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Does increasing the biltricide (praziquantel) treatment frequency reduce liver damage in children?

Submission date
23/08/2019

Recruitment status
No longer recruiting

Registration date
05/09/2019

Overall study status
Completed

Last Edited
13/06/2025

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Schistosomes are worm infections that can cause liver damage. We have seen evidence of this liver damage in children in Hoima District. Currently your community is provided with the drug praziquantel (biltricide tablets) once per year through the national treatment programme known as MDA. We have found liver damage due to schistosomes to be very common in your district despite the MDA programme. As praziquantel (biltricide tablets) is the only treatment available for schistosomes, we want to see if treating children more than once a year reduces the amount of liver damage seen. We want to find out if increasing the amount of praziquantel (biltricide tablets) given to children reduces their worm infections (Schistosomes) and liver disease.

Who can participate?
Children aged 6-14 can participate in the trial. We plan to include 600 participants from primary schools in Hoima District. Participation in this trial is completely voluntary.

Your child may not participate in the trial if they have had swelling of the face or neck following previous treatment with praziquantel (biltricide tablets) and have lived in the local area for less than two years.

What does the study involve?
The trial involves comparing three different praziquantel (biltricide tablets) treatment plans. Your child will be allocated to one of the treatments for this trial in a random way (by chance). Your child will have an equal chance of receiving praziquantel (biltricide tablets) once, twice or four times a year. For each treatment, children will receive praziquantel (biltricide tablets) following the procedure used by the Uganda Department of Health during school-treatment days. The amount of praziquantel (biltricide tablets) to be received by a child will be determined by their height. A teacher who is trained to treat the children will provide the praziquantel tablets, which the children are to swallow. A member of the study team will observe the treatment to ensure that it is conducted properly.

Prior to receiving praziquantel (biltricide tablets) we will carry out an ultrasound examination, which uses sound waves to create an image of your child's liver. It will not cause any discomfort. Your child will be asked to provide three stool samples and one urine sample. These samples will be used to determine how many schistosomes (worms) your child is infected with. We will also collect parasites from these samples to examine the parasites' genetic code. Three more stool samples and one urine sample will be collected four-weeks after treatment, to see how successful the drug has been, and what schistosome worms and parasites survived. An 8ml blood sample, equivalent to one and a half teaspoons, will be collected from your child. This blood sample will be used to measure how your child's body responds to the parasite. We will relate what we measure in blood samples to the children's liver images. Collecting blood can sometimes cause bruising.

The treatment phase of the trial will last two years. The assessments will be repeated once a year. In total your child will provide 18 stool samples, 6 urine samples and 3 blood samples of 8ml.

All information collected about your child as a result of their participation in the trial will be kept strictly confidential. The results will be anonymous and your child will not be identifiable from any of the data produced. Anonymous datasets from the trial will be made available to other researchers. We will report the overall results to your community. Once the trial has finished, the once per year provision of praziquantel (biltricide tablets) will continue through the national treatment programme (MDA).

What are the possible benefits and risks of participating?
There is no guarantee that your child will benefit from taking part in this trial. They may experience improvement in their disease. However, information collected as part of their participation may be used by the Ugandan Government to improve schistosome treatment programmes in the future. You will not receive any payment for your child participating in this trial but we will compensate the school time missed through your child's participation in this trial. This will be through the provision of school stationery.

Praziquantel (biltricide tablets) have been used for many years and its side-effects are well known. The risks that a single dose of praziquantel can have are mild and short-lived side effects. Headaches and abdominal pain, with or without nausea or vomiting, are very common. Dizziness, drowsiness, a rash and diarrhoea are common.

In very rare cases, intense itchy skin or swelling of the lips and tongue have been reported. In the very unlikely event that your child experiences either of these or your child is feeling very unwell, please contact your trial manager immediately. Their number will be given to you in a patient information sheet before the start of treatment.

As praziquantel (biltricide tablets) passes through the body quickly, with any drug left after killing of the worms passed in the urine within 2 days after treatment, the increased doses in two of the treatment groups should not make these effects or risks worse. To help reduce the side effects we will provide your child with food prior to treating them with praziquantel (biltricide tablets).

Where is the study run from?
The trial is run and managed by the Vector Control Division – Ministry of Health, Uganda in collaboration with Makerere University, University of Cambridge, and Cambridge University Hospitals Trust.

When is the study starting and how long is it expected to run for?
August 2018 to August 2024

Who is funding the study?
The trial is funded by the European and Developing Countries Clinical Trials Partnership Programme (EDCTP).

Who is the main contact?
Dr Shona Wilson
sw320@cam.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Katrina Gatley

ORCID ID
https://orcid.org/0000-0003-2622-1373

Contact details
Cambridge Clinical Trials Unit
Box 401
Cambridge University Hospitals NHS Foundation Trust
Addenbrooke's Hospital Level 6
Coton House
Hills Road
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 216740
cuh.cctu@nhs.net

Type(s)
Scientific

Contact name
Dr Shona Wilson

ORCID ID
https://orcid.org/0000-0001-5725-4376

Contact details
Department of Pathology
University of Cambridge
Tennis Court Road
Cambridge
United Kingdom

CB2 1QP
+44 1223 333338
sw320@cam.ac.uk

Additional identifiers

Protocol serial number
CCTU0255

Study information

Scientific Title
Impact of increased praziquantel frequency on childhood fibrosis in persistent schistosomiasis morbidity hotspots. A phase IV CTIMP trial

Acronym
FibroScHot

Study objectives
Increasing praziquantel treatment frequency will be an effective disease control strategy in hotspots of schistosomiasis morbidity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/06/2019, Vector Control Division Research Ethics Committee (15 Bombo Road Kampala Uganda; 256-414-253407; vcdmohrec@gmail.com), REC ref: UG-REC-018; PI Ref: VCDREC/110
2. Approved 23/08/2019, Uganda National Council for Science and Technology (Plot 6, Kimera Road, Ntinda), ref: HS 2625
3. Approved 23/01/2020, Uganda National Drug Authority (Secretariat office, Kampala, PO Box 23096), ref: CTC 0122/2020
4. Approved 09/04/2019, University of Cambridge, Human Biology Research Ethics Committee (17 Mill Lane, Cambridge, CB2 1RX, UK; 44-223 766894; cb480@admin.cam.ac.uk), ref: HBREC. 2018.32

Study design
Phase IV single-centre randomized open-label trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Periportal fibrosis of the liver caused by schistsosomiasis mansoni

Interventions

Current intervention as of 12/04/2023:
This trial is designed to align with the national Uganda Neglected Tropical Disease Control Programme, Mass Drug Administration with Praziquantel (MDA), which is a public health programme. The public health programme is delivered annually through the primary schools and the control arm for this trial mimics the annual public health programme.

The IMP is praziquantel, the dose is ~40 mg/kg, dependent on standardised and verified dose pole. This is the method used to determine dose for the MDA. Maximum dose 5 x 600 mg tablets. The IMP is given orally after food. Children who are treated with praziquantel will be directly observed for 1 hour with follow-up the next day. Total treatments detailed below include an end-of-trial final treatment. The trial runs over 50 months: the treatment period over 2 years.

Randomisation will be stratified by school. Individuals will be randomised on a 1:1:1 ratio into the control or intervention arms. The sample size is 600 primary school-aged children entering the treatment phase with 200 randomised into each of the three arms. If required additional enrolment will be conducted prior to the first treatment to maintain this sample size.

Assessments during the trial:
2 x 3 days screening for S. mansoni egg counts and ultrasonography examination, conducted prior to the first and final treatments of all trial arms.
3 x 3 day-annual 4-week follow up screen for S. mansoni egg counts. Stool samples will be collected at approximately 4 weeks post treatment to assess treatment efficacy.

Intervention period:
Control arm: 3 treatments of praziquantel, one treatment provided annually.
Intervention arm 1: 5 treatments, provided bi-annually at ~6 months apart
Intervention arm 2: 9 treatments, provided quarterly at ~3 months apart.
Timings of treatments are shown in the Schedule of Assessments. Their exact timing is dependent on the timings of the Ugandan school terms for that year.

Follow-up period:
Outcome assessments will be conducted approximately 2 years after the first annual treatment of individuals in all arms of the study (Ultrasound Examination and the collection of stool samples). The assessments will involve up to 3 days of samples for each individual.

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Previous intervention:
This trial is designed to align with the national Uganda Neglected Tropical Disease Control Programme, Mass Drug Administration with Praziquantel, (MDA) which is a public health programme. The public health programme is delivered annually through the primary schools and the control arm for this trial mimics the annual public health programme.

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Randomisation will be stratified by school. Individuals will be randomised on a 1:1:1 ratio into the control or intervention arms. Six hundred primary school-aged children will be enrolled in the study and 200 randomised into each of the three arms.

Assessments during the trail:
2 x 3 day-annual screening period for S. mansoni egg counts and ultrasonography examination. The Ultrasound Examination and the collection of stool samples will be collected up-to 2-weeks prior to treatment with praziquantel.
3 x 3 day-annual 4-week follow up screen for S. mansoni egg counts. Stool samples will be collected at 4-weeks post treatment to assess treatment efficacy.

Intervention period:
Control arm: 3 treatments of Praziquantel, provided annually.
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Follow-up period:
Outcome assessments will be conducted two years after the first annual treatment of individuals in all arms of the study (Ultrasound Examination and the collection of stool samples). The assessments will be conducted over 3-days for each individual.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
Prevalence of periportal fibrosis, defined as Niamey Protocol pattern scores of C, D, E or F, measured at 2-year follow-up

Key secondary outcome(s))
Schistosoma mansoni infection intensities are measured using Kato-Katz faecal egg counts at 2-year follow-up

Completion date
31/08/2024

Eligibility

Key inclusion criteria
1. Have a parent/guardian who has given written/marked informed consent for the child to participate
2. Given written/marked informed assent to participate
3. Aged 6-14 years of age
4. Born or resident within the community in which their school is situated for >=2 years

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 years

Upper age limit
14 years

Sex
All

Total final enrolment
851

Key exclusion criteria
1. History of facial oedema after treatment with praziquantel

Added 12/06/2020:
2. Known neurocysticercosis or ocular cysticercosis

Date of first enrolment
20/02/2020

Date of final enrolment
28/04/2023

Locations

Countries of recruitment
Uganda

Study participating centre
School of Public Health, Makerere University
New Mulago Hill Road
Kampala
Uganda
UG

Study participating centre
Vector Control Division, Uganda Ministry of Health
15 Bombo Road
Kampala

Uganda
UG

Sponsor information

Organisation
Cambridge University Hospital Trust

Organisation
The Chancellor, Masters and Scholars of the University of Cambridge

Funder(s)

Funder type
Government

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership (EDCTP), The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
A proportion of the dataset will be made available to open archiving platforms as per ‘Pilot on Open Research Data in Horizon 2020’ commitments, specific of which will be decided at a later date.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	14/10/2024	18/12/2024	No	No
Protocol file	version 4.22	23/11/2022	22/04/2024	No	No
Statistical Analysis Plan	version 2.0	23/06/2022	22/01/2024	No	No
Statistical Analysis Plan	version 3.0	05/06/2024	25/06/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes