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Evaluating the safety and immune response to RH5 blood-stage malaria vaccine in adults, young children and infants living in Tanzania

Submission date
23/04/2020

Recruitment status
No longer recruiting

Registration date
02/07/2020

Overall study status
Completed

Last Edited
20/09/2021

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

Background and study aims
Malaria is a disease that is responsible for illnesses and deaths among many Tanzanians, especially young children and pregnant women. There are drugs to treat malaria but there is presently no vaccine available for general use to protect against malaria. The aim of this study is to assess in healthy adults, young children and infants the safety of the malaria vaccines ChAd63 RH5 and MVA RH5 and their ability to make an immune response that can prevent malaria parasites from getting into the red blood cells and hence prevent infection. Both vaccines proved to be safe to-date and well-tolerated in 24 adult participants from the UK. This will be the first time the vaccine is given to people living in areas where malaria is common.

Who can participate?
Healthy adults (aged 18-35 years), young children (1-6 years) and infants (6-11 months) living in the Bagamoyo district, Pwani, Tanzania

What does the study involve?
Two vaccines, ChAd63 RH5 and MVA RH5, will be tested in this study. ChAd63 RH5 consists of a virus called ChAd63 that is genetically changed so that it expresses a malaria protein called RH5. MVA RH5 is a different virus (MVA) that was genetically changed in the same way as ChAd63. Both ChAd63 and MVA viruses are genetically changed so that they are unable to grow in humans. The protein RH5 is used by a parasite like a key to get into red blood cells, after which people are sick. By giving people ChAd63 RH5 and MVA RH5 it is hoped the body will develop an immune response against this protein so that the body will prevent the parasite from using RH5 to get into the blood cells and hence stops the infection. To test how well the RH5 vaccine works, participants in the control group will receive the rabies vaccine. The rabies vaccine is a registered vaccine which helps prevent infection with the rabies virus. All the vaccines in this study will be injected into the muscles of the left shoulder.

What are the possible benefits and risks of participating?
Future generations will benefit if ChAd63 RH5 and MVA RH5 proves to be safe and effective and is licensed for use to prevent malaria. Participants will receive free medical attention during the

entire study period. This will include treatment of any symptoms caused by the vaccines, as well as treatment for any acute illnesses or injuries occurring during the study period, free of charge. All expected and unexpected acute illnesses or injuries that are related or not related to the study product/procedures and that occur during the study period will be covered up to an established limit by the project or insurance.
The risks associated with participating in the study include side effects in the participant's arm that may occur because of the injection of the vaccines or blood sample collection. These include redness (or change in the colour of the skin), swelling, itching, bruising, soreness, warmth or infection at the injection site. These side effects are expected to be minor in nature and may not need treatment unless otherwise decided by a study doctor. MVA vaccines have tended to cause more reaction at the vaccine site than ChAd63 vaccines in previous studies. As with other vaccines, participants may experience fever, fatigue, headache, chills or joint and muscle aches, tiredness and feeling generally unwell with the first 24 hours after vaccination which normally resolve within 48 hours. The majority of these symptoms are likely to be mild/moderate but there is a possibility of severe symptoms occurring. Participants may also have other reactions to ChAd63 RH5 and MVA RH5 that at this time are unknown. With any vaccination, there is a rare risk of other serious reactions, which may be related to the nervous system. One of these, called Guillain-Barré syndrome, is an illness in which people can develop severe weakness and may be fatal. However, these reactions were not seen with the types of vaccines used in this study. If participants have any concerns after being vaccinated they can contact one of the study Investigators (who are available 24 hours a day) or community health worker using the emergency contact details provided once they have been vaccinated. There is a small chance that participants could have an allergic reaction to ChAd63 RH5, MVA RH5 or rabies vaccine. An allergic reaction may range from being mild, such as a rash, to being severe and life-threatening. Medicines and equipment needed to treat allergic reactions are available at the Clinical Trial Facility and the Bagamoyo District Hospital. It is currently unknown whether the vaccines being tested are safe during pregnancy. For this reason, it is important that all women use adequate contraception throughout the trial. To ensure this all women aged 18-35 years will receive Depo-Provera every 3 months for contraception. If participants were to become pregnant during the trial they will be withdrawn from the study, although follow up will continue for safety reasons. Finally, there will be blood taken during the study, which may cause minor bruising and local tenderness. This amount is within the safe limit accepted by medical professionals and is not expected to cause health problems.

Where is the study run from?
This study will take place at the Clinical Trial Facility (CTF) located in Bagamoyo (Tanzania)

When is the study starting and how long is it expected to run for?
March 2018 to February 2019

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

Who is the main contact?
1. Dr Ally Olotu
aolotu@ihi.or.tz
2. Prof. Simon Draper
simon.draper@ndm.ox.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03435874

Secondary identifying numbers
VAC070

Study information

Scientific Title
A Phase Ib age de-escalation dose-escalation randomized, double-blind, controlled study of the safety and immunogenicity of ChAd63 RH5 and MVA RH5 given intramuscularly at 0 and 2 months in healthy adults, children and infants in Tanzania

Study objectives
This Phase Ib trial aims to assess the safety, tolerability and immunogenicity of ChAd63-RH5 administered with MVA-RH5 in a heterologous prime-boost regimen. It is envisioned that RH5-specific immunity elicted from the vaccine will contribute towards controlling Falciparum malaria.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 15/11/2017, Oxford Tropical Research Ethics Committee (University of Oxford, Research Services, University Offices, Wellington Square, Oxford, OX1 2JD, UK; +44 (0) 1865 (2) 82106; oxtrec@admin.ox.ac.uk), ref: 29-17

2. Approved 27/11/2017, National Institute for Medical Research (NIMR, 3 Barack Obama Drive, PO Box 9653, 11101 Dar es Salaam, Tanzania; Tel: +255 (0)22 2121400; ethical nimr.or.tz), ref: NIMR/HQ/R.8c/Vol. I /1088
3. Approved 20/12/2017, Tanzania Food and Drugs Authority (TFDA, Nelson Mandela Road, Mabibo - External, PO Box 77150, Dar Es Salaam, Tanzania; +255 (0)22 2450512/2450751 /2452108, +255 (0)658 445 222/685 701 735/777 700 002; info@tfda.go.tz), ref: TFDA0017/CTR /0015/5

Study design
Phase Ib age de-escalation dose-escalation randomized double-blind controlled interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Plasmodium falciparum malaria

Interventions
Heterologous prime-boost with the candidate malaria vaccines ChAd63 RH5 and MVA RH5 against control vaccine (Rabies vaccine). Given intramuscularly at 0 and 2 months (respectively) in healthy adults, children and infants

Randomized (2:1 ratio)
Method of randomization: stratified randomization

Group 1 Active
n=6. Age 18-35 years. 5 x 10e10 vp ChAd63 RH5 at D0 and 2 x 10e8 pfu MVA RH5 at D56

Group 1 Comparator
n=3. Age 18-35 years. Rabies vaccine at D0 and D56

Group 2a Active
n=6. Age 1-6 years. 1 x 10e10 vp ChAd63 RH5 at D0 and 1 x 10e8 pfu MVA RH5 D56

Group 2a Comparator
n=3. Age 1-6 years. Rabies vaccine at D0 and D56

Group 2b Active
n=12. Age 1-6 years. 5 x 10e10 vp ChAd63 RH5 at D0 and 2 x 10e8 pfu MVA RH5 D56

Group 2b Comparator
n=6. Age 1-6 years. Rabies vaccine at D0 and D56

Group 3a Active
n=6. Age 6-11 months. 1 x 10e10 vp ChAd63 RH5 at D0 and 1 x 10e8 pfu MVA RH5 D56

Group 3a Comparator
n=3. Age 6-11 months. Rabies vaccine at D0 and D56

Group 3b Active
n=12. Age 6-11 months. 5 x 10e10 vp ChAd63 RH5 at D0 and 2 x 10e8 pfu MVA RH5 D56

Group 3b Comparator
n=6. Age 6-11 months. Rabies vaccine at D0 and D56

Total duration of follow up: 16 weeks after last vaccination (6 months from recruitment)

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
1. ChAd63 RH5 2. MVA RH5 3. Rabies vaccine

Primary outcome measure
1. Solicited symptoms after vaccination. Frequency and severity (according to internationally recognised grading tables) of local and systemic solicited adverse events will be recorded for 7 days after each vaccination. For each, a causal relationship between the adverse event and IMP will be assigned.
2. Unsolicited symptoms after each vaccination. Frequency and severity (according to internationally recognised grading tables) of unsolicited adverse events will be recorded for 28 days after each vaccination. For each, a causal relationship between the adverse event and IMP will be assigned.
3. Serious adverse events during the study period, recorded from first dose of vaccine to end of study (approximately 6 months from first vaccination)
4. All serious adverse events from the first dose of IMP until the end of the study (approximately 6 months from first vaccination) recorded, causality assigned and reported to the Chief Investigator (as the Sponsor's representative) within 24 hours of the Investigator being aware of the suspected SAE. The Safety Monitoring Committee will be notified immediately by the PI if SAEs are deemed possibly, probably or definitely related to study interventions

Secondary outcome measures
1. Anti-RH5 antibody concentration measured by ELISA at baseline, and days 14 (adults only), 28, 56, 70, 84, 112, 140 and 168 after the first vaccination
2. Quality of antibody responses to RH5, measured by an assay of growth inhibition activity of sera from vaccinees on a panel of P. falciparum parasites. Measured at baseline, and days 14

(adults only), 28, 56, 70, 84, 112, 140 and 168 after the first vaccination
3. Avidity of anti-RH5 antibodies measured by ELISA and surface plasmon resonance (SPR) and /or other assays (to be defined) at baseline, and days 14 (adults only), 28, 56, 70, 84, 112, 140 and 168 after the first vaccination
4. Cellular immune responses to the RH5 measured by ELISpot assay and/or Intracellular Cytokine Staining (ICS) and/or other assays (to be defined) at baseline, and days 14 (adults only), 28, 56, 70, 84, 112, 140 and 168 after the first vaccination

Overall study start date
20/03/2018

Completion date
26/02/2021

Eligibility

Key inclusion criteria
Group 1: Healthy male or female adults aged 18-35 years at the time of enrolment with signed consent
Group 1 (Female only participants): Must be non-pregnant (as demonstrated by a negative urine pregnancy test), and provide consent of their willingness to take Depo-Provera contraceptive during the study and safety follow-up period
Groups 2a & 2b: Healthy male or female young children aged 1-6 years at the time of enrolment with signed consent obtained from parents or guardians
Groups 3a & 3b: Healthy male or female infants aged 6-11 months at the time of enrolment with signed consent obtained from parents or guardians
Planned long-term (at least 9 months from the date of recruitment) or permanent residence in Bagamoyo town
Adults with a Body Mass Index (BMI) 18 to 30 Kg/m2; or young children and infants with Z-score of weight-for-age within ±2SD

Participant type(s)
Healthy volunteer

Age group
Mixed

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Both

Target number of participants
63

Total final enrolment

Key exclusion criteria
1. Clinically significant congenital abnormalities as judged by the PI or other delegated individual
2. Clinically significant history of skin disorder (psoriasis, contact dermatitis etc.), allergy, cardiovascular disease, respiratory disease, endocrine disorder, liver disease, renal disease, gastrointestinal disease and neurological illness as judged by the PI or other delegated individual.
3. Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; recurrent, severe infections and chronic (more than 14 days) immunosuppressant medication within the past 6 months (inhaled and topical steroids are allowed)
4. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
5. Weight for age z-scores below 2 standard deviations of normal for age
6. History of allergic disease or reactions likely to be exacerbated by any component of the vaccines, e.g. egg products, Kathon, neomycin, betapropiolactone
7. Any history of anaphylaxis in relation to vaccination
8. Clinically significant laboratory abnormality as judged by the PI or other delegated individual
9. Blood transfusion within one month of enrolment
10. History of vaccination with previous experimental malaria vaccines
11. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
12. Participation in another research study involving receipt of an investigational product in the 30 days preceding enrolment, or planned use during the study period
13. Seropositive for hepatitis B surface antigen (HBsAg) or hepatitis C (HCV IgG)
14. Any other finding which in the opinion of the PI or other delegated individual would increase the risk of an adverse outcome from participation in the trial
15. Likelihood of travel away from the study area
16. Positive malaria by blood smear at screening
17. Female participant who is pregnant, lactating or planning pregnancy during the course of the trial
18. Scheduled elective surgery or other procedures requiring general anaesthesia during the trial
19. Any other significant disease, disorder or situation which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial

Date of first enrolment
31/03/2018

Date of final enrolment
27/02/2019

Locations

Countries of recruitment
Tanzania

Study participating centre

Ifakara Health Institute Clinical Trial Facility
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Bagamoyo
Tanzania
PO Box 74

Sponsor information

Organisation
University of Oxford

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Sponsor type
University/education

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ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

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
Publication of results expected mid-late 2021.

Intention to publish date
31/01/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Ally Olotu (aolotu@ihi.or.tz) and Prof. Simon Draper (simon.draper@ndm.ox.ac.uk). Types of data to be shared: Data will be stored and extracted in coded form, and therefore confidential/identifiable information will not be shared. Data will include safety data (clinical and laboratory endpoints) and immunogenicity data (ELISA and ELISPOT data). The trial will be 'discoverable' through trial registration (ClinicalTrials.gov registry) and afterwards by dissemination of results through conference presentations and publications (in high-quality open-access peer-reviewed journals, and deposited in PubMed Central enabling public access). The study will comply with the University of Oxford's guidance: http://researchdata.ox.ac.uk/home/sharing-your-data/. With whom: With collaborative laboratories and scientists working in the field of malaria vaccines. Consent has been obtained from volunteers for sharing anonymous data. Data will be maintained confidential until the appropriate intellectual property has been filed (if required), and findings have been published in open access research journals in a timely manner. Thereafter it can be made available to users as described above. We will share anonymous data only as per the consent provided by volunteers.

IPD sharing plan summary
Available on request