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A study to assess the safety and efficacy of an experimental malaria vaccine by infecting vaccinated and unvaccinated volunteers with malaria parasites

Submission date
05/02/2025

Recruitment status
Recruiting

Registration date
02/07/2025

Overall study status
Ongoing

Last Edited
10/09/2025

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 an infectious disease caused by the Plasmodium parasite and is a major public health problem in many parts of the world. Malaria is spread by the bite of an infected mosquito. There are six species of the Plasmodium parasite that are known to cause malaria in humans. Of these six species, Plasmodium falciparum causes the most sickness and death globally, with an estimated 241 million cases of malaria and 619,000 deaths worldwide in 2021. This is a clinical trial assessing a new malaria vaccine candidate called R78C. In this study, R78C will be used alone or in combination with another malaria vaccine called RH5.1. Both of these vaccines are protein vaccines and are modified parts of the proteins that the malaria parasite uses to enter red blood cells. We would like to find out whether these vaccines are safe and effective.

Who can participate?
We will recruit two groups of healthy volunteers from the Oxford area.

What does the study involve?
The first group will have 13 participants who will receive three doses of the vaccine (R78C /RH5. 1 with Matrix M). We will recruit a second group of 'control' participants. These participants will not receive any vaccinations. Up to 11 participants from each group will then be infected with malaria under controlled conditions (called a 'malaria challenge') and followed up closely by the study team. Participant will also have a fine needle aspiration (optional). If our vaccine works, the diagnosis of malaria should be delayed in participants who received the vaccine, compared to those who did not.

What are the possible benefits and risks of participating?
Benefits:
Participants will not benefit directly from participation in this study. However, it is hoped that the information gained from this study will contribute to the development of a safe and effective P. falciparum vaccine. Participants will also receive information about their general

health status.
Risks:
1. Venepuncture: The maximum volume of blood drawn over the study should not compromise healthy participants. However, the additional effect of malarial infection on potential anaemia is acknowledged. Therefore, full blood counts will be monitored throughout the challenge period and participants less than 50kg will be excluded.
2. Venepuncture/cannulation: There may be bruising, tenderness, pre-syncope or syncope associated with venepuncture or cannulation. To reduce these risks, venepuncture and cannulation will be performed by appropriately trained staff members according to the local SOP.
3. Vaccinations: Local adverse events are likely to include: pain, erythema, swelling, itching and warmth. Foreseeable systemic adverse events would include: headache, fatigue, myalgia, arthralgia, malaise, feverishness, fever and nausea. The majority of adverse events are foreseen to be mild to moderate in nature, however, rarely, these may be severe. Of the systemic adverse events following receipt of Matrix-M, myalgia is the most common. Myocarditis/pericarditis has infrequently been reported in clinical trials using the Novavax COVID-19 vaccine which is given in Matrix-M adjuvant. However, causal relationship to Matrix-M has not been established. Any participants in this trial who present with or describe concerning symptoms will be carefully assessed with appropriate referral if necessary. Guillain-Barré syndrome or immune-mediated reactions including serious allergic reactions may occur, but this should be extremely rare. Serious allergic reactions including anaphylaxis could also occur and for this reason participants will be observed for an hour after each vaccination and vaccinated in a clinical area where Advanced Life Support trained physicians, equipment and drugs are immediately available.
4. Risk of blood borne Infection: Experimentally induced blood-stage malaria infection involves the administration of parasitised red blood cells. The process constitutes a small blood transfusion and therefore the risk of transmission of a blood borne infection cannot be completely ruled out. The donors were tested negative for HIV, Hepatitis A, B and C, Syphilis, HTLV1 and Ross River virus. Over 430 volunteers have received the inoculum and there have been no serious adverse events, and no cases of blood borne infection associated with this. Although the donors are antibody positive for EBV and CMV, risk of transmission has been greatly reduced by leukodepletion of the donor blood and washing of the blood with clinical grade saline prior to use. The risk of transmission of variant Creutzfeldt Jacob Disease appears remote. The donors are Australian residents, where no cases of either Bovine Spongiform Encephalopathy in cattle or vCJD in humans have been reported. As well as the measures outlined above, the risk of infection is further reduced by the very small size of the inoculum. Serum from participants will be collected before and after challenge for storage in case further safety testing may be necessary.
5. Malaria infection: Participants are likely to develop symptomatic malaria following CHMI, including feverishness, fever, tachycardia, hypotension, chills, rigors, sweats, headache, anorexia, nausea, vomiting, diarrhoea, myalgia, arthralgia, low back pain, thrombocytopenia and lymphopenia. Malaria can be fatal and participants will be followed up closely post-challenge and only enrolled in the study if they are deemed reliable and capable of complying with the intensive follow-up schedule. If necessary, participants may be admitted for in-patient care. Participants will be followed-up daily initially following challenge. Once parasite count rises, participants will be followed-up with twice daily in-person visits and provided with antimalarials at diagnosis. The clone of malaria is known to be sensitive to antimalarials including chloroquine, Riamet, Malarone and Fansidar.
6. Medications: Malarone may cause headache, diarrhoea, nausea, vomiting, stomach pain, dizziness rash, fever, low mood, reduced appetite, cough or sleep disturbance. Riamet may cause headache, dizziness, abdominal pain and loss of appetite, sleeping problems, palpitations, nausea, vomiting, diarrhoea, pruritus, skin rash, cough, muscle or joint pain and fatigue. Participants will be screened for contraindications and any side effects will be recorded,

