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Combined strategies to accelerate onchocerciasis (river blindness) elimination in Cameroon

Submission date
04/07/2025

Recruitment status
No longer recruiting

Registration date
31/07/2025

Overall study status
Ongoing

Last Edited
30/07/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Onchocerciasis, also known as river blindness, is a disease caused by a parasitic worm and spread by blackflies. The usual way to control it is through yearly community treatment with a drug called ivermectin. However, in some areas, even after many years of treatment, the disease is still common. One reason is that some people can't take ivermectin safely, especially those who also have another parasite called Loa loa, which can cause serious side effects. This study is testing new ways to fight onchocerciasis, including a different drug called doxycycline (DOX) and a method to reduce blackfly populations by treating their breeding sites with a chemical called temephos. The goal is to see if these new approaches can help eliminate the disease more effectively.

Who can participate?
People aged 15 to 70 years who are generally healthy and either have at least one detectable nodule caused by the parasite or test positive for the parasite in their skin can take part in the study.
Children aged between 5 and 14 years living in the study area will participate only in the pre-screening and the follow up at 20 months (nodule palpation, skin snipping, finger prick). Children between 2 – 3 years will be included only in the prevalence assessment at baseline

What does the study involve?
Participants will be divided into different groups depending on where they live. Some will receive the standard ivermectin treatment, while others will also take doxycycline for six weeks. In some areas, blackfly breeding sites will be treated weekly for 10 weeks to reduce the number of flies that spread the disease. The study team will monitor how well these treatments work by checking the number of parasites in people and the number of blackflies in the area.

What are the possible benefits and risks of participating?
All participants will receive some form of treatment and care. Those with nodules will be offered surgery to remove them about 20 months after treatment begins. If doxycycline proves effective, all participants will be offered this treatment at the end of the study. Risks include

possible side effects from the medications, discomfort from blood tests and skin samples, and minor risks from the surgery.

Where is the study run from?
The study is being led by the Parasite and Vector Biology Research Unit at the University of Buea in Cameroon. Participants will be recruited from several communities in the Nkam-Wouri and Sanaga river basins.

When is the study starting and how long is it expected to run for?
January 2024 to September 2027

Who is funding the study?
The study is funded by the German Federal Ministry of Research, Technology and Space (BMFTR) through the Research Networks for Health Innovations in Sub-Saharan Africa.

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Additional identifiers

Protocol serial number
TAKeOFF2_RT5 - 01

Study information

Scientific Title
Field trials of health interventions: a combination of test and treat with doxycycline and ground larviciding with Temephos to accelerate onchocerciasis elimination in Cameroon

Acronym
TAKeOff 2 DOX -GL

Study objectives
Administration of DOX 100mg/d for 42 days will have a macrofilaricidal effect or lead to permanent sterility of the living female adult O. volvulus worms without inducing adverse and severe adverse reactions in individuals co-infected with Loa loa.
Ground larviciding in addition to T&T with DOX would have an added benefit to reduce the O. volvulus transmission.
Offering an alternative treatment to IVM, community members who are reluctant to engage with the CDTi will be able to access treatment for onchocerciasis.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 02/05/2025, Comite National D'Ethique de la Recherche pour la Sante Humaine (CNERSH) (P.O Box 1937, Yaoundé, -, Cameroon; +237-222-234-579; minsanterecherche@yahoo.fr), ref: 2025/04/1797/CE/CNERSH/SP

2. submitted 23/06/2025, The Ethikkommission an der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn (Venusberg-Campus 1, Bonn, 53127, Germany; +49 228 287 51931; ethik@ukbonn.de), ref: 2025-204-BO

Study design
Field-based controlled parallel-group open-label phase III trial

Primary study design
Interventional

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Onchocerciasis (river blindness)

Interventions
The study is a prospective, stratified randomized, controlled, open-label, parallel-group, interventional phase III trial with blinded endpoint evaluation as the histologists and the persons responsible for PCR assessment will be blinded to treatment assignment. Participants who meet the inclusion criteria will be allocated to participate in this clinical trial.

Treatment arm A (experimental):
DOX 100 mg/d for 6w on top of CDTi plus ground larviciding

Treatment arm B (experimental):
DOX 100 mg/d for 6w on top of CDTi

Treatment arm C (experimental):
Standard CDTi plus ground larviciding.

Treatment arm D (control):
Standard CDTi

Duration of treatment and follow-up for all study arms

Visit 1 Pre-Screening:
• For Humans (5-70 years old): Informed consent for screening, biobanking and data protection, demographic data, presence of onchocercomata, palpation of onchocercomata, skin snipping, finger prick
• OV16 testing in children of 2-3 years
• Mapping of river basins (Transmission zones): Capture of blackflies with description of vectors species and infectivity rates.

Visit 2 Screening:
For 15-70 years old: Informed consent for trial, medical history, physical examination, prior therapies/medication, concurrent medication, skin examination, laboratory assessments of blood and urine, pregnancy testing, vital signs (plus skin snipping, finger prick and palpation of onchocerca nodules in case of visit 1 is more than 28 days ago)
For Vector control intervention: Head of community Informed consent for vector control intervention, Inventory of non-target fauna within the rivers and sensitivity testing of Simulium larvae before larviciding

For treatment arms A and B:
Visit 3 Treatment Period (42 days (7 range days) + end of treatment day):
Recheck of in- and exclusion criteria (in case important examinations were carried out more than 28 days before Visit 3 day 1)
Day 1: review of inclusion/exclusion criteria, pregnancy testing (if not done on the day before), concurrent medication, application of IMP
Day 2 – 13: concurrent medication, application of IMP, AE and SAE assessment
Day 14: concurrent medication, application of IMP, AE and SAE assessment, after 14 th treatment (+2 range days) pregnancy test for female participants
Day 15 – Day 27: concurrent medication, application of IMP, AE and SAE assessment
Day 28: concurrent medication, application of IMP, AE and SAE assessment, after 28 th treatment (+2 range days) pregnancy test for female participants
Day 29 – Day 42: concurrent medication, application of IMP, AE and SAE assessment
After Day 42 —End of Treatment analysis (+3 range days), concurrent medication, AE and SAE assessment, pregnancy test for female participants

For treatment arms C and D:
Visit 3 (6 weeks follow up after inclusion):
Concurrent medication, AE and SAE assessment

For Vector control intervention:
(10 weeks)
Ground larviciding with Temephos (recommended dosage range between 0.06 and 0.12 l/m3/s) every week

Visit 4:
6 months (-2/+4 weeks (range) after visit 3 day 1): AE/SAE assessment (all treatment arms), concurrent medication, skin snipping

Visit 5:
12 months follow-up (12 months ± 4 weeks (range) after visit 3 day 1): SAE assessment (all treatment arms), concurrent medication, skin snipping, finger prick

Visit 6:
20 months follow-up, Nodulectomies for nodule positive participants (20 months -2/+4 months (range) after visit 3 day 1): additional information about nodulectomy including additional (renewal of) informed consent for nodulectomy, SAE assessment (all treatment groups), concurrent medication, blood and urine sampling, pregnancy test for female participants, vital signs, physical examination, palpation of onchocercomata, skin snipping, finger prick, skin examination
For participants of 5-14 years at baseline: follow-up assessment: palpation of onchocercomata, skin snipping, finger prick

Visit 7:
Wound dressing (1 day after Visit 6, then every other day until all wounds are healed) concurrent medication, AE and SAE assessment

Visit 8:
End of clinical trial (approximately 6 months after nodulectomy (Visit 6))

Visit 9
Approximately 3 years after treatment onset, OV16 testing in children of 2-3 years (children born after treatment onset)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Doxycycline, Temephos (Abate 500EC)

Primary outcome(s)
Number and percentage of participants without live female worms with normal embryogenesis (participants with dead or sterile worms only by histology plus patients who no longer have palpable nodules) 20 (-2/+4) months after treatment onset/study start.

Key secondary outcome(s))
1. Number (%) of participants without palpable nodules 20 (-2/+4) months after study start.
2. Measurement of treatment effects on worm vitality, fertility and Wolbachia by immunohistology and qPCR after 20 (-2/+4) months.
3. Reduction/Absence of MF in the skin compared to baseline at 6, 12 and 20 (-2/+4) months after treatment onset.
4. Assessment of treatment effects on Wolbachia/MF (qPCR) at different time points; 6, 12 and 20 (-2/+4) months compared to baseline.
5. Nodule and MF prevalence in children (5-14 years) at baseline and 20 months after treatment.
6. OV16 prevalence in children (2-3 years) at baseline and in the same age group (children born after treatment start) 36 months after treatment onset.
7. Number (%) of infective vectors at baseline, 12 and 20 months after study start.
8. Monitoring the CDTi compliance before and during the study period.
9. Assessment of the perception of DOX +/- ground larviciding in a community-based approach.
10. Adverse events (AEs) as well as Serious Adverse Events (SAEs) in response to the different treatments will be assessed and described (DOX within the scope of daily observed treatment and ground larviciding in the scope of inventory of non-target fauna within the rivers diversity and abundance of non-target species in rivers before and after larviciding).

Completion date
30/09/2027

Eligibility

Key inclusion criteria

General inclusion criteria for prevalence assessment and compliance monitoring (incl. skin biopsies, nodule palpation):
1. Age 2-3 years for prevalence assessment using antibody test otherwise age: ≥ 5 years for all other assessments
2. Willingness to participate in the study by signing the Informed Consent Form (ICF)

Participants will only be included in the study (incl. nodulectomies) if they meet all of the following criteria:
1. Age: 15-70 years
2. Presence of at least one Onchocerca nodule detected by palpation and/or OV MF-positive
3. No previous history of adverse drug reaction with tetracyclines
4. Participants with the ability to follow study instructions and are likely to attend and complete all required visits

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
2 years

Upper age limit
70 years

Sex
All

Key exclusion criteria
General exclusion criteria:
1. Participants not able to give consent
2. Participants who are unable to understand the nature, scope, significance, and consequences of this trial
3. Simultaneous participation in any clinical trial
4. Any significant medical condition other than filarial infections, including but not limited to autoimmune disorders, chronic respiratory conditions, and any diagnosed psychological or psychiatric disorders (e.g., schizophrenia, depression, epilepsy, Parkinson's disease, autism), which in the opinion of the study investigator or trial clinician might interfere with the conduct of the study

Exclusion from DOX treatment study (treatment arm A and B):
5. Body weight < 40 kg
6. Pregnant or breastfeeding women
7. Women of childbearing potential who are not willing or able to use methods to prevent pregnancy for the entire treatment duration plus 4 weeks after treatment end, in addition to hormonal contraception (e.g., condoms), unless surgically sterilized/hysterectomized or other criteria deemed reliable by the investigator

8. Known hepatic or renal dysfunction, disease of the central nervous system (CNS), blood disorder, or asthma
9. History of alcohol or drug abuse
10. Known history of hypersensitivity to the investigational drug or to drugs with a similar chemical structure: DOX or any member of the tetracyclines (e.g., Chlortetracycline, Minocycline)
11. History of photosensitivity/phototoxicity reactions after taking drugs
12. Concomitant medication with drugs interacting with DOX, including:
12.1. Antacids containing aluminium, magnesium, or sucralfate (if unable to discontinue)
12.2. Other antibiotics than doxycycline (if unable to discontinue)
12.3. Diuretics or sulfonylureas
12.4. Coumarin or warfarin (if unable to discontinue)
13. Participants with a physical or psychiatric condition which, at the investigator's discretion, may put the participant at risk, confound trial results, or interfere with participation
14. Evidence of clinically significant neurological, cardiac, pulmonary, hepatic, or renal disease based on participant history, physical exam, and/or lab results, which may interfere with the study

Laboratory values leading to exclusion:
15. Serum creatinine > 2× upper limit of normal (ULN)
16. AST (GOT) > 2× ULN
17. ALT (GPT) > 2× ULN
18. γ-GT > 2× ULN
19. Platelet count < 100,000/µL
20. Hemoglobin < 7 g/dL
21. Positive pregnancy test (blood or urine)

CDTi exclusion criteria (all treatment arms):
22. Loa loa MF count > 8,000 MF/mL
23. History of serious adverse events (SAEs) to ivermectin

Date of first enrolment
07/07/2025

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
Cameroon

Study participating centre
University of Buea, Parasite and Vector Biology Research Unit, University of Buea
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Sponsor information

Organisation
University of Buea

ROR
https://ror.org/041kdhz15

Funder(s)

Funder type
Government

Funder Name
German Federal Ministry of Research, Technology and Space (BMFTR)

Funder Name
Research Networks for Health Innovations in Sub-Saharan Africa

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date