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Test and treat for regional elimination of lymphatic filariasis

Submission date
15/03/2022

Recruitment status
No longer recruiting

Registration date
29/03/2022

Overall study status
Ongoing

Last Edited
27/08/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Lymphatic filariasis is a parasitic disease caused by microscopic, thread-like worms that infect the lymph system. The worms are transmitted by mosquitoes that take up baby worms (microfilariae) during a blood meal and can later pass the developed larvae to another person. The infection can cause fluid collection and swelling (lymphedema) but can also go unnoticed by the infected person. Previous studies showed that doxycycline 100-200 mg given daily for 4-6 weeks could kill the adult worms and therefore is more effective in fighting the disease than the standard mass drug administration used in Ghana and Tanzania. Another promising treatment is the double-drug combination using moxidectin plus albendazole (MoxA). ALB is an approved drug for the treatment of lymphatic filariasis (LF). Moxidectin (Mox) has a similar safety profile as ivermectin and is approved for another filarial disease that causes river blindness (onchocerciasis). MoxA is currently being evaluated in several clinical trials, including treatment against LF. Because these treatments target adult worms, they will potentially eliminate parasite reservoirs within transmission units and across entire countries/regions. In order to eliminate this disease and prevent infection of more people, it is important to find and treat all infected people, even if they are not aware of the infection. Therefore, the aim of this study is to find the best way to reach this goal and finally eliminate lymphatic filariasis.

Who can participate?
Everybody aged 5 years or older living in one of the trial areas in Ghana and Tanzania will be screened for the parasite Wuchereria bancrofti, however, the actual treatment and control groups will include participants from age 14 to 70 years.

What does the study involve?
Lymphatic filariasis infected participants from six hotspots study areas in Ghana and Tanzania (three hotspots per country) will be treated with doxycycline 100 mg for 5 weeks (35 days) plus a single dose of ivermectin plus albendazole at the end of the DOX treatment or 8 mg moxidectin plus 400 mg albendazole (MoxA). A control group will only be given the standard MDA medication, ivermectin 200 mcg/kg plus albendazole 400 mg (“IA”).
Each of the six study areas will be assigned randomly to one of the following groups: group A, (interventional; “DOX”), group B (interventional, “MoxA”) or group C (control, “IA”). All participants from the communities randomized to group A (“DOX”) or group C (control group)

will receive ivermectin 200 mcg/kg plus albendazole 400 mg (“IA”) in cooperation with the national programs at the study start. Participants of communities randomized to group B (MoxA) will not receive “IA” but a MoxA single dose. In the case of MF-positive participants at 12 months in any of the three groups, these participants will receive IA one more time at 12 months (groups A and C) or MoxA one more time or also IA (group B).
At study start and around 12 and 24 months later, blood, urine and stool samples (some participants) will be collected. Men will be asked for an ultrasound examination of their scrotum to confirm infection (optional). A questionnaire about acute attacks is carried out at every contact with the study team.

What are the possible benefits and risks of participating?
Benefits to the participant include a thorough medical evaluation and participants will get medical support throughout the study (also for unrelated problems). The risks to participants are side effects caused by the licensed study drugs doxycycline or ivermectin, moxidectin and albendazole. In rare cases, blood sampling could cause infection or nerve damage. In the event of side effects caused by the study drugs or treatments, participants are treated and followed up by the research team until they are resolved.

Where is the study run from?
1. Kumasi Centre for Collaborative Research (KCCR) (Ghana)
2. The National Institute for Medical Research (NIMR) (Tanzania)

When is the study starting and how long is it expected to run for?
August 2020 to April 2027

Who is funding the study?
Research Networks for Health Innovations in Sub-Saharan Africa sponsored by the Federal Ministry of Education and Research (BMBF) (Germany)

Who is the main contact?
Ghana: Prof. Alexander Yaw Debrah email yadebrah.chs@knust.edu.gh
Tanzania: Dr Akili Kalinga email: akili.kalinga@nimr.or.tz

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Additional identifiers

Protocol serial number
TAKeOFF-7- 0218

Study information

Scientific Title
Comparing the effectiveness of test and treat approaches with doxycycline or moxidectin /albendazole vs ivermectin/albendazole for targeted elimination of lymphatic filariasis in a Phase III clinical trial

Acronym
TAKeOFF – Test&Treat

Study objectives
To assess the effectiveness of the respective treatments by comparing the percentage of circulating filarial antigen (CFA)-negative eligible participants 24 months after treatment onset

Ethics approval required
Old ethics approval format

Ethics approval(s)

1. Approved 08/10/2024, Committee for Human Research, Publication and Ethics (CHRPE) of the Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana (College of Health Sciences, School of Medicine and Dentistry, University Post Office, Kumasi, Ghana; +233 (0)322063248; chrpe@knust.ede.gh), ref: CHRPE/AP/1115/24
2. Approved 11/02/2025, Ghana Health Service Ethics Review Committee (GHS-ERC), Accra, Ghana (Research & Development Division, Ghana Health Service, Ethics Review Committee, PO Box MB 190, Accra, Ghana; +233 (0)302 960628; ethics.research@ghs.gov.gh), ref: GHS. 25/052
3. Approved 02/04/2025, Ghana Food and Drugs Authority (Ghana FDA) (PO Box CT 2783, Cantonments - Accra, Ghana;
+233 (0)30 223 3200; fda@fda.gov.gh), ref: FDA/HPT/VVC/CTD/CTA/25/0035
4. Approved 21/05/2025, Tanzania Medicines and Medical Devices Authority (TMDA Headquarters, Plot No. 56/1, Block E, Kisasa B Centre, Hombolo Road, PO Box 1253, Dodoma, Tanzania; +255 (0)26 2961989; info@tmda.go.tz), ref: BC.69/96/32/2
5. Approved 13/02/2025, National Institute for Medical Research (NIMR) Institutional Review Boards (National Institute for Medical Research, 3 Barack Obama Drive, PO Box 9653, 11101 Dar es Salaam, Tanzania; +255 (0)22 2121400; ethics@nimr.or.tz), ref: NIMR/HQ/R.8a/Vol.IX/4833
6. Approved 05/02/2025, Ethikkommission an der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn (Venusberg-Campus 1, Bonn, 53127, Germany; +49 (0) 22828751931; ethik@ukbonn.de), ref: 2024-350-BO

Primary study design
Interventional

Study design
Community-based parallel-assigned (three-group) interventional Phase III trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lymphatic filariasis (LF)

Interventions
Current interventions as of 14/03/2025:
The study involves treatment according to the area the participant is living in:
1. DOX 100: doxycycline 100 mg/d for 5 weeks (100 mg tablet/day orally), on top of standard MDA. Doxycycline will be given weekly to any formally trained nurse working in the Community-based Health Planning and Services (CHPS) premises. Participants will be required to come to the CHPS compound twice a week to receive the drugs until treatment is completed.
2. MoxA: Moxidectin 8 mg plus albendazole 400 mg single dose
“MoxA” treatment will be administered under the supervision of a trial clinician Participants in the MoxA group will be followed up for a period of 24 months without any additional treatment with the exemption of MF-positive participants at 12 months. These participants will receive MoxA one more time or IA in cooperation with the national MDA programmes
3. Control: Standard MDA; ivermectin 200 mcg/kg plus albendazole 400 mg single dose

Participants in this group will receive IVM + ALB (“IA”) at baseline in parallel to the treatments in groups A and B and again after 12 months if the participant is MF-positive at this time point. IA

will be administered in cooperation with the national MDA programmes.
At baseline and around 12 and 24 months after treatment onset, participants will undergo specific blood measurements to determine the infection status.

Timepoints:
V1: pre-screening (all community volunteers)
V2: baseline screening (all FTS+ volunteers, >5 years)
V3: treatment (volunteers eligible for treatment)
V4: 8 weeks follow-up, safety assessment (volunteers eligible for treatment)
V5: 1 year follow-up (volunteers eligible for treatment).
V6: 2 years follow-up (all community volunteers)

Previous interventions:
The study involves treatment according to the area the participant is living in:
1. DOX 100: doxycycline 100 mg/d for 5 weeks (100 mg tablet/day orally), on top of standard MDA. Doxycycline will be given weekly to any formally-trained nurse working in the Community-based Health Planning and Services (CHPS) premises. Participants will be required to come to the CHPS compound twice a week to receive the drugs until treatment is completed.
2. IDA: ivermectin 200 µg/kg once followed by one dose of ivermectin 200 µg/kg plus diethylcarbamazine 6 mg/kg plus albendazole 400 mg after 5±1 weeks on top of standard MDA IDA treatment will be administered under the supervision of a trial clinician. In addition, all participants will receive a single dose of ivermectin 5±1 weeks before IDA to clear potential Onchocerca volvulus microfilaria.
3. Control: Standard MDA as part of the national MDA treatment program

Standard MDA for all treatment arms will be administered as part of the national MDA treatment program without interference by the study team. If MDA is stopped in the study area, participants in the MDA-only group will not receive any drugs.

The trial is not randomized and not blinded. Communities are chosen to minimize the side effects of the treatments: the area with the lowest prevalence of Onchocerciasis will receive treatment 2. From the remaining areas, the one with a higher prevalence of LF will receive treatment 1.

Standard mass drug administration (MDA) will be given in the course of the national programs without interference from the study team. Therefore, MDA is not considered a trial intervention and can be stopped or changed by the national MDA program at any time.

At baseline and around 12 and 24 months after treatment onset, participants will undergo specific blood measurements to determine the infection status.

Timepoints:
V1: pre-screening (all community volunteers)
V2: baseline screening (all FTS+ volunteers, >5 years)
V3: treatment (volunteers eligible for treatment)
V4: 8 weeks follow-up (volunteers eligible for treatment)
V5: 1 years follow-up (volunteers eligible for treatment)
V6: 2 years follow-up (all community volunteers)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Doxycycline, ivermectin, moxidectin, albendazole

Primary outcome(s)
Percentage of CFA-negative individuals, measured by Filariasis Test Strip (FTS) test, among the eligible participants at 24 months after treatment onset

Key secondary outcome(s)
Current secondary outcome measures as of 14/03/2025:
1. Endpoints on an individual level (eligible participants):
1.1. Proportion of participants with FTS score reduction compared to baseline at 12 and 24 months after treatment onset.
1.2. Proportion of FTS-negative individuals at 12 months after treatment onset.
1.3. Change of quantitative CFA measured by Og4C3 ELISA in all eligible participants at 12 and 24 months after treatment onset
1.4. Proportion of MF-negative individuals, determined by microscopy in night blood, at 12 and 24 months after treatment onset (Participants who are MF-positive at 12 months and receive an additional round of IA or MoxA will be analyzed as treatment failures at 24 months even if they become negative after the second treatment)
1.5. Change in MF loads, determined by microscopy in night blood, at 12 and 24 months after treatment onset
1.6. Proportions of eligible men with or without live W. bancrofti in the scrotum (filarial dance sign), determined by ultrasound examination at 24 months after treatment onset
1.7. Changes in levels of biomarkers, e.g., VEGF, CEACAM, MMPs, miRNA, NATOG or metabolites in blood and/or urine that could be responsible for differences in disease development and/or drug responsiveness, measured using flow-cytometry or PCR at V2, V5 and V6
1.8. Adverse events (AE) will be assessed for “MoxA”, “DOX” and “IA” as described below:
1.8.1. Occurrence of AE
1.8.2. Intensity of AE (Grade 0 (none), Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe)
1.8.3. Serious Adverse Events
1.8.4. Relation to treatment (definite, probable, possible, remote, not related)
1.8.5. Outcome of AE (restored, improved, unchanged, deteriorated, death, unknown, overcome with sequelae)
1.8.6. Intervention
1.9. In Ghana only: Changes in the microbiome from stool analysis before and after treatment and between people with differences in disease development and/ or drug responsiveness.
2. Endpoints on community level:
2.1. Proportion of FTS-negative volunteers in the whole community 24 months after treatment onset
2.2. Proportion of MF-negative individuals, determined by microscopy in night blood, from the FTS+ participants in the community 24 months after treatment onset
2.3. In Ghana only: Prevalence of previous SARS-CoV-2 contact in an LF endemic area using dry blood spots collected during the pre-screening visit (finger prick)
3. Endpoints on treatment monitoring and treatment decisions:
3.1. Proportions of people compliant with DOX or MoxA treatment in the respective community assessed using direct CRF entries and diary cards filled by the nurses at every contact after the first treatment to the end of treatment
3.2. Proportion of community members taking MDA as reported by participating community

members 24 months after treatment onset and random cross-checking of approximately 5% of the population with the MDA documentation of the national program
3.3. Modelling of saved MDA rounds by administration of one-time treatment with DOX or MoxA using the collected data at V1, V2, V5, V6
3.4. Costs for DOX, MoxA and MDA treatment calculated for all timepoints based on:
3.4.1. Medication costs
3.4.2. Expenses for the training of involved personnel/health workers
3.4.3. Travel and shipment costs to deliver medications to the villages
3.4.4. Number of needed treatment rounds
For all endpoints: the 24-month follow-up for untreated participants (on community level) will be based on the schedule of the assigned treatment group of the community.

Previous secondary outcome measures:
1. Percentage of CFA-negative volunteers, measured by FTS test, among the whole community at 24 months after treatment onset
2. Percentage of CFA-negative individuals, measured by FTS test, from the eligible participants at 12 months post-treatment
3. Percentage of microfilariae (MF)-negative individuals, measured by FTS test, from the eligible participants at 12 and 24 months after treatment onset
4. Percentage of MF-negative individuals, determined by microscopy in night blood, from the FTS+ participants in the community 24 months after treatment onset
5. Change in MF loads, determined by microscopy in night blood, at 12 and 24 months in the eligible participants after treatment onset
6. Change of quantitative CFA measured by Og4C3 ELISA in the eligible participants at 12 and 24 months after treatment onset
7. Number of people positive for OV16 in all trial communities measured using the SD BIOLINE Oncho/LF IgG4 Biplex-Test at baseline (V2)
8. Percentage of eligible men without live W. bancrofti in the scrotum, determined by ultrasound examination at 12 and 24 months after treatment onset
9. Number of people experiencing (S)AEs after IDA treatment which can be linked to a missed infection with O. volvulus determined by active (day 1-3) and passive (day 4-7) observations up to 7 days after treatment
10. Percentage of people treated with doxycycline or IDA per protocol in the respective community using direct CRF entries and diary cards filled by the nurses at every contact after the first treatment to the end of treatment
11. Percentage of community members taking MDA as reported by participating community members 24 months after treatment onset and random cross-checking of approximately 5% of the population with the MDA documentation of the national program
12. Modelling of saved MDA rounds by administration of one-time treatment with DOX or IDA using collected data at V1, V2, V5, V6
13. Costs for DOX, IDA and MDA treatment calculated for all timepoints based on:
13.1. Medication costs
13.2. Expenses for the training of involved personnel/health workers
13.3. Travel and shipment costs to deliver medications to the villages
13.4. Number of needed treatment rounds
14. Changes in levels of biomarkers, e.g. VEGF, CEACAM, MMPs, miRNA, NATOG or metabolites in blood and/or urine that could be responsible for differences in disease development and/or drug responsiveness, measured using flow cytometry or PCR at V2, V5 and V6
15. Changes in the microbiome measured using stool analysis before and after treatment and between people with differences in disease development and/or drug responsiveness

Assessment of safety:
Adverse events (AE) will be assessed for DOX and IDA as described below at [timepoints]:
1. Occurrence of AE
2. Intensity of AE (Grade 0 (none), Grade 1 (mild), grade 2(moderate) grade 3 (severe)
3. Serious adverse events
4. Relation to treatment (definite, probable, possible, remote, not related)
5. Outcome of AE (restored, improved, unchanged, deteriorated, death, unknown, overcome with sequelae)
6. Intervention

(For all endpoints: follow-ups for untreated participants based on the schedule group A)

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Age ≥5 years
2. LF-infected person (CFA positive)
3. Able and willing to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
5 Years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 14/03/2025:
Specific exclusion criteria for DOX 100 participants:
1. Age <14 years or >70 years
2. Body weight <40 kg
3. Pregnant or breastfeeding women
4. Women of childbearing potential not using an agreed method of contraception (including abstinence; oral contraceptives are not allowed because of interaction with trial drugs)
5. Known hepatic or renal dysfunction or disease of the central nervous system (CNS)
6. History of alcohol or drug abuse
7. History of serious adverse reactions to doxycycline or other tetracyclines
8. History of photosensitivity reactions after taking drugs.
9. Concomitant medication with antacids containing aluminium, magnesium or sucralfate and

not able to discontinue
10. Concomitant medication with other antibiotics than doxycycline and not able to discontinue
11. Concomitant medication with diuretics, sulfonylurea or coumarin (coumadin)
12. Any significant condition other than filariasis (including medical and psychological/psychiatric disorder) which in the opinion of the study investigator might interfere with the conduct of the study

Laboratory values that will lead to exclusion:
1. Positive urine pregnancy test

Specific exclusion criteria for MoxA participants:
1. Pregnant or breastfeeding women
2. Women of childbearing potential not using an agreed method of contraception during and for one month following treatment (e.g. condoms, abstinence; contraceptives are not an agreed method because of interaction with trial drugs)
3. Known hepatic or renal dysfunction or disease of the central nervous system (CNS)
4. History of alcohol or drug abuse
5. History of serious adverse reactions to ivermectin or albendazole

Laboratory values that will lead to exclusion:
1. Positive urine pregnancy test

Specific exclusion criteria for Group C “IA” ; (MDA medication) participants
1. Pregnant or breastfeeding women
2. Known hepatic or renal dysfunction or disease of the central nervous system (CNS) or blood disorder or asthmatic
3. Concomitant medication with warfarin and not able to discontinue
4. History of drug or alcohol abuse
5. History of serious adverse reactions to ivermectin or albendazole

Previous exclusion criteria:
Specific exclusion criteria for DOX 100 participants:
1. Age <14 years or >70 years
2. Body weight <40 kg
3. Pregnant or breastfeeding women
4. Women of childbearing potential not using an agreed method of contraception (including abstinence; oral contraceptives are not allowed because of interaction with trial drugs)
5. Known hepatic or renal dysfunction or disease of the central nervous system (CNS)
6. History of alcohol or drug abuse
7. History of serious adverse reactions to doxycycline or other tetracyclines
8. History of photosensitivity reactions after taking drugs.
9. Concomitant medication with antacids containing aluminium, magnesium or sucralfate and not able to discontinue
10. Concomitant medication with other antibiotics than doxycycline and not able to discontinue
11. Concomitant medication with diuretics, sulfonylurea or coumarin (coumadin)
12. Any significant condition other than filariasis (including medical and psychological/psychiatric disorder) which in the opinion of the study investigator might interfere with the conduct of the study

Laboratory values that will lead to exclusion:
1. Positive urine pregnancy test

Specific exclusion criteria for IDA participants:
1. Age <18 years and >70 years
2. Pregnant or breastfeeding women
3. Women of childbearing potential not using an agreed method of contraception (including abstinence; oral contraceptives are not allowed because of interaction with trial drugs)
4. Known hepatic or renal dysfunction or disease of the central nervous system (CNS)
5. History of alcohol or drug abuse
6. History of serious adverse reactions to ivermectin, diethylcarbamazine or albendazole
7. Any significant condition other than filariasis (including medical and psychological/psychiatric disorder) that in the opinion of the study investigator might interfere with the conduct of the study

Laboratory values that will lead to exclusion:
1. Positive urine pregnancy test
2. Detection of Onchocerca volvulus MF in skin snips after ivermectin but prior to IDA treatment

No exclusion criteria apply to participants from the control group (MDA only)

Date of first enrolment
01/12/2024

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
Ghana

Tanzania

Study participating centre
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Sponsor information

Organisation
Kumasi Centre for Collaborative Research in Tropical Medicine

ROR
https://ror.org/032d9sg77

Organisation
National Institute for Medical Research

ROR
https://ror.org/05fjs7w98

Funder(s)

Funder type
Research organisation

Funder Name
Research Networks for Health Innovations in Sub-Saharan Africa sponsored by the Federal Ministry of Education and Research (BMBF), Germany

Results and Publications

Individual participant data (IPD) sharing plan
Sharing anonymized clinical data is encouraged in the publication process to maximize the value of clinical trials with minimal impact on participants (i.e. reducing the number of clinical trials). All data shared with other researchers working on LF outside the study team will be anonymized and cannot be tracked back to the participants. The informed consent forms (ICFs) will contain a section regarding personal data where participants will be informed who will get access to their data in what form.

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