ adenocarcinoma who have received a prior trastuzumab-based regimen,[7] and is being investigated as first-line therapy in the phase 3 ARTEMIDE-Gastric01 (NCT06764875) and DESTINY-Gastric05 (NCT06731478) studies in patients with HER2-positive locally advanced or metastatic gastric or GEJ cancer.
- Here we report the design of GEMINI-PeriOp Gastric (NCT07069712), a phase 2 study evaluating rilvegostomig with or without an antibody-drug conjugate plus chemotherapy given as neoadjuvant and adjuvant therapy for locally advanced resectable gastric, GEJ, or esophageal adenocarcinoma.

Study design and treatment

- GEMINI-PeriOp Gastric is an ongoing, open-label, phase 2 platform study.
- The study currently comprises three substudies in approximately 150 patients overall (**Figure 1**).
  - New substudies may be added in the future to evaluate additional treatment regimens.
- Rilvegostomig monotherapy will be given for up to 1 year after completing adjuvant combination therapy in all three substudies based on the MATTERHORN study outcomes.[3]
- Safety and efficacy endpoints will be measured in each substudy until completion.

Figure 1. Study design



*Rilvegostomig monotherapy will be given for up to 1 year as maintenance therapy in this setting based on the MATTERHORN study outcomes.[3]
CLDN18.2, claudin 18.2; ECOG PS, Eastern Cooperative Oncology Group performance status; FLOT, 5-fluorouracil + leucovorin (isovorin in Japan) + oxaliplatin + docetaxel; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; PD-L1, programmed cell death ligand-1

Key inclusion criteria

- Aged ≥18 years.
- Locally advanced resectable gastric, GEJ, or esophageal adenocarcinoma.
- Eastern Cooperative Oncology Group performance status of 0 or 1.
- Adequate organ and bone marrow function.
- Body weight >35 kg.

Key exclusion criteria

- Prior anticancer treatment or surgery for the current gastric, GEJ, or esophageal adenocarcinoma.
- Any known or suspicious distant metastasis.
- Active or prior documented autoimmune or inflammatory disorders requiring systemic treatment with steroids or other immunosuppressive treatment.
- Uncontrolled infections, including chronic or active hepatitis B.
- Central nervous system pathology (with exceptions).
- History of noninfectious interstitial lung disease (ILD)/pneumonitis, or current or suspected ILD/pneumonitis.
- History of another primary malignancy.
- Receipt of immunosuppressive medication within 14 days prior to the first dose of study treatment.
- Additional substudy-specific exclusion criteria also apply.

Study endpoints

Primary endpoints

- Safety and tolerability of perioperative therapy.
- Pathological complete response rate.

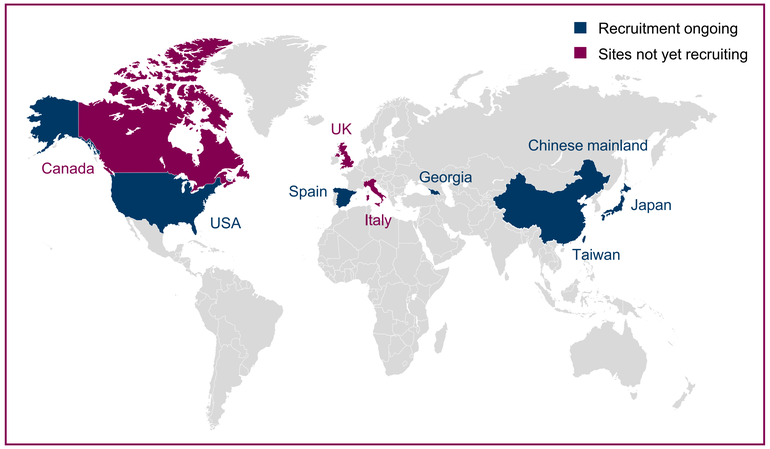
Secondary endpoints

- Surgery completion rate as planned.
- Complete resection rate.
- Tumor downstaging following neoadjuvant therapy and following surgery.
- Event-free survival.
- Disease-free survival.
- Objective response rate following neoadjuvant therapy.
- Overall survival.
- Pharmacokinetics and immunogenicity.

Study status

- The study status in participating locations is shown in **Figure 2**.
- Enrollment began in July 2025 and primary completion is anticipated in December 2026.

Figure 2. Study status by location



References:

1. Zhang X, et al. *Lancet Oncol* 2021;22:1081–92.
2. Al-Batran S-E, et al. *Lancet* 2019;393:1948–57.
3. Janjigian YY, et al. *N Engl J Med* 2025;393:217–30.
4. Xu D, et al. *Immunobiology* 2020;225:151915.
5. Rivera Herrero F, et al. *Ann Oncol* 2024;35(suppl_2):Abstract 1422P.
6. Janjigian YY, et al. *J Clin Oncol* 2025;43(suppl_4):Abstract TPS507.
7. US Food and Drug Administration. ENHERTU® Prescribing Information (Daiichi Sankyo, Inc.) 2025. Available at: https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Enhertu&inline=true (Accessed November 2025).

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Disclosures

Ziyu Li has no conflicts to report.

Co-authors – please refer to the abstract.

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