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The effect of intensive treatment for schistosomiasis on response to vaccines among island adolescents in Uganda

Submission date
12/03/2019

Recruitment status
No longer recruiting

Registration date
01/05/2019

Overall study status
Completed

Last Edited
21/10/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Infectious diseases remain very common in low-income countries (LICs). Vaccines protect people against infectious diseases, but several important vaccines do not work as well in LICs compared to high-income countries (HICs) and in rural, compared to urban, settings. One possible reason for this might be that people living in these settings are more likely to have worm infections. Worm infections impact on the immune system and may change an infected person's response to a vaccine. This study aims to investigate whether treating adolescents infected with schistosomiasis, a parasitic worm infection, before vaccination, will lead to a better immune response to these vaccines.

Who can participate?
Healthy volunteer children (aged 9-17, with no gender restriction) from selected schools located in the Koome islands of Lake Victoria, Uganda. Schistosomiasis is very common in this area.

What does the study involve?
Children are randomly allocated to receive either intensive or standard praziquantel treatment for schistosomiasis. Intensive praziquantel treatment is three doses, 2 weeks apart, of praziquantel before vaccination followed by quarterly praziquantel for a period of one year. Standard praziquantel treatment is once a year. They are then vaccinated against tuberculosis, yellow fever, human papilloma virus (which can cause cancer of the cervix [or opening] of the womb, and other cancers), typhoid and tetanus. Four weeks after vaccination, their immune responses to each vaccine are measured.

What are the possible benefits and risks of participating?
Participants will benefit from receiving the vaccines and treatments as they are expected to provide protection against infectious diseases. Participants and their families, schools and communities will benefit from improved understanding of schistosomiasis and vaccines. No major risks to the participants are anticipated since all the treatments and vaccines to be given are licensed and known to be safe. The main risk to participants will be time lost from school work, and the researchers will work with teachers and parents to minimise this. Very rarely, a

vaccine may cause a severe allergic reaction, so individuals who have previously suffered a possible allergic reaction to drugs or vaccines or their components will not be included in the study.

Where is the study run from?
The host institution for the study will be the Medical Research Council/Uganda Virus Research Institute and London School of Hygiene and Tropical Medicine Uganda Research Unit (MRC/UVRI & LSHTM), Entebbe, Uganda.

When is the study starting and how long is it expected to run for?
May 2018 to August 2020

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof. Alison Elliott
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Contact information

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Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
v1

Study information

Scientific Title
Population differences in vaccine response: the role, reversibility and mediators of immunomodulation by chronic infections in the tropics (POPVAC).

Trial Protocol A: the effect of intensive treatment for schistosomiasis on response to vaccines among island adolescents in Uganda

Acronym
POPVAC trial A

Study objectives
Schistosoma mansoni infection suppresses responses to unrelated vaccines, and this effect can be reversed, at least in part, by intensive praziquantel treatment intervention.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 05/09/2018, MRC/UVRI and LSHTM Uganda Research Unit Research Ethics Committee (Plot 51-59, Nakiwogo Road, Entebbe, P.O. Box 49, Entebbe-Uganda; +256 414 320 385/6; directoruvri@uvri.go.ug), ref: GC/127/18/09/680
2. Approved 07/05/2019, Uganda National Council for Science and Technology (Plot 6, Kimera Road, Ntinda, P.O. Box 6884, Kampala-Uganda; +256 414 705500; infor@uncst.go.ug), ref: HS 2486
3. Approved 28/05/2019, National Drug Authority (Plot 19 Lumumba Avenue, P.O. Box 23096, Kampala, Uganda; +256 417 788 100; ndaug@nda.or.ug), ref: 351/NDA/DPS/05/2019
4. Approved 05/06/2019, London School of Hygiene and Tropical Medicine Interventional Ethics Committee (Keppel Street, London WC1E 7HT; +44(0)20 7636 8636; ethics@lshtm.ac.uk), ref: 16032

Study design
Single-centre open individually randomised two parallel group trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
School

Study type(s)
Other

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Vaccine responses

Interventions
A randomisation code will be generated by the trial statistician using a randomly permuted block size. Participants will be allocated in a 1:1 ratio to receive either intensive or standard praziquantel treatment. Participants in the intensive arm will receive three doses of praziquantel (PZQ) (40mg/kg, assessed by height pole) each two weeks apart (the last of these 2-4 weeks before immunisation), followed by quarterly PZQ (approximately; timings adjusted to accommodate school terms) during follow up. Participants in the standard arm will receive annual PZQ (Uganda Ministry of Health (MoH) policy) given after immunisation and after primary endpoint sampling.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
1. BCG: BCG-specific IFN-gamma ELIspot response 8 weeks post BCG immunisation
2. YF-17D: neutralising antibody titres (plaque-reduction neutralisation test) at 4 weeks post YF immunisation
3. Ty21a: Salmonella typhi lipopolysaccharide (LPS)-specific immunoglobulin(Ig)G concentration at 4 weeks post Ty21a immunisation
4. HPV: IgG specific for L1-proteins of HPV-16/18 at 4 weeks post HPV priming immunisation
5. Td: tetanus and diphtheria toxoid-specific IgG concentration at 4 weeks post Td immunisation

Secondary outcome measures
Current secondary outcome measures as of 24/07/2019:
1. Protective immunity. Proportions with protective neutralising antibody (YF); protective IgG levels (TT); seroconversion rates (Ty21a) at 4 weeks post the corresponding immunisation
2. Response waning. Primary outcome measures (all vaccines) repeated at week 52, and area-under-the curve (AUC) analyses
3. Priming versus boosting. Effects on priming versus boosting will be examined for HPV only,

comparing outcomes 4 weeks after the first, and 4 weeks after the second vaccine dose
4. Current S. mansoni infection status and intensity. This will be determined by serum/plasma levels of circulating anodic antigen (CAA). The method is quantitative, highly specific for Schistosoma infection, and much more sensitive than the conventional Kato Katz method. CAA will be assessed retrospectively on stored samples collected at baseline, on immunisation days, and on primary and secondary endpoint days.

Previous secondary outcome measures:
1. Protective immunity. Proportions with protective neutralising antibody (YF); protective IgG levels (TT); seroconversion rates (Ty21a) at 4 weeks post the corresponding immunisation
2. Response waning. Primary outcome measures (all vaccines) repeated at week 52, and area-under-the curve (AUC) analyses
3. Priming versus boosting. Effects on priming versus boosting will be examined for HPV only, comparing outcomes 4 weeks after the first, and 4 weeks after the second vaccine dose

Overall study start date
01/05/2018

Completion date
30/11/2020

Eligibility

Key inclusion criteria
1. Attending the selected school and planning to continue to attend the school for the duration of the study
2. Aged 9 to 17 year and enrolled in primary 4, 5 or 6
3. Written informed consent by parent or guardian
4. Written informed assent by participant
5. Agree to avoid pregnancy for the duration of the trial (female only)
6. Willing to provide locator information and to be contacted during the course of the trial
7. Able and willing (in the investigator's opinion) to comply with all the study requirements

Participant type(s)
Healthy volunteer

Age group
Child

Lower age limit
9 Years

Upper age limit
17 Years

Sex
Both

Target number of participants
480

Total final enrolment
479

Key exclusion criteria
1. Clinically significant history of immunodeficiency (including HIV), cancer, cardiovascular disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness
2. History of serious psychiatric condition or disorder
3. Concurrent oral or systemic steroid medication or the concurrent use of other immunosuppressive agents within 2 months prior to enrolment
4. History of allergic reaction to immunisation or any allergy likely to be exacerbated by any component of the study vaccines including egg or chicken proteins
5. History of previous immunisation with YF, oral typhoid or HPV vaccine; previous immunisation with BCG or Td at age >5 years
6. Tendency to develop keloid scars
7. Haemoglobin less than 82g/L
8. Positive HIV serology
9. Positive pregnancy test
10. Female currently lactating, confirmed pregnancy or intention to become pregnant during the trial period
11. Use of an investigational medicinal product or non-registered drug, live vaccine, or medical device other than the study vaccines for 30 days prior to dosing with the study vaccine, or planned use during the study period
12. Administration of immunoglobulins and/or any blood products within the three months preceding the planned trial immunisation date

Date of first enrolment
08/07/2019

Date of final enrolment
23/08/2019

Locations

Countries of recruitment
Uganda

Study participating centre
MRC/UVRI and LSHTM Uganda Research Unit
Plot 51-59 Nakiwogo Road
Entebbe
Uganda
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Sponsor information

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London School of Hygiene and Tropical Medicine

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Sponsor type
University/education

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ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Current publication and dissemination plan as of 05/05/2022:
The trial protocol has been published. The main trial results will be submitted for publication in early 2023.

Previous publication and dissemination plan as of 10/06/2020:
The researchers plan to publish the study protocol on around 01/12/2019. They will also add the statistical analysis plan to the trial registration before database lock. They then plan to publish the results of the trial in a high-impact peer-reviewed journal with an intention to publish date of 31/08/2021.

Previous publication and dissemination plan:
The researchers plan to publish the study protocol on around 01/12/2019. They will also add the statistical analysis plan to the trial registration before database lock. They then plan to publish the results of the trial in a high-impact peer-reviewed journal with an intention to publish date of 31/08/2021.

Intention to publish date
01/07/2024

Individual participant data (IPD) sharing plan
The de-identified individual participant data that underlie the results reported in journal articles will be stored in a non-publically available repository (LSHTM Data Compass), together with a data dictionary. This will be done at the time of publication. Each dataset will be allocated a unique digital object identifier (DOI). Researchers who would like to access the data may submit a request through LSHTM Data Compass, detailing the data requested, the intended use for the data, and evidence of relevant experience and other information to support the request. The request will be reviewed by the Principal Investigator in consultation with the POPVAC Steering Committee, with oversight from the UVRI and LSHTM ethics committees. In line with the MRC policy on Data Sharing, there will have to be a good reason for turning down a request. Patient Information Sheets and consent forms specifically referenced making anonymised data available and this has been approved by the relevant ethics committees. Researchers given access to the data will sign data sharing agreements which will restrict the use to answering pre-specified research questions.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Statistical Analysis Plan		01/11/2019	19/03/2020	No	No
Statistical Analysis Plan	version v2.0	01/12/2020	27/01/2021	No	No
Protocol article		16/02/2021	05/05/2022	Yes	No
Protocol article	scientific rationale and cross-cutting analyses	16/02/2021	26/10/2022	Yes	No
Participant information sheet	Information sheet for participants 9 to 12 years old	05/09/2020	09/07/2024	No	Yes
		01/11	21/10		

Results article	/2024	/2024	Yes	No