Background There is no consensus on the beneficiary population, regimen selection, and efficacy evaluation of neoadjuvant therapy for locally advanced gastric cancer. Existing evidence shows that neoadjuvant chemoradiotherapy can increase pCR, reduce tumor staging, and improve R0 resection rate for locally advanced gastric cancer. However, due to the insufficiently high pCR and survival benefits, there is an urgent need for more effective neoadjuvant treatment regimens to improve patient outcomes. Immune checkpoint inhibitor (ICI) combined with chemotherapy has become a standard first-line treatment for gastroesophageal junction adenocarcinoma (GEJ) and gastric adenocarcinoma. In addition, radiotherapy combined with ICI may enhance the efficacy of immunotherapy. Preliminary studies have shown that short-course radiotherapy combined with ICIs and chemotherapy for neoadjuvant treatment of colorectal cancer has good efficacy and safety. Envafolimab is the world’s first approved novel subcutaneously injectable PD-L1 inhibitor, which can significantly improve treatment convenience and compliance, and has shown good efficacy in multiple solid tumors including gastric cancer, small cell lung cancer, and liver cancer. The purpose of this study is to explore the efficacy and safety of short-course radiotherapy combined with envafolimab, recombinant human vascular endothelial inhibitor, and SOX regimen for neo-adjuvant treatment of resectable locally advanced gastric/gastroesophageal junction adenocarcinoma.

Methods This study is a prospective, single-arm, phase II clinical trial (NCT05387681). The study plans to recruit 35 newly diagnosed patients with locally advanced gastric/gastroesophageal junction adenocarcinoma (aged 18–75 years; cT2–4aN+ M0; ECOG score ≤1). Patients who meet the inclusion criteria will receive preoperative short-course radiotherapy according to the study plan, with a tumor dose of 25Gy (5Gy/day × 5 days, from day 1 to day 5). After a one-week rest, they will receive three cycles of envafolimab (300 mg/dose, Q3W, subcutaneous injection) combined with recombinant human vascular endothelial inhibitor (210 mg, Q3W, intravenous pump infusion, given on the first three days of each cycle), and SOX regimen treatment. Radical surgery will be performed 2–4 weeks after the completion of the last neoadjuvant treatment, and adjuvant therapy will be administered based on staging, followed by survival follow-up. The primary endpoint of the study is the pathological complete response rate (pCR), and the secondary endpoints include R0 resection rate, major pathological response (MPR), and safety.

Trial Registration This study for ClinicalTrials.gov identifier (NCT number): NCT05387681

Ethics Approval This study has been approved by the Medical Ethics Committee of the Union Hospital Tongji Medical College Huazhong University of Science and Technology, with review number UHCT-IEC-SOP-016–03-03.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.