Informed Consent Form

Project Title: A Phase III Randomized Controlled Study Comparing High-Dose Rituximab (500 mg/m²) Combined with the CHOP Regimen to Standard-Dose Rituximab (375 mg/m²) Combined with the CHOP Regimen in Male Patients with Newly Diagnosed Advanced Diffuse Large B-Cell Lymphoma

Informed Consent Form Version: 2.0, July 5, 2024
Research Institution: Sun Yat-sen University Cancer Center
Principal Investigator: Yi Xia

Patient Name: Patient Initials:

Dear Participant,

We invite you to participate as a subject in a clinical trial. This informed consent form provides you with information to help you decide whether to participate in this clinical trial. Please take some time to read the following content carefully. If you have any questions or terms you do not understand, feel free to 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 the Sun Yat-sen University Cancer Center.

1. Background of the Study

Lymphoma is one of the most common malignant tumors. In China, the estimated number of new cases of lymphoma in 2022 was about 100,000, ranking tenth among all malignant tumors, with approximately 60,000 deaths. Rituximab (R) combined with cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP regimen) is one of the first-line recommended treatments for diffuse large B-cell lymphoma (DLBCL). Previous studies have shown that using a higher dose of rituximab can improve the poor prognosis of male patients without increasing toxicity. We have noted that few clinical studies specifically target male patients with advanced (Ann Arbor stage III-IV) DLBCL, and whether increasing the dose affects the safety of rituximab remains to be answered. Therefore, our study will focus on exploring the impact of different doses of rituximab on modified PFS and OS in male patients with advanced DLBCL.

2. Objective of the Study

To compare the modified progression-free survival (modified-PFS) between high-dose rituximab (500 mg/m²) combined with the CHOP regimen and standard-dose rituximab combined with the CHOP regimen in previously untreated (treatment-naive, TN) male patients with stage III-IV diffuse large B-cell lymphoma (DLBCL).

3. Study Procedure

This study is a multicenter, randomized controlled Phase III clinical trial designed to primarily evaluate progression-free survival (PFS) in previously untreated (treatment-naive, TN) male patients with stage III-IV diffuse large B-cell lymphoma (DLBCL) when comparing high-dose rituximab (500 mg/m²) combined with the CHOP regimen to standard-dose rituximab combined with the CHOP regimen.

After signing the informed consent form and before randomization begins, all participants must provide sufficient tumor biopsy samples for confirmation of DLBCL through HE staining and immunohistochemistry (IHC) testing at a central laboratory. Qualified participants will be randomly assigned in a 1:1 ratio to either the experimental group (rituximab 500 mg/m²) or the control group (rituximab 375 mg/m²). Participants will undergo six cycles of R-CHOP treatment (21 days per cycle), followed by two cycles of rituximab maintenance therapy (21 days per cycle). During the study, there will be no cross-dosing between the two groups.

"Randomization" means you will be assigned to a treatment group randomly to reduce bias. You have a 1 in 2 chance of receiving rituximab 375 mg/m² and a 1 in 2 chance of receiving rituximab 500 mg/m². The specific group assignment will be determined randomly by a computer program. Neither you nor your doctor can choose which drug you will receive. This ensures that the study drug is evaluated in a fair manner.

4. Participant Responsibilities

To ensure the successful and smooth conduct of this study, please cooperate with the following:

- Follow the medication schedule and undergo examinations as arranged by the researcher.
- Do not change your current treatment or start any new treatments without confirming with the study doctor.
- Inform the study doctor about any health issues, even if you think they are not significant.
- Tell the study doctor about all other medications you are using, both before and during the study, including herbal medicines, other than the study drug.
- If you terminate the study treatment early for any reason, please complete the final evaluation with the study doctor.
- Participate in routine examinations to ensure your safety.
- Accurately record your medication diary card as required and submit it to your study doctor at your next visit.

5. Risks and Discomforts of Participating in the Study

Risks Associated with Chemotherapy Drugs:

- Hematological toxicity such as neutropenia (possibly with fever), anemia, and thrombocytopenia

- Gastrointestinal adverse reactions (diarrhea, nausea, vomiting, constipation, decreased appetite)
- Infections (upper and lower respiratory tract infections, pneumonia, urinary tract infections, sepsis, etc.)
- Infusion reactions
- Liver adverse reactions such as elevated transaminases
- Renal adverse reactions such as elevated creatinine
- Fatigue/weakness
- Skin toxicity
- Tumor lysis syndrome (TLS)
- Reproductive toxicity
- Hepatitis B virus reactivation
- Urinary tract reactions
- Neurotoxicity
- Aseptic necrosis of the femoral head
- Cushing's syndrome
- Cytokine release syndrome (CRS)

Procedure-Related Risks:

Blood drawn for laboratory tests may cause bruising at or near the site where the needle enters the vein and increase the risk of infection.

As the effects of the drugs used in this study on infants are unknown, you and your partner must use contraception during the trial. If your partner becomes pregnant while you are on medication or within 90 days after you stop taking the medication, you must inform your doctor.

If you undergo subsequent treatments after completing the treatment in this study protocol, such as local radiotherapy, surgery, or interventional therapy for the primary or metastatic lesions, you may experience risks related to these treatments.

Common Risks Associated with Radiotherapy:

- Salivary gland and oral reactions: inhibition of salivary gland secretion, acute and chronic reactions of the oral mucosa
- Damage to sensory organs
- Radiation pneumonitis
- Common Risks Associated with Surgery:
- Anesthetic complications
- Intraoperative bleeding, massive bleeding, shock
- Injury to surrounding tissues or organs
- Intraoperative and postoperative infections
- Common Risks Associated with Interventional Surgery:
- Allergic reactions
- Injury to adjacent organs
- Complications related to endovascular stenting
- Toxic and side effects caused by contrast agents and chemotherapy drugs

6. Benefits of Participating in the Study

During this trial, your condition may be controlled or relieved, but there is also the

possibility of disease progression. The research team will make diagnostic and treatment decisions based on changes in your condition. In this trial, the sponsor has purchased medical insurance for you to cover certain risks associated with the trial.

7. Alternative Treatments

In addition to participating in this study (or if you choose not to participate), you can also follow clinical guidelines to select other treatment options. Please discuss these and other possible choices with your doctor.

8. Related Costs of Participating in the Study

All medications for this study must be paid for by the patient.

9. Compensation

During your participation in this clinical study, if any study-related injury or serious adverse event occurs, the sponsor will cover the treatment costs and provide appropriate compensation in accordance with Chinese law.

However, study-related injuries do not include those arising from the following circumstances:

- The natural progression of underlying diseases or conditions
- Your negligence or intentional misconduct (e.g., failure to strictly adhere to this consent form, study protocol, or instructions provided by the study doctor or research staff)

10. Insurance

The sponsor has purchased liability insurance for this clinical trial.

11. Right to Refuse Participation or Withdraw from the Study

You may choose not to participate in this study or withdraw at any stage without any reason, and your medical treatment and rights will not be affected. However, any data collected about you before withdrawal will be legally processed, and if your data has already been integrated into the study, it may not be feasible to remove it due to cost constraints. In such cases, it may still be used in the study, provided your privacy is protected. 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 a screening to confirm if you are a suitable candidate.

12. Privacy and Confidentiality

During the study, your personally identifiable information, such as your name and gender, will be replaced with codes or numbers and kept strictly confidential. Only the relevant doctors will know your personal information, ensuring your privacy rights are well protected. The study results may be published in journals, but no personally identifiable information about you will be disclosed.

If you agree to participate in this study, all your medical records will be accessible to authorized personnel of the research unit initiating this study, relevant authorities, or independent ethics committees to verify the study's proper conduct. Signing the informed consent form indicates your agreement to this access.

13. How to Obtain Assistance During the Study

If you have any questions about participant rights during the study, you can contact the Ethics Committee of the Sun Yat-sen University Cancer Center at 020-87343009.

If you fully understand the content of this research project and agree to participate, you will sign this informed consent form. It will be made in duplicate, with one copy retained by the researcher and one by the participant or their authorized representative.

Clinical Research Project Title:

Signature of the Participant or Legal Representative:

Consent Statement:

I confirm that I have read and understood the informed consent form for this study. The potential issues and solutions during the study have been explained to me, and I have had the opportunity to ask questions.

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

I acknowledge that the study team members and the Ethics Committee of the Sun Yat-sen University Cancer Center have the right to review study records and case data. I agree to allow these individuals to access my study records and understand that the information will be kept confidential.

I agree to participate in this study.

Full Name of Participant:

Date: Year ___ Month ___ Day ___

Full Name of Participant's Legal Representative:

Date: Year ___ Month ___ Day ___

Relationship to Participant: _____ (If the representative is not a close relative, is there an authorization letter from the participant? Yes [ ] No [ ])

To be completed by the physician conducting the informed consent process:

Researcher Statement: I confirm that I have explained and discussed the nature, purpose, requirements, and potential risks of this study with the participant. I have also discussed alternative treatment options and ensured that a copy of this informed consent form has been given to the participant for their records.

Full Name of Researcher:

Date: Year ___ Month ___ Day ___