Participant information for participating in medical scientific research

Coadministration of genetically attenuated GA2 malaria parasites with adjuvants

Coadministration of genetically attenuated Plasmodium falciparum Δmei2 (GA2) sporozoites with adjuvants – a proof of principle study

Introduction

Dear reader,

With this letter, we would like to ask you to take part in a medical study. Participation is voluntary. You can read about the medical study in this information sheet, what it means for you, and what the pros and cons are. It is a lot of information. Please read the information and decide if you want to take part.

Ask your questions

You can take your decision based on the information in this information sheet. We also suggest that you do this:

- Ask your questions to the investigator who gave you this information.
- Talk to your partner, family or friends about this study.
- Ask questions to the independent expert, dr. A.H.E. Roukens.
- Read the information on www.rijksoverheid.nl/mensenonderzoek.

1. General information

The Leiden University Medical Center (LUMC) has set up this study. This study is conducted by researchers (physicians, nurses, doctor's assistants and student-assistants) in the LUMC in Leiden. Participants in medical-scientific studies are often called study subjects. Both patients and healthy people can be study subjects. For this study, we are recruiting a total of 66 healthy study subjects aged 18 to 35. The Central Committee for Research with Human Subjects (In Dutch: Centrale Commissie Mensgebonden Onderzoek (CCMO)) approved this study.

2. What is the purpose of this study?

In this study, we investigate a genetically attenuated malaria parasite: the GA2 parasite. A previous study showed that administration of the GA2 parasite with mosquito bites is safe, and does not cause malaria.

In this study, we investigate how well the GA2 parasite can induce protection against malaria after one administration with 10 or 50 mosquito bites. We also investigate if the protection increases if we coadminister adjuvants at the site of the mosquito bites. The adjuvants are: the BCG vaccine, the yellow fever vaccine and imiquimod cream.
We also compare the effect of the GA2 parasite with the effect of a placebo. A placebo is a product without the active ingredient: a 'fake product'. Since the GA2 parasites will be administered by mosquito bites, the placebo will consist of bites by mosquitoes that are not infected with malaria.

3. What is the background of this study?

Every year, approximately half a million people die of malaria, mostly young children in Africa. The malaria parasite is transmitted by mosquito bites. The development of an effective vaccine against malaria is necessary to protect these children against malaria before they get sick.
The GA2 is a malaria parasite that has been attenuated by genetic modification. Because of these changes, the parasite is not able to cause malaria. The parasite can train the immune system to recognize and clear malaria parasites. We thus hope that the GA2 parasite can be used as a vaccine against malaria in the future. In order to achieve this, we must learn how we can improve the training of the immune system by GA2. Therefore, we now want to investigate adjuvants. Adjuvants are additives that are added to a vaccine in order to improve immune activation.
In previous studies, it was found that one and 3 times 50 mosquito bites with GA2 parasites led to good protection against malaria. In this study we will investigate the protection after 1 time 10 or 50 mosquito bites in combination with adjuvants.

4. How will the study be carried out?

How long will the study take?
In case you participate in the study, it will take approximately three months. During the study, you will visit the LUMC a total of 27 times in 12 weeks. Additionally, you will receive three phone calls. After that, there will be two follow-up visits, at 8 and 21 weeks after the end of the trial.

Step 1: screening visit
The screening visit will take about one and half hours. We want to know if you are eligible to take part. That is the reason that the investigator is doing some checks:

- Discussing your medical history and that of your close family members.
- Physical examination. For example, the investigator can listen to your heart and lungs, and will measure your blood pressure and heart rate.

- Blood test. The investigator will take some blood from you. We will test your blood for HIV, Hepatitis B and Hepatitis C. We will tell you if you have one of these diseases.
- Electrocardiogram (ECG).
- Urine test for the use of drugs such as cocaine, amphetamines and cannabis.
- Pregnancy test for women (performed on the day before every mosquito exposure).

Please note: it is possible that you are not eligible for this study, even if you are healthy. The investigator will tell you more about this.

Step 2: exposure to the genetically attenuated parasite by mosquitoes (immunization)
The exposure to the GA2 parasites will take place in the LUMC and will take a whole working day.

There will be four groups in this study:

- BCG adjuvant group: This group consists of a total of 5 people, who will be exposed to the bites of 10 GA2-infected mosquitoes and the BCG vaccine.
- Yellow fever vaccine adjuvant group: This group consists of a total of 5 people, who will be exposed to the bites of 10 GA2-infected mosquitoes and the yellow fever vaccine.
- Imiquimod adjuvant group: This group consists of a total of 5 people, who will be exposed to the bites of 10 GA2-infected mosquitoes and imiquimod cream.
- Control: This group consists of a total of 2 people, who will be exposed to the bites of 10 **uninfected** mosquitoes only. This is the placebo group.

You will be assigned to a group at random by drawing lots. Both you and the investigator will know in which of the two groups you are participating.

The mosquito bites and the administration of the adjuvants will be done on the same region on the upper arm.

Back-up study subjects stay in the trial until the exposure the genetically attenuated parasite. A back-up subject attends the screening visit and study day 1 and attends study day 2 (exposure to GA2 parasites) as a back-up (see appendix C for study days). If one of the other study subjects drops out before the exposure, a back-up study subject can replace this participant.

Step 3: infection with malaria
Six weeks after the last exposure to the genetically attenuated parasites, you will be infected with malaria to see if you are protected (= immune). This will be done in the LUMC and will take a whole working day .The malaria infection will be done by exposing you to 5 infected mosquitoes on the forearms. After the exposure, you will visit the LUMC **on a daily basis for two week**s for malaria blood tests. These control visits will take 15 minutes and will be held between **7:00 and 8:30 in the morning.** Once we see that you have malaria you will be treated with the anti-malarial drug Malarone.

If you did not develop malaria 28 days after the exposure, you will receive the Malarone treatment as a safety measure. If a study subject does not tolerate the use of Malarone, or if the treatment with Malarone is not effective, the anti-malarial drug Riamet will be used as a treatment.

Blood tests

At every study visit to the LUMC, blood tests will be done. The investigator will do this by collecting 1 to 10 vials of blood each time. In total, we will not collect more than 500 mL of blood over a 4-month period. This amount does not cause problems in adults. For comparison: if you give blood at the blood bank, you give 500 mL at a time. With the blood test, we test these things:

- Do you have malaria?
- Do you have other side effects caused by the exposure to attenuated malaria parasites?
- How does your immune system responds to the attenuated parasites?

Appendix C has a list of the exact measurements we carry out during each visit.

5. What agreements do we make with you?

We want the study to go well. That is why we will make the following agreements with you:

- You visit every appointment.
- You will not perform intensive physical activities (more than normal) after being exposed to the mosquito bites.
- You will not travel abroad for 28 days after being exposed to the mosquito bites, and will not go to malaria-endemic regions during the study.
- You will not take part in other medical research during this study.
- You carry a participant card of the study with you. In your wallet, for example. It states that you are taking part in this study. And who should be warned in case of an emergency. Show this card when you visit another doctor.
- You should contact the investigator in the following situations:
    - You want to start taking other medication. Also if these are homoeopathic remedies, natural remedies, vitamins or over-the-counter medicines.
    - You are hospitalised or get treatment in a hospital.
    - You suddenly have problems with your health.
    - You no longer want to take part in the study.
    - Your telephone number, address or email address changes.

Is it OK for you to get pregnant during the study?

Women who are pregnant or breastfeeding cannot take part in this study. Women should also not get pregnant during the study. Malaria can affect an unborn child, by, for instance, causing growth retardation. The investigator will tell you how best to prevent pregnancy. Talk to your partner about this.

Pregnant after all?

If you do become pregnant during the study, inform the investigator immediately. In this case, you should stop participating in the study as soon as possible in consultation with the investigator.

Are you allowed to donate blood during the study?

You are not allowed to donate blood or plasma during the study. You are not allowed to donate blood for at least 3 years following the end of the study. You will no longer be able to donate whole blood if antibodies against malaria remain detectable in your blood. However, you can still (continue to) donate plasma after this study has ended.

6. Which side effects, adverse effects or inconveniences may you encounter?

The GA2 parasites may cause side effects. The following side effects are very common (in 1 in 10 people or more):

- Redness around the area exposed to mosquitoes;
- Itching around the area exposed to mosquitoes;
- Darkening of the skin at the site of the mosquito bites;
- Mild headaches;
- Mild muscle aches;
- Feeling of weakness and/or malaise.

Blisters on the mosquito bites may occur (1 in 10 – 100 persons).

A rare side effect are elevated liver enzymes in the blood.

An anti-allergy cream (antihistamine) is commonly used to alleviate the side effects of the mosquito bites. In some cases, the use of antihistamine tablets or anti-inflammatory (corticosteroid) cream is needed.

The adjuvants

BCG vaccine (group A): the BCG vaccine will be injected into the skin with a small needle. Six to eight weeks after the vaccination a small pustule or sore develops that may leak fluid. This heals after a couple of weeks with a scar. Side effects that occur occasionally (in 1 in 100 – 1.000 persons) are: fever or headache. Side effects that occur rarely (in 1 in 1.000 – 10.000 persons) are: allergic reactions, abscesses, bone infections or generalised BCG infection. From the moment of BCG vaccination onward, future tuberculosis skin test (Mantoux test) will become positive.

Yellow fever vaccine (group B): the yellow fever vaccine will be injected into the skin with a small needle. Very frequent side effects (in more than 1 in 10 persons) are: pain, tenderness, redness, swelling or itch on the injection site, headache, vomiting, muscle ache and fever between day 4 and 14 after vaccination. Common (in 1 in 10 – 100 persons) side effects are: nausea, joint pain and rash.

Occasionally (in 1 in 100 - 1.000 persons) stomach ache or dizziness occurs. Severe side effects of the yellow fever vaccine are very rare (less than 1 in 10.000 persons).

Imiquimod cream (group C): after the application of the cream, itch at the site of application is very common (more than 1 in 10 people). Common (in 1 in 10 – 100 people) side effects are: pain, burning sensation, redness or pimples appear at the application site or the development of flu-like symptoms.

Infection with malaria

Infection with malaria parasites may result in malaria. This risk will differ from group to group. We expect all the study subjects in the placebo group (group E) to develop malaria. For the other groups (A to D), the risk is unknown but expected to be lower. Most people who develop malaria, experience some symptoms, lasting two to three days on average.

The main symptoms of malaria are:

- Headache;
- Fever;
- Shivering;
- General weakness and fatigue;
- Muscle and joint pain;
- Nausea;
- Dizziness.

The following side effects are rare but can be serious:

- Increase in liver enzymes;
- Inflammation of the heart muscle.

Immediately contact the investigator if you:

- Have pain in your chest;
- Become ill and get fever with or without shivering.

The anti-malarial drug Malarone

The anti-malarial drug Malarone may cause side effects. The following side effects are very common (more than 1 in 10 people): stomach ache, nausea, throwing up, diarrhoea and headache. Common (1 in 10 – 100) side effects are: decreased appetite, dizziness, difficulty sleeping, gloominess, vivid dreams, itch or rash. Occasionally (1 in 100 – 1.000 people), palpitations, anxiety, hair loss or hives occurs. Rarely (1 in 1.000 – 10.000), hallucinations occur.

The antimalarial drug Riamet

If the exceptional situation occurs that you do not tolerate the use of Malarone, or when it is not effective to treat the malaria, the drug Riamet will be used as treatment. Common side effects are:

headache, dizziness, palpitations, nausea, throwing up, tummy ache, diarrhoea, fatigue, muscle- or joint ache. In rare cases, further treatment is needed after Riamet when the parasite has not been treated effectively.

Inconvenience during blood sampling

Blood sampling can lead to inconvenience such as:

- Pain;
- Bruising.

7. What are the pros and cons if you take part in the study?

Taking part in the study can have pros and cons. We will list them below. Think about this carefully and talk to other people about it.

You do not benefit from taking part in this study yourself. But if you take part you will help the investigators to get more insight into the prevention of malaria.

Taking part in the study can have these cons:

- You may experience the side effects or adverse effects of the exposure to genetically attenuated parasites and of the infection with the unattenuated parasites, as described in Section 6.
- There may be some discomfort from the measurements during the study. For example: taking a blood sample can be a little painful. Or you could get a bruise as a result.
- Taking part in the study will cost you extra time.
- You have to comply with the study agreements.

You do not wish to participate in the study?

It is up to you to decide if you wish to participate in the study.

8. When will the study end?

The investigator will let you know if there is any new information about the study that is important to you. The investigator will then ask you if you want to continue to take part.

In these situations, the study will stop for you:

- All checks according to the schedule are finished.
- You have become pregnant.
- You want to stop participating in the study yourself. You can stop at any time. Report this to the investigator immediately. You do not have to explain why you want to stop. If you want to stop after you having been exposed to genetically attenuated parasites, you still have to take the anti-malarial drug Malarone and visit the hospital a few times for your own safety
- The investigator thinks it is better for you to stop. In this case, you still have to take the anti-malarial drug Malarone and visit the hospital a few times for your own safety.
- One of the following authorities decides that the study should stop:
    - The LUMC,

- The government,
- The Medical Ethics Review Committee assessing the study.

What happens if you stop participating in the study?
The investigators use the data and body materials (blood) that have been collected up to the moment that you decide to stop participating in the study.
The whole study is finished when all the study subjects are done.

9. What happens after the study has ended?

Will you get the results of the study?
About 6 months after you took part in the study, the investigator will inform you about the most important results of the study. The investigator may also tell you what group you were in. Do you prefer not to know? Please tell the investigator. He/she will not tell you in that case.

10. What will be done with your data and body material?

Are you taking part in the study? Then you also give your consent to collect, use and store your data and body material.

What data do we store?
We store these data:
- your name;
- your sex;
- your address;
- your date of birth;
- your bank details (for payment at the end of the trial);
- details about your health;
- (medical) information that we collect during the study.

What body material do we store?
We will store blood in vials.

Why do we collect, use and store your data and samples?
We collect, use and store your data and your body material to answer the questions of the this study. And to be able to publish the results.

How do we protect your privacy?
To protect your privacy, we give a code to your data and your body material. We only put this code on your data and body material. We keep the key to the code in a safe place in the hospital. When we process your data and body material, we always use only that code. Even in reports and publications about the study, nobody will be able to see that it was about you.

A copy of your signed consent form will be stored in the LUMC. This study also requires the investigator at the LUMC to access your personal data. You must provide separate consent for this on the consent form. Even in reports and publications about the study, nobody will be able to see that it was about you.

Who can see your data?

Some people can see your name and other personal information without a code. These are people checking whether the investigators are carrying out the study properly and reliably. These persons can access your data:

- Members of the committee that keeps an eye on the safety of the study;
- An auditor who works for the LUMC;
- National and international supervisory authorities.

These people will keep your information confidential. We ask you to give permission for this access. The Healthcare and Youth Inspectorate (in Dutch: *Inspectie Gezondheidszorg en Jeugd)* can see this information without your permission.

For how long will we store your data and bodily matter?

We store your data in the LUMC for 25 years. We will also store body materials in the LUMC. They will be stored for 25 years in order to be able to make new assessments related to this study. If no longer needed, we will destroy your body material.

Can we use your data and body material for other research?

Your data and your (remaining) body material may also be important after this study for other medical research in the field of malaria. For this purpose, your data and body material will be stored in the LUMC for 25 years. Please indicate in the consent form whether you agree with this. If you do not give permission for this, you can still participate in the study.

What will happen if there are accidental discoveries?

It is possible that during the study we discover something that is important to your health. In that case, the investigator will contact your general practitioner. You will then discuss what needs to be done with your doctor or specialist. With the form, you give consent to inform your doctor or specialist.

Can you take back your consent for the use of your data?

You can take back your consent for the use of your data at any time. This applies both to the use in this study and to the use in other medical research. But please note: if you take back your consent, and the investigators have already collected data for research, they are still allowed to use this information.

The investigators will destroy your body material after you take back your consent. But if assessments with your body material have been carried out, the investigator can continue to use the results.

Do you want to know more about your privacy?

Do you want to know more about your rights when processing personal data? Visit https://www.autoriteitpersoonsgegevens.nl/en.

Do you have questions about your rights? Or do you have a complaint about the processing of your personal data is processed? Please contact the person who is responsible for processing your personal data. For the present, this is:

- The LUMC, see Appendix A for contact details and website.
- If you have complaints about how your personal data is processed, we advise you to first discuss the matter with the research team. For further privacy-related information, refer to the privacy statement of the LUMC on the LUMC website: see Appendix A. You can also contact the Data Protection Officer at the LUMC. Alternatively, you can submit a complaint to the Dutch Data Protection Authority.

Where can you find more information about the study?
More information about the study can be found on the following website: www.ClinicalTrials.gov. After the study, the website may display a summary of the study results. You can find this study by searching for 'NCT05468606'.

11. Will you be reimbursed for taking part in the study?

The testing and treatment for the study will not cost you anything. If you are eligible and you take part in this study, you will receive an reimbursement.

The reimbursement consists of:
- €50,- per control visit/follow-up visit,
- €25,- per phone call control,
- €150,- for exposure to GA2 parasites,
- €150,- for infection with malaria,
- a bonus of €100,- after the last follow-up visit.

The total reimbursements amounts to €1.875,-. For back-up study subjects the total reimbursement is €150,-. You do not receive separate compensation for travel costs.

If you are excluded from the study by the investigator due to a medical reason, you will receive the full reimbursement. If you quit the study before it is completed, you will receive less compensation. The compensation for taking part in this study should possible be declared to the Tax and Customs Administration as 'income from other work'. When needed, ask the National Tax Administration (in Dutch: *de Belastingdienst*) for more information.

12. Are you insured during the study?

Insurance has been taken out for everyone who takes part in this study. The insurance pays for damage caused by the study. But not for all damage. You can find more information about this insurance and any exceptions in **Appendix B**. It also says who you can report damage to.

13. We will inform your general practitioner

The investigator will send your general practitioner a letter to let them know that you are taking part in the study. This is for your own safety.

14. Do you have any questions?

You can ask questions about the study to the research team. Would you like to get advice from a neutral party? Then contact dr. A.H.E. Roukens. She knows a lot about the study but is not involved in it.
You can find her contact details in **appendix A**.
Do you have a complaint? Discuss it with the investigator. Would you prefer not to? Then please contact the complaints committee at the LUMC. **Appendix A** explains how you can do this.

15. How can I provide consent for the study?

You can first think carefully about this study. Then you tell the investigator if you understand the information and if you want to take part or not. If you want to take part, fill in the consent form that you can find with this information sheet during the screenings visit. You and the investigator will both get a signed version of this consent form.

16. Appendices accompanying this information

A. Contact details
B. Information about the insurance
C. Overview of measurements
D. Consent form

Appendix A: Contact details

Principal investigator

Prof. dr. M. Roestenberg

Department of Parasitology

Tel: 06-20942061

E-mail: vaccinonderzoek@lumc.nl

Independent expert

Dr. A.H.E. Roukens

Department of Infectious Diseases LUMC

Tel: 071-52662613

E-mail: A.H.E.Roukens@lumc.nl

Complaints

If you have a complaint about the study, you can contact Team Klachten of the LUMC via e-mail: patientenservicebureau@lumc.nl. You can also contact the Patiëntenservicebureau by phone: 071-5262989, during office hours. They will process your complaint according to the applicable regulations.

Privacy & rights

If you have questions about the protection of your privacy, you can contact the data protection officer at the LUMC (FG) via privacy@lumc.nl. For more information about your rights, you can contact the LUMC

Contact details LUMC

Albinusdreef 2

2333 ZA Leiden

Central telephone number: +31(0)71-5269111

For further information about your rights, please visit the website of the LUMC.

https://www.lumc.nl/12367/Deelnemers-wetenschappelijk-onderzoek/

Appendix B: Information about the insurance

The LUMC has taken out insurance for everyone who takes part in the study. The insurance pays for the damage you have suffered because you participated in the study. This concerns damage you suffer during the study or within 4 years after your participation in the study has ended. You must report damage to the insurer within 4 years.

Have you suffered damage due to the study? Please report this to this insurer:

The insurer for this study is:	
Name:	Centramed
Address:	Maria Montessorilaan 9, 2719 DB Zoetermeer
Telephone:	+31 (0)70-3017070
E-mail:	info@centramed.nl
Policy number:	624.530.305

The insurance will pay maximum €650,000 per person and €5,000,000 for the whole study (and €7,500,000 per year for all studies by the same client).

Please note that the insurance does **not** cover the following damage:

- Damage due to a risk about which we have given you information in this sheet. But this does not apply if the risk turned out to be greater than we previously thought. Or if the risk was very unlikely.
- Damage to your health that would also have happened if you had not taken part in the study.
- Damage that happens because you did not follow directions or instructions or did not follow them properly.
- Damage to the health of your children or grandchildren.
- Damage caused by a treatment method that already exists. Or by research into a treatment method that already exists.

These provisions can be found in the 'Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015' ('Medical Research (Human Subjects) Compulsory Insurance Decree 2015'). This decision can be found in the Government Law Gazette (https://wetten.overheid.nl).

Appendix C: Overview of visits and measurements

Day	Location/Time & duration	Activity
Screening visit	LUMC (by appointment), duration: 1 – 1,5 hours	Explanation about the study and possibility to ask questior The informed consent form will be signed. You will be asked about your age, sex, body weight and height. Medical history of participant and of participant's close relatives will be collected. The following tests and assessments will be carried out: - Temperature, blood pressure, heart; - Physical examination; - Electrocardiogram (ECG); - Blood sampling and blood examination; - Urine sampling for drug test;
Study day 1: Control visit (day before exposure to genetically attenuated parasites)	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	All study subjects will be given a trial diary for noting side effects. The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Only for women: pregnancy test.
Study day 2: **Exposure to genetically attenuated malaria parasite by 10 mosquito bites**	LUMC, duration: a whole working day	Study subjects will be exposed to the genetically attenuated parasite (and possibly an adjuvant) through mosquito bites. The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 3: Phone call control	Phone call, duration: 2-15 minutes	The following tests and assessments will be carried out: - Assessment of side effects; - Assessment of trial diary.
Study day 4: Control visit	LUMC, between 7:00 and 8:30 a.m. duration: 5 minutes	The following tests and assessments will be carried out: - Blood sampling and blood examination;
Study day 8: Control visit	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.

Study day 11: Control visit	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 16: Control visit	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 43: Control visit (day before infection with malaria)	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 44: **Infection with malaria parasites by 5 mosquito bites**	LUMC, duration: a whole working day	Study subjects will be exposed to the genetically attenuated parasite for the first time via mosquito bites. The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 50 to 65: **Daily control visit**	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 68: Phone call control	Phone call, duration: 2-15 minutes	The following tests and assessments will be carried out: - Assessment of side effects; - Assessment of trial diary.
Study day 72: **Control visit + treatment**	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 74: Phone call control	Phone call, duration: 2-15 minutes	The following tests and assessments will be carried out: - Assessment of side effects; - Assessment of trial diary.
Study day 75: Control visit	LUMC, between 7:00 and 8:30 a.m.,	The following tests and assessments will be carried out: - Temperature;

	duration: 15 minutes	- Blood sampling and blood examination; - Assessment of side effects; - Assessment of trial diary.
Study day 79: **Control visit + end of study**	LUMC, between 7:00 and 8:30 a.m., duration: 15 minutes	The following tests and assessments will be carried out: - Temperature; - Blood sampling and blood examination; - Assessment of side effects; - Assessment and collection of trial diary.
Study day 135: Follow-up visit	LUMC	The following tests and assessments will be carried out: - Blood sampling and blood examination;
Study day 226: Follow-up visit	LUMC	The following tests and assessments will be carried out: - Blood sampling and blood examination;

[1] When a participant develops malaria earlier, it will be treated on the same day with Malarone.

Appendix D: Consent form study subjects

Belonging to the study called " Coadministration of genetically attenuated Plasmodium falciparum Δmei2 (GA2) sporozoites with adjuvants – a proof of principle study":

- I have read the information sheet. I was able to ask questions. My questions have been answered well enough. I had enough time to decide if I wanted to take part.
- I know that taking part is voluntary. I also know that at any time I can decide not to take part in the study. Or to stop taking part. I do not have to explain why.
- I give the investigator consent to inform my general practitioner or specialist treating me that I am taking part in this study.
- I give consent to give my doctor or specialist information about accidental discoveries made during the study that are important for my health.
- I give consent to collect and use my data and/or body material (blood). The investigators only do this to answer the question of this study.
- I know that some people will be able to see all of my data to review the study. These people are mentioned in this information sheet. I give consent to let them see my data for this review.
- For women: I know that I cannot get pregnant during the study.
- For women: The investigator discussed with me how I can best prevent becoming pregnant.

- Please tick yes or no in the table below.

I give consent to store my data to use for other research, as stated in the information sheet.	**Yes ☐**	**No☐**
I give consent to have my (remaining) body material stored for use in other research, as stated in the information sheet. The body material is stored for this purpose for another 25 years.	**Yes ☐**	**No☐**
I give consent to ask me after this study if I want to participate in a follow-up study.	**Yes ☐**	**No☐**

- I want to take part in this study.

My name is (participant):

Signature:

Date (DD/MMM/YYYY) : ____ / _____ / _____ Time __ : __ (24h notation)

I declare that I have fully informed this subject about the study mentioned.

If any information becomes known during the study that could influence the subject's consent, I will let this subject know in good time.

Investigator name (or their representative):

Signature:

Date (DD/MMM/YYYY) : ____ / _____ / _____ Time __ : __ (24h notation)

De participant will receive the entire patient information form, together with a certified copy of the signed informed consent form.