

# Assessment of the effects on immunity of azithromycin in pulmonary tuberculosis patients

<b>Submission date</b> 16/10/2024	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 22/10/2024	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/10/2024	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Tuberculosis (TB) is a serious infectious disease with high morbidity and mortality rates, especially in developing countries. Even if appropriate and timely initiation of the standard treatment regimen eradicates *Mycobacterium tuberculosis*, up to half of tuberculosis survivors have some form of persistent lung dysfunction due to an exacerbated inflammatory response. Azithromycin suppresses the production of inflammatory cytokines and as such is a promising adjunct to current tuberculosis treatment to prevent long-term pulmonary complications. The objective of the AZT-TB project is to conduct a pilot clinical study evaluating the immunomodulatory effects of azithromycin in Congolese patients with pulmonary tuberculosis.

### Who can participate?

Patients aged 18 to 80 years old who have a clinical diagnosis of drug-sensitive pulmonary tuberculosis

### What does the study involve?

This study will examine whether adding azithromycin to standard care has beneficial effects on lung health, as measured by chest X-rays and lung function tests.

### What are the possible benefits and risks of participating?

#### Fair subject selection

Consistent with the scientific purpose, people will be chosen in a way that minimizes risks and enhances benefits to patients and society. Patients who will accept the risks and burdens of research will be in a position to enjoy its benefits, and those who may benefit will share some of the risks and burdens.

#### Favorable risk-benefit ratio

Everything will be done to minimize the risks and inconvenience to research patients, to maximize the potential benefits, and to determine that the potential benefits to patients and Congolese society are proportionate to, or outweigh, any risk or burden.

#### Briefly

Benefits: to have full access to clinicians during more than one-year follow-up and to have access

to treatment not only for TB but for some diseases like malaria. To participate in a study that will impact the lives of all future TB patients because data will be carefully analysed and will contribute to future decisions by health stakeholders.

#### Respect for potential and enrolled subjects

Individuals will be treated with respect from the time they are approached for possible participation—even if they refuse enrollment in a study—throughout their participation and after their participation ends.

#### This includes:

Respecting their privacy and keeping their private information confidential

Respecting their right to change their mind, to decide that the research does not match their interests, and to withdraw without penalty

Informing them of new information that might emerge in the course of research, that might change their assessment of the risks and benefits of participating

Monitoring their welfare and, if they experience adverse reactions, untoward events, or changes in clinical status

Ensuring appropriate treatment and, when necessary, removal from the study

Informing them about what was learned from the research

#### Risks:

To have external people know about your personal life conditions but the confidentiality will be strictly kept therefore this risk is minimized. Individuals will give informed consent in which individuals (1) are accurately informed of the purpose, methods, risks, benefits, and alternatives to the research, (2) understand this information and how it relates to their clinical situation or interests, and (3) make a voluntary decision about whether to participate.

#### Where is the study run from?

Congolese Foundation for Medical Research (Fondation Congolaise Pour La Recherche Médicale)

#### When is the study starting and how long is it expected to run for?

October 2020 to December 2024

#### Who is funding the study?

European and Developing Countries Clinical Trials Partnership

#### Who is the main contact?

Prof Francine Ntoumi, fntoumi@fcrm-congo.com, ffntoumi@hotmail.com

## Contact information

#### Type(s)

Public, Scientific, Principal investigator

#### Contact name

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## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **Protocol serial number**

TMA2019CDF-2737

## **Study information**

### **Scientific Title**

Assessment of immunomodulatory effects of azithromycin in pulmonary tuberculosis patients

### **Acronym**

AZT-TB

### **Study objectives**

Azithromycin in combination with standard care may prevent the formation of persistent lung lesions via its immunomodulatory effects

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 08/10/2020, Institutional Ethics Committee of The Congolese Foundation for Medical Research (CERMI, cite de la recherche ex-ORSTOM, quartier Château-d'eau, Brazzaville, XXXX, Congo; +242 06 672 31 22; kcaryel@yahoo.fr), ref: 029/CIE/FCRM/2020

### **Study design**

Interventional prospective randomized two-arm open-label pilot study

### **Primary study design**

Interventional

### **Study type(s)**

Other

### **Health condition(s) or problem(s) studied**

Pulmonary tuberculosis

### **Interventions**

This study is a prospective randomized study that will be carried out to evaluate the immunomodulatory effect of azithromycin in tuberculosis patients. A sputum smear microscopy, Xpert MTB/RIF, a mycobacterial culture and a chest x-ray will be performed to diagnose pulmonary tuberculosis in patients with suspicious symptoms of tuberculosis (including cough > two weeks, weight loss, fatigue, fever, sweats nocturnal). Online probe testing (LPA) will be performed using the Genotype MTBDR test (no longer commercially available), to exclude patients with drug-resistant tuberculosis from the study. The HIV test will be carried out according to the guidelines of tuberculosis management and HIV-positive patients will be excluded from the study. The patients will be enrolled after consent and ethical approval. A manual method of randomization (flip a coin and get heads = with or tails = without) will be used to allocate patients to the standard of care (2HRZE/4HR) with or without azithromycin treatment. The study will be conducted as an open-label study. Azithromycin will be administered at an initial dose of 500 mg followed by 250 mg once a day daily for 28 days in the form of a film-coated tablet. Patients in both arms of treatment will be stratified according to disease severity, age and gender. The patients will be recruited over 12 months and followed for 12 months. The study will enrol 50 adults (>18 years) of both sexes with a first episode of tuberculosis pulmonary, seronegative, sensitive to all first-line drugs and living at Brazzaville. Patients in both treatment arms will be matched as much as possible for disease severity, age and sex. Pulmonary manifestations will be evaluated at each follow-up consultation using a chest x-ray and pulmonary function test.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

2HRZE/4HR, Azithromycin

### **Primary outcome(s)**

The following primary outcome measures will be assessed before randomization, week 2, months 1, 2, 6 and 12:

1. Chest radiographic abnormalities measured using chest X-rays
2. Function measured using a pulmonary function test
3. Serum inflammatory cytokine levels measured using Magpix Luminex immunoassay

### **Key secondary outcome(s)**

The following secondary outcome measures will be assessed before randomization, week 2, months 1, 2, 6 and 12:

1. Sputum inflammatory cytokine levels measured using Magpix Luminex immunoassay
2. Serum blood cells measured using an automat Cyan Hemato
3. Sputum inflammatory cell count measured using Magpix Luminex immunoassay

### **Completion date**

31/12/2024

## **Eligibility**

### **Key inclusion criteria**

1. Clinical diagnosis of drug-sensitive pulmonary tuberculosis (molecular test identification of the Mtb complex; absence of resistance genes such as rpoB, inhA, katG)
2. Written informed consent

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Mixed

### **Lower age limit**

18 years

### **Upper age limit**

80 years

### **Sex**

All

### **Total final enrolment**

50

### **Key exclusion criteria**

1. The patient has reported a history of treatment for tuberculosis
2. Patients under 18 years old
3. Pregnancy or breastfeeding
4. Patients with hypersensitivity to macrolide antibiotics
5. Treatment with a macrolide during the previous month
6. Treatment with tetracycline during the previous month
7. Treatment with any inhaled or oral corticosteroid within the previous month
8. Concomitant treatment with analgesics (NSAIDs)/immunosuppressants (except paracetamol)
9. Digoxin treatment
10. Patients with gastrointestinal disorders, such as diarrhea and vomiting ( $\geq$  grade 2, observed)
11. Patients with a history of cholestatic jaundice/liver dysfunction associated with previous use

of Azithromycin

12. Other known respiratory diseases, including bronchiectasis, pulmonary fibrosis, disease pulmonary vascular or lung cancer

13. HIV infection or AIDS

**Date of first enrolment**

31/10/2020

**Date of final enrolment**

31/10/2023

## Locations

**Countries of recruitment**

Congo

**Study participating centre**

**Centre Antituberculeux (CAT) de Brazzaville**

Boulevard Denis Sassou Nguesso

Brazzaville

Congo

COG

## Sponsor information

**Organisation**

Fondation Congolaise Pour La Recherche Médicale

**ROR**

<https://ror.org/023f4f524>

## Funder(s)

**Funder type**

Research organisation

**Funder Name**

European and Developing Countries Clinical Trials Partnership

**Alternative Name(s)**

Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European &

Developing Countries Clinical Trials Partnership (EDCTP), The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

### Funding Body Type

Private sector organisation

### Funding Body Subtype

International organizations

### Location

Netherlands

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publically available repository (currently unknown). Clinical and socio-demographic data will be shared as soon as the trial is completed and the results published. To request access please contact the Principal investigator, Prof Francine Ntoumi, [fntoumi@fcrm-congo.com](mailto:fntoumi@fcrm-congo.com), [ffntoumi@hotmail.com](mailto:ffntoumi@hotmail.com), after first publication in 2027. Consent from participants was required and obtained. Data anonymization was undertaken via a code given at enrolment and only PI and co-Pi may link the code to an individual name.

### IPD sharing plan summary

Stored in publicly available repository

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>			21/10/2024	No	No