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Antibiotic targeting of Wolbachia endosymbiotic bacteria as a new approach to the treatment of filarial (Wuchereria bancrofti) infection and disease

Submission date
10/02/2006

Recruitment status
No longer recruiting

Registration date
22/02/2006

Overall study status
Completed

Last Edited
25/09/2009

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

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EC CONTRACT IC-A4-CT 2002-10051

Study information

Scientific Title

Acronym
WOLBACHFIL

Study objectives
Wolbachia are symbiotic endobacteria in filarial nematodes that have recently emerged as targets for an improved chemotherapy of filariasis by tetracycline antibiotics, with the potential to close the gap left open in current mass treatment programs. The purpose of this project was:
1. To obtain the optimal regimen with anti-Wolbachia antibiotics leading to Wolbachia depletion and sterilization or killing of adult worms in human filariasis.
2. To analyze the role of Wolbachia in inflammatory processes which lead to disease manifestations (hydrocele, lymphedema, acute episodes of lymphangitis)
3. To investigate the role of Wolbachia release by microfilaricidal therapy in the induction of side effects. In their combination, the studies will allow us to assess the role of Wolbachia in the pathogenesis and as targets for the long-needed second punch for sustained interruption of transmission.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical clearance has been obtained from the Liverpool School of Tropical Medicine Research Ethics Committee on 06/12/2001, reference number 01.74 for the whole EC contract and from the Committee on Human Research Publications and Ethics, School of Medical Sciences, University of Science and Technology, Kumasi, Ghana on 20/01/2003

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

Health condition(s) or problem(s) studied
Lymphatic filariasis due to infection with Wuchereria bancrofti

Interventions
Study drugs and treatment regimens:
1. 200 mg doxycycline per day orally for six weeks plus a single dose of ivermectin (150 µg/kg) plus albendazole (400 mg), four months after the start of doxycycline administration
2. Placebo matching doxycycline orally for six weeks plus a single dose of ivermectin (150 µg/kg) plus albendazole (400 mg), four months after the start of doxycycline-placebo administration
3. 200 mg doxycycline per day orally for three weeks plus a single dose of ivermectin (150 µg/kg) plus albendazole (400 mg), four months after the start of doxycycline administration
4. Placebo matching doxycycline orally for three weeks plus a single dose of ivermectin (150 µg /kg) plus albendazole (400 mg), four months after the start of doxycycline-placebo administration

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
1. Doxycycline 2. Ivermectin 3. Albendazole

Primary outcome measure
1. Depletion of Wolbachia (gene copies per Mf by quantitative Polymerase Chain Reaction [PCR])
2. Subsequent decline in microfilaraemia (according to Mf half-life) due to inferred sterility of adult worms
3. Macrofilaricidal effects, as assessed by ultrasonography and by reduction of circulating filarial antigen in serum
4. Decrease in size and grade of chronic pathology and frequency of acute inflammatory episodes

Secondary outcome measures
Reduction in adverse reaction to ivermectin treatment

Overall study start date
01/12/2002

Completion date
31/05/2005

Eligibility

Key inclusion criteria
For all participants: subjects of both sexes, aged 18-50 years, who have given informed consent (written or thumb print) were evaluated. Minimum criteria was body weight >40 kg. Participants

were only included in case they met the following criteria: normal renal and hepatic laboratory profiles for aspartate aminotransferase (AST) (0-40 IU/l), alanine aminotransferase (ALT) (0-45 IU /l), creatinine 53-126 µmol/l) as measured by dipstick chemistry.

For microfilaraemic participants: minimum criteria was microfilarial (Mf) counts >50 Mf/ml (finger pricks taken from night blood between 8 and 10 p.m., counted through a blood counting chamber, e.g. Sedgewick®.

For patients with early or chronic signs of disease: microfilaraemic or amicrofilaraemic, clinical manifestation of hydrocele and/or lymphedema.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
240

Key exclusion criteria
1. Pregnancy (pregnancy test)
2. Lactation
3. Intolerance to ivermectin or doxycycline
4. Chronic diseases
5. Alcohol or drug abuse
6. Anti-filarial therapy within the last two years

Date of first enrolment
01/12/2002

Date of final enrolment
31/05/2005

Locations

Countries of recruitment
Germany

Ghana

Study participating centre
Institute of Medical Microbiology
Bonn
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Sponsor information

Organisation
European Commission

Sponsor details
European Commission
Research Directorate-General
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Sponsor type
Other

Website
http://www.europa.eu.int

ROR
https://ror.org/00k4n6c32

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, Ευρωπαϊκής Επιτροπής, Европейската комисия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságról, Europese Commissie,

Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration