ISRCTN74599367 https://doi.org/10.1186/ISRCTN74599367

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

Submission date
16/10/2024

Recruitment status
No longer recruiting

Registration date
22/10/2024

Overall study status
Completed

Last Edited
21/10/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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

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Additional identifiers

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

Primary study design
Interventional

Study design

Interventional prospective randomized two-arm open-label pilot study

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 (≥ 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)

The European & Developing Countries Clinical Trials Partnership, The European & Developing Countries Clinical Trials Partnership (EDCTP), European and Developing Countries Clinical Trials, 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, 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, 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?
Protocol file			21/10/2024	No	No