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Dose-finding and pharmacokinetic studies of praziquantel in children infected with schistosomes

Submission date
05/11/2014

Recruitment status
No longer recruiting

Registration date
28/11/2014

Overall study status
Completed

Last Edited
04/06/2018

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Schistosomiasis is a neglected tropical disease caused by parasites called blood flukes that live in fresh water, such as rivers and lakes. Symptoms of the disease can follow 1 of 2 patterns. Acute schistosomiasis symptoms develop within a few weeks and include a high temperature, muscle aches, a skin rash and cough. Chronic schistosomiasis symptoms can occur months, or even years, later and include cystitis, passing blood in urine, bloody diarrhoea, vomiting blood, abdominal pain and paralysis of the legs. There is only one treatment of the disease, the drug praziquantel. When given to children, praziquantel is administered empirically, that is at a dose that has been seen to work before, rather than based on scientific theory, and there have not been, to date, any studies that have looked into how the drug is absorbed, metabolised and excreted (i.e. drug disposition) in children. This study looks at how well different doses of the drug work and how safe it is to use when given to school-age and preschool-age children infected with either Schistosoma mansoni or Schistosoma haematobium by measuring praziquantel disposition using dried blood spot technology, a method where blood sample is blotted and dried onto filter paper and then taken to a laboratory for analysis.

Who can participate?
School-aged and preschool-aged children infected with either Schistosoma mansoni or Schistosoma haematobium

What does the study involve?
Children are randomly allocated to one of four different groups. Children in three of the groups are treated with a single specific dose of oral praziquantel, namely 20 mg/kg, 40 mg/kg, or 60 mg /kg. The fourth group is a control group and the children are given a placebo (dummy pill). Two stool or urine samples are collected on different days over a 5-day period. Their medical history is also assessed with a standardised questionnaire and they undergo a full clinical examination. Blood samples are taken at different points post-dosing and sent away for analysis. The success of the treatment is determined 19-25 days post-treatment by collecting another two stool or

urine samples, on consecutive days, and microscopically examined for schistosome eggs. Children are considered schistosome negative (and therefore cured) if no eggs have been found in the stool or specimens.

What are the possible benefits and risks of participating?
Praziquantel is well known, widely used in mass treatment programs and has little adverse events (headache, abdominal pain etc). All children enrolled in the study will benefit from a clinical examination and treatment against helminths. There is no risk in participating in the study.

Where is the study run from?
The study will take place in an schistosome endemic area of Cote d'Ivoire (Ivory Coast)

When is the study starting and how long is it expected to run for?
November 2014 to August 2015

Who is funding the study?
European Research Council (Belgium)

Who is the main contact?
Prof. Jennifer Keiser

Contact information

Type(s)
Scientific

Contact name
Dr Jennifer Keiser

Contact details
Swiss Tropical and Public Health Institute
Basel
Switzerland
4051

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Dose-finding and pharmacokinetic studies of praziquantel in school-aged and preschool-aged children infected with Schistosoma mansoni and Schistosoma haematobium

Acronym
Prazschisto

Study objectives
To compare the efficacy and safety of three oral praziquantel dosages: 1) 20 mg/kg, 2) 40 mg/kg, 3) 60 mg/kg in school-aged and preschool-aged children infected with either Schistosoma mansoni or S. haematobium and to measure praziquantel disposition in both age groups using dried blood spot technology. The primary objective of the trial is to determine the dose-response of praziquantel in pre-school and school- aged children infected with either S. mansoni or S. haematobium.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethikkommission Nordwest und Zentralschweiz, 09/07/2014, ref: EKNZ 2014-162
2. Comite National d'ethique et de la recherche, 22/7/2014, ref: CNER 2014, No. 50

Study design
Randomized controlled phase 2 single-blind dose-finding trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Schistosomiasis

Interventions
Children will be randomized using a computer-generated stratified block randomization code to 4 treatment arms:
Praziquantel (20, 40 and 60 mg/kg) (single oral dose) and placebo

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Praziquantel

Primary outcome measure
Cure rate (21 days post-treatment)

Secondary outcome measures
1. Egg reduction rate (21 days post-treatment)
2. Safety (2h, 24h, 48, 72 h post-treatment)
3. Pharmacokinetic parameters (sampled within 24 hours post-treatment)

Overall study start date
15/11/2014

Completion date
01/08/2015

Eligibility

Key inclusion criteria
1. Written informed consent signed by parents and/or legal guardian; and oral assent by children
2. Able and willing to be examined by a study physician at the beginning of the study and 3 weeks after treatment
3. Able and willing to provide two stool and urine samples at the beginning of the study and 3 weeks after treatment
4. Able and willing to provide 11 finger prick blood samples for PK studies
5. Infected with S. mansoni (study 1) or S. haematobium (study 2), as assessed by the presence of egg(s) in the stool (S. mansoni) or urine (S. haematobium)
6. Absence of major systemic illnesses (e.g. clinical malaria or hepato-splenic schistosomiasis) as assessed by a medical doctor, upon initial clinical assessment
7. No known allergy to study medications

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
640

Key exclusion criteria
1. No written informed consent by parents and/or legal guardian
2. Presence of any abnormal medical condition, judged by the study physician

3. History of acute or severe chronic disease such as liver or renal disease
4. Recent use of anthelminthic drug (within past 4 weeks)
5. Administration of any investigational product or use of any investigational device within 30 days prior to praziquantel administration. Subjects who have used drugs that may affect the pharmacokinetics of praziquantel from 15 days before dosing until the last PK sample, e.g., phenytoin, barbiturates, primidone, carbamazapine, oxcarbazepine, topiramate, felbamate, rifampicin, nelfinavir, ritonavir, griseofulvin, oral ketoconazole
6. Consumption of substances known to be potent inhibitors or inducers of CYP P450s such as grapefruit juice, grapefruit juice containing products, and herbal remedies or dietary supplements containing St. Johns Wort, in the two weeks before dosing
7. Attending other clinical trials during the study
8. Negative diagnostic result for Schistosoma

Date of first enrolment
15/11/2014

Date of final enrolment
01/08/2015

Locations

Countries of recruitment
Côte d'Ivoire

Switzerland

Study participating centre
Swiss Tropical and Public Health Institute
Basel
Switzerland
4051

Sponsor information

Organisation
European Research Council

Sponsor details
Covent Garden
Place Charles Rogier 16
1210 Saint-Josse-ten-Noode
Brussels
Belgium
1210

Sponsor type

Government

ROR
https://ror.org/0472cxd90

Funder(s)

Funder type
Government

Funder Name
European Research Council

Alternative Name(s)
ERC

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	21/02/2017		Yes	No
Results article	results	01/07/2017		Yes	No
Results article	results	01/06/2018		Yes	No