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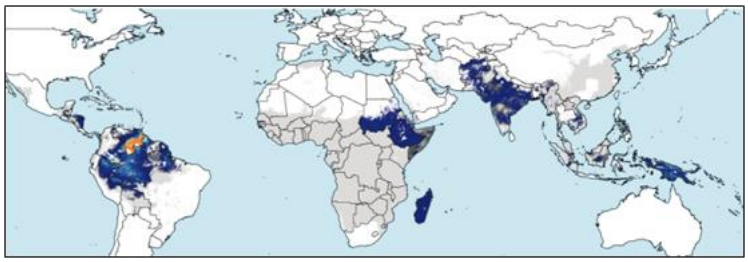
BIO-006: ABBREVIATED PARTICIPANT INFORMATION SHEET

Development of a relapsing *P. vivax* Controlled Human Malaria Infection model

Why are we conducting this study?

Plasmodium vivax malaria

Malaria is a disease caused by a parasite infection called *Plasmodium* which is 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.



***P. vivax* geographical distribution**

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.

Relapsing malaria

A particular feature of *P. vivax* is that, unlike other malaria species, it produces an inactive dormant form of infection called a hypnozoite. Hypnozoites hide in the liver and can later reawaken to cause another active malaria infection. This can occur several times over the months after the mosquito bite which introduced the infection in the first place. It is estimated that 80-90% of all *P. vivax* malaria cases are due to these "relapse" infections.

The BIO-006 study

We are conducting the BIO-006 study 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.

What's the aim of the study?

The BIO-006 study will provide us with valuable information about relapse malaria infections. Success would mean that we could repeat a similar study in the future to test new vaccines or medications that could be used to treat or prevent relapsing malaria, and ultimately prevent unnecessary illness and suffering.

Thank you for your interest in the BIO-006 study. Help us in the fight against malaria!

Who can take part?

- ✓ Healthy adult age 18-45 years
- ✓ Not had malaria before
- ✓ Able to attend visits over a **7.5** month study period

You may be able to take part!

Please see the full version of the Participant Information Sheet BIO-006 PIS for a complete list of eligibility criteria

What does the study involve?

1. Malaria challenge

We would like to study relapsing malaria by performing a malaria challenge, a deliberate malaria infection introduced in carefully controlled conditions. The malaria infection will be administered by mosquito bites, on a designated day **Radboud University Medical Center (RUMC) in Nijmegen, Netherlands**. The malaria challenge therefore involves travelling to the Netherlands for approximately 2 nights. Travel, accommodation and food will be organised and paid for by the study team. You will need to have the necessary passport +/- visa requirements to travel to the Netherlands. All other appointments will be conducted at the **Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) at Churchill Hospital in Oxford**.

The malaria challenge follow-up visits are very important. We will assess you by phone once a day for the first 6 days. From the day 7 onwards we will see you daily at the CCVTM clinic in Oxford. At these appointments, we will take a small blood sample to see if there are any detectable malaria parasites in your blood. This will continue until 21 days after malaria challenge or until you are diagnosed with malaria, whichever happens sooner.

Once the study team confirms the diagnosis of malaria, you will be treated with tablets (such as Riamet or Malarone). Both these tablets are effective at treating active malaria infections. However, they do not treat inactive malaria infections (i.e. dormant *P. vivax* hypnozoites). This is because we want to study relapsing malaria infections that occur from reactivating hypnozoites.

Did you know that approximately 600 people have previously had a malaria challenge as part of a research study in Oxford?

Watch this video hear about their experiences
<https://www.youtube.com/watch?v=Pjn77B-gnIE >

2. Relapsing malaria infection

We will monitor you closely for the following 6 months for relapsing malaria infections. You will be required to attend a fortnightly clinic at CCVTM. You will also be able to contact the study doctor at any time (i.e. 24/7) if you think you are developing symptoms of malaria infection (e.g. fever). Relapse infections will be treated as before with Riamet or Malarone to clear the active infection.

We expect you to experience approximately 2-3 relapse infections in 6 months. However, it is important to em**phasise** that relapsing infections are unpredictable and variable. They may occur at any time. Some people may develop symptoms of malaria due to a relapse infection, some people may not. Some people may not experience any relapse malaria infections.

3. Definitive malaria treatment

Approximately 6.5 months following the malaria challenge all participants will receive tablets to treat any active malaria infection (Riamet or Malarone) *and* another medication called Primaquine to completely clear any inactive dormant infection. Primaquine tablets are taken for 14 days and prevent future relapse infections from occurring. The last in-person visit will take place 7.5 months following the malaria challenge.

4. Long-term follow-up

We will email you fortnightly until 1 year following the malaria challenge, and then annually for another four years. This is to ensure you have not experienced any unexpected relapse malaria infections.

Blood tests will be performed at most in-person study visits.

What does the schedule look like?

Aim

To develop a method of safely and effectively introducing relapsing malaria in healthy volunteers by Controlled Human Malaria Infection (CHMI) administered by mosquito-bite

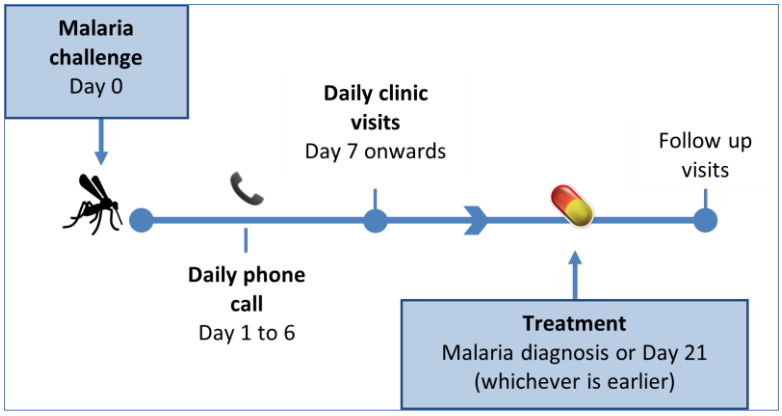
Day 0 – Day 28

Malaria challenge

Primary malaria infection

Treatment of active infection

Riamet (or Malarone) only



Month 1 – Month 6.5

Relapse follow-up period

Fortnightly clinic
Study doctor 24/7

Relapse malaria infection

Treatment of active infection

Riamet (or Malarone) only

Month 6.5 – Month 7

Definitive malaria treatment

Riamet (or Malarone)
AND
Primaquine

Last in-person visit
Month 7.5

Email follow-up
Fortnightly month 8-12
Annually year 2 - 5

Key Facts

Malaria challenge administered at RUMC, Nijmegen, Netherlands: 2 night/3 day trip

Total visits: Approximately 51 study visits*

Study duration: 7.5 months in person, email follow-up until 5 years

Compensation: Approximately £5,510*

***Actual no. of visits & compensation will depend on number of relapse infections. Above figures assume 2 relapse infections and attendance at all study visits.**

Is there anything else I should know?

- **Travel restrictions**

In the Netherlands, there will not be an opportunity to extend your travel or participate in activities beyond the scope of the malaria challenge. Following your return from the Netherlands, you will be required to remain in Oxfordshire (or the surrounding area) until you complete treatment of the primary *P. vivax* infection (approximately 28 days following malaria challenge). After this, you will be asked to remain within travelling distance of Oxford until Primaquine treatment is completed (i.e. approximately 7 months). This is because we need to be able to assess and treat you promptly if you develop a malaria infection. Short trips to other areas of the UK may be possible following discussion with the study team. However, you must not travel abroad until completion of Primaquine treatment (i.e. approximately 7 months).

- **Are there any risks or benefits of participating?**

Untreated malaria infection can result in serious illness. Therefore, it is important that you attend all the clinic visits and take the anti-malarial treatment as advised. There may be some redness and itching following the mosquito bites. You may experience early symptoms or malaria infection such as a fever, chills, headache, muscle aches, diarrhoea and vomiting. We will provide medication to help. Participating in this study will not benefit you directly. However, it will greatly improve our understanding of relapsing malaria and will help us develop a new method of testing new vaccines against relapsing malaria. Please see the Participant Information Sheet – full version for more information about risks and benefits of participating.

- **How would you look after my data and research samples?**

This is explained in more detail in the Participant Information Sheet – full version **BIO-006 PIS**. We will only use information that we need for the research study. Everyone involved in this study will keep your data safe and secure. We will follow all privacy rules. All study samples will be stored in a pseudonymised form. This means that your study number rather than your personal details will be on them. With your consent, we may store your samples and research data for the purpose of malaria research. We will make sure no-one can work out who you are from any reports we write.

- **How do I sign up?**

Thank you for your interest! To express an interest in participating in the BIO-006 study, please complete our online questionnaire.

- **Visit our website https://www.ovg.ox.ac.uk/studies/bio006**
- **Scan the QR code**

The questionnaire takes 3-5 minutes and will ask questions to see if you could be eligible for participation. It will also ask for your contact details and permission to contact you so that we can arrange an in-person appointment.

- **What happens next?**

The next step is a screening appointment with one of the study doctors. This appointment lasts 1-2 hours and involves a detailed discussion about the trial, review of the full eligibility criteria, blood tests and a medical examination.

- **How long are the other visits?**

The malaria challenge will take most of the morning or afternoon. However, the other study visits are much quicker and generally take no more than 30 minutes. These generally fit around normal working or studying patterns for most people.

- **How do I find out more information?**

More detailed information about this study can be found in the Participant Information Sheet – full version**.** **BIO-006 PIS** We require you to read this document before you can be part of this study. Find out more about participating in a malaria challenge study from some of our previous volunteers in our malaria challenge video. **Watch this Video** Please feel free to contact us using the details below. We would be more than happy to answer any questions!

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