Informed Consent Form for Study Participants

Medical Research Title:	Randomized, Double-Blind, Placebo-Controlled Clinical Study of the Efficacy and Safety of Tocilizumab in Chinese Adults with Anti-MDA5 Antibody-Positive Dermatomyositis
Protocol Number (if applicable):	PROMIS-RCT-I
Research Center:	Peking Union Medical College Hospital
Principal Investigator:	Wang Qian
Informed Consent Form Version Number:	2.0
Informed Consent Form Version Date	November 1, 2025
Subject Name:	
Subject ID:	

Dear Participant:

We would like to invite you to participate in a clinical study titled "A Randomized, Double-Blind, Placebo-Controlled Clinical Study of the Efficacy and Safety of Tocilizumab in Chinese Adults with Anti-MDA5 Antibody-Positive Dermatomyositis."

Please read this informed consent form carefully before you decide whether or not to participate. You may ask the investigator any questions you have, or consult with your family, friends, or others. Once you decide to participate in this study, you will be required to sign this informed consent form.

1. Background of the Study

Dermatomyositis (DM) is a chronic inflammatory autoimmune disease primarily affecting the skin and skeletal muscles. Anti-MDA5 antibody-positive dermatomyositis (anti-MDA5-DM) is the most common and severe subtype of DM, characterized by ulcerative skin lesions and rapidly progressive interstitial lung disease (RP-ILD). Anti-MDA5-DM exhibits the poorest prognosis among DM subtypes, with acute respiratory failure due to RP-ILD being the primary cause of mortality. Current clinical management relies predominantly on empirical regimens, lacking high-quality evidence-based medical evidence. The treatment of MDA5-DM-related ILD is often combined with glucocorticoid and calcineurin inhibitors (such as cyclosporine and tacrolimus) . However, even with intensive therapy combining corticosteroids and calcineurin inhibitors, approximately 50% of patients experience persistent ILD progression, with some requiring advanced life support. Consequently, developing targeted therapies with proven efficacy represents an urgent clinical need.

Tocilizumab is a humanized monoclonal antibody targeting the IL-6 receptor, exerting therapeutic effects by specifically blocking the IL-6 signaling pathway. Research indicates that IL-6, as a key pro-inflammatory factor, plays a crucial role in the pathogenesis of anti-MDA5-DM, potentially directly mediating inflammatory responses and tissue damage processes. Clinical observations reveal significantly elevated serum IL-6 levels in RP-ILD patients, with high IL-6 levels closely associated with poor patient outcomes. Based on this, tocilizumab, by precisely inhibiting the IL-6 signaling pathway, can effectively control excessive inflammatory responses, improve clinical symptoms, and potentially delay disease progression, offering a new targeted therapeutic option for anti-MDA5-DM treatment.

Currently, approved indications for tocilizumab worldwide do not include anti-MDA5-DM. Therefore, its use in treating anti-MDA5-DM constitutes off-label use. Our research team is the first internationally to report the clinical efficacy of tocilizumab in treating anti-MDA5-DM. Among 6 patients with anti-MDA5-DM complicated by ILD who showed poor response to conventional corticosteroid plus immunosuppressive therapy, 5 (83.3%) demonstrated significant improvement in respiratory symptoms and pulmonary imaging findings after adding tocilizumab. This confirms the treatment regimen's favorable efficacy and safety profile. Subsequent case reports further validated these findings, providing crucial evidence for tocilizumab's application in anti-MDA5-DM therapy.

Currently, the potential efficacy of tocilizumab in anti-MDA5-DM treatment has garnered attention in multiple domestic and international expert consensus statements. These consensus documents suggest considering its inclusion in treatment regimens for dermatomyositis,

particularly anti-MDA5-DM cases. However, as existing studies are predominantly small-sample case reports or case series lacking evidence from rigorously designed randomized controlled trials (RCTs), all consensus statements maintain a cautious stance and refrain from making explicit recommendations. To confirm the clinical value of tocilizumab, large-scale, multicenter clinical studies are still needed to systematically evaluate its precise efficacy and long-term safety, thereby providing more reliable evidence-based medical support for clinical practice. Therefore, this study proposes to conduct a prospective, multicenter, randomized, placebo-controlled clinical trial to further provide high-quality evidence on the efficacy and safety of tocilizumab in anti-MDA5-DM treatment. This is expected to address the current lack of definitively effective drugs for this disease and offer a new therapeutic option for this rare but severely debilitating autoimmune disorder.

Please be informed that this study has been approved by the Ethics Review Committee of Peking Union Medical College Hospital.

2. What is the purpose of this clinical study?

The aim of this study was to evaluate the efficacy and safety of these drugs by conducting a 16-week multicenter, prospective, randomized, placebo-controlled clinical trial, to systematically evaluate the efficacy and safety of tocilizumab in the treatment of Chinese adult anti-MDA5-DM patients, and to provide high-quality clinical evidence for the clinical application of tocilizumab in this disease.

[Comment: Change 'was' to 'is' to reflect ongoing study.]

If this study confirms the efficacy and safety of tocilizumab in treating anti-MDA5-DM, it will help address the current lack of therapeutic options for this disease. It holds promise as a new treatment choice for anti-MDA5-DM, potentially improving treatment standards, reducing patient mortality, enhancing quality of life, alleviating the burden on families and society, and saving healthcare costs.

3. Research methods

- This is an intervention study and the subjects will be divided into two groups: Experimental Group and control group. The ratio of entry to the two groups is 1:1, the grouping is done at random (like a lottery), and neither you nor the researcher can choose in advance which group to join.
- The experimental group will receive standard therapy combined with tocilizumab injection. The control group will receive standard therapy combined with placebo intravenous infusion (the placebo resembles the study drug but contains no active ingredients). Neither you nor your study doctor will know whether you are receiving the study drug or placebo. In emergencies, your study doctor may access your group assignment through a specific protocol if necessary.
- About 110 people nationwide will participate in the study. Each study participant will participate in the trial for 16 weeks.
  [Comment: Clarify total enrollment: 'Approximately 110 participants nationwide'.]

4. Study Procedure

- Before commencing any study-related activities, you must first sign this informed

consent form.

- During the screening period, the investigator will ask about and collect your personal information, past medical history, and concomitant medications. You will be scheduled for clinical laboratory tests, myositis antibody panel, pulmonary function tests, and chest CT scans.
- If you are eligible, the investigator will initiate the study treatment. Enrolled patients will be randomly assigned in a 1:1 ratio to one of two groups:
  ① Tocilizumab treatment group: Standard therapy regimen (prednisone (<1 mg/kg/d) combined with one calcineurin inhibitor [tacrolimus 1 mg bid or cyclosporine 3-5 mg/kg/d]) plus tocilizumab injection (8 mg/kg , injected 4 times at weeks 0,2,4, and 8, respectively, intravenously).
  ② Placebo Treatment Group: Standard treatment regimen combined with placebo intravenous infusion.
- You are required to attend weekly follow-up visits at the hospital at weeks 4, 8, and 16 post-treatment as per the protocol. During these visits, the investigator will arrange for the following examinations: vital signs, physical examination, complete blood count, liver and kidney function tests, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum ferritin, creatine phosphokinase (CK), arterial blood gas analysis, oxygenation index (PaO_2/FiO_2, and oxygen saturation (SpO_2).
- On the enrollment day and at the 4th, 8th, and 16th week follow-ups, the investigator will arrange for a professional to conduct a face-to-face interview with you to complete several scales: Cutaneous Damage Assessment in Dermatomyositis (CDASI), Myositis disease activity assessment visual analogue scale (MYOACT), the International Myositis Assessment, and the Clinical Study Group-defined Total Immunosuppression Score (TIS). These scales are designed to assess and monitor your disease activity and will take approximately an additional half hour.
- Your use of prednisone and other medications and adverse events should be recorded throughout the study. You do not need offline hospital follow-up at week 12, the investigator will arrange for a professional to contact you by telephone.
  [Comment: Replace 'offline' with 'in-person'.]

5. How the Study Ends

- All follow-up for this study will last 16 weeks. After the study ends, you will no longer receive the study medication and will continue treatment according to standard clinical practice.
- During follow-up visits, your doctor will evaluate your overall condition. If no significant therapeutic effect is observed or your condition worsens, you will be withdrawn from the study and transitioned to an alternative treatment regimen.
- You may choose to withdraw from the study at any time during its duration. and may be asked to do so by the study physician for your health and benefit. Before you quit, your doctor may arrange for you to be examined to ensure a safe exit.
- The study may be terminated by the study doctor, the study sponsor, regulatory authorities, or the ethics committee at any time during the study.

6. Study Benefits

- Participating in this study may improve your health, but we cannot guarantee that you will experience improvement.
- Your participation may help physicians learn more about tocilizumab treatment for anti-MDA5 antibody-positive adult dermatomyositis. Study results may guide future treatment approaches for this condition.
- If this study confirms the efficacy and safety of tocilizumab for treating anti-MDA5-DM, it will help address the current lack of treatment options for this disease. It holds promise as a new therapeutic choice for anti-MDA5-DM, potentially improving treatment standards, reducing mortality rates, enhancing patients' quality of life, alleviating the burden on families and society, and saving healthcare costs.

7. Risks and Inconveniences of the Study

All research involves known and unknown risks. Some risks are minor and temporary, while others may be serious or permanent. Whether, what and how severe the risks will be varies from person to person. Your study doctor will take all necessary precautions and closely monitor your condition. If you experience any discomfort, please inform your study doctor immediately so that appropriate treatment can be provided promptly.

Known Potential Risks and Side Effects of the Study Drug: Adverse reactions reported in clinical studies include: 1. Infections and infestations (upper respiratory tract infection, cellulitis, herpes labialis, herpes zoster, diverticulitis); 2. Gastrointestinal disorders (abdominal pain, oral ulceration, gastritis, stomatitis, gastric ulcer); 3. Skin and subcutaneous tissue disorders (rash, pruritus, urticaria); 4. Various neurological disorders (headache, dizziness); 5. Various abnormal test results (elevated liver aminotransferases, weight gain, elevated total bilirubin); 6. Vascular and lymphatic disorders (hypertension); 7. Blood and lymphatic system disorders (leukopenia, neutropenia); 8. Metabolic and nutritional disorders (hypercholesterolemia, hypertriglyceridemia); 9. Systemic disorders and administration site conditions (peripheral edema, hypersensitivity reactions); 10. Respiratory, thoracic, and mediastinal disorders (cough, dyspnea); 11. Eye disorders (conjunctivitis); 12. Renal and urinary disorders (nephrolithiasis); 13. Endocrine disorders (hypothyroidism).

Risks associated with study procedures: This study protocol does not involve any additional invasive examinations.

Risks related to pregnancy and lactation: There is insufficient data on the use of tocilizumab in pregnant women, and its effects on the fetus and mother remain unclear. Therefore, women who are pregnant, breastfeeding, or planning to conceive during the study period are ineligible to participate. Participants of childbearing potential must use effective contraception throughout the study.

Potential inconveniences of participating in this study: You will be required to attend follow-up visits at the hospital on the day of enrollment and at weeks 4, 8, and 16 post-enrollment. A telephone follow-up will be conducted at week 12. Face-to-face interviews will be conducted on the day of enrollment and at weeks 4, 8, and 16, which may require an additional 30 minutes of your time. You will be required to document your use of prednisone and other medications throughout the study. Please carefully consider these inconveniences when deciding whether to

participate.

It is crucial that you immediately report any side effects or discomfort to your study physician during the study period. The study physician may provide alternative medications to manage side effects and will conduct close follow-up as needed based on your condition. If you or your study physician determine that you cannot tolerate these side effects, the study medication may be discontinued entirely, and you may withdraw from this study.

The following measures are typically in place to address potential risks during the study:

Serious adverse reactions previously reported with tocilizumab primarily include infections and hypersensitivity reactions. Should you develop a serious infection, opportunistic infection, or sepsis, the study physician will interrupt tocilizumab treatment until your infection is controlled. Should you develop a new infection during tocilizumab treatment, you will undergo prompt and comprehensive diagnostic evaluation, receive appropriate antimicrobial therapy, and be closely monitored. In the event of a rapid-onset allergic reaction or other severe hypersensitivity reaction, immediate appropriate treatment will be administered, tocilizumab will be discontinued, and tocilizumab therapy will be permanently terminated.

To ensure trial safety, this study implements multi-tiered risk mitigation measures. First, stringent subject screening criteria exclude high-risk populations, reducing adverse event likelihood at the source. Second, based on prior research data, optimized dosing and treatment protocols maintain tocilizumab within safe ranges to balance efficacy and safety. Additionally, all investigators undergo specialized training to ensure proficiency in emergency protocols and standardized operating procedures, enabling swift and standardized responses to unforeseen events. Finally, this study will purchase clinical trial liability insurance. Should you experience adverse events leading to personal injury or death due to the investigational drug, compensation will be provided in accordance with the insurance contract.

8. Alternative Options

If you choose not to participate in this study, you may opt for the conventional standard treatment regimen (prednisone (<1 mg/kg/d) combined with a calcineurin inhibitor [tacrolimus 1 mg bid or cyclosporine 3-5 mg/kg/d]). For patients with inadequate response to the above standard treatment, studies suggest alternative approaches beyond tocilizumab, including JAK inhibitors, plasma exchange, or lung transplantation. However, the efficacy of these treatments remains uncertain. Your study doctor will explain the potential benefits and risks of these treatments.

9. New Information During the Study

During the study, if the investigator obtains new important information related to the research, we will promptly inform you and allow you to decide whether to continue participating in this study.

10. Study-Related Costs

- You will not be responsible for any study-related costs, including the study drugs used in this research (tocilizumab, control drug).
  [Comment: Clarify: '(tocilizumab or placebo)'.]

- Costs associated with standard clinical care, such as corticosteroids, immunosuppressants, and routine tests (complete blood count, urinalysis, liver/kidney function tests, chest CT, etc.), are the patient's responsibility.
- You will not receive compensation for participating in this clinical study. However, you will receive a transportation allowance of 200 yuan per visit and a nutritional allowance of 100 yuan per blood draw.
- Compensation will be transferred to your bank account within three months after each visit.

11. Research-Related Adverse Events

- If you experience any discomfort during the study, please contact your study physician promptly. The physician will guide you on subsequent diagnosis and treatment. The investigator has purchased insurance for this study. Should your health be harmed as a result of participating in this study, the insurance company will be responsible for providing treatment costs and compensation.

12. How My Samples Will Be Handled

- During the study, 10-12 mL of your blood will be collected at the following time points: screening period, randomization, and weeks 4, 8, and 16. These samples will be used for the following tests: complete blood count (CBC), liver and kidney function tests, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), creatine kinase (CK), serum ferritin, arterial blood gas analysis, and KL-6.
- Samples sent to our hospital will be destroyed according to standard medical procedures after use. Samples sent to external laboratories will be destroyed upon completion of the study.
- Your biological samples will be used solely for the purposes described in this study protocol and this informed consent form.
- Should you withdraw from the study early, no new samples will be collected; however, samples or data already collected or analyzed will be retained.

13. Confidentiality Policy

- This study may collect or process your personal and medical information, including but not limited to: your name, gender, date of birth, address, telephone number, diagnosis and treatment, examinations and tests, medical imaging, etc.
- Your personal information will be used solely for the purposes described in the study protocol and this informed consent form.
- The medical information obtained from your participation in this study will be kept confidential. No personally identifiable information will be disclosed when the study results are published in academic journals.
- The investigator will be responsible for storing and using all your personal data in this study. Members of the research team, research supervisors, the ethics committee, or the Clinical Research Oversight Department may have access to your personal data.

14. Funding Sources Potential Conflicts of Interest

The researchers have no conflicts of interest related to this study.

15. Voluntary Participation

Your participation is entirely voluntary. You may choose not to participate or withdraw from this study at any time during its course. This will not affect your relationship with your healthcare provider, and your routine medical care will remain unaffected.

16. Participant considerations

- Please truthfully inform the study doctor about your health status and any past or current medications you are taking;
- Please take your medication as prescribed and attend follow-up appointments at the hospital on time;
- If you experience any discomfort, please inform your study doctor promptly;
- During the study, you must not take the following medications: JAK inhibitors (tofacitinib, ruxolitinib, baricitinib, abulastinib, upadacitinib), other immunosuppressive drugs (methotrexate, azathioprine, mycophenolate mofetil, etc.);
- Avoid smoking and alcohol consumption during the study period;
- Avoid pregnancy or causing your partner to become pregnant during the study. If you plan to become pregnant or become pregnant during the study, inform your study doctor immediately.

17. Contact

If you experience any discomfort or have questions about this study, you may contact the investigator:

Position: Research Assistant	Name: Wu Chanyuan	Phone Number: 18612672717

If you have any questions regarding your rights as a research participant, you may contact the Ethics Committee:

Position: Ethics Secretary	Name: Li Jiayue	Phone Number: 010-69156874

Thank you for reading and considering participation in this study.

18. Signature Page

Subject:

I acknowledge the following information:

（1） I have read and understood the above informed consent information and have had sufficient time to consider whether to participate in the study.

（2） All my questions have been answered to my satisfaction.

（3） I voluntarily participate in this study and agree to follow the study procedures.

（4） I understand that I may withdraw from this study at any time without providing any reason, and my treatment or rights will not be affected.

（5） I have received a copy of the informed consent document and the signed consent form for my personal records.

（6） I consent to the collection and use of my samples as described in this informed consent statement.

（7） I consent to the collection and use of my personal information in this study.

（8） I understand that I may be contacted in the future to obtain permission for this study or any related sub-studies.

By signing this document, I agree to participate in this study as stated in the informed consent form and consent agreement.

Participant Name (Regular script): _____

Subject Signature:_____ Date:

The following applies only to incapacitated subjects, requiring guardian signature.

[Participant Name (Regular script):_____ , Guardian's Relationship to Participant_____ .]

Guardian Name (Regular script):_____ Contact Number:

Guardian Signature:_____ Date:

The following applies only to subjects who cannot read or write. A fair witness must sign.

Witness Name (Regular script):_____ Contact Number:

Witness Signature:_____ Date:

Investigator/Authorized Personnel Name (Regular script):

Investigator/Authorized Personnel Signature:_____ Date: