ISRCTN95289709 https://doi.org/10.1186/ISRCTN95289709

A study to compare two dosing regimens for a new malaria vaccine

Submission date
13/01/2023

Recruitment status
No longer recruiting

Registration date
25/04/2023

Overall study status
Ongoing

Last Edited
23/05/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Malaria is a major public health problem. There were around 240 million cases of malaria and 627,000 deaths worldwide in 2020. Most of the deaths are in children under five living in Africa. It is a major problem for those who live in affected areas and for travellers. There is a great need for a safe, effective malaria vaccine. This study is being done to evaluate an experimental malaria vaccine for its safety. We will also look at the body's immune response to the vaccine. The vaccine being tested in this study is called RH5.1. This is given with an adjuvant called "Matrix-M". This is a substance to improve the body's response to vaccination. The aim is to use vaccines and adjuvants to help the body make an immune response against parts of the malaria parasite. This study will assess the safety of the vaccines in healthy participants and the response of the human immune system to the vaccines.

Who can participate?
Healthy adults aged 18 to 50 years

What does the study involve?
Participants are given three doses of the RH5.1 vaccines at two different dose levels (10 and 50 micrograms; µg). One group will have three doses of 10 µg given at 0, 1 and 6 months whilst the other will receive two doses of 50 µg (at 1 and 2 months) followed by a 10 µg dose at 6 months - known as a 'delayed fractional dose'. The researchers will then do blood tests and collect information about any symptoms that occur after vaccination.

What are the possible benefits and risks of participating?
Information from previous studies suggests that a delayed fractional dose improves the immune response to the vaccine, particularly in terms of the antibody response. The researchers suspect that this improvement is due to the delay in dosing, rather than the reduction in dose, and this study will help to answer that. Having a vaccine at a single dose is important for efficient production and dosing for vaccines rolled out in national programs so being able to move away from 'delayed fractional dose' regimens to 'delayed final dose' regimens will be important for vaccine development.
The amount of blood taken at each visit will vary between around 14 ml (about 3 teaspoons) to a maximum of 86 ml (about 6 tablespoons). The volume of blood being taken over the course of

the trial should not cause any problems in healthy people. There may be some temporary mild discomfort, including bruising and tenderness at the site where the blood is taken. Participants may feel faint as a result of collecting blood. Blood will be collected by trained staff and participants will be able to lie down for blood tests if necessary.
If abnormal results or undiagnosed conditions are found in the course of the study these will be discussed with participants and with their agreement the participant's GP may also be informed.
The most common side effects experienced by participants who have previously received RH5.1 /Matrix-M are described below.
We expect that most symptoms will be mild. However, some may be moderate or severe. All symptoms should resolve completely within a few days. Participants may experience any of the following side effects:
Injection site pain is most likely mild. However, there is a chance this could be moderate or severe in intensity.
Redness, swelling, itching and warmth at the vaccine site. Symptoms are likely to be mild if present. However, there is a chance this could be moderate or severe in intensity.
A 'flu-like' illness within 24 hours of vaccination which usually resolves within 48 hours. This can include headache, muscle aches, joint aches, feverishness, tiredness, nausea and feeling generally unwell. The majority of general symptoms are likely to be mild. There is a possibility of moderate or severe symptoms occurring.
With any vaccination, there is a low risk of serious reactions. These may be related to the nervous system or the immune system.
Severe allergic reactions to vaccines (anaphylaxis) are very rare but can be fatal. The researchers will have doctors qualified in the management of anaphylaxis at each vaccination. Appropriate equipment and medication will also be present.
Reactions in the nervous system are also extremely rare. However, vaccines can cause an illness called Guillain-Barré syndrome. This is an illness in which people can develop severe weakness. It may be fatal. However, these reactions have not previously been seen with the type of vaccine used in this study.
Study doctors will be available 24 hours a day in the adverse event follow-up period post-vaccination, and participants will be encouraged to contact them if concerned.
We now have over 2 years of experience conducting trials during the COVID-19 pandemic. We have developed protocols to keep our volunteers safe and trials running. As the public health situation evolves, we may change some of these procedures, in line with the most up-to-date guidance from the UK Health Security Agency (UKHSA) and the UK Government. To minimise the number of people in the building during study visits, we will give participants a specific appointment time for all study visits.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
January 2023 to August 2025

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

Who is the main contact?
Dr Ruth Payne (PI), r.o.payne@sheffield.ac.uk

Contact information

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1005754

ClinicalTrials.gov number
NCT06141057

Secondary identifying numbers
BIO-002, IRAS 1005754, CPMS 55207

Study information

Scientific Title
Phase I clinical trial to assess the safety and immunogenicity of the malaria vaccine candidate RH5.1 soluble protein in Matrix-MTM using two dosing regimens

Acronym
BIO-002

Study objectives
Primary objectives:
1. To assess the safety of RH5.1 soluble protein in Matrix-M in healthy adult volunteers at different doses.

Secondary objectives:
1. To assess the humoral immunogenicity of RH5.1 soluble protein with Matrix-M when administered to healthy adult volunteers at different doses.
2. To compare the anti-RH5 serum IgG functional immunogenicity between the two dose regimens – assessment of serum anti-RH5 IgG quantity, functional quality and longevity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/04/2023, London - Chelsea Research Ethics Committee (Research Ethics Committee (REC) London Centre, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)20 7104 8150; chelsea.rec@hra.nhs.uk), ref: 23/LO/0058

Study design
Single-centre randomized single-blind interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Malaria (African strain)

Interventions
Participants are randomised through the REDCap database.
Group 1: 10 µg of RH5.1 with 50 µg of Matrix-M given on Day 0, Day 28 and Day 182, Intramuscular injection in the deltoid region of the non-dominant arm. Follow up until Day 547 (with visit window applied).
Group 2: 50 µg of RH5.1 with 50 µg of Matrix-M at Day 0 and Day 28 and reduced dosage 10 µg of RH5.1 with 50 µg of Matrix-M at Day 182. The route of administration and follow-up activity is the same as Group 1.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
RH5.1

Primary outcome measure
1. Occurrence of solicited local reactogenicity signs and symptoms for 7 days following each vaccination Listed signs and symptoms (Pain, Itching, warmth, Feverish, Muscle Aches, Joint Aches, Headache, Fatigue, Nausea, Generally Unwell) measured using a 0-3 grading scale on Day 0 to Day 6 following each vaccination.
2. Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following each vaccination Listed signs and symptoms (Pain, Itching, warmth, Feverish, Muscle Aches, Joint Aches, Headache, Fatigue, Nausea, Generally Unwell) measured using a 0-3 grading scale on Day 0 to Day 6 following each vaccination.
3. Occurrence of unsolicited adverse events for 28 days following the vaccination Participant

listed signs and symptoms measured using a 0-3 grading scale from Day 0 to Day 28 following each vaccination.
4. Change from baseline for safety laboratory measures for 28 days following vaccination Listed laboratory measures measured using appropriate laboratory parameters on Day 0 to Day 28 following each vaccination.
5. Occurrence of serious adverse events during the whole study duration SAEs measured using a 0-3 grading system during the whole study duration.

Secondary outcome measures
1. Serum ELISA response:
1.1. Quantitative antigen-specific IgG antibody levels (µg/mL readout) over time – analysis of peak responses and longevity anti-RH5 specific total IgG quantity assessed by standardised ELISA at every vaccination and follow-up visits.
1.2. Antigen-specific antibody subclass/isotype analysis anti-RH5 specific total IgG1, IgG2, IgG3, IgG4, IgA and IgM responses assessed by standardised isotype/subclass ELISA at baseline, peak and late timepoints
1.3. Antigen-specific antibody avidity analysis anti-RH5 specific total IgG avidity responses assessed by chaotropic displacement ELISA at baseline, peak and late timepoints
2. In vitro GIA against 3D7 clone P. falciparum parasites using purified total IgG and a single-cycle pLDH readout assay anti-RH5 specific purified IgG growth inhibition activity as determined by growth inhibition assay at baseline and peak responses.
3. Purified IgG ELISA versus GIA titration "Quality Analysis" Quality (concentration of RH5 specific total IgG required to give 50% growth inhibition) analysis – GIA titre determined as per 2. Purified IgG tested on 1. And plotted against each other to give EC50%.
4. Total IgG serum concentration determination Serum total IgG concentration determined by HPLC at GIA timepoints (baseline and peak response) to allow normalisation of actual physiological responses.

Overall study start date
09/01/2023

Completion date
31/08/2025

Eligibility

Key inclusion criteria
1. Healthy adult aged 18 to 50 years
2. Able and willing (in the Investigator's opinion) to comply with all study requirements
3. Willing to allow the Investigators to discuss the volunteer's medical history with their GP
4. Participants of childbearing potential only: must practice continuous effective contraception for the duration of the study (see section 9.9)
5. Agreement to refrain from blood donation for the duration of the study
6. Able and willing to provide written informed consent to participate in the trial

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
24

Total final enrolment
23

Key exclusion criteria
1. History of clinical malaria (any species) or previous participation in any malaria (vaccine) trial or controlled human malaria infection (CHMI) study
2. Travel to a clearly malaria endemic locality during the study period or within the preceding 6 months
3. Use of immunoglobulins or blood products (e.g. blood transfusion) in the last 3 months
4. Receipt of any vaccine in the 30 days preceding enrolment, or planned receipt of any other vaccine within 30 days following each study vaccination, with the exception of COVID-19 vaccines, which should not be received between 14 days before to 7 days after any study vaccination
5. Receipt of an investigational product in the 30 days preceding enrolment, or planned receipt during the study period
6. Concurrent involvement in another clinical trial involving an investigational product or planned involvement during the study period
7. Prior receipt of an investigational vaccine likely to impact on interpretation of the trial data, as assessed by the Investigator
8. 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)
9. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine
10. Any history of anaphylaxis
11. Pregnancy, lactation or intention to become pregnant during the study
12. Body mass index of <18.5 or >35
13. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
14. History of serious psychiatric condition that may affect participation in the study
15. Any other serious chronic illness requiring hospital specialist supervision
16. Suspected or known current alcohol misuse as defined by an alcohol intake of greater than 25 standard UK units every week
17. Suspected or known injecting drug use in the 5 years preceding enrolment
18. Hepatitis B surface antigen (HBsAg) detected in serum
19. Seropositive for hepatitis C virus (antibodies to HCV) at screening (unless volunteer has taken part in a prior hepatitis C vaccine study with confirmed negative HCV antibodies prior to participation in that study, and negative HCV ribonucleic acid (RNA) PCR at screening for this study)

20. Volunteers unable to be closely followed for social, geographic or psychological reasons.
21. Any clinically significant abnormal finding on biochemistry or haematology blood tests, urinalysis or clinical examination. In the event of abnormal test results, confirmatory repeat tests will be requested. Procedures for identifying laboratory values meeting exclusion criteria are shown in SOP VC027
22. Any other significant disease, disorder, or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data
23. Inability of the study team to contact the volunteer's GP to confirm medical history and safety to participate

Date of first enrolment
15/06/2023

Date of final enrolment
28/02/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Hallamshire Hospital
Glossop Road
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Sponsor information

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University of Oxford

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Sponsor type

University/education

Website
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ROR
https://ror.org/052gg0110

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
1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Submission to regulatory authorities

Following publication of the results from this trial, primary research data will be made available for future analysis upon request by other researchers. The data will be anonymised. Trial participants will be informed of this.

Intention to publish date
31/07/2026

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No