Establishing a Single-sex Controlled Human Schistosoma mansoni Infection Model: safety and dose finding

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Primary objective: To investigate the safety, tolerability and infectivity of male Schistosoma mansoni cercariae in healthy Schistosoma-naïve volunteers. Exploratory objectives: To investigate the kinetics of controlled infection with male...

Ethical review	Approved WMO
Status	Completed
Health condition type	Helminthic disorders
Study type	Interventional

Summary

ID

NL-OMON46890

Source
ToetsingOnline

Brief title
Controlled Human Schistosoma mansoni Infection (CoHSI1)

Condition

- Helminthic disorders

Synonym
bilharzia, Schistosomiasis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Veni

Intervention

Keyword: controlled infection, Schistosoma mansoni

Outcome measures

Primary outcome

- Frequency and magnitude of adverse events after controlled human Schistosoma mansoni infection with male cercariae.

- The number of male cercariae at which 100% volunteers show detectable Schistosoma mansoni circulating anodic antigen.

Secondary outcome

- Time to positive serum and urine CAA (Circulating Anodic Antigen) test;

- Comparison of the height of the peak serum CAA concentration in different dose groups.

- Humoral (antibody) responses directed against Sm antigens

- Cellular responses directed against Sm antigens

- Changes in microbiome after controlled human Schistosoma mansoni infection with male Sm cercariae.

Study description

Background summary

Schistosomiasis is a parasitic disease of global importance, for which no vaccine exists. Vaccine candidates are tested for efficacy in large-scale Phase 2 and 3 field trials in Schistosoma-endemic areas, where the endpoint is usually the incidence of infection or disease following natural exposure. Such trials therefore require long duration and/or large population sizes in order to obtain a good estimate of the effect size. Conducting controlled, experimental infection studies have been shown to eliminate several drawbacks of the traditional proof-of-efficacy approach. This study thus aims to develop

a novel controlled human schistosomiasis infection model that can be used to provide early proof-of-concept data on candidate schistosomiasis vaccines and are an innovative approach to study schistosome immune responses.

Study objective

Primary objective:
To investigate the safety, tolerability and infectivity of male Schistosoma mansoni cercariae in healthy Schistosoma-naïve volunteers.

Exploratory objectives:
To investigate the kinetics of controlled infection with male Schistosoma mansoni cercariae in healthy Schistosoma-naïve volunteers.
To investigate immunological, metabolic and microbiome changes after infection with Schistosoma mansoni male cercariae.

Study design

Open label intervention study

Intervention

Groups of 3 or 7 volunteers will be exposed to 10, 30 and 20 cercariae. Depending on the outcome of infection, the dose will be adapted or additional volunteers will be exposed to the same number of cercariae. Volunteers will visit the clinical trial centre weekly after infection to record adverse events.

Study burden and risks

Volunteers will be requested to visit the trial centre on a weekly basis for 12 weeks. After this bi-weekly visits will follow until week 24. Final follow up visit will be after one year. Blood and urine sampling will take place at every visit. They will keep a diary to register adverse events during 24 weeks. Volunteers will be dermally exposed to single-sex cercariae once. They may experience adverse events, such as malaise, fatigue or Katayama fever. Twelve weeks after infection, they will be treated with praziquantel to cure the Schistosoma infection, which is known to give gastrointestinal side effects. Praziquantel may be repeated at 18 weeks. There is no benefit to participation in the trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject is aged * 18 and * 45 years and in good health.
2. Subject has adequate understanding of the procedures of the study and agrees to abide strictly thereby.
3. Subject is able to communicate well with the investigator, is available to attend all study visits.
4. Subject will remain within Europe (excluding Corsica) during the study period and is reachable by mobile telephone from week 3 to week 12 of the study period.
5. Subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period.
6. For female subjects: subject agrees to use adequate contraception and not to breastfeed for the duration of study.
7. Subject has signed informed consent.

Exclusion criteria

1. Any history, or evidence at screening, of clinically significant symptoms, physical signs or abnormal laboratory values suggestive of systemic conditions, such as cardiovascular, pulmonary, renal, hepatic, neurological, dermatological, endocrine, malignant, haematological, infectious, immune-deficient, psychiatric and other disorders, which could compromise the health of the volunteer during the study or interfere with the interpretation of the study results. These include, but are not limited to, any of the following:
- body weight <50 kg or Body Mass Index (BMI) <18.0 or >30.0 kg/m2 at screening;
- positive HIV, HBV or HCV screening tests;
- the use of immune modifying drugs within three months prior to study onset (inhaled and topical corticosteroids and oral anti-histamines exempted) or expected use of such during the study period;
- history of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years;
- any history of treatment for severe psychiatric disease by a psychiatrist in the past year;
- history of drug or alcohol abuse interfering with normal social function in the period of one year prior to study onset.
- Any clinically significant abnormalities (including extended QT interval) on electrocardiogram
2. The chronic use of any drug known to interact with praziquantel, or artesunate or lumefantrine metabolism (e.g. phenytoïn, carbamazepine, phenobarbital, primidon, dexamethason, rifampicine, cimetidine, flecaïnide, metoprolol, imipramine, amitriptyline, clomipramine, class IA and III anti-arrythmics, antipsychotics, antidepressants, macrolides, fluorchinolones, imidazole- and triazole antimycotics, antihistamines)
Because lumefantrine may cause extension of QT-time, chronic use of drugs with effect on QT interval are excluded from the study.
3. For female subjects: positive urine pregnancy test at screening.
4. Any history of schistosomiasis or treatment for schistosomiasis.
5. Positive serology for schistosomiasis or elevated serum or urine CAA at baseline.
6. Known hypersensitivity to or contra-indications (including co-medication) for use of praziquantel or, artesunate or lumefantrine.
7. Being an employee or student of the department of parasitology or infectious diseases of the LUMC.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	28-09-2016
Enrollment:	17
Type:	Actual

Ethics review

Approved WMO

Date:	14-09-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	27-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-09-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	18-12-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02755324
CCMO	NL57697.058.16

Study results

Date completed: 21-01-2019

Results posted: 27-02-2020

First publication
27-02-2020