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

Submission date
11/03/2009

Registration date
21/04/2009

Last Edited
03/02/2016

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

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

Plain English summary of protocol
Not provided at time of registration

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

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

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

Secondary outcome measures
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).

Overall study start date
15/03/2009

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

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
500

Key exclusion criteria

1. Known intolerance to the study drugs (doxycycline, rifampicin)
2. Pregnancy (if not obvious, all women are tested by dipstick chemistry (ß-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
53105

Sponsor information

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Sponsor type
University/education

Website
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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, 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

Publication and dissemination plan

There will be a publication of the results; a manuscript is currently in preparation

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request