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Wolbachia endobacteria in filarial infections - exploring their usefulness as targets for novel chemotherapies that are anti-filarial and improve lymphoedema

Submission date	Recruitment status	[_] Prospectively registered
19/01/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/02/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
14/08/2012	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
1/81 306

Study information

Scientific Title
Wolbachia endobacteria in filarial infections - exploring their usefulness as targets for novel chemotherapies that are anti-filarial and improve lymphoedema: a randomised double blind placebo-controlled trial

Study objectives
Filarial infections belong to the major diseases in sub-Saharan Africa and are strongly associated with poverty. At present, World Health Organization (WHO) led control activities in Africa mainly rely on mass administration of microfilaricidal drugs, with a measure of success. However, it has become clear that new, complementary therapies, ideally being macrofilaricidal, must be developed for sustainable control.

In lymphatic filariasis (LF), there is the additional need to deliver new therapies for lymphatic pathology, i.e. lymphoedema and urogenital pathology such as hydrocele and lymphocele, which are not targeted by current mass drug administrations. Depletion of Wolbachia essential endosymbionts of filariae with doxycycline, an approach established by our group, resulted in macrofilaricidal activity in LF. The present study hypothesises that Wolbachia also play a major role in inducing and maintaining lymphatic pathology, and that doxycycline may therefore improve lymphoedema.

The aim of this project is:
1. To analyse to what extent lymphoedema is caused by Wolbachia. To this, the Wolbachia-depleting antibiotic doxycycline will be compared with amoxicillin, which does not target Wolbachia but only opportunistic exogenous bacteria that may worsen lymphoedema.
2. To analyse the role of Wolbachia in the systemic immune responses in lymphoedema patients, by comparing immune responses before and after Wolbachia depletion

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Committee on Human Research Publication and Ethics, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana approved on 25th November 2005

Study design
Randomised double blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lymphatic filariasis (Wuchereria bancrofti)

Interventions
Study drugs and treatment regimens:
1. 200 mg/day doxycycline for 6 weeks
2. 1000 mg/day amoxicillin for 6 weeks
3. Placebo for 6 weeks

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Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Doxycycline, amoxicillin

Primary outcome(s)
Reduction of the stage of lymphoedema and number of acute attacks, measured pre-treatment as well as 3 months, 12 months and 24 months after the start of drug administration

Key secondary outcome(s))
1. Reduction in circulating filarial antigen levels as a measure of a macrofilaricidal effect of doxycycline
2. Change in systemic immune responses

All measured pre-treatment as well as 3 months, 12 months and 24 months after the start of drug administration.

Completion date
30/03/2009

Eligibility

Key inclusion criteria
1. Men and women aged between 18 - 60 years
2. Resident in the village for five years or more

3. Clinical stage of lymphoedema (1 - 5) of at least one extremity
4. Good general health without any clinical condition requiring long-term medication
5. Minimum body weight 40 kg

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy (if not obvious all women are tested by dipstick chemistry: beta-human chorionic gonadotrophin [BhCG])
2. Currently breast-feeding
3. Evidence of clinically significant neurological, cardiac, pulmonary, hepatic, rheumatological, or renal disease by history, physical examination, and/or laboratory tests
4. Behavioural, cognitive or psychiatric disease that, in the opinion of the investigator, affects the ability of the volunteer to understand and cooperate with the study protocol
5. Laboratory evidence of liver disease (aspartate aminotransferase [AST], alanine aminotransferase [ALT] and/or gamma-glutamyl transferase [gGT] greater than 1.25 times the upper limit of normal of the testing laboratory)
6. Laboratory evidence of renal disease (serum creatinine greater than 1.25 times the upper limit of normal of the testing laboratory)
7. Other condition that, in the opinion of the investigator, would jeopardise the safety or rights of a volunteer participating in the trial or would render the subject unable to comply with the protocol
8. Volunteer has abused alcohol or illicit drugs during the past 6 months by history
9. History of severe allergic reaction or anaphylaxis
10. Intolerance to doxycycline or amoxicillin

Date of first enrolment
01/12/2005

Date of final enrolment
30/03/2009

Locations

Countries of recruitment
Germany

Ghana

Study participating centre
Institute of Medical Microbiology, Immunology and Parasitology
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Sponsor information

Organisation
Volkswagen Foundation (VolkswagenStiftung) (Germany)

ROR
https://ror.org/03bsmfz84

Funder(s)

Funder type
Research organisation

Funder Name
Volkswagen Foundation (VolkswagenStiftung) (Germany) (ref: 1/81 306)

Alternative Name(s)
VolkswagenStiftung, The Volkswagen Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2012		Yes	No