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Pre-treatment of loiasis caused by the parasitic African eye worm Loa loa in Gabon with the antiparasitic medication albendazole among patients with a high risk of adverse events after another antiparasitic administration, ivermectin

Submission date
22/11/2022

Recruitment status
No longer recruiting

Registration date
29/11/2022

Overall study status
Completed

Last Edited
19/08/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
In areas where onchocerciasis (river blindness) and loiasis (caused by the parasitic African eye worm Loa loa, so called because it localizes to the conjunctiva of the eye) are co-endemic, the Community-Directed Treatment with Ivermectin (CDTI) strategy for onchocerciasis control is hampered by the presence of hypermicrofilaremic individuals who have Loa loa microfilaraemia exceeding 8,000 microfilariae per milliliter of blood (mf/ml). They are at risk of developing post-treatment severe and/or serious adverse reactions (SARs) after ivermectin (IVM) administration. These SARs are frequent in almost 10.0% of the exposed population of loiasis hyperendemic settings such as in Gabon where both filariasis is endemic, and where Loa infection prevalence exceeds 40.0% in some villages with Onchocerca volvulus-infected individuals. A treatment that can safely reduce high Loa loa microfilaremia (HLMF) below the risk threshold for SARs for a time sufficiently long enough to implement IVM mass drug administration, would be a major contribution to efforts to control and eliminate onchocerciasis. Antifilarial albendazole is considered an alternative to diethylcarbamazine and IVM for the treatment of loiasis that can reduce hypermicrofilaraemia by at least 50% or even below 8,000 mf/ml for at least 4 months. Moreover, this drug is equally effective on soil-transmitted helminthiases (STH) which are also prevalent in loiasis-onchocerciasis co-endemic settings. We hypothesize that a 30-day treatment of HLMF patients with albendazole will be sufficient to reduce the microfilaraemia below the threshold of 8,000 mf/ml and will allow this neglected population to be eligible for the CDTI for onchocerciasis control in co-endemic areas. The objective of this study is to assess and compare the safety and effects of two daily doses of albendazole for 30 days for the treatment of hypermicrofilaremic loiasis in Bitam and Minvoul villages in Gabon with Loa loa-Onchocerca volvulus and STH co-endemicity.

Who can participate?
Adults aged between 18 and 75 years old in Bitam and Minvoul villages in Gabon

What does the study involve?
After biological examinations, positive patients with Loa loa microfilaremia will be approached and asked if they consent to participate in the study and stay within the study area for 2 years. A total of 105 hypermicrofilaraemic individuals will be randomly put in one of the treatment arms. The comparator arm will be composed of 35 low microfilaraemic patients (> 8,000 mf/ml) treated with 400mg albendazole. The experimental arms will comprise people with > 8,000 mf /ml treated with 400 and 800 mg albendazole. The Adequate Clinical and Parasitological Response (ACPR) defined as the reduction of microfilaraemia below 8,000mf/ml will be determined for all groups at day 30. For the first time albendazole pharmacokinetic and metabolites will be determined in filarial-infected individuals using high-performance liquid chromatography and analysed according to the microfilaraemia. The follow-up will last 180 days and the parasite clearance as well as impact on STH prevalence will be evaluated. This will be the first study in Gabon evaluating a pretreatment test and treatment strategy for onchocerciasis control including loiasis and STH.

What are the possible benefits and risks of participating?
Patients will be managed for microfilaremic loiasis first. According to the National Ethical Committee for Research in Gabon, blood count, malaria, intestinal and urine diagnosis will be also performed. Closed management of known adverse events of the albendazole treatment with the administration of antiH2 molecule will be carried out mainly for pruritus. Blood collection may cause local inflammation and pain. Also, participants will be inconvenienced by being expected to attend daily appointments for one month due to the medical appointment each day with the study team.

Where is the study run from?
Université des Sciences de la Santé (Gabon)

When is the study starting and how long is it expected to run for?
June 2019 to February 2023

Who is funding the study?
European and Developing Countries Clinical Trial Partnership (EDCTP) (Netherlands)

Who is the main contact?
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Contact information

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Protocol number: 0053/2022/CNER/P/SG

Study information

Scientific Title
Pre-treatment of hypermicrofilaremic loiasis for eligibility to the community-directed ivermectin intervention for onchocerciasis control in co-endemic settings of Gabon

Acronym
PHYLECOG

Study objectives

Albendazole has been safely used for the reduction of Loa loa microfilaraemia but there is no formal recommendation for this purpose or for loiasis treatment. We hypothesize that a 30-day treatment in patients with hypermicrofilaraemic loiasis will be sufficient to reduce the microfilaraemia below the threshold of 8,000 microfilariae (mf)/ml and allow this neglected population to be eligible for the community-directed ivermectin (CDTI) intervention for onchocerciasis control in co-endemic areas. Moreover, a trial investigating albendazole pharmacokinetic (PK) data and its relationship with microfilaraemia will demonstrate its curative effect.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/11/2021, Ethical National Committee for the Research (B.P. 2117 - Libreville, Gabon; +241 77 56 41 95 - HB; gaboncner49@gmail.com), ref: none provided

Study design
Interventional single-blind non-randomized phase IIb trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Hypermicrofilaremic loiasis

Interventions
A 30-day treatment of albendazole will be given in three experimental groups: a control group (< 8000 microfilariae (mf)/ml) who will receive 400 mg albendazole, and two experimental groups (> 8000 mf/ml) who will receive 400 and 800 mg albendazole. A histamine Type-2 receptor antagonist (H2 blocker; 10 mg/kg) will also be given for 7 first days of the treatment. Blood samples for parasitological diagnosis (direct examination and leukoconcentration) will be performed on Day (D0) before the initiation of the treatment, at D2, 7,14 and 28. Socioeconomic and demographic data, clinical signs and adverse events will be recorded on a standardized Case Report Form.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Albendazole

Primary outcome measure
Day 30 Adequate Clinical and Parasitological Response (ACPR) measured using parasitological diagnosis (direct examination and leukoconcentration techniques) for blood count of microfilariae, clinical diagnosis for the disappearance of loiasis symptoms and pharmacokinetic (PK) measurements with high-performance liquid chromatography (HPLC) on day 30

The ACPR corresponds to the reduction of microfilaraemia below the threshold of 8,000 mf/m without parasite recrudescence (recurrence).

Secondary outcome measures
Variables measured using parasitological diagnosis by direct examination and leukoconcentration techniques on blood samples:
1. Day 30 crude ACPR measured using microscopy on day 30
2. Day 60 crude ACPR measured using microscopy on day 60
3. Day 90 crude ACPR measured using microscopy on day 90
4. Day 180 total microfilaraemia clearance on day 180
5. Microfilaraemia at baseline then at 48 h, and on days 7, 14, 30, 60, 90, and 180
6. Time to microfilaraemia clearance per individual
7. Time to microfilaraemia reduction until 8,000 mf/ml
8. Time to recrudescence or re-infection, per individual
9. Observed microfilaraemia reduction rate (MRR) on days 7, 14, 30, 90, and 180
10. Observed frequency of soil-transmitted helminthiases (STH) at baseline and on day 90 after inclusion

Overall study start date
15/06/2019

Completion date
28/02/2023

Eligibility

Key inclusion criteria
1. Age between 18 and 75 years with a weight below 90.1 kg
2. Positive for hypermicrofilaremic loiasis (> 8000 mf/ml for the treatment arm and under 8,000 mf/ml for the comparative arm) by blood microscopic direct examination
3. Signed written informed consent
4. Agree to comply with study procedures, including the provision of a blood sample and two stool samples at the beginning (baseline) and approximately six months after treatment
5. Willingness to stay in the village over the following 2 years

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
105

Key exclusion criteria
1. Presence of acute or uncontrolled systemic illnesses (e.g. severe anemia, infection, clinical malaria) as assessed by a medical doctor, upon initial clinical assessment and liver function tests
2. Known or reported history of chronic illness such as HIV, acute or chronic hepatitis, cancer, diabetes, chronic heart disease or renal disease
3. Prior treatment with anthelmintics (eg, diethylcarbamazine [DEC], suramin, ivermectin, mebendazole or albendazole) within 4 weeks before the screening
4. Known or suspected allergy to benzimidazoles
5. Pregnant (urine testing) or breastfeeding women

Date of first enrolment
13/11/2022

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
Gabon

Study participating centre
Université des Sciences de la Santé
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Sponsor information

Organisation
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Sponsor type
University/education

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https://ror.org/00yk3tm64

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, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
The Ministry of Health, the national control program, the ethics committee, the Woleu-Ntem local authorities, chiefs of the villages as well as the village communities will be informed of the

results of the study. Meetings will be organized. A sensitization will be performed to show the importance to conduct clinical trials or research through the presentation results session.
At the national level, team members will be responsible for informing the National Control. Program and National Health Authorities on the progress being made, study partial and final reports and future plans. These can be done through policy briefs, and specific meetings with stakeholders. A user-friendly version of the annual report on program achievements will be distributed to national health and higher education authorities. The study report will be validated and sent to all parties. Results will be presented during meetings, conferences and publications in high-impact peer-reviewed journals. Scientific publications will be distributed using open access while ensuring the circulation of standard protocols and scientific information.

Intention to publish date
30/04/2023

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Preprint results		17/08/2024	19/08/2024	No	No