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A study to examine the effects of preoperative envafolimab and chemotherapy in advanced stomach and gastroesophageal junction cancer

Submission date
30/01/2024

Recruitment status
No longer recruiting

Registration date
31/01/2024

Overall study status
Completed

Last Edited
31/01/2024

Condition category
Cancer

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This study is about a new preoperative treatment for stomach and gastroesophageal junction cancer. Usually, immune checkpoint inhibitors, which help the immune system recognize and fight cancer by targeting the programmed cell death receptor-1 (PD-1) and its ligand (PD-L1), are given through an IV (intravenous injection) method. This can be inconvenient for patients and sometimes they may have trouble sticking with the treatment.
Envafolimab is a new drug in this category that specifically targets PD-L1. It's a smaller, more soluble type of PD-L1 antibody, which means it can get into tissues faster and can be given as a simple injection under the skin, but not through an IV method. This will streamline the process for patients receiving treatment.
The effects of immune checkpoint inhibitors within the context of preoperative cancer treatment, especially in cases of stomach and gastroesophageal junction cancers, have not been fully established. Early results from other studies suggest that combining immune treatment with chemotherapy before surgery could be helpful, but it's not yet clear how effective envafolimab is in this situation. This particular study is trying to find out the benefits and harms of using envafolimab combined with a specific chemotherapy regimen (called SOX, which includes S-1 and oxaliplatin) before surgery in patients with advanced stomach and gastroesophageal junction cancers that can still be surgically removed.

Who can participate?
Patients aged between 18 and 70 years with advanced stomach and gastroesophageal junction cancers that can still be surgically removed

What does the study involve?
The study treatment is a combination of envafolimab and SOX chemotherapy. Specifically, participants will receive envafolimab injections at a dosage of 300 mg every 3 weeks for a total of three cycles before surgery. In addition, the SOX regimen will be administered, consisting of IV oxaliplatin at a dose of 130 mg/m² on the first day of each cycle, and oral S-1, ranging from 40 to 60 mg twice daily from day 1 to day 14, repeated every 3 weeks for three cycles as part of the preoperative treatment. Following 3 to 6 weeks after the last dose of neoadjuvant therapy,

patients will undergo a D2 gastrectomy (removal of stomach and lymph nodes), depending on their suitability for surgery.

What are the possible benefits and risks of participating?
Participants will receive a thorough anti-tumor treatment that integrates both medical and surgical approaches. The research team will provide assistance to ensure that participants can complete all treatments within the designated treatment cycles promptly and effectively. As the first subcutaneous PD-L1 inhibitor, envafolimab has demonstrated a more satisfactory effectiveness and safety profile compared to other approved PD-1/PD-L1 inhibitors, based on early data. This could potentially offer enhanced therapeutic benefits and improved patient convenience due to its subcutaneous administration. As with any medical treatment, envafolimab may cause side effects.

Where is the study run from?
West China Hospital (China)

When is the study starting and how long is it expected to run for?
June 2023 to March 2025

Who is funding the study?
Beijing Bethune Charitable Foundation (China)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
HX-H2401022

Study information

Scientific Title
Neoadjuvant envafolimab plus chemotherapy for locally advanced gastric or gastroesophageal junction adenocarcinoma: a single-arm Phase II trial

Acronym
NEO-EGA

Study objectives
In patients with locally advanced gastric cancer, neoadjuvant chemotherapy may downstage both the T and N stages, thereby increasing tumor resectability and potentially improving long-term survival outcomes. Envafolimab, as the first globally approved subcutaneously injectable PD-L1 antibody, presents a promising therapeutic advancement. The combination of preoperative PD-L1 antibody therapy with chemotherapy may represent a novel approach to treating locally advanced gastric cancer. This strategy is anticipated to enhance response rates, increase resectability, and diminish the likelihood of recurrence.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/11/2023, Biomedical Ethics Review Committee of the West China Hospital of Sichuan University (No.37 Guoxue Lane, Wuhou District, Chengdu, 610041, China; +86 (0)28 85423237; huaxilunli@163.com), ref: 2023(1652)

Study design

Single-center open-label single-arm Phase II interventional clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Locally advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma

Interventions
Experimental intervention:
Envafolimab (subcutaneous injection, 300 mg, Q3W, three cycles before surgery)

Other interventions:
1. SOX (intravenous oxaliplatin 130 mg/m² d1, oral S-1 40~60 mg BID d1~14, Q3W, three cycles before surgery)
2. Gastrectomy with D2 lymphadenectomy will be scheduled within 4–6 weeks after the last dose of neoadjuvant treatment. The scope of gastrectomy will be determined by the location and extent of the primary tumor to ensure an adequate surgical resection margin.

The study intervention comprises a combination of envafolimab and SOX chemotherapy. Specifically, participants will receive envafolimab subcutaneous injections at a dosage of 300 mg every 3 weeks (Q3W), for a total of 3 cycles before surgery. In addition, the SOX regimen will be administered, consisting of intravenous oxaliplatin at a dose of 130 mg/m² on the first day (d1) of each cycle, and oral S-1, ranging from 40 to 60 mg twice daily (BID) from day 1 to day 14 (d1-14), repeated every 3 weeks for three cycles as part of the preoperative treatment. Following 3 to 6 weeks after the last dose of neoadjuvant therapy, patients will undergo a D2 gastrectomy, contingent upon their clinical suitability for surgery.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Envafolimab, oxaliplatin, S-1

Primary outcome(s)
Pathologic complete response rate (pCR i.e., 0% residual tumor per tumor bed), measured after surgical resection

Key secondary outcome(s))
1. R0 resection rate (i.e., complete removal of the tumor with a tumor-free margin) measured at the time of surgical resection
2. Major pathological response rate (MPR i.e., residual tumor cells below 10% in the resected specimen), measured after surgical resection
3. Objective response rate (ORR) by RECIST v1.1, defined as the proportion of subjects with complete response or partial response, measured radiologically after completion of neoadjuvant

therapy.
4. Surgery-related outcomes such as intraoperative bleeding, operative time, time to first passage of flatus/stool, and length of postoperative hospital stay, measured using patient medical records during hospitalization
5. Safety endpoints include immune-related adverse events (irAEs), chemotherapy-related AEs, and surgical AEs (i.e., complications occurring during or within 30 days of surgery), measured according to National Cancer Institute Common Terminology Criteria for Adverse Events and Clavien-Dindo Classification

Completion date
15/03/2025

Eligibility

Key inclusion criteria
1. Individuals of any gender, aged between 18 and 70 years
2. Eastern Cooperative Oncology Group performance (ECOG) performance status of 0 or 1, no surgery contraindications. The individual must have no surgical contraindications and possess a physical condition along with adequate organ function to ensure the safe completion of abdominal surgery
3. Diagnosis of primary resectable, histologically confirmed cT3/4aN+M0 gastric or GEJ adenocarcinoma, as determined by CT/MRI
4. Absence of peritoneal metastases, as determined by laparoscopic exploration
5. No prior cancer treatment (e.g. radiotherapy, chemotherapy, targeted therapy, immune checkpoint inhibitors)
6. Fully informed about the study and voluntarily sign an informed consent form

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Key exclusion criteria
1. Patients with distant metastases or primary tumors deemed non-resectable
2. Previous or concurrent other malignancies (except completely resected basal cell carcinoma, stage I squamous cell carcinoma, carcinoma in situ, intramucosal carcinoma, superficial bladder cancer or any other malignancies that have not recurred for at least 5 years)

3. Allergies towards drug ingredients or excipients in this study, or history of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins
4. Any active autoimmune disease or documented history of serious autoimmune disease within the past 2 years requiring systemic therapy (i.e., with the use of disease-modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.
5. Prior allogeneic stem cell or solid organ transplantation, with exceptions for transplants not requiring ongoing immunosuppression, such as corneal or hair transplantation
6. History of non-infectious pneumonitis that required steroid treatment, current pneumonitis, or a history of or current interstitial lung disease
7. Conditions requiring systemic treatment with either corticosteroids (>10mg daily prednisone equivalents) or other immunosuppressive medications within 14 days of study drug administration. Inhaled or topical steroids and adrenal replacement doses >10mg daily prednisone equivalents are permitted in the absence of active autoimmune disease
8. History of gastrointestinal hemorrhage within 4 weeks before enrollment or patients with a high risk of hemorrhage
9. Pregnancy or breastfeeding or intention of becoming pregnant during study treatment or within months after the last dose of study treatment.
10. Known history of human immunodeficiency virus (HIV), active Hepatitis B or Hepatitis C
11. Significant cardiovascular disease (such as New York Heart Association Class II or greater cardiac disease, myocardial infarction or cerebrovascular accident) within 6 months before initiation of study treatment, unstable arrhythmia or unstable angina
12. Treatment with a live, attenuated vaccine within 4 weeks before initiation of study treatment or anticipation of need for such a vaccine during study treatment
13. Inadequate hematologic or organ function evidenced, defined by the following laboratory test results, obtained within 7 days before initiation of study treatment:
13.1. ALT/AST >3× upper limit of normal (ULN)
13.2. Total bilirubin > 1.5×ULN. For participants with a history of Gilbert's Syndrome, total bilirubin > 3×ULN at screening
13.3. Serum creatinine level >1.5×ULN and creatinine clearance <40 ml/min
13.4. Absolute value of neutrophils < 1.0 × 10^9 / L
13.5. Platelet count <90 × 10^9 / L
13.6. Hemoglobin <90g / L
14. Any medical or psychological condition, organ dysfunction, or significant social circumstances, including but not limited to uncontrolled diabetes, hypertension, pulmonary diseases, atrial fibrillation, pericardial effusion, mental illness, substance abuse, or other significant systemic diseases, as assessed by the investigator. These conditions must be considered likely to:
14.1. Impair the participant's ability to provide informed consent
14.2. Negatively impact the participant's ability to comply with and fully participate in the study
14.3. Compromise the interpretation of study results

Date of first enrolment
26/02/2024

Date of final enrolment
30/01/2025

Locations

Countries of recruitment
China

Study participating centre
West China Hospital of Sichuan University
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Sponsor information

Organisation
West China Hospital of Sichuan University

ROR
https://ror.org/007mrxy13

Funder(s)

Funder type
Charity

Funder Name
Beijing Bethune Charitable Foundation (STLKY0090)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author (Bo Zhang, zhangbo_scu@scu.edu.cn) on reasonable request. The researchers have a data-sharing plan for investigator and external requests, only for legitimate research purposes and reasonable data requirements. The data of patients will be strictly anonymized to protect patients from being identifiable. Data would typically only be available to share at the end of the study. The sharing process will be carried out in strict compliance with both local legal regulations and ethical review.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes