Informed Consent Form

Version 2.0

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Protocol Title

Validation of an Intensified Treatment Strategy for Disseminated MAC Infection: A Four-Drug Regimen Adding a Fluoroquinolone (Levofloxacin or Moxifloxacin) to the Standard Triple Therapy — A Multicenter, Randomized, Controlled Clinical Trial

Sponsor/Lead Institution

Shanghai Public Health Clinical Center

Principal Investigator

Liu Li

Dear Research Participant:

Because you may meet the eligibility criteria for this study, we invite you to participate. Please read this informed consent form carefully and make your decision with caution as to whether to participate. Participation in this study is entirely voluntary.

Before making your decision, you should understand the purpose, methods, possible benefits, and risks of this study. This process is called "informed consent." This study has been submitted for ethical review as required and may only be implemented after written approval by the Ethics Committee. If there is anything you do not understand, please feel free to consult the study doctor or study staff at any time. Before making your decision, you may take the unsigned consent form home and discuss it with your family, friends, or anyone you trust. You have the right to refuse participation or withdraw from the study at any time without penalty and without affecting the medical services and rights you are entitled to receive. If you decide to participate in this study, you will need to sign this consent form; you will receive a signed copy of the consent form.

1. Why is this study being conducted?

1.1 Study Background

Disseminated infection with the Mycobacterium avium complex (MAC) is one of the important opportunistic infections in patients with advanced HIV infection. Current treatment generally uses the standard triple regimen of "macrolide + ethambutol + a third drug (such as rifabutin/rifampin)." However, in patients with a high bacterial burden, profound immunosuppression, or concomitant bacteremia, the early culture conversion rate remains limited, and management of drug interactions and adverse reactions is complex. Fluoroquinolones (such as levofloxacin or moxifloxacin) have in vitro activity against some mycobacteria, and short-term addition during the intensive phase may enhance early bactericidal activity, but its true benefit and safety still need to be verified through randomized controlled trials.

1.2 Study Objective
This study aims to evaluate whether a four-drug regimen, in which a fluoroquinolone (levofloxacin or moxifloxacin) is added during the intensive phase on the basis of standard triple anti-MAC therapy, can improve the culture conversion rate of specimens at Day 28 (±3 days) and systematically assess its safety.

1.3 Study Methods
This study is a prospective, multicenter, randomized, controlled, parallel-group, open-label clinical trial. Eligible participants who sign the consent form will be randomly assigned in a 1:1 ratio to one of the following two groups:
(1) Standard triple-therapy group (control): macrolide (azithromycin or clarithromycin) + ethambutol + a third drug (rifabutin/rifampin, etc., according to center routine).
(2) Four-drug group (experimental): on the basis of the standard triple therapy, a fluoroquinolone (levofloxacin or moxifloxacin) will be added for the first 8 weeks of the intensive phase.

Both groups will continue prior antiretroviral therapy (ART), or start ART within 2 weeks after initiation of anti-MAC therapy (as determined by the study doctor based on assessment of drug interactions).

1.4 Study Procedures (What will you experience?)
After you sign the consent form, the study doctor will screen you and confirm whether you meet the eligibility criteria. If eligible and enrolled by randomization, you will receive treatment and follow-up according to the study protocol. Study follow-up time points usually include: screening period (D-7 to D0), baseline/randomization (D0), D7 (±2 days), D14 (±3 days), D28 (±3 days), D56 (±7 days), D84 (±7 days), and W24 (±14 days); if necessary, follow-up may be extended (e.g., to W48) to assess long-term safety and recurrence.

1.5 Examinations, Data, and Sample Collection Required
During the study, the following may be performed or collected (as arranged by the doctor):
• Medical history inquiry and physical examination: symptoms, signs, vital signs, body weight, etc.;
• Medication reconciliation and adherence assessment: study drugs, ART, and other concomitant medications;
• Laboratory tests: blood routine tests, liver and kidney function, electrolytes (including potassium/magnesium), etc., and inflammatory markers if necessary;
• Electrocardiogram (ECG): at baseline and during the intensive phase as specified by the protocol, or additionally if symptoms such as palpitations or syncope occur;
• Vision/color vision screening: because ethambutol may affect the optic nerve, regular assessment is required;
• Pathogen testing: baseline culture and repeat culture at D28 (primary endpoint), and repeat testing may also be performed at time points such as D56/D84;
• HIV-related tests: viral load, CD4, etc. (according to center routine and protocol

requirements);
• Collection of blood, urine, and stool samples.

Your examination results and study-related information will be recorded in the case report form (CRF) and managed using a code instead of your name.

2. How many people will participate in this study?
This study plans to enroll a total of 124 participants across multiple centers (approximately 62 in each group), with the final number depending on the actual enrollment.

3. How long will this study last?
The enrollment period is expected to last approximately 12 months. After enrollment, you will be followed for at least 24 weeks (about 6 months); if evaluation of recurrence or long-term safety is needed, the study doctor may recommend extending the follow-up.

4. Source of Funding
Source of funding for this project: *National Science and Technology Major Project for Prevention and Control of Emerging and Re-emerging Infectious Diseases and Major Infectious Diseases*.

5. Is participation voluntary?
Yes. Your participation in this study is completely voluntary. You may withdraw from the study at any time without giving any reason, and you will not be discriminated against or retaliated against, nor will it affect your access to routine medical services and related rights. The study doctor may also terminate your continued participation in the study under the following circumstances:
• Continuing participation may not be in your best interest;
• You develop severe adverse reactions that you cannot tolerate;
• You are unable to comply with study requirements or there are other reasonable medical/management reasons;
• The sponsor or regulatory authorities decide to terminate the study early.

6. What will you need to do for this study?
• Provide accurate and truthful personal and medical history information to the study staff;
• Return to the hospital according to the follow-up schedule or cooperate with telephone/online follow-up (if applicable);
• Take medications regularly as instructed by the doctor and report any missed doses/discontinuation;
• Inform the study staff promptly of any discomfort, symptom changes, or new medications during the study;
• Try not to participate in other medical studies during the study period;
• If you are a woman of childbearing potential, effective contraception must be used during the study; if pregnancy is suspected, inform the study doctor immediately.

7. Possible benefits of participating in this study?
Direct benefits: After participating in this study, you will receive standardized treatment and closer follow-up monitoring, and may experience improvement in your condition or faster microbiological clearance, but benefit cannot be guaranteed.

Potential benefits: The information obtained from this study may help improve future treatment strategies for disseminated MAC infection, benefiting more patients with similar conditions.

8. What are the risks of participating in this study?

8.1 Risks related to routine clinical procedures
• Blood draw/specimen collection: may cause pain, bruising, bleeding, infection, dizziness, etc.;
• ECG: a non-invasive test, generally without significant risk;
• Vision/color vision screening: generally no risk;
• Other tests: handled according to the discomforts or risks that may occur with routine clinical examinations.

8.2 Risks related to the study drugs (main concerns)
The study drugs are all commonly used clinical medications, but adverse reactions may still occur. Common or important risks include, but are not limited to:
(1) Macrolides (azithromycin/clarithromycin): gastrointestinal discomfort (nausea, diarrhea), abnormal liver function, rash, and in a small number of cases may affect the ECG (QT interval), etc.;
(2) Ethambutol: optic neuropathy (decreased vision, abnormal color vision, etc.);
(3) Rifabutin/rifampin and other rifamycins: abnormal liver function, gastrointestinal reactions, rash, blood cell reduction, etc., and they interact with some anti-HIV drugs, possibly requiring adjustment of the regimen or dose;
(4) Fluoroquinolones (levofloxacin/moxifloxacin, used only in the four-drug group during the intensive phase): gastrointestinal reactions, central nervous system reactions such as dizziness/insomnia, abnormal blood glucose, tendinitis/tendon rupture, peripheral neuropathy (which may persist or be irreversible), rash/allergic reactions, and risk of QT interval prolongation and arrhythmia (moxifloxacin requires relatively greater attention).

To minimize risk, the study doctor will assess your ECG, electrolytes, and other conditions before enrollment; during the study, ECG and laboratory indices will be monitored regularly, and related drugs will be adjusted or discontinued according to your condition. If significant discomfort or abnormal test results occur, the study doctor will take medical measures in a timely manner.

8.3 Other possible risks
• Drug interactions: study drugs may interact with ART or other concomitant medications, leading to reduced efficacy or increased adverse reactions;
• Immune reconstitution inflammatory syndrome (IRIS): after initiation or adjustment of

ART, some patients may experience worsening inflammatory responses requiring further evaluation and management;
• Risk of privacy disclosure: the study will adopt coding and access control measures, but there remains a very low risk of information disclosure.

If you experience any discomfort during the trial, please report it to the study staff immediately. The study staff will take appropriate medical measures in a timely manner. If the study doctor believes that you cannot tolerate the study or that continued participation is not in your safety interests, you may be asked to withdraw from this study.

9. If I do not participate in this study, are there alternative treatment options?
You may choose not to participate in this study and receive routine medical care. Standard treatment for disseminated MAC infection is usually the standard triple regimen, or other appropriate anti-MAC regimens and supportive treatment selected by the clinician according to your condition. You may discuss with your attending physician which diagnostic and treatment option is more suitable for you.

10. Will my information be kept confidential?
If you decide to participate in this study, your personal information will be protected. Study data will be identified using a code rather than your name. Study results may be published at academic conferences or in medical journals, but no information that can identify you will be disclosed. Within the scope permitted by laws and regulations, only authorized personnel (such as study staff, ethics committees, government regulatory authorities, etc.) may access study-related records as required and are obliged to maintain confidentiality.

11. Do I need to pay any fees to participate in the study?
Medical expenses during the study may include routine clinical care costs and study-related testing costs. Some study-related tests/follow-up costs that are not part of routine clinical care may be covered by the research funding (subject to notification by the study center); other routine clinical care costs will still be settled in the usual manner (insurance/self-pay, etc.).

12. Will I receive any compensation?
This study does not involve corresponding compensation.

13. What if I am harmed as a result of the study?
If your health is harmed or you feel unwell due to participation in this study, please inform the study doctor promptly. We will immediately take the necessary medical measures to protect your health.

14. Will I be informed in a timely manner of information that may affect my continued participation?
During the trial, if the study staff learns of important new information that may affect

your decision to continue participation, we will inform you promptly so that you can decide whether to continue or withdraw.

15. Can I withdraw from the study?
You may withdraw from the study at any time without giving a reason. Withdrawing from the study will not affect your subsequent access to routine medical services. When you decide to withdraw, please inform the study doctor promptly so that the doctor can discuss subsequent diagnostic and treatment arrangements with you.

In principle, after you withdraw, the investigator will securely retain the study-related information already generated until final retention and destruction as required. In very rare circumstances, even if you have withdrawn from the study or the study has ended, the investigator may still continue to use the collected de-identified study data, for example: if removing the data would affect the scientific validity of the study results or safety evaluation; or if regulatory authorities need to review the records in accordance with the law.

16. Who should I contact if I have questions or difficulties?
If you have any questions about this study or experience discomfort during the study, please contact the study doctor/study team:
Contact person: ___Liu Li_____ Phone: *18916091026*_____

If you have questions related to your rights/interests, or wish to report difficulties, dissatisfaction, or concerns encountered during participation in this study, or wish to provide comments and suggestions regarding this study, please contact the Ethics Committee of Shanghai Public Health Clinical Center:
Phone: 021-37990333-8349 Email: lunliweiyuanhui2009@126.com

— Participant Signature Page —

Informed Consent Statement:
I have been informed of and understand the purpose, background, procedures, risks, and possible benefits of this study. I have had sufficient time to ask questions and have received satisfactory answers. I have been informed whom to contact if I have any questions, difficulties, or concerns during the study. I have read this informed consent form and voluntarily agree to participate in this study. I know that I may choose not to participate or withdraw at any time during the study, and this will not affect my access to normal medical services.

Participant Signature: _____ Date: ____/____/____
Contact Number: _____

(If the participant has no or limited legal capacity, the legal representative must sign.)
Legal Representative Signature: _____ Date: ____/____/____
Contact Number: _____

(If the participant cannot read this consent form, an independent witness must sign.)
Independent Witness Signature: _____ Date: ____/____/____
Contact Number: _____

Investigator Signature: _____ Date: ____/____/____
Contact Number: _____