# ARTEMIDE-Gastric01: a phase 3 randomized study of rilvegostomig with fluoropyrimidine and trastuzumab deruxtecan as first-line treatment for locally advanced or metastatic HER2-positive gastric or gastroesophageal junction cancer

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## Plain language summary

**Why are we performing this research?**

- Stomach cancer, also known as gastric cancer (GC), is a common cancer that is often diagnosed at an advanced stage when the cancer has spread from its original site to other parts of the body. In some cases, stomach cancer can form where the stomach meets the esophagus (known as the gastroesophageal junction [GEJ])
- Approximately a fifth of people with GC/GEJ cancer (GEJC) have tumors with an elevated level of a protein called human epidermal growth factor receptor 2 (HER2)
- Drugs that target the HER2 protein, combined with chemotherapy and sometimes immunotherapy, are used to treat advanced GC/GEJC
- Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate (a chemotherapy with a linker [deruxtecan], joined to an antibody [trastuzumab]) that kills cancer cells by targeting the HER2 protein
- Rilvegostomig is a drug that blocks both PD-1 and TIGIT proteins to help the immune system kill cancer cells
- The aim of the ARTEMIDE-Gastric01 study is to find out if rilvegostomig treatment combined with T-DXd and chemotherapy can stop GC/GEJC cancer from worsening and extend how long patients live

**How are we performing this research?**

- Patients with advanced GC/GEJC who have not received prior treatment for their cancer will be randomly assigned to one of three treatment groups: rilvegostomig plus T-DXd plus chemotherapy; pembrolizumab plus trastuzumab plus chemotherapy; or rilvegostomig plus trastuzumab plus chemotherapy
- Patients will receive treatment until their cancer worsens or they decide to stop treatment due to unacceptable side effects, or for another reason
- The study will measure how long patients live without their cancer getting worse and how long they live overall

**Who will participate in this study?**

- Approximately 840 adults with previously untreated HER2-positive advanced GC/GEJC will be enrolled from 28 countries and regions globally

**Where can I access more information?**

- This study is ongoing, and no results are available yet; completion is expected in November 2030
- More information on the ARTEMIDE-Gastric01 study can be found at ClinicalTrials.gov (NCT06764875): https://clinicaltrials.gov/study/NCT06764875. You may also speak to your doctor about clinical studies

## Background

- Gastric cancer is the fifth most common cancer globally[1] and is often diagnosed at an advanced stage with poor prognosis;[2] 5-year relative survival for advanced gastric cancer is approximately 5%[3]
- HER2 overexpression/amplification occurs in up to 22% of GC/GEJC tumors[4] and for patients with HER2-positive tumors, standard of care treatment includes HER2-targeting agents plus chemotherapy[5]
- In patients with advanced HER2-positive GC/GEJC and programmed cell death ligand-1 (PD-L1) combined positive score (CPS) ≥1, adding immune checkpoint inhibition to HER2-targeting treatment and chemotherapy has shown clinical benefit[6,7]
- Pembrolizumab (a programmed cell death-1 [PD-1] inhibitor) in combination with trastuzumab (an anti-HER2 monoclonal antibody) and chemotherapy has demonstrated improvements in progression-free survival[6] (PFS) and overall survival[7] (OS) versus trastuzumab plus chemotherapy and is an approved first-line treatment for HER2-positive advanced GC/GEJC with PD-L1 CPS ≥1[8]
- PD-1 and T cell immunoreceptor with Ig and ITIM domains (TIGIT) are inhibitory immune receptors that are frequently co-expressed on T cells;[9,10] dual inhibition of PD-1 or PD-L1 and TIGIT has shown encouraging results across multiple tumor types, without major increases in high-grade toxicity compared with PD-1 or PD-L1 inhibition[11]

## Rationale

- Rilvegostomig is a humanized immunoglobulin G1 bispecific monoclonal antibody that targets both PD-1 and TIGIT receptors, and is designed to be Fc-reduced[12]
- Rilvegostomig has shown encouraging efficacy with manageable safety as monotherapy in metastatic non-small cell lung cancer[13] and in combination with chemotherapy in HER2-negative advanced GC/GEJC[14]
- T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, a tetrapeptide-based cleavable linker, and a topoisomerase I inhibitor pay load. T-DXd is approved for the treatment of locally advanced or metastatic HER2-positive GC/GEJC following a trastuzumab-based regimen[15]
- T-DXd in combination with fluoropyrimidine and pembrolizumab has shown promising antitumor activity in first-line HER2-positive metastatic GC/GEJC[16]
- The ARTEMIDE-Gastric01 (NCT06764875) study will assess the efficacy and safety of rilvegostomig in combination with T-DXd and fluoropyrimidine in patients with HER2-positive GC/GEJC whose tumors express PD-L1 with a CPS ≥1

## ARTEMIDE-Gastric01 (NCT06764875) study design and participating countries and regions

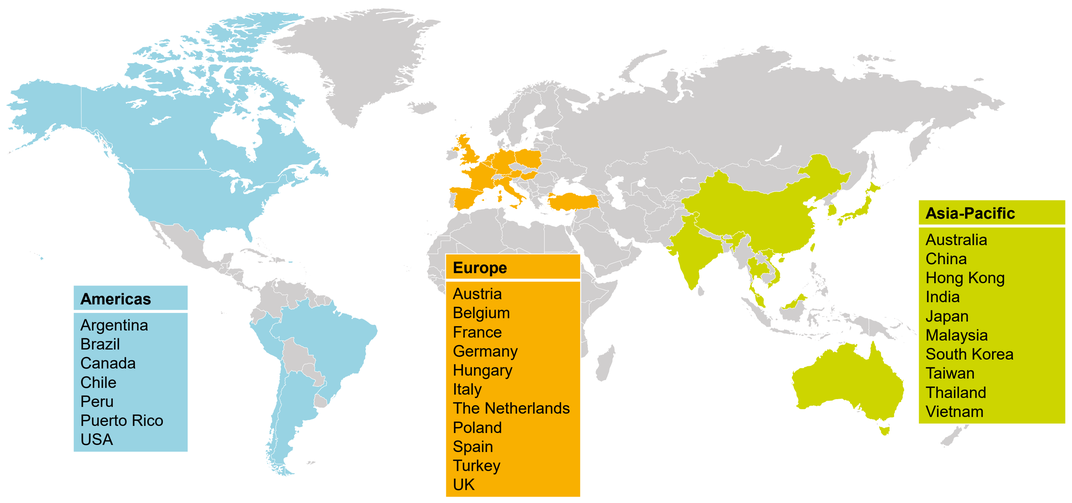
**A phase 3, randomized, open-label, sponsor-blinded, multicenter, global study to assess the efficacy and safety of rilvegostomig in combination with T-DXd and fluoropyrimidine versus pembrolizumab with trastuzumab and chemotherapy**

Histologically confirmed HER2-positive, locally advanced or metastatic GC/GEJC with PD-L1 CPS ≥1 and no prior systemic therapy for advanced disease
Approximately 840 patients randomized 1:1:1*

| Arm A | Arm B | Arm C |
|---|---|---|
| **Rilvegostomig IV Q3W** plus **T-DXd 5.4 mg/kg IV Q3W** plus fluoropyrimidine | Pembrolizumab 200 mg IV Q3W plus trastuzumab 6 mg/kg† IV Q3W plus platinum-based chemotherapy | **Rilvegostomig IV Q3W** plus trastuzumab 6 mg/kg† IV Q3W plus platinum-based chemotherapy |
| **Fluoropyrimidine:** Investigator's choice of capecitabine 750 mg/m² PO BID for 14 days Q3W, OR 5-FU 600 mg/m²/day IV‡ Q3W | **Platinum-based chemotherapy:** Investigator's choice of cisplatin 80 mg/m² IV (up to 6 cycles) plus 5-FU 800 mg/m²/day IV‡ Q3W, OR oxaliplatin 130 mg/m² IV (up to 8 cycles) plus capecitabine 1000 mg/m² PO BID for 14 days Q3W | |

*All randomized patients will receive an assigned treatment until either unacceptable toxicity or progressive disease (as defined by RECIST v1.1). Patients who continue to show clinical benefit can stay on treatment after progressive disease. †Patients will be given 8 mg/kg as a loading dose, followed by 6 mg/kg for the subsequent cycles. ‡Given as a continuous infusion over 24 hours for the first 5 days of each cycle (120 hours or per local practice).
5-FU, 5-fluorouracil; BID, twice daily; CPS, combined positive score; GC, gastric cancer; GEJC, gastroesophageal junction cancer; HER2, human epidermal growth factor receptor 2; IV, intravenous; PD-L1, programmed cell death ligand-1; PO, orally; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; T-DXd, trastuzumab deruxtecan.

**Enrollment start: March 2025 | Expected study completion: November 2030**




## Key inclusion criteria

- Adults aged ≥18 years
- Histologically confirmed, unresectable, locally advanced or metastatic GC/GEJC
- HER2-positive (immunohistochemistry [IHC] 3+ or IHC 2+ in-situ hybridization-positive)
- Confirmed PD-L1 expression with a CPS ≥1
- No prior systemic therapy for advanced disease
- World Health Organization or Eastern Cooperative Oncology Group performance status 0 or 1
- Measurable target disease assessed by the Investigator, based on RECIST v1.1

## Key exclusion criteria

- Lack of physiological integrity of the upper gastrointestinal tract
- Known dihydropyrimidine dehydrogenase enzyme deficiency
- History of another primary malignancy, except for those treated with curative intent and no known active disease within 3 years
- Spinal cord compression or brain metastases, unless asymptomatic, treated, stable, and not requiring treatment
- History of interstitial lung disease/pneumonitis or clinically significant lung illnesses
- Uncontrolled or active infectious disease or history of active primary immunodeficiency
- Active or prior autoimmune or inflammatory disorders requiring chronic treatment

## Study endpoints

1° PFS*† and OS‡ (Arm A vs Arm B)

2° Key secondary: PFS*† and OS‡ (Arm C vs Arm B)

2°
- PFS§
- Objective response rate†§
- Duration of response†§
- Safety and tolerability
- Pharmacokinetics
- Immunogenicity
- Patient-reported outcomes

*PFS is defined as time from randomization until progression or death. †Assessed by blinded independent central review according to RECIST v1.1. ‡OS is defined as time from randomization until the date of death. §Assessed by Investigator.

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**Poster**

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## Disclosures

Rui-Hua Xu reports consulting or advisory roles for Astellas Pharma, AstraZeneca, BeiGene, CPPC, Hutchison MediPharma, Hengrui Pharmaceutical, Innovent Biologics, Junshi Pharmaceuticals, Keymed Biosciences, Merck Serono, QiLu Pharmaceutical, and Roche. Co-authors – please refer to the abstract.

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