

# Comparison of doxycycline alone vs doxycycline plus rifampicin in their efficacy against onchocerciasis

<b>Submission date</b> 11/03/2009	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 21/04/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 03/02/2016	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

Not provided at time of registration

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## **Additional identifiers**

**Protocol serial number**  
Grant ref: 39284

## **Study information**

**Scientific Title**  
Comparison of doxycycline alone vs doxycycline plus rifampicin in their efficacy against onchocerciasis: a randomised double-blind placebo-controlled trial

**Acronym**  
A-WOL Oncho

### **Study objectives**

1. To refine existing regimes of drugs with known activity against Wolbachia (doxycycline, rifampicin):
  - 1.1. To provide a shortened treatment period compared to the gold-standard (200mg doxycycline per day for 6 weeks) using the combination of doxycycline and rifampicin.
  - 1.2. To provide a reduction of the daily dosage of doxycycline from 200mg to 100mg.
  - 1.3. To evaluate if the treatment with rifampicin alone has an equivalent effect compared to doxycycline alone.

2. To use immune and metabolite profiling to identify markers of infection and macrofilaricidal activity to provide accurate and sensitive diagnostic tools for individual treatment and control programme monitoring and evaluation.

Added 25/01/2016:

The registration was initiated on 11/03/2009 and finalised on 21/04/2009 after payment was received. Following the prospective submission on 11/03/2009, there were no subsequent changes to the protocol. The recruitment started on 15/03/2009, after initiation of public registration.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Germany: Ethical Committee, University Clinic Bonn, Faculty of Medicine, Bonn, approved on 11/08/2008

Ghana: Committee on Human Research Publication and Ethics, Kwame Nkrumah University of Science and Technology, Kumasi, approved on 29/07/2008

### **Study design**

Randomised double-blind placebo-controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Onchocerciasis (*Onchocerca volvulus*)

### **Interventions**

The participants will be randomised and assigned to one of the following five treatment regimens:

Treatment regimen 1 (n=150):

- a. 6 weeks doxycycline 200 mg (2 capsules/day)
- b. 6 weeks placebo matching rifampicin (3 or 4 capsules/day)

Treatment regimen 2 (n=100):

- a. 6 weeks doxycycline 100 mg (1 capsule/day) plus placebo matching doxycycline 100 mg (1 capsule/day)
- b. 6 weeks placebo matching rifampicin (3 or 4 capsules/day)

Treatment regimen 3 (n=100):

- a. 3 weeks doxycycline 200 mg followed by 3 weeks placebo (2 capsules/day)
- b. 3 weeks rifampicin (10 mg/kg BW per day) followed by 3 weeks placebo (3 or 4 capsules/day)

Treatment regimen 4 (n=100)

- a. 6 weeks rifampicin (10 mg/kg BW per day) (3 or 4 capsules/day)
- b. 6 weeks placebo matching doxycycline (2 capsules/day)

Treatment regimen 5 (n=50)

- a. 6 weeks placebo matching doxycycline (2 capsules/day)
- b. 6 weeks placebo matching rifampicin (3 or 4 capsules/day)

Volunteers for this study are recruited based on the inclusion and exclusion criteria and treated directly in their villages (Upper- and Lower Denkyira Districts, Dunkwa on Offin, Central Region; Amansie Central and Adanse South Districts, Ashanti Region). The study-drugs will be distributed ad personam by the research staff and drug intake monitored on a daily basis for 6 weeks.

To assess the skin microfilarial load, skin biopsies are taken pre-treatment, as well as at 6 and 20 months after treatment.

Nodulectomies to assess worm vitality and embryogenesis will be performed 6 and 20 months after the start of drug administration. Onchocercomata will be removed under local anaesthesia in the hospital. Patients will be kept in hospital for one day after operation for observation before being discharged. Wound dressing will continue in the villages until all the wounds are healed.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Doxycycline, rifampicin

### **Primary outcome(s)**

Rates of nodules (onchocercomata) with normal embryogenesis assessed by histology 6 and 20 months after the start of drug administration.

### **Key secondary outcome(s)**

1. Evaluation of worm embryogenesis (normal embryos/degenerated embryos/no embryos) assessed by histology from onchocercomata excised 6 and 20 months after the start of drug administration
2. Macrofilaricidal activity of the different treatment arms assessed by histology from onchocercomata excised 20 months after the start of drug administration
3. Reduction or absence of Wolbachia bacteria in adult worms assessed by immunohistology (using anti-Wolbachia antibodies) and polymerase chain reaction (PCR) measured 6 and 20 months after the start of drug administration
4. Microfilarial load in the skin measured pre-treatment as well as 6 and 20 months after the start of drug administration
5. Parasite specific immuno-globulin subclasses and cytokine responses/angiogenesis factors measured pre-treatment as well as 6 and 20 months after the start of drug administration

For all the above mentioned primary and secondary outcome measures: Treatment regimens 2 to 4 will subsequently be tested first for superiority compared to placebo (regimen 5) and second for equivalence to the standard therapy (regimen 1).

### **Completion date**

31/12/2011

# Eligibility

## Key inclusion criteria

1. Men and women between 18-55 years
2. Good general health without any clinical condition requiring long-term medication and with normal renal and hepatic laboratory profiles
3. Body weight (BW): 40-70 kg
4. Presence of at least 1 palpable onchocercoma

## Participant type(s)

Patient

## Healthy volunteers allowed

No

## Age group

Adult

## Lower age limit

18 years

## Upper age limit

55 years

## Sex

All

## Key exclusion criteria

1. Known intolerance to the study drugs (doxycycline, rifampicin)
2. Pregnancy (if not obvious, all women are tested by dipstick chemistry ( $\beta$ -hCG), the test will be carried out pre-treatment and every 2 weeks during treatment)
3. Currently breast-feeding
4. History of severe allergic reaction or anaphylaxis
5. History of alcohol or drug abuse
6. Evidence of clinically significant neurological, cardiac, pulmonary, hepatic, metabolic, rheumatologic or renal disease as assessed by history of participants, physical examination, and /or laboratory examinations including blood and urine analyses
7. Laboratory evidence of liver disease (alanine aminotransferase [ALT], gamma-GT greater than 1.25 times the upper limit of normal results as stated by the manufacturer of dipstick tests, Roche)
8. Laboratory evidence of renal disease (serum creatinine greater than 1.25 times the upper limit of normal results as stated by the manufacturer of dipstick tests, Roche)
9. Laboratory evidence of diabetes (urine dipstick chemistry)
10. Behavioural, cognitive or psychiatric disease that, in the opinion of the trial clinician, affects the ability of the participant to understand and comply with the study
11. Severe asthma (emergency room visit or hospitalisation)
12. Undergone splenectomy
13. Participation in other drug trials concurrent with this study

14. Any other condition that, in the opinion of the investigator (trial clinician), would risk the safety or rights of a participant in the trial or would render the subject unable to comply with the protocol

**Date of first enrolment**

15/03/2009

**Date of final enrolment**

28/04/2009

## **Locations**

**Countries of recruitment**

Germany

Ghana

**Study participating centre**

**University of Bonn**

Bonn

Germany

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## **Sponsor information**

**Organisation**

Liverpool School of Tropical Medicine (UK)

**ROR**

<https://ror.org/03svjbs84>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Bill and Melinda Gates Foundation

**Alternative Name(s)**

Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United States of America

## **Results and Publications**

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Available on request