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Repurposing fusidic acid as a therapeutic for onchocerciasis

Submission date
13/03/2026

Recruitment status
Not yet recruiting

Registration date
13/03/2026

Overall study status
Ongoing

Last Edited
13/03/2026

Condition category
Infections and Infestations

[X] 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
This study, called FAME-ENDPOINT, is investigating whether a treatment called fusidic acid can become a new, shorter treatment for river blindness. River blindness is caused by a parasite that lives in the skin and eyes, and although there have been regular distributions of treatment to entire communities for years to prevent it spreading, it still affects many people in Cameroon and other parts of the world. Parasitic worms live and breed in raised nodules in the skin and produce baby worms.

Who can participate?
We plan to include about 264 adults aged 18 to 60 years who have river blindness. Everyone who takes part will be helping us understand whether new treatments can improve health in their communities.

What does the study involve?
The study is testing several different treatments. Some people will receive fusidic acid for a short time, some will receive albendazole, some will get both medicines together, and some will receive doxycycline, which is an older treatment. One group will not receive treatment at the start, but all participants will be offered the usual ivermectin medicine after 6 months. Everyone has an equal chance of being placed in any group.

What are the possible benefits and risks of participating?
The main reason for the study is to see whether these treatments can weaken or kill the adult worms by removing a bacteria they depend on to survive. We will also check that the medicines are safe and well-tolerated. At the end of the study, participants will have the opportunity to have their nodules removed. The risk is that some of these medications have not been tested in onchocerciasis, so participants may experience some side effects, although none are expected.

Where is the study run from?
The study is run at the Manjo Clinical Research Centre (Cameroon). Trial Management is being provided by the Global Health Trials Unit at the Liverpool School of Tropical Medicine (UK), and data management is being provided by the University Hospital Bonn (Germany). Analysis of the samples will occur at all three institutions.

When is the study starting and how long is it expected to run for?
August 2026, and expected to recruit participants until April 2027

Who is funding the study?
The study is co-funded by Global Health European and Developing Countries Clinical Trials Partnership (EDCTP3) Joint Undertaking and Foreign, Commonwealth & Development Office (FCDO) – UK aid

Who is the main contact?
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Study information

Scientific Title
Repurposing fusidic acid as a short-course treatment to target wolbachia in onchocerciasis – a randomized controlled open-label Phase IIa/b trial

Acronym
FAME-ENDPOINT

Study objectives
The primary estimand is to evaluate the efficacy (difference in percentage of female adult worms without Wolbachia at 6 months) of each of four fusidic acid (FA) regimens, compared to no treatment, in adult participants with confirmed Onchocerca volvulus infection who are alive and have at least one live female adult worm at 6 months follow-up.

The primary endpoint is absence of Wolbachia in a live female adult worm at 6 months measured by immunohistology, versus presence of Wolbachia. This outcome is summarised as the percentage of live adult female worms without Wolbachia at 6 months follow-up, calculated as a percentage as the number of live adult female worms without Wolbachia at 6 months, divided by the number of live adult female worms at 6 months, multiplied by 100.

The primary analysis of the primary endpoint is a superiority comparison of each FA monotherapy to no treatment and a superiority comparison of the combination treatment of FA and Albendazole, versus no treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Treatment

Study type(s)

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

Interventions
The anti-Wolbachia strategy is a clinically validated disease-modifying approach in onchocerciasis, with doxycycline providing established proof of concept through consistent Wolbachia depletion (>90%), long-term sterilisation, and macrofilaricidal activity.

Fusidic acid (FA) is a licensed, off-patent antibiotic with over 60 years of clinical use and a well-characterised human safety profile. Preclinical in vitro studies and filarial infection models demonstrate potent anti-Wolbachia activity of FA across parasite life stages, including adult worms, achieving depletion levels comparable to – or exceeding – those observed with doxycycline. Although rodent pharmacokinetics are suboptimal, human pharmacokinetic exposure is approximately 20–30-fold higher, with predictable accumulation during repeated dosing. Pharmacokinetic-pharmacodynamic (PK/PD) modelling based on these data predicts that a short-course oral FA (≥7 days) at standard systemic doses can achieve Wolbachia depletion levels associated with durable sterilisation and macrofilaricidal effects.

Doxycycline (200 mg once daily for 28 days) is included as a positive control and biological benchmark, representing the most robustly validated anti-Wolbachia regimen in onchocerciasis. A no-treatment arm allows assessment against natural disease progression, with ethical safeguards ensured through provision of standard-of-care ivermectin to all participants at 6 months.

Albendazole is a benzimidazole FDA-approved drug, 400 mg once daily for 3 days, included within this trial to contextualise effects relative to a regimen with minimal macrofilaricidal activity. Albendazole (400 mg/day for 3 days) is added to the antibiotic regimen because, in a randomized pilot trial in onchocerciasis, co-administration of albendazole with a shortened 3-week doxycycline course showed signals of improved parasitological activity compared with doxycycline alone. Specifically, the combination arm achieved a higher proportion of adult female worms depleted of Wolbachia (81.4% vs 64.1% with doxycycline 3 weeks) and showed a trend toward stronger downstream effects on worm reproduction (reduced normal embryogenesis) relative to control. (Klarmann-Schulz U, Specht S, Debrah AY, et al. Comparison of Doxycycline, Minocycline, Doxycycline plus Albendazole and Albendazole Alone in Their Efficacy against Onchocerciasis in a Randomized, Open-Label, Pilot Trial. PLoS Negl Trop Dis 2017; 11(1): e0005156.) Albendazole may provide an additive effect in combinations and could be a potential strategy to enhance efficacy in FA regimens.

Preclinical filariasis studies further indicate that albendazole can act as a pharmacological synergist with anti-Wolbachia agents (e.g., tetracyclines or rifamycins), enabling larger Wolbachia depletions, embryostasis, and treatment shortening compared with anti-Wolbachia monotherapy, even when albendazole alone has negligible anti-Wolbachia activity at clinically relevant exposures. (https://doi.org/10.1073/pnas.1710845114 Turner JD, Sharma R, Al Jayoussi

G, et al. Albendazole and antibiotics synergize to deliver short-course anti-Wolbachia curative treatments in preclinical models of filariasis. Proceedings of the National Academy of Sciences 2017; 114(45): E9712-E21.)

Combined with ivermectin for the treatment of soil-transmitted helminths and lymphatic filariasis in adults and children aged over 5 years, a combination of high dose albendazole and rifampicin is one of only two clinical candidates potentially addressing the TPP suited for use in onchocerciasis / loiasis regions. Other microfilaricide candidates entered into clinical development are the combination treatment ivermectin, diethylcarbamazine and albendazole (IDA). The combination of FA with ALB is thus being investigated, with pilot trials in Ghana endemic for onchocerciasis demonstrating an additive effect of ALB (3d) when used alongside DOX for embryogenesis degradation. Preclinical rodent studies have also demonstrated that when ALB is co-treated with the anti-wolbachial AWZ1066, there is significantly augmented Wolbachia depletion within germline and hypodermal tissues of B. malayi female worms.

Ivermectin is a well-established microfilaricidal agent with extensive global use in mass drug administration programmes for onchocerciasis. It rapidly reduces skin microfilariae densities and thereby decreases transmission and short-term morbidity. However, ivermectin has no clinically meaningful macrofilaricidal activity against adult Onchocerca volvulus worms and does not permanently sterilise adult females. Repeated annual or biannual administration is therefore required to maintain microfilarial suppression over many years. Therefore, ivermectin is not expected to influence the primary endpoint (Wolbachia depletion in adult female worms) or key secondary histological outcomes when administered at 6 months, as these endpoints reflect biological processes occurring prior to ivermectin exposure. Its use therefore preserves scientific validity while maintaining ethical acceptability.

In accordance with ICH-GCP E6 (R3), the trial design leverages existing non-clinical and clinical knowledge to justify first-in-indication use while minimising unnecessary participant risk and avoiding unjustified exposure escalation.

Randomisation to one of each of the eight arms will be equal and stratified by site and number of nodules per patient (1, 2+) and use random block sizes. A computer-generated centralised list will be produced by the Global Health Trials Unit, by a statistician not directly involved in this trial. Opaque envelopes will be used to conceal allocation, and the envelopes will be stored in a lockable cabinet in a secure location at the trial site. No adaptive randomisation or minimisation procedures are employed. Randomisation will be in a 1:1:1:1:1:1:1:1. The arms are:
1. FA 1 g once daily, 7 days
2. FA 0.75 g twice daily, 7 days
3. FA 1 g once daily, 14 days
4. FA 0.75 g twice daily, 14 days
5. Albendazole 400 mg once daily, 3 days
6. FA 0.75 g twice daily, 14 days + albendazole: 400 mg once daily, 3 days (days 1-3)
7. Doxycycline 200 mg once daily, 28 days
8. No treatment

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

Fusidic acid, albendazole, doxycycline

Primary outcome(s)

1. The efficacy (difference in percentage of live female adult worms without Wolbachia at 6 months) of each of four different fusidic acid (FA) regimens, compared to no treatment, in participants with confirmed Onchocerca volvulus infection who are alive and have at least one live female adult worm at 6 months follow-up, measured using absence vs presence of Wolbachia in live female adult worms measured by immunohistology, calculated as the percentage of live adult female worms without Wolbachia at 6 months follow-up (% = the number of live adult female worms without Wolbachia at 6 months / live adult female worms at 6 months x 100), at 6 months

2. The efficacy of combination of 14 days FA (0.75 g twice daily) plus 3 days albendazole (D1-3, 400 mg once daily) compared to no treatment in participants with confirmed Onchocerca volvulus infection who are alive and have at least one female adult worm at 6 months follow-up, measured using absence vs presence of Wolbachia in live female adult worms measured by immunohistology, calculated as the percentage of live adult female worms without Wolbachia at 6 months follow-up (% = the number of live adult female worms without Wolbachia at 6 months / live adult female worms at 6 months x 100), at 6 months

Key secondary outcome(s))

1. The efficacy of albendazole compared to no treatment in participants with confirmed Onchocerca volvulus infection who are alive and have at least one female adult worm at 6 months follow-up, measured using absence of Wolbachia in live female adult worms at 6 months

2. The efficacy of doxycycline compared to no treatment in participants with confirmed Onchocerca volvulus infection who are alive and have at least one female adult worm at 6 months follow-up, measured using absence of Wolbachia in live female adult worms at 6 months

3. The efficacy of a combination of 14 days FA (0.75 g twice daily) plus 3 days albendazole (D1-3, 400 mg once daily) compared to albendazole in participants with confirmed Onchocerca volvulus infection who are alive and have at least one female adult worm at 6 months follow-up, measured using absence of Wolbachia in live female adult worms at 6 months

4. Wolbachia depletion in nodules in participants with confirmed Onchocerca volvulus infection who are alive and have at least one evaluable nodule at 6 months follow-up, measured using PCR (FtsZ/Actin ratio per nodule) at 6 months

5. Embryogenesis in evaluable live adult female worms measured using immunohistology, categorised per evaluable live adult female worm as one of two categories; i) normal; ii) degenerated, oocytes only or empty uterus, at 6 months

6. Free microfilariae in nodules measured using immunohistology (absence of free microfilariae [mf] in the nodule) at 6 months

7. Onchocerca mf in the skin measured using microfilariae per skin snip at 3 and 6 months

8. Worm mortality measured using the number of dead adult female worms / all adult female worms x 100 (vitality = 100 - worm mortality %) at 6 months

9. Wolbachia clearance in each arm measured using absence of Wolbachia in all evaluable nodules for each participant at 6 months

10. Wolbachia in the skin Onchocerca mf measured using PCR (FTsZ/actin per patient) at baseline, 3 and 6 months

11. The safety profile of study treatment regimens measured using incidence of serious adverse events, incidence of serious adverse reactions, incidence of all adverse events, incidence of all adverse reactions at 6 months

12. Exploratory outcome: the acceptability of alternative treatment regimens from the perspective of patients and providers measured using interviews and focus group discussions at pre, during, and post-trial commencement

13. Exploratory outcome: broader health and wellbeing outcomes of alternative treatment regimens measured using interviews, roundtable discussions, and consultation meetings at pre, during, and post-trial commencement

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Aged 18 to 60 years inclusive at the time of screening
2. Body weight: ≥50 kg at screening
3. Confirmed infection:
3.1. Presence of skin microfilariae confirmed by skin snip/biopsy (indicator of live female O. volvulus worms)
3.2. At least one palpable subcutaneous Onchocerca nodule confirmed by clinical examination
4. General health: Considered to be in good general health as determined by medical history, physical examination, and clinical judgment of the investigator
5. Laboratory parameters: Screening laboratory results within acceptable ranges (see appendix 3), including:
5.1. AST, ALT, and γ-GT ≤upper limit of normal (ULN)
5.2. Serum creatinine ≤ULN
5.3. Haemoglobin (Hb) ≥8 g/dL
6. No ongoing clinical condition requiring regular medication that may interact with the trial interventions
7. Able and willing to provide written informed consent and to comply with all trial procedures and follow-up visits

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Pregnant or breastfeeding women (confirmed by pregnancy test at screening).
2. Presence of Loa loa microfilaremia (confirmed by capillary blood smear), due to increased risk of severe adverse events with standard treatment.
3. Any severe or uncontrolled chronic medical condition that, in the opinion of the investigator, could interfere with trial participation or safety (e.g., significant cardiovascular, neurological, or metabolic disease).
4. Current use of medications known to interact with fusidic acid or doxycycline, or that could confound safety assessments – see section 7.8.1 for prohibited concomitant therapies.
5. Known hypersensitivity to fusidic acid, doxycycline, or any excipients of the trial interventions.
6. Participation in another clinical trial of an investigational product within 30 days prior to screening or during the study period.
7. Inability or unwillingness to comply with the contraceptive requirements of the trial (see Appendix 3 for the requirements).
8. Inability or unwillingness to provide written informed consent, or inability to understand the nature, scope, and potential consequences of the trial.
9. Any other condition or circumstance that, in the opinion of the investigator, may compromise the participant's safety, the validity of the trial results, or their ability to comply with the study protocol.

Date of first enrolment
31/08/2026

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
Cameroon

Study participating centre
Manjo Clinical Research Centre
Cameroon

Sponsor information

Organisation
University of Buea

ROR
https://ror.org/041kdhz15

Funder(s)

Funder type

Funder Name
Foreign, Commonwealth and Development Office

Alternative Name(s)
Foreign, Commonwealth & Development Office, Foreign, Commonwealth & Development Office, UK Government, FCDO

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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

IPD sharing plan summary
Not expected to be made available