INFORMED CONSENT FORM

A Prospective, Single-Arm, Single-Center Phase II Clinical Trial of Iparomlimab and Tuvonralimab as Neoadjuvant Immunotherapy for Microsatellite Instability-High / Mismatch Repair-Deficient Locally Advanced Gastric Adenocarcinoma

Version Number: 1.1, dated 21 April 2026

Study Institution: Peking University Cancer Hospital

Patient Name:	**Patient Name Initials:**
Patient Address:	**Patient Telephone:**

Dear **_____ (Mr./Ms.):**

We hereby invite you to participate in this study as a research subject. This informed consent form provides information to help you decide whether to participate in this study. Please take the time to read the following content carefully. If you have any unclear questions or technical terms, you may discuss them with the relevant physician.

Your participation in this study is entirely voluntary. This study has been reviewed and approved by the Ethics Committee of Peking University Cancer Hospital.

1. Study Background

Gastric cancer is a highly prevalent gastrointestinal malignancy in China. According to the World Health Organization, gastric cancer ranks fifth in incidence and third in mortality among all malignancies worldwide, surpassed only by lung cancer and liver cancer. The situation for the prevention and control of gastric cancer in China is particularly severe; newly diagnosed cases in China account for more than 40% of the global total each year, and the overall incidence in East Asia accounts for 58% of global cases. The annual number of newly diagnosed patients in China approaches 400,000, and the mortality rate has long remained high. More importantly, nearly 90% of patients with gastric cancer in China have advanced-stage disease at the time of diagnosis, and the 5-year survival rate of these patients is only 10% to 49%. Effective treatment of locally advanced gastric cancer therefore remains a core challenge for clinical oncology in China. Surgical resection is the principal modality of gastric cancer treatment, and D2 radical gastrectomy has become the classical standard for curative surgery. Even with continuous optimization of surgical techniques and perioperative management, however, the local recurrence rate after surgery alone remains as high as 24% to 54%, and the prognosis of most patients with recurrence is extremely poor within a short period. Currently, neoadjuvant therapy is the conventional preoperative regimen for locally advanced gastric cancer recommended by major domestic and international guidelines; it can effectively

reduce tumor size and increase the rate of radical resection, but it is not appropriate for all subtypes of gastric cancer.

dMMR/MSI-H represents a distinctive molecular subtype of gastric cancer. In these patients, loss of mismatch repair gene function leads to microsatellite sequence abnormalities, resulting in tumors with high immunogenicity. The core clinical characteristic of this subtype is its very poor response to conventional neoadjuvant therapy: patients derive no benefit from such therapy, and authoritative guidelines worldwide do not recommend standard regimens for them. To date, no unified consensus has been reached on perioperative treatment for dMMR/MSI-H locally advanced gastric cancer, and current recommendations are limited to participation in immunotherapy clinical trials or regular follow-up observation. Specific therapeutic options for this population are urgently needed in clinical practice. The advent of immunotherapy has changed this situation: immune checkpoint inhibitors are highly effective in this subtype. Multiple clinical studies have shown that PD-1 inhibitor monotherapy or dual immune combination as neoadjuvant therapy can substantially increase the rates of pathological complete response (pCR) and major pathological response (MPR), with long-term progression-free survival significantly superior to conventional treatment. Immunotherapy has become the core therapeutic direction for dMMR/MSI-H gastric cancer.

Iparomlimab and tuvonralimab (QL1706) is the world's first PD-1/CTLA-4 bifunctional combination antibody, developed on the MabPair® biotechnology platform. It consists of an anti-PD-1 antibody and an anti-CTLA-4 antibody combined in a precise 2:1 ratio, and is capable of simultaneously blocking two key immune checkpoint pathways to achieve synergistic antitumor effects. Compared with the conventional two-drug regimen of a PD-1 inhibitor combined with a CTLA-4 inhibitor, QL1706 demonstrates more favorable pharmacokinetic characteristics, stronger target specificity, and reduced off-target effects, effectively lowering the incidence of adverse reactions. Furthermore, dual-pathway blockade is achieved with a single agent without the need for additional co-administration, substantially improving patient compliance. This drug has previously demonstrated excellent antitumor efficacy and manageable safety in clinical studies of multiple tumor types, including cervical cancer, hepatocellular carcinoma, and non-small cell lung cancer.

Conducting a prospective, single-arm, single-center Phase II clinical trial of QL1706 as neoadjuvant therapy for dMMR/MSI-H locally advanced gastric adenocarcinoma is of substantial clinical and scientific value. This study is the first in China to explore the therapeutic value of QL1706 in the perioperative management of this gastric cancer subtype. It can effectively fill the research gap in this field and provide new reference for clinical practice. The study will also systematically validate the efficacy and safety of this drug, laying a solid foundation for subsequent multicenter, randomized, controlled Phase III studies. In addition, the study will concurrently investigate therapy-related biomarkers and explore mechanisms of resistance and organ-preservation strategies, supporting the realization of precision individualized care for gastric cancer. In the long term, this study is expected to transform the perioperative treatment model for dMMR/MSI-H gastric cancer, provide superior

therapeutic options for patients with this specific subtype, and promote clinical innovation and standardized development of gastric cancer immunotherapy.

2. Study Objectives

The primary objective of this study is to evaluate the efficacy of iparomlimab and tuvonralimab in improving perioperative treatment of MSI-H/dMMR locally advanced gastric adenocarcinoma. The secondary objective is to evaluate the safety and long-term benefit of iparomlimab and tuvonralimab in improving perioperative treatment of MSI-H/dMMR locally advanced gastric adenocarcinoma.

3. Study Procedures

This study is a prospective, single-arm, single-center Phase II clinical trial of iparomlimab and tuvonralimab as neoadjuvant immunotherapy for MSI-H/dMMR locally advanced gastric adenocarcinoma, with a planned enrollment of 30 patients. The study population consists of patients with MSI-H/dMMR locally advanced gastric adenocarcinoma. Your treating physician will explain the details of the study to you and, after obtaining your consent, will begin screening. After screening, if you meet the protocol requirements and are approved by the investigator, you will formally enter the study. The specific study procedures are as follows:

3.1 Screening Period

Within 28 days before receiving the study drug treatment, your study physician will explain this study to you. If you agree to participate in this study, please sign this informed consent form.

You will be asked to cooperate with the study physician or study personnel to complete the following procedures:

- You will be asked to provide demographic information, such as date of birth and ethnicity.
- You will be asked about your previous medical history and any medications you have used in the past.
- Your body temperature, pulse, respiratory rate, and blood pressure, as well as your height and body weight, will be measured.
- ECOG performance status assessment: this is an overall assessment of your performance status, which will be scored by your physician.
- A physical examination will be performed.
- A 12-lead electrocardiogram (ECG) and echocardiography will be performed (results from examinations previously performed at the study center are acceptable, provided that they were completed within 28 days before the first dose of the study drug). These examinations are used to assess your cardiac function.

- Blood and urine samples will be collected to assess your general health, including complete blood count, biochemistry, urinalysis with urinary sediment, coagulation function, the 8-item pituitary panel, and virology testing (hepatitis B, hepatitis C, and human immunodeficiency virus).
- If you are a woman of childbearing potential, a urine or blood pregnancy test will be performed within 7 days before the first dose of the study drug.
- Adverse events occurring after the signing of the informed consent form will be assessed.
- You will be asked about concomitant medications used since signing the informed consent form.
- Your disease status will be evaluated, including CT (computed tomography) or MRI (magnetic resonance imaging) scans to measure and record tumor size. Please undergo additional imaging assessments as recommended by your physician. The above are routine procedures for tumor status evaluation and will be performed regardless of whether you participate in this study. The frequency of assessments in this study is comparable to that of standard clinical care.

Please inform your physician promptly of any condition that may be related to the treatment. After all screening procedures are completed, your study physician will conduct an evaluation to determine whether you are eligible to participate in this study.

The examinations performed during the screening phase are part of routine clinical care. Results of examinations conducted at this study center before you signed the informed consent form may be used to assess your eligibility to participate in the study, in which case you will not need to repeat them. After all evaluations during the screening period, if the study physician determines that you are eligible, you will be scheduled to enter the treatment phase. If the study physician determines that you are not suitable for this study, he or she will inform you and assist in arranging alternative treatment outside the study.

3.2 Treatment Period

Neoadjuvant Therapy:

Iparomlimab and tuvonralimab 5 mg/kg, intravenous infusion, on Day 1 of each 21-day cycle.

A total of 4 cycles of neoadjuvant therapy will be administered.

Surgery:

Radical surgery will be performed within 4 to 8 weeks after the completion of neoadjuvant therapy. The surgical approach will be determined based on tumor location, stage, and tumor regression, including total gastrectomy, proximal gastrectomy, and distal gastrectomy.

Adjuvant Therapy:

Postoperative adjuvant therapy will begin within 4 to 6 weeks after surgery, consisting of 4 cycles of iparomlimab and tuvonralimab.

Iparomlimab and tuvonralimab 5 mg/kg, intravenous infusion, on Day 1 of each 21-day cycle.

During the neoadjuvant and adjuvant therapy periods, you must attend scheduled visits with the study

physician on Days 7, 14, and 21 of each treatment cycle. At each visit, you will be asked to cooperate with the study physician or study personnel to complete the following procedures. Safety-related examinations must be completed before each dose, and blood sampling must not occur earlier than 3 days before dosing (for the first neoadjuvant treatment cycle, blood sampling may occur within 7 days before dosing). Dosing can be initiated only after the study physician has reviewed the examination results and determined that they meet the criteria for continued treatment.

- Limited physical examination based on your symptoms, including vital signs and body weight measurement.
- The study physician will score your performance status (activities of daily living).
- Complete blood count, biochemistry, amylase and myocardial enzymes, urinalysis with urinary sediment, the 8-item pituitary panel, and electrocardiogram. If screening examinations were completed within 7 days before the first dose of Cycle 1, they do not need to be repeated.
- On Days 8 and 15 after dosing, complete blood count will be repeated; if myelotoxicity occurs, dosing will be adjusted in a timely manner.
- Within 3 days before the second through fourth doses: vital signs, body weight measurement, ECOG performance status, physical examination, complete blood count, biochemistry, amylase and myocardial enzymes, urinalysis with urinary sediment, the 8-item pituitary panel, and electrocardiogram.
- Imaging examinations: plain CT of the chest; plain plus contrast-enhanced CT or plain plus contrast-enhanced MRI of the abdomen and pelvis; plain plus contrast-enhanced CT or plain plus contrast-enhanced MRI of any other site suspected of metastasis based on the investigator's judgment (per clinical indication); CT or MRI of the brain (per clinical indication); bone scan (per clinical indication); PET-CT (per clinical indication). Imaging is performed every 6 weeks (± 3 days), calculated from the date of the first dose.

During the surgical treatment period, you will be asked to cooperate with the study physician or study personnel to complete the following examinations:

- Preoperative physical examination, including vital signs and measurement of height and body weight.
- Preoperative scoring of your performance status (activities of daily living) by the study physician.
- Preoperative scoring of your nutritional status by the study physician.
- Within 7 days before surgery: laboratory tests including complete blood count, biochemistry, amylase and myocardial enzymes, coagulation function, blood type, infection screening, urinalysis with urinary sediment, the 8-item pituitary panel, and tumor markers.
- Preoperative cardiopulmonary assessment: electrocardiogram, 24-hour ambulatory electrocardiogram, cardiac ultrasound, pulmonary function test, and B-mode ultrasound of bilateral carotid arteries and bilateral lower extremity veins.

- Postoperatively, the study physician or study personnel will, based on your postoperative recovery, periodically monitor complete blood count, biochemistry, amylase and myocardial enzymes, and coagulation function, and will monitor vital signs daily.

4. Matters Requiring Your Cooperation

To facilitate the successful conduct of this study, after you agree to participate, we will conduct regular follow-up on your therapeutic response and quality of life. Follow-up will continue until 3 years after surgery and will include two parts: safety follow-up and survival follow-up.

Safety Follow-up: The safety follow-up period extends from the last dose of the study drug or from the date of surgery to 30 ± 7 days thereafter, or until the initiation of other antitumor therapy (whichever occurs first), during which adverse events (AE) and concomitant medications and treatments will be assessed.

Survival Follow-up: After the safety follow-up, survival follow-up will be conducted. Using the last safety follow-up as the reference time point, follow-up will be performed every 6 months (± 2 weeks), including telephone follow-up, to record whether you have received any other antitumor therapy since the previous follow-up. If other treatment is received, the treatment regimen, number of cycles, best therapeutic response, and time to disease progression must be recorded.

During this period, please cooperate with the following requirements:

- Take medications and undergo examinations as arranged by the investigator.
- Do not arbitrarily change your current treatment or initiate any new treatment without confirmation from the study physician.
- Inform the study physician of any health-related issues, even those that you consider minor.
- Inform the study physician of all medications you have used (including traditional Chinese herbal medicines) other than the study drug, both before and during participation in the study.
- If you discontinue study treatment prematurely for any reason, please complete the final assessment by the study physician.
- Because the drugs used during treatment may be harmful to fetal development, please use medically accepted effective contraceptive methods (including barrier contraception, surgical contraception, and abstinence) from the time of signing the informed consent form until 120 days after the last dose. Routine examinations will be required to ensure your safety.
- Please cooperate with the study physician in completing the necessary periodic examinations during treatment.
- Please cooperate with the study physician in evaluating your current medical history, prior treatment history, concomitant diseases, concomitant medications, allergy history, vital signs, and comprehensive physical examination, and in scoring your overall condition; also cooperate with the collection of various clinical examination data, including blood pressure, complete blood

count, urinalysis, electrocardiogram, biochemistry, amylase, the 8-item pituitary panel, and CT/MRI imaging.

5. Biological Sample Collection

Please cooperate with the study physician in the collection of biological samples, including peripheral blood, urine, and feces, before treatment, after 2 cycles of treatment, before surgery, and 1 month after surgery. At each time point, 5 mL of peripheral blood, 10 mL of urine, and 10 g of feces will be collected. Peripheral blood will be used for circulating tumor cell detection. Tissue specimens will be collected as fresh-frozen samples and used to screen for treatment-related biomarkers, with sample size approximately that of a red bean and on the condition that pathological diagnosis is not affected. Biological samples will be used solely for the exploration of biomarkers and mechanisms of resistance related to gastric adenocarcinoma, and all samples will be destroyed within 3 years after the end of clinical study enrollment. All matters concerning human genetic resources data will strictly comply with the National Regulations on the Management of Human Genetic Resources. Your privacy and security will be strictly protected throughout this process.

6. Risks and Discomforts of Participating in the Study

6.1 Adverse Reactions Possibly Caused by Neoadjuvant and Adjuvant Therapy

The investigational drug iparomlimab and tuvonralimab is a marketed product. Its adverse reactions are predominantly immune-related, including pneumonitis, diarrhea and colitis, hepatitis, nephritis, hypothyroidism or hyperthyroidism, adrenal insufficiency, hyperglycemia or type 1 diabetes mellitus, thrombocytopenia, pancreatitis, and myocarditis.

6.2 Surgical Risks

During anesthesia, possible events include anesthetic drug allergy, cardiovascular and cerebrovascular complications, airway injury due to endotracheal intubation, and respiratory dysfunction. During the surgical procedure, possible events include intraoperative injury to important organs, vascular bleeding, and intra-abdominal infection. Postoperatively, possible complications include intra-abdominal bleeding, anastomotic leakage, duodenal stump leakage, anastomotic bleeding, intestinal obstruction, intra-abdominal or pelvic infection, respiratory tract infection, urinary tract infection, lower extremity venous thrombosis, pulmonary embolism, and incisional infection, fat liquefaction, dehiscence, or delayed healing.

6.3 Imaging Examination Risks

During imaging examinations, contrast media allergy may occur, including rash, asthma, hypotension, dizziness, and anaphylactic shock.

6.4 Risk of Disease Progression

Malignant tumors may progress rapidly, and no treatment can completely prevent the development of drug resistance. If neoadjuvant therapy is ineffective, rapid tumor progression may occur, and some patients may lose the opportunity for surgery. The study team will perform imaging reassessment every 2 cycles during treatment. If there is a risk of progression, a multidisciplinary team (MDT) discussion will be convened to evaluate your treatment options.

6.5 Unknown Risks

There may be currently unforeseen risks and adverse reactions. You may experience changes similar to the adverse reactions described above, and you may also experience previously unreported unknown adverse reactions. During the treatment process, please contact the study physician promptly if you experience any discomfort or adverse reactions. In addition, any treatment may prove ineffective, and the disease may continue to progress because of treatment failure or because of comorbid diseases.

All of the risks described above, including "adverse reactions possibly caused by neoadjuvant and adjuvant therapy," "surgical risks," "imaging examination risks," "risk of disease progression," and "unknown risks," may be life-threatening when severe.

7. Benefits of Participating in the Study

After participating in this study, the direct benefits you may obtain include suppression or prevention of tumor cell growth, reduction of the postoperative recurrence rate, and improvement of quality of life. However, this is a clinical study, and it is currently uncertain whether the study drug and study regimen will be effective for you. There is no guarantee that you will derive direct medical benefit from participating in this study. In addition, the data obtained from this study may help to deepen the medical community's understanding of this disease and related treatment regimens, and may provide reference for the treatment of similar patients in the future, but this does not constitute direct benefit to you personally.

8. Alternative Treatments

Participation in this study is voluntary; you are not required to participate in this study to receive treatment for your disease. In addition to participating in this study, you have other treatment options, such as other immunotherapies, direct surgical treatment, and participation in other clinical studies. Your study physician will discuss with you the other available treatment measures or drugs and will discuss the risks and benefits of these treatments. If you decide not to participate in this study, your medical care will not be affected.

9. Costs Related to Participation in the Study

You will not receive payment for participating in this study. During the study, iparomlimab and tuvonralimab will be provided free of charge. The imaging and laboratory examinations in this study are mainly used for assessment of disease status, evaluation of efficacy, and safety monitoring; these

examinations are conducted as part of routine clinical care and follow-up and are not added as a result of participation in the study. Therefore, the costs of various examinations during disease treatment, the costs of other treatments, and the costs of treatment and examination for concomitant diseases will be borne by the subject.

10. Compensation

You will not receive additional compensation for participating in this study.

11. Indemnification

If a study-related injury occurs during your participation in this clinical study, the study sponsor will assume corresponding liability for compensation in accordance with applicable laws and regulations.

12. Right to Refuse to Participate or to Withdraw from the Study

You may choose not to participate in this study and have the right to withdraw at any stage of the trial without providing any reason. Your medical care and rights will not be affected as a result. However, processing of data obtained before your withdrawal is lawful, and these data may continue to be used in this study with protection of your privacy. Once you decide to participate in this study, please sign this informed consent form to indicate your agreement. Before entering the study, the physician will conduct screening to confirm whether you are a suitable candidate. During the study, if new information emerges that may affect your willingness to continue participation, you will be informed promptly and may need to sign a new informed consent form.

The study physician will actively terminate your participation in the study under the following circumstances:

- Disease progression or inability to tolerate study treatment.
- New information indicating that study treatment cannot provide you with optimal benefit.
- If the study physician believes that continued participation in the study would be detrimental to you, he or she may discontinue your participation at any time without obtaining your consent.
- The Ethics Committee and the regulatory authorities may also terminate your participation in the study as appropriate.

If the study is stopped, you will be informed, and your study physician will assist in arranging your subsequent treatment. If you withdraw from the study prematurely for any reason, the study physician will ask you to return to the study center to complete the end-of-treatment visit. You may also be contacted thereafter or scheduled for follow-up to collect a small amount of data regarding your health status. If you withdraw from the study, study data obtained prior to your withdrawal may still be used to the extent permitted by applicable laws and regulations.

13. Privacy and Confidentiality

During the study, your name, sex, and other personally identifiable information will be replaced by codes or numbers and kept strictly confidential. Only the relevant physicians will know your personal information, and your privacy will be well protected. Study results may be published in journals, but no personally identifiable information of yours will be disclosed.

If you agree to participate in this study, all of your medical records may be reviewed by relevant personnel from the sponsoring institution, the relevant regulatory authorities, or the independent Ethics Committee in order to verify that the study is being conducted appropriately. Signing the informed consent form indicates that you agree to allow such review.

14. How to Obtain Help During the Study

You may obtain information about this study and its progress at any time. If you have any questions related to this study, please contact Wang Anqiang, telephone: 88196967 / 88196970.

If you have questions during the study regarding the rights of research participants, you may contact the Ethics Committee of Peking University Cancer Hospital, telephone: 010-88196391, 010-88196861.

Informed Consent Signature Page

If you fully understand the content of this study and agree to participate, please sign this informed consent form. The form will be prepared in duplicate, with one copy retained by the investigator and one copy retained by the subject or his or her legally authorized representative.

Clinical Study Title: A Prospective, Single-Arm, Single-Center Phase II Clinical Trial of Iparomlimab and Tuvonralimab as Neoadjuvant Immunotherapy for Microsatellite Instability-High / Mismatch Repair-Deficient Locally Advanced Gastric Adenocarcinoma.

To be signed by the subject or his or her legal guardian

Statement of Consent:

1. I confirm that I have read and understood the informed consent form for this study. The problems that may arise during the study and their corresponding solutions have been explained to me, and I have had the opportunity to raise my own questions.

2. I understand that participation in this study is voluntary, and that refusal to participate will not affect any of my entitlements.

3. I have been informed that the physician participating in the study, the relevant officer in charge of this work at Peking University Cancer Hospital, and the Medical Ethics Committee of Peking University Cancer Hospital have the right to review the study records and case data. I agree that the above personnel may directly access my study records, and I understand that the above information will be handled confidentially.

4. I agree to participate in this study.

Subject's full name and signature: _____ Date (YYYY/MM/DD): _____

Legally authorized representative: _____ Date (YYYY/MM/DD): _____

Relationship to the subject: _____ (If the representative is a non-relative authorized agent, is there a letter of authorization from the subject? Yes □ No □)

To be completed by the physician conducting the informed consent process

Investigator's Statement: I confirm that I have explained and discussed with the patient the nature, objectives, requirements, and possible risks of this study, and have also discussed alternative treatment options. I confirm that a copy of this informed consent form has been provided to the subject for retention.

Investigator's full name and signature: _____ Date (YYYY/MM/DD): _____