

# 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

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<b>Registration date</b> 16/01/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 23/05/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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

## Contact information

### Type(s)

Public

### Contact name

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**Additional identifiers**

## Clinical Trials Information System (CTIS)

Nil known

## Integrated Research Application System (IRAS)

342867

## ClinicalTrials.gov (NCT)

Nil known

## Protocol serial number

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

## Study type(s)

Treatment

## 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(s)

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

## Key secondary outcome(s)

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

## 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 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](http://www.tops.org.uk)).

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Upper age limit**

45 years

### **Sex**

All

### **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  $\geq 5\%$  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**

United Kingdom

England

## **Study participating centre**

### **Oxford Vaccine Group**

Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)

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## **Sponsor information**

### **Organisation**

University of Oxford

### **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

## 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?
<a href="#">Protocol file</a>	version 1.1	27/11/2024	10/01/2025	No	No
<a href="#">Protocol file</a>	version 2.0	17/02/2025	13/03/2025	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes