**Efficacy and Safety of Serplulimab Combined with SOX and Nab-paclitaxel as Neoadjuvant Treatment for Locally Advanced Gastric cancer or Adenocarcinoma of Esophagogastric junction: A Multicenter Randomized Controlled Trial**

# Informed Consent Form

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# Informed Consent · Informed Notification page

**Dear Patient,**

We sincerely welcome your participation in the **"Efficacy and Safety of Serplulimab Combined with SOX and Nab-paclitaxel as Neoadjuvant Treatment for Locally Advanced Gastric cancer or Adenocarcinoma of Esophagogastric junction: A Multicenter Randomized Controlled Trial"** Before deciding whether to enroll, please carefully review the following information, which outlines the study's purpose, procedures, duration, potential benefits, risks, and discomforts. You are encouraged to discuss this with family members or consult your physician for further clarification to aid your decision-making process.

## I. Study Overview

### 1. Study Objectives

To evaluate the **efficacy and safety** of Serplulimab combined with the SOX regimen (S-1 + Oxaliplatin) and Nab-Paclitaxel in treating locally advanced gastric carcinoma (GC) or gastroesophageal junction (GEJ) adenocarcinoma.

### 2. Study Background

Gastric cancer ranks as the fifth most common malignancy globally and the third leading cause of cancer-related mortality, with half of global cases occurring in Eastern Asia. In China, 679,000 new cases and 498,000 deaths were estimated in 2015, positioning GC as the second most prevalent and fatal malignancy. Prognosis remains poor, underscoring its significant threat to public health. Risk factors include age, male gender, smoking, radiation exposure, family history, Helicobacter pylori infection, and dietary habits (e.g., low fruit/vegetable intake, high salt, and smoked foods). *H. pylori* induces chronic gastritis, gastric atrophy, and subsequent metaplasia, dysplasia, and carcinogenesis.

**Current Treatment Landscape**

Curative surgical resection remains the primary approach for non-metastatic GC, yet post-operative recurrence rates reach 40–80%, with a 5-year survival rate of 30–60%. Perioperative therapy (neoadjuvant chemotherapy + surgery + adjuvant chemotherapy) has demonstrated superiority over surgery alone by reducing tumor burden, improving R0 resection rates, enhancing survival outcomes, and maintaining postoperative safety. Neoadjuvant chemotherapy enables tumor downstaging, predicts chemosensitivity, and correlates with pathological complete response (pCR), a prognostic marker for overall survival (OS).

**Key Clinical Evidence**

The RESOLVE Phase III trial (presented at ESMO 2019) compared perioperative SOX (C arm) with postoperative XELOX (A arm) or SOX (B arm) in 1,022 patients. Perioperative SOX

improved R0 resection rates (92.88% vs. 86.47% in A arm; 87.83% in B arm) and 3-year disease-free survival (62.02% vs. 54.78%, P=0.045). A French Phase III trial reported 84% R0 resection with PF neoadjuvant chemotherapy vs. 73% with surgery alone (P=0.04). Studies on XELOX, FOLFOX, and SP regimens demonstrated ORRs of 70–75.5% and R0 resection rates of 81.3–87.8%. The FLOT4 trial showed superior R0 resection with FLOT (5-FU, docetaxel, oxaliplatin, leucovorin) vs. ECF/ECX (85% vs. 78%, P=0.0162).

**3. Study Design**

This trial employs a randomized, double-blind, multicenter framework to assess the efficacy and safety of Serplulimab combined with the SOX regimen (S-1 + Oxaliplatin) and Nab-Paclitaxel in patients with locally advanced GC or GEJ adenocarcinoma.

**Primary Endpoint**

Pathological Complete Response (pCR) Rate.

**Secondary Endpoints**

Efficacy Metrics: Objective Response Rate (ORR)，Major Pathological Response (MPR)，R0 Resection Rate，Progression-Free Survival (PFS), and Overall Survival (OS)

Safety Assessments: Treatment-related adverse events (graded per NCI-CTCAE v5.0 criteria). Surgical safety parameters: Postoperative complications, 30-day mortality, hospitalization duration.

Patient-Reported Outcomes (PROs):Quality of life (QoL) evaluations using validated scales (e.g., EORTC QLQ-C30/STO22).

Exploratory Objectives: Biomarker Analysis:Correlation of PD-L1 expression with treatment response. Identification of novel biomarkers (e.g., tumor immune microenvironment profiling). Dynamic monitoring via circulating tumor DNA (ctDNA) to predict therapeutic efficacy and recurrence.

## II. Participant Responsibilities

Prior to study enrollment, please complete requisite examinations in collaboration with your physician to ascertain eligibility for participation in this clinical investigation. Should you satisfy all inclusion criteria without violating exclusion parameters, consent to participate, and receive medical confirmation of suitability, the investigational protocols will proceed as delineated below:

**Patients will undergo randomized allocation to receive either:**

- **Serplulimab + SOX + Nab-Paclitaxel neoadjuvant chemotherapy for 3 cycles**
- **SOX + Nab-Paclitaxel neoadjuvant chemotherapy alone for 3 cycles**

Postoperative adjuvant chemotherapy (Serplulimab+SOX+Nab-Paclitaxel or SOX+

Nab-Paclitaxel alone) will be administered based on clinical evaluation.

**Serplulimab Protocol**

Every 3 weeks (21 days) was given as one dosing cycle, 4.5mg was given intravenously on the first day of each cycle, and the infusion time was within 60 minutes. Up to 8 cycles. Dose adjustment is not allowed and delayed dosing is allowed.

**Chemotherapy Protocol (SOX+ Nab-Paclitaxel)**

1 cycle every 3 weeks (21 days). Dose adjustment is allowed and delayed dosing is allowed.

**Nab-Paclitaxel**: 260 mg/m2, intravenous infusion, d1, infusion greater than 30 minutes.

**Oxaliplatin (OXA)**: 130mg/m2, intravenous infusion, d1, infusion greater than 2 hours.

**Tegafur, Gimeracil and Oteracil Potassium Capsule (S-1)**: Taken orally after breakfast and dinner twice daily, d1-14.

Initial measurement (by Tegafluormeter) is distributed on the basis of body surface area (BSA) :

BSA less than 1.25m2, 40mg/ time;

BSA greater than or equal to 1.25m2 less than 1.5m2, 50mg/ time;

BSA greater than 1.5m2, 60mg/ time;

**Administration Sequence**

the experimental group was given drug treatment in sequence on the first day of each cycle, with intravenous infusion of PD-1 monoclonal antibody first, followed by chemotherapy with albumin paclitaxel combined with SOX at an interval of at least 1 hour; The control group was given albumin paclitaxel combined with SOX chemotherapy on the first day of each cycle. BSA greater than 1.5m2, 60mg/ time; The dosing time window is ±3 days, but within 72 hours prior to each dosing, subjects must complete an examination that includes all clinical requirements to assess tolerance for continued dosing.

During the treatment you will need to undergo the following tests: Demographic data, screening for infectious diseases (hepatitis B, hepatitis C, syphilis, AIDS), lung function, 12-lead electrocardiogram, and imaging of tumor lesions (CT or.) were collected after signing informed consent 14 days before treatment MRI and gastroscopic biopsy data, previous disease history, previous medication history, drug allergy history, tobacco and alcohol history, pathological assessment, nutritional risk screening, adverse events, and drug combination. ECOG score, thyroid function, coagulation function, tumor markers, dysphagia score, blood pressure test, vital signs, physical examination, blood routine, urine routine, blood biochemistry, stool occult blood, adverse events and drug combination were completed within 7 days before the start of the study drug treatment, and the admission criteria were checked.

We may conduct further analyses on your **remaining biopsy tissue** and **residual blood samples** to investigate underlying biological mechanisms. These tests **will not result in any additional adverse effects** or risks to you.

Adverse events and drug combinations/concomitant treatments were recorded from the time the informed consent was signed to 90 days after the last dose.

**If you do not meet the inclusion criteria or you do not wish to participate in this study:** You can choose other feasible treatment options, such as other chemotherapy, radiotherapy, direct surgery and other treatment means, the specific treatment plan your doctor will communicate with you according to your condition.

## III. The benefits and possible risks and inconvenience brought to you by participating in this study

The examination items involved in this study are necessary for routine diagnosis and treatment of esophageal cancer (hemuria routine, liver and kidney function, electrolyte, CT, pathology, etc.), and do not involve additional special medical examination.

1. We cannot guarantee that you will benefit from treatment with this protocol.

2. By participating in this study, you and the community will likely benefit from this study, and you will be more closely followed and observed by your doctor. Benefits also include the possibility that your condition will improve.

3. All therapeutic drugs have the potential to cause side effects. The study data showed that the most common adverse events in combination with chemotherapy were Anaemia, Decreased neutrophil count, Decreased leukocyte count, Decreased platelet count; Hypothyroidism; Decreased appetite; Nausea; Fatigue; Alanine aminotransferase increased. The study data showed that the common adverse events in combination with chemotherapy were Lymphocyte count decreased; Hyperthyroidism; Hypoalbuminemia, Hyperglycemia or diabetes mellitus, Hyponatremia, Hypokalemia, Hypomagnesemia, Hyperuricemia, Hypocalcemia, Hypophosphatemia, Hypochloremia, Hypo-/Hyperkalemia; Dysesthesia, Dizziness, Headache; Urinary tract infection; Arrhythmia; Hypertension; Vomiting, Constipation, Diarrhea, Abdominal pain, Abdominal distension; Hepatitis; Alopecia, Rash, Dermatitis, Pruritus; Musculoskeletal pain, Arthralgia; Proteinuria, Hematuria, Renal impairment; Pyrexia, Malaise, Edema, Chest discomfort; Insomnia; Aspartate aminotransferase increased, Blood lipid increased, Blood bilirubin increased, Thyroid function test abnormal, Myocardial necrosis markers increased, Blood creatinine increased, Gamma-glutamyltransferase increased, Weight decreased, Blood alkaline phosphatase increased, Blood lactate dehydrogenase increased, Electrocardiogram abnormal, Blood urea increased, Weight increased, Blood myoglobin increased, Activated partial thromboplastin time prolonged. The study data showed that the occasional adverse events in combination with

chemotherapy were Leukocytosis, Febrile neutropenia, Neutrophil count increased, Bone marrow suppression; Hypophysitis, Thyroid disorders, Adrenal-related disorders, Thyroiditis; Hyperphosphatemia, Hypercalcemia, Hypermagnesemia, Electrolyte imbalance, Malnutrition, Hypoglycemia, Diabetic ketoacidosis, Iron deficiency, Tumor lysis syndrome; Peripheral neuropathy, Somnolence, Encephalitis, Tremor, Ataxia, Memory impairment, Syncope; Upper respiratory tract infection, Herpes simplex, Septic shock, Herpes zoster; Pericardial effusion, Heart failure, Myocardial ischemia, Atrial fibrillation, Myocarditis, Acute coronary syndrome, Cardiomyopathy; Hypotension, Phlebitis, Flushing; Hiccups, Hemoptysis, Dyspnea, Pleural effusion, Tachypnea, Respiratory failure, Oropharyngeal pain, Epistaxis, Pneumothorax, Rhinorrhea; Dysphagia, Dry mouth, Reflux, Stomatitis, Dyspepsia, Colitis, Gastritis, Gastrointestinal disorders, Pancreatitis, Oral ulcer, Upper gastrointestinal hemorrhage; Pigmentation disorder, Dry skin, Erythema, Psoriasis, Hyperhidrosis, Nail discoloration, Vitiligo, Epidermolysis; Muscular weakness, Musculoskeletal stiffness, Rheumatoid arthritis; Chills, Non-cardiac chest pain, Chest pain, Influenza-like illness; Motion sickness, Deafness, Tinnitus, Vertigo; Amylase increased, Pro-N-terminal brain natriuretic peptide increased, Brain natriuretic peptide increased, Alpha-hydroxybutyrate dehydrogenase increased, Lipase increased, Glycosuria, Platelet count increased, Transaminases increased, Fibrin D-dimer increased, C-reactive protein increased, Low-density lipoprotein increased, Glomerular filtration rate decreased, Globulin decreased, Fibrin degradation products increased, Eosinophil count decreased, Cardiac function test abnormal, Blood homocysteine increased, Lipoprotein a increased. **If you experience any discomfort, new changes in your condition, or unexpected events during the study, regardless of suspected relation to the medication, promptly notify your physician. He/she will assess and manage accordingly.**

4. We may conduct further analyses on your **remaining biopsy tissue** and **residual blood samples** to investigate underlying biological mechanisms. These tests **will not result in any additional adverse effects** or risks to you.

5. Any treatment may be ineffective or other co-morbidities may occur due to the tumor. During the trial, if your doctor finds the above situation, he may suggest you to change to other treatment measures, such as local radiotherapy, chemotherapy and other treatment means. Your doctor in charge of the specific treatment plan will communicate with you according to your condition, and the study will purchase insurance for the subjects.

## IV. Are there any costs associated with participating in this study?

You will receive Serplulimab medication free of charge for participating in this clinical study. However, you will be responsible for covering the costs of chemotherapy drugs, routine diagnostic tests (including blood and urine tests, liver and kidney function tests, electrolyte tests, CT scans, pathological examinations, etc.), and surgical fees. This study does not involve any additional

specialized medical examinations.

## V. Confidentiality of Your Personal Information

1.Your medical records (study files, case report forms, and test reports) will be securely stored at the hospital. Relevant test results will be documented in your medical records by your physician.

2.Access to your medical records will be granted to investigators, sponsor representatives, ethics committees, and drug regulatory authorities. Any public reports related to this study will not disclose your personal identity.

3.Privacy protection: We will safeguard the confidentiality of your medical information to the fullest extent permitted by law.

## VI. You Have the Right to Obtain Additional Information

1.You may ask any questions regarding this study at any time.

2.If any significant information arises during the study that may affect your willingness to continue participation, your physician will promptly notify you.

## VII. Voluntary Participation and Withdrawal

1.Participation in this trial is completely voluntary. You may refuse to participate or withdraw from the study at any time during the research process. This decision will not affect your relationship with your physician or your medical or legal rights.

2.Your physician or the investigator may discontinue your participation in this study at any time if it is deemed necessary for your best interests.

3.If you withdraw from the study for any reason, you may be asked about your medication usage. If required by your physician, you may also need to undergo relevant laboratory tests and physical examinations.

If you have any questions about the procedure of this study, you can consult **Dr. Li Zhenshun** at **15922893108** . If you have any questions about your rights and interests to participate in this study, you can consult **the ethics committee of Xijing hospital of Air force Medical university** at **(029) 84771794**.

# Informed consent· Signature page

**Title of clinical study：** **Efficacy and Safety of Serplulimab Combined with SOX and Nab-paclitaxel as Neoadjuvant Treatment for Locally Advanced Gastric cancer or Adenocarcinoma of Esophagogastric junction: A Multicenter Randomized Controlled Trial**

## Declaration of consent:

I have read the above introduction about this clinical study, and have the opportunity to discuss and ask questions with doctors about this clinical study. All my questions were answered satisfactorily.

I know the possible risks and benefits of participating in this clinical study. I know that participating in the clinical study is voluntary. I confirm that I have had enough time to consider this and understand that:

- I can always ask the doctor for more information.
- I can withdraw from this clinical study at any time without discrimination or retaliation, and my medical treatment and rights will not be affected.
- I also know that if I withdraw from clinical research halfway, I will tell the doctor about the changes of my condition and complete the corresponding physical and chemical examination, which will be very beneficial to the whole condition.
- If I need to take any other treatment due to the change of my condition, I will consult the doctor in advance or tell the doctor truthfully afterwards.
- I agree with the ethics committee or its representative to access my clinical research data.
- I will receive a signed and dated copy of the informed consent form.
- Finally, I decided to agree to participate in this clinical study and promise to follow the doctor's advice as much as possible.

**Subject Signature：** _____ **ID Number：** _____

**Contact Number：** _____ **Date of Signature：** _____

（***Applicable only if the subject lacks legal capacity or has limited capacity***）

**Legal Representative：** _____ **ID Number：** _____

**Relationship：** _____ **Contact Number：** _____

**Reason for Signature：** _____ **Date of Signature：** _____

I confirm that I have explained the details of this clinical study to the patient, including its rights, possible benefits and risks, and gave him a copy of the signed informed consent form.

**Doctor signature：** _____ **Date of Signature：** _____

**Contact Number：** _____