MAMAH trial Informed Consent

This form covers the woman and infant. It must be signed by the woman participating in the study (and in some countries by a legal guardian according to national policies).

Title of the study
Evaluation of the safety and efficacy of dihydroartemisinine-piperaquine (DHA-PPQ) for intermittent preventive treatment of malaria in HIV-infected pregnant women.

Introduction
The Barcelona Institute for Global Health (ISGlobal) in Spain is coordinating a study to evaluate drugs to prevent malaria in pregnant women from Gabon and Mozambique.

The study will be testing if a drug called dihydroartemisinine-piperaquine (DHA-PPQ) can prevent pregnant women receiving cotrimoxazole and antiretroviral therapy from malaria while they are using treated mosquito nets. As you know, sometimes you may have malaria without feeling sick. Malaria may be hidden in the placenta and can cause baby to be born small and weak, even if you never feel sick. The baby may also be born too early. If the woman is infected with HIV, this increases even more her chances of getting malaria and makes it difficult to treat.

Right now pregnant women who are infected with the HIV receive cotrimoxazole to prevent infections (including malaria). Also, they must take antiretroviral therapy for controlling the infection and to avoid transmission of the virus to their baby while pregnant. The preventive antimalarial drug that is currently recommended to HIV-uninfected women, cannot be given to HIV-infected women because all the medicines received can have interaction with each other. That is why it is necessary to look for anti-malarial drugs to prevent malaria in pregnant women. Of the current available antimalarial drugs for pregnant women, dihydroartemisinine-piperaquine is the most promising.

You are being asked to participate because the initial screening makes you eligible to join the study. Before you decide if you wish to be in this study, you will be informed about the study and about things that you will be asked to do if you agree to join.

Purpose of the study and study groups
The information coming from this study will help to prevent malaria in African women infected with HIV.

The trial will compare dihydroartemisinine-piperaquine (DHA-PPQ) to placebo (a substance similar to DHA-PPQ but without any effect) as prevention for malaria in pregnancy together with using cotrimoxazole, antiretrovirals and insecticide treated mosquito nets. There will be 664 pregnant women from Mozambique and Gabon enrolled in this study.

Some women in the study will be receiving dihydroartemisinine-piperaquine and other placebo. Also you will be given cotrimoxazole and antiretrovirals to take with you home and administer one tablet every day to prevent any infection. Neither the study team nor you can pick the study group as this could affect the study results. You will be put into one of the two groups by chance.

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Participants from both groups will have the same study visits. Before you learn about the study, it is important that you know that your participation in this study is voluntary and you may decide not to participate, not to have the tests, or to withdraw from the study at any time.

Let me explain to you what we mean by placebo. The placebo is a tablet that looks like dihydroartemisinine-piperaquine tablet but it does not have the ingredients that the dihydroartemisinine-piperaquine has and it will not prevent against malaria. You will receive either dihydroartemisinine-piperaquine or placebo by chance.

What happens during the study

If you agree to be in this study, your first visit will continue today, after you read, discuss, and sign or put thumbprint on this form.

You will be asked to come back to the clinic monthly before delivery. In addition, you must agree to deliver your baby at the study facility rather than at home. Because you have HIV virus, you will be offered drugs (antriretrovirals) for your treatment and for the prevention of mother to child transmission of HIV as per routine antenatal care and will be followed up as usual.

If you agree to be in this study:

- We will first ask you some questions about yourself and your health
- We will ask you to give information on where you live and how to keep in contact with you. The study staff will use this information to visit you at home to see how you are feeling and to remind you about your study visits.
- A study clinician will examine you and will check your pregnancy status
- You will also be asked to give a venous blood sample at the first visit for tests of your blood
- At the first study visit at the clinic, in the presence of the study nurse, you will take either dihydroartemisinine-piperaquine or placebo (assigned by chance)
- The following day and the day after you will be visited by study personnel at horme to complete the three day course treatment of DHA-PPQ
- Subsequent doses of DHA-PPQ or placebo will be given to you at the next scheduled monthly ANC clinic visit at least one month apart
- You will also receive cotrimoxazole and ARV drugs to take home and take it once a day as per routine ANC care
- In case you will be unwell with malaria or other infection, you will have additional blood tests done and if needed you will be given medicine and asked to come back here as scheduled by study staff
- At enrolment you will receive a long lasting insecticide treated net and will be told how to use it
- You and your baby will receive a unique identification number (ID) and identification study card, which you will be requested to present to the study staff at every visit
- Even though you will receive drug for malaria prevention (if in dihydroartemisinine-piperaquine group), it is possible that you may still get sick. Therefore you will be asked to come to the clinic whenever you feel unwell, get fever or any other symptoms.
- At delivery you will be visited during in the labour ward and you and your new-born baby will be examined by the study personnel.
- In addition to venous blood being collected from you, also a sample of cord blood will be taken to be tested for malaria
- A piece of placenta will be examined at the study laboratory and also tested for malaria
- Blood sample will be taken from your baby for malaria tests

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- You must agree to deliver at the health facility but in case you deliver at home, the study staff will visit you as soon as possible but not later than one week after delivery and will ask you questions about your delivery and about health of your infant. At this visit you and your infant will be examined by the study personnel. Blood sample will be taken from you and your baby for tests of malaria
- When your baby is born, your child will be followed up until he/she is 12 months old
- You will be asked to come back with your new-born to the study clinic around 1, 6 , 9 and 12 months after delivery.
- One month after birth and at 12 months, a blood sample will be collected from your baby for HIV testing
- During these visits we will exam your baby to see if your baby is growing well
- If your child has signs of malaria, blood will be taken for tests and appropriate treatment given
- Study staff will visit you at home a few times after delivery to exam your baby

Unscheduled visits

- Throughout the twelve months of your baby's life she/he will be attended by the study staff when you bring her/him to the clinic. During those visits study nurses will exam your child and only if necessary take a sample of blood and provide treatment.
- You can come to the clinic at any time during this study. If you feel discomfort or are in pain, you should call the study staff or come to the clinic.
- You can also ask any questions at any point during the study, even during time other than your scheduled visit

Alternatives to joining the study

If you choose not to participate in this study or to leave the study after enrolment you are encouraged to come to this ANC for your routine visits and for any questions or concerns you may have related to your pregnancy. You will receive standard ANC care as before. We will refer you to another doctor if necessary.

Risks or discomforts *(