monitored and appropriately dealt with by study doctors. As Riamet may increase the QT interval, Riamet will not be given to participants at risk for QT prolongation. Cyclizine and paracetamol are well tolerated, however, there is a risk of an allergic reaction and other minor side effects. Study staff will monitor and treat these if they occur.
7. Transfusion reaction: The donor is Blood Group O and Rh negative and the blood is leukodepleted, minimising this risk. Participants will be reviewed 15 minutes and 1 hour after receiving the inoculum before being allowed to leave the clinic.

FNA is safe but, as with any medical procedure, it carries some risks:
• Pain: The FNA should not be any more uncomfortable than a blood test. Any tenderness afterwards will resolve. You can take a simple painkiller like paracetamol if you need it. Avoid taking aspirin, as this may increase the risk of bruising.
• Bleeding: The needle used is very slim but bleeding under the skin may sometimes occur after the
FNA. It usually stops quickly by itself. Any bruising will fade within 2 weeks.
• Infection after FNA is rare. If you get redness, pain and/or tenderness in the days afterwards, you
may need antibiotic treatment.
• Damage to nearby tissues and organs: it is possible for the needle used in an FNA procedure to damage underlying structures; however, such occurrences are extremely rare. Among these, a rare
but potential complication of ultrasound-guided FNA of axillary (armpit) lymph nodes is a pneumothorax. This occurs when air leaks into the space between the lung and chest wall, which can cause pain and, in some cases, difficulty breathing. A small pneumothorax can heal by itself with rest. To date, this complication has only been reported in a single case study and a separate clinical trial conducted at the University of Oxford. Fine needle aspiration procedures are conducted under ultrasound guidance to prevent this from happening.

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

When is the study starting and how long is it expected to run for?
November 2025 to September 2026

Who is funding the study?
University of Oxford (UK)

Who is the main contact?
info@ovg.ox.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
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Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010837

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
BIO-005

Study information

Scientific Title
An open label phase I/IIa clinical trial to assess the safety, immunogenicity and efficacy of the blood-stage malaria vaccine candidates R78C and RH5.1 in Matrix-M

Acronym
BIO-005

Study objectives
We will assess:
• The safety of the vaccine in healthy participants.
• The ability of the vaccine to prevent malaria illness

We will assess the response of the human immune system to the vaccine.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 09/04/2025, South Central - Oxford A Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, United Kingdom; +44 207 104 8118; oxforda.rec@hra.nhs.uk), ref: 25/SC/0053

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Healthy volunteers, testing investigational Malaria vaccines

Interventions
Current interventions as of 10/09/2025:

We will testing the safety and efficacy of the vaccines, R78C and RH5.1, which are given in combination with the adjuvant Matrix-M. Group 1 participants will receive the combination of 10 ug of RH5.1 with 10 ug of R78C (with 50 ug Matrix M), given in a 0,1,6-month regimen. Group 2 will be a control group and will not receive any vaccinations. Safety will be assessed in vaccinated participants by follow up and collected of solicited and unsolicited adverse events after each vaccination. Efficacy will be tested by time to malaria diagnosis at blood stage controlled human malaria infection.

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Previous interventions:

We will testing the safety and efficacy of the vaccines, R78C and RH5.1, which are given in combination with the adjuvant Matrix-M. Group 1 participants will receive the combination of 10 ug of RH5.1 with 10 ug of R78C (with 50 ug Matrix M), given in a 0,1,2-month regimen. Group 2 participants will be returning participants from a previous vaccine trial (VAC089). They will receive one 'booster' dose of vaccine: either 10 ug of R78C or the combination of 10ug R78C with 10 ug RH5.1 (both with 50ug of Matrix M), depending on Group allocation. Group 3 will be a control group and will not receive any vaccinations. Safety will be assessed in vaccinated participants by follow up and collected of solicited and unsolicited adverse events after each vaccination. Efficacy will be tested by time to malaria diagnosis at blood stage controlled human malaria infection.

Intervention Type
Biological/Vaccine

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
R78C, RH5.1, Matrix M

Primary outcome(s)
Current primary outcome measure as of 10/09/2025:

1. Solicited local and systemic adverse events measured after vaccination until day 7 post vaccination.
2. Unsolicited adverse events measured after each vaccination until day 28 post vaccination.
3. Change from baseline measured for safety laboratory measures for 28 days following vaccination
4. Medically attended adverse events collected during the entire study period
5. Serious adverse events (which includes AESIs) collected during the entire study period.
6. Comparison of time to diagnosis measured between Groups 1 and 2

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Previous primary outcome measure:

1. Solicited local and systemic adverse events measured after vaccination until day 7 post vaccination.
2. Unsolicited adverse events measured after each vaccination until day 28 post vaccination.
3. Change from baseline measured for safety laboratory measures for 28 days following vaccination
4. Medically attended adverse events collected during the entire study period
5. Serious adverse events (which includes AESIs) collected during the entire study period.
6. Comparison of time to diagnosis measured between Groups 1, 2 and 3 (Groups 2a and 2b will be pooled)

Key secondary outcome(s))
Current secondary outcome measures as of 10/09/2025:

1. Quantitative antigen-specific IgG antibody levels (µg/mL readout) measured over time – analysis of peak responses and longevity
2. In vitro GIA against 3D7 clone P. falciparum parasites measured using purified total IgG and a single-cycle pLDH readout assay
3. Purified IgG ELISA versus GIA titration “Quality Analysis”
4. Frequency of vaccine-specific B cells in axillary lymph nodes as measured by flow cytometry

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Previous secondary outcome measures:

1. Quantitative antigen-specific IgG antibody levels (µg/mL readout) measured over time – analysis of peak responses and longevity
2. In vitro GIA against 3D7 clone P. falciparum parasites measured using purified total IgG and a single-cycle pLDH readout assay

Completion date
31/03/2026

Eligibility

Key inclusion criteria

Current inclusion criteria as of 10/09/2025:

1. Healthy adult aged 18 to 45 years.
2. Able and willing (in the Investigator's opinion) to comply with all study requirements.
3. Willing to allow the Investigators to access participant's electronic medical records and discuss the participant's medical history with their GP.
4. Able and willing to provide written informed consent to participate in the trial.
5. Participants of childbearing potential only: must practice continuous effective contraception for the duration of the study.
6. Negative haemoglobinopathy screen (including screening for sickle cell disease and alpha and beta thalassaemia) and normal G6PD levels.
7. Agreement to permanently refrain from blood donation, as per current UK Blood Transfusion and Tissue Transplantation Services guidelines.
8. Reachable (24 hours a day) by mobile phone during the period between CHMI and completion of antimalarial treatment.
9. Willing to take a curative anti-malaria regimen following CHMI.
10. Able to answer all questions on the informed consent questionnaire correctly at first or second attempt.
11. Willing to be registered on the TOPS database (The Over volunteering Prevention System; www.tops.org.uk).

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8. Reachable (24 hours a day) by mobile phone during the period between CHMI and completion of antimalarial treatment.
9. Willing to take a curative anti-malaria regimen following CHMI.
10. Able to answer all questions on the informed consent questionnaire correctly at first or second attempt.
11. Willing to be registered on the TOPS database (The Over volunteering Prevention System; www.tops.org.uk).

Group 2 only:
12. Participant in Group 1, 2 or 4 of the VAC089 trial.

Participant type(s)

Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 10/09/2025:

