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A study testing the safety and practicality of infecting healthy UK adults with malaria to understand how the parasite grows and how the body responds

Submission date
10/01/2025

Recruitment status
No longer recruiting

Registration date
16/01/2025

Overall study status
Ongoing

Last Edited
23/05/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[X] 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 disease caused by a parasite infection called Plasmodium, transmitted by mosquitoes. Plasmodium vivax is the most widespread of all the Plasmodium species known to cause malaria in humans with approximately 3.3. billion people living in areas at risk of infection. P. vivax causes significant health problems in many areas of the world. Between 2018-2022, more than 5 million P. vivax infections occurred every year. After being bitten by a mosquito carrying the malaria parasite, people usually develop symptoms of infection (such as fever, headache, and muscle aches) within 1-2 weeks. Most malaria infections can be successfully treated with tablets. However, without early effective treatment, P. vivax malaria can lead to severe illness and even death. A particular feature of P. vivax is that, unlike other malaria species, it also produces an inactive dormant form of infection called a hypnozoite. The word hypnozoite is a name derived from the Greek word “hypnos” meaning sleep. Hypnozoites hide in the liver and can later reactivate or reawaken to cause another active malaria infection. This can occur several times over the months (or even years) after the mosquito bite which introduced the infection in the first place if left untreated. It is estimated that 80-90% of all P. vivax malaria cases are due to relapse infections. Study BIO-006 is being conducted to try and find out more about relapsing malaria infections. It is a malaria challenge study. This means it involves deliberately infecting volunteers with malaria in a safe and controlled way. Participants will be deliberately infected with relapsing P. vivax infections over 6 months, each of which will be treated with tablets to clear the active infection. At the end of this period, all participants will be treated with tablets to clear any active and inactive malaria parasites (hypnozoites) in the liver, to prevent any further infections from occurring. The BIO-006 study will provide us with valuable information about relapse malaria infections. It is also a proof-of-concept study, meaning that, although malaria challenges by mosquito bites have been safely performed in previous studies, participants have never been allowed to experience relapsing infections. Success will mean that a similar study could be repeated in the future (in the knowledge that it works) to test new vaccines or medications that could be used to treat or prevent relapsing malaria infections.

Who can participate?
Participants will be healthy adults between 18 to 45 years of age.

What does the study involve?
All participants will attend a screening appointment to ensure they are eligible to undergo a malaria challenge and take part in this study. Eligible participants will be exposed to mosquitoes carrying the malaria infection in a safe and controlled way. The participants will deliberately experience relapsing P. vivax infections over 6 months. During each relapse, they will be treated with tablets to clear the active infection. At the end of this period, all participants will receive treatment with tablets to clear both active and inactive malaria parasites (hypnozoites) in the liver, preventing any further infections. Participants will attend study visits over 7.5 months, followed by a fortnightly email questionnaire for 4 months and then annually for 4 years. Some of the study visits will consist of a blood draw to check for general health, look at the immune response and ensure the active malaria infection has cleared and also collection of information on serious adverse events.

What are the possible benefits and risks of participating?
Participating in this study will not provide a direct benefit. However, the information gained from the study will help develop a new method of testing future curative and preventative therapies for relapsing malaria such as vaccines. As 80-90% of P. vivax malaria cases are thought to be due to relapsing infections, this will be an invaluable platform to develop treatments that may help in the pursuit of malaria eradication.

Temporary localised bruising and discomfort can occur at the site of blood sampling. Mosquito bites may cause local inflammatory reactions with redness, itching, swelling, scaling and/or tenderness. Topical antihistamine cream will be provided to help with these symptoms. Untreated malaria infection can result in serious illness; therefore, participants must attend all follow-up visits and take the anti-malarial treatment as advised

Where is the study run from?
Oxford Vaccine Group, Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), University of Oxford (UK)

When is the study starting and how long is it expected to run for?
December 2024 to February 2030

Who is funding the study?
Innovate UK – Horizon Europe Consortium (OptiVivax)

Who is the main contact?
Nelly Owino, nelly.owino@paediatrics.ox.ac.uk

Study website
https://www.ovg.ox.ac.uk/studies/bio006

Contact information

Type(s)
Public

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Type(s)
Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
342867

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 65371, UK Research and Innovation (UKRI) Grant Code: 10077974

Study information

Scientific Title
BIO-006: A clinical study to assess the safety and feasibility of relapsing P. vivax controlled human malaria infection through experimental sporozoite infection of healthy malaria-naïve UK adults, and to characterise parasite growth and immune responses to primary and relapsing P. vivax infection

Study objectives
This study assesses the safety and feasibility of controlled primary and relapsing human P. vivax malaria infection with the PvW1 clone in five healthy volunteers.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/12/2024, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8178; berkshire.rec@hra.nhs.uk), ref: 24/SC/0355

Study design
Non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital, Laboratory

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Specialty: Infection, Primary sub-specialty: Tropical Medicine; Health Category: Infection

Interventions
The sporozoite Controlled Human Malaria Infection (CHMI) will be administered by exposure of participants to the bites of five infectious laboratory-reared Anopheles stephensi mosquitoes by placing their forearms over the container of the mosquitoes for 5-10 minutes.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. Safety of primary and relapsing P. vivax infection following sporozoite-administered CHMI measured using (S)AE occurrences throughout the study and by the end of the in-person follow-up period (month 7.5) and long-term safety data from remote follow-up period (month 8 – year 5)
2. Primary P. vivax infection following sporozoite-administered CHMI measured by detectable parasitaemia using qPCR +/- clinical symptoms by day 21
3. The frequency of P. vivax relapse infections measured by the number of malaria episodes confirmed using qPCR occurring within a 6-month follow-up period after treatment of primary infection, and time to relapse infection by month 7

Secondary outcome measures
The following will be assessed at C-2, C+7, C+14, C+21, at every fortnightly relapse clinic until C+196:
1. Secondary outcome: Serological response to a panel of P. vivax antigens measured using ELISA
2. Exploratory outcomes:
2.1. Gametocyte induction following primary and each relapse P. vivax infection measured using a qPCR assay
2.2. Cellular responses measured using flow cytometry
2.3. Functional anti-parasitic activity in purified total IgG measured using growth inhibition assay screening

Overall study start date
19/12/2024

Completion date
26/02/2030

Eligibility

Key inclusion criteria

1. Healthy, malaria-naïve adult aged 18 to 45 years
2. Able and willing to provide informed consent to participate in the study
3. Able and willing (in the opinion of the Investigator) to comply with all study requirements
4. Willing to allow the Investigators to access participant's electronic medical records or discuss the participant's s medical history with their GP
5. Participants of childbearing potential only: must practice continuous highly effective contraception until 3 months after completion of Primaquine treatment
6. Negative haemoglobinopathy screen (including sickle cell disease and alpha and beta thalassaemia)
7. Normal G6PD screen
8. Agreement to refrain from blood donation until at least 3 years following completion of Primaquine treatment, as per current UK Blood Transfusion and Tissue Transplantation Services guidelines
9. Able to answer all questions on the informed consent questionnaire correctly at first or second attempt
10. Able to travel to CCVTM easily
11. Able to travel to the Netherlands for malaria challenge with the necessary passport +/- visa requirements
12. Reachable 24 hours a day by mobile phone during the period between CHMI and completion of Primaquine treatment
13. Willing to take anti-malarial treatment for i) primary P. vivax infection ii) any relapse P. vivax infections and iii) at the end of relapse follow-up period as outlined in schedule of study procedures
14. Willing to remain in Oxfordshire (or surrounding area) following malaria challenge (after return from the Netherlands) until completion of treatment of primary P. vivax infection
15. Willing to remain within travelling distance of Oxfordshire (or surrounding area) following treatment of primary P. vivax infection until completion of Primaquine treatment (month 7). Absolute necessity is to remain on the UK mainland within 1-2 hours of secondary care NHS hospital.
16. Willing to be registered on the TOPS database (The Over volunteering Prevention System; www.tops.org.uk).

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Both

Target number of participants
Planned Sample Size: 5; UK Sample Size: 5

Total final enrolment
5

Key exclusion criteria
1. Red blood cells negative for the Duffy antigen/chemokine receptor (DARC)
2. CYP2D6 genotype suggestive of poor or intermediate metabolism of Primaquine
3. Body weight < 50kg or Body Mass Index (BMI) < 18.0 at screening
4. History of clinical malaria (any species) or previous participation in any malaria vaccine trial or CHMI
5. Travel to a clearly malaria endemic locality during the study period or within the preceding six months
6. Receipt of immunoglobulins or blood products (e.g. blood transfusion) in the last three months
7. Receipt of an investigational product in the 30 days preceding enrolment (or planned receipt during the study period) likely to impact on interpretation of the trial data or the P. vivax parasite as assessed by the Investigator
8. Concurrent involvement in another clinical trial involving an investigational product or planned involvement during the study period
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. Any history of severe allergy or anaphylaxis
11. Use of systemic antibiotics with known anti-malarial activity within 30 days of CHMI (e.g. trimethoprim-sulfamethoxazole, doxycycline, tetracycline, clindamycin, erythromycin, fluoroquinolones and azithromycin)
12. Use of anti-malarials within 30 days of CHMI
13. Any clinical condition known to prolong the QT interval
14. History of cardiac arrhythmia, including clinically relevant bradycardia
15. Disturbances of electrolyte balance, e.g. hypokalaemia or hypomagnesaemia
16. Family history of congenital QT prolongation or sudden death
17. An estimated ten-year risk of fatal cardiovascular disease of > = 5% at screening, as determined by the Systematic Coronary Risk Evaluation (SCORE2) shown in Appendix A
18. Use of medications known to have a potentially clinically significant interaction with both Riamet and Malarone
19. Use of medications known to have a potentially clinically significant interaction with Primaquine
20. Any other contraindications/known hypersensitivities to both Riamet and Malarone
21. Any other contraindications/known hypersensitivities to Primaquine
22. 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
23. Pregnancy, lactation or intention to become pregnant during the study
24. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
25. History of serious psychiatric condition that may affect participation in the study
26. Any other serious chronic illness requiring hospital specialist supervision
27. Suspected or known current alcohol misuse
28. Suspected or known injecting drug use in the 5 years preceding enrolment
29. Hepatitis B surface antigen (HBsAg) detected in serum
30. 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) qPCR at screening for this study)

31. Participants unable to be closely followed for social, geographic or psychological reasons.
32. 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 Appendix B. 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 B.
33. Any other significant disease, disorder, or finding (in the opinion of the Investigator) 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
34. Inability of the study team to confirm medical history via electronic records or contact the participant's GP to confirm medical history

Date of first enrolment
13/01/2025

Date of final enrolment
12/03/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford Vaccine Group
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Sponsor type
Hospital/treatment centre

Website
https://www.ox.ac.uk

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
26/02/2031

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request directed to Angela Minassian (angela.minassian@paediatrics.ox.ac.uk), Chief Investigator or upon written approval of the sponsor.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	27/11/2024	10/01/2025	No	No
Protocol file	version 2.0	17/02/2025	13/03/2025	No	No