1. History of clinical malaria (any species) or previous participation in any malaria vaccine trial
2. Planned travel to a clearly malaria-endemic locality during the study period or previous travel to a malaria endemic locality within the preceding six months.
3. Use of immunoglobulins or blood products (e.g. blood transfusion) in the last three 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 and flu vaccines, which should not be received between 14 days before to 7 days after any study vaccination.
5. Receipt of a vaccine within 2 weeks before the day of CHMI or planned receipt of a vaccine prior to expected completion of antimalarial treatment (around 2 to 3 weeks after day of challenge based on experience in previous P. falciparum CHMI studies to date).
6. Receipt of an investigational product in the 30 days preceding enrolment, or planned receipt during the study period.
7. Concurrent involvement in another clinical trial involving an investigational product or planned involvement during the study period.
8. Prior receipt of an investigational vaccine likely to impact on interpretation of the trial data, as assessed by the Investigator.
9. 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).
10. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine.
11. Any history of anaphylaxis.
12. Pregnancy, lactation or intention to become pregnant during the study.
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.
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 participant 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. Body weight <50 kg or Body Mass Index (BMI) <18.0 kg/m² at screening.
21. Use of systemic antibiotics with known antimalarial activity within 30 days of CHMI (e.g. trimethoprim-sulfamethoxazole, doxycycline, tetracycline, clindamycin, erythromycin, fluoroquinolones and azithromycin).
22. Use of anti-malarials within 30 days of CHMI.
23. An estimated ten-year risk of fatal cardiovascular disease of ≥5% at screening, as determined by the Systematic Coronary Risk Evaluation 2 (SCORE2).
24. Use of medications known to cause prolongation of the QT interval and existing contraindication to the use of Malarone.
25. Use of medications known to have a potentially clinically significant interaction with Riamet and Malarone.
26. Any other contraindications/known hypersensitivities to both Riamet and Malarone.
27. Any clinical condition known to prolong the QT interval.
28. History, or evidence at screening, of clinically significant arrhythmias, including clinically relevant bradycardia, prolonged QT interval or other clinically relevant ECG abnormalities.
29. Disturbances of electrolyte balance, e.g. hypokalaemia or hypomagnesaemia.
30. Family history of congenital QT prolongation or sudden death.
31. Positive family history in both 1st AND 2nd degree relatives <50 years old for cardiac disease.
32. History of sickle cell anaemia, sickle cell trait, thalassaemia or thalassaemia trait, G6PD deficiency or any haematological condition that could affect susceptibility to malaria infection.
33. Participants unable to be closely followed for social, geographic or psychological reasons.
34. Any clinically significant abnormal finding on biochemistry or haematology blood tests or clinical examination. The normal range of results for each blood parameter is shown in Appendix A. In the event of abnormal test results, confirmatory repeat tests will be requested. Procedures for identifying laboratory values meeting exclusion criteria are described in Appendix A
35. Any other significant disease, disorder, or finding which may significantly increase the risk to the participant because of participation in the study, affect the ability of the participant to participate in the study or impair interpretation of the study data.
36. Inability of the study team to confirm medical history via electronic records or by contacting the participant's GP.

Additional exclusion criteria for optional FNA in Groups 1 and 2:
• Regular use of anticoagulation or antiplatelet medication likely to induce bruising or bleeding on fine needle aspiration.
• Any confirmed or suspected bleeding disorders.
• History of lymphatic disorders (e.g. lymphoedema).
• History of allergic disease or reactions to local anaesthetic such as lidocaine.
• Any history of anaphylaxis in relation to local anaesthetic such as lidocaine.

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Previous exclusion criteria:

1. History of clinical malaria (any species) or previous participation in any malaria vaccine trial (with the exception of Groups 1, 2 or 4 of VAC089) or previous participation in CHMI.
2. Planned travel to a clearly malaria-endemic locality during the study period or previous travel to a malaria endemic locality within the preceding six months.
3. Use of immunoglobulins or blood products (e.g. blood transfusion) in the last three 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 and flu vaccines, which should not be received between 14 days before to 7 days after any study vaccination.
5. Receipt of a vaccine within 2 weeks before the day of CHMI or planned receipt of a vaccine prior to expected completion of antimalarial treatment (around 2 to 3 weeks after day of challenge based on experience in previous P. falciparum CHMI studies to date).
6. Receipt of an investigational product in the 30 days preceding enrolment, or planned receipt during the study period.
7. Concurrent involvement in another clinical trial involving an investigational product or planned involvement during the study period.
8. Prior receipt of an investigational vaccine likely to impact on interpretation of the trial data, as assessed by the Investigator.
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10. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine.
11. Any history of anaphylaxis.
12. Pregnancy, lactation or intention to become pregnant during the study.
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.
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22. Use of anti-malarials within 30 days of CHMI.
23. An estimated ten-year risk of fatal cardiovascular disease of ≥5% at screening, as determined by the Systematic Coronary Risk Evaluation 2 (SCORE2).
24. Use of medications known to cause prolongation of the QT interval and existing contraindication to the use of Malarone.
25. Use of medications known to have a potentially clinically significant interaction with Riamet and Malarone.
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clinical examination. The normal range of results for each blood parameter is shown in Appendix A. In the event of abnormal test results, confirmatory repeat tests will be requested. Procedures for identifying laboratory values meeting exclusion criteria are described in Appendix A
35. Any other significant disease, disorder, or finding which may significantly increase the risk to the participant because of participation in the study, affect the ability of the participant to participate in the study or impair interpretation of the study data.
36. Inability of the study team to confirm medical history via electronic records or by contacting the participant's GP.

Date of first enrolment
04/08/2025

Date of final enrolment
01/07/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
University/education

Funder Name
University of Oxford

Alternative Name(s)

University in Oxford, Oxford University, , Universitas Oxoniensis, uniofoxford

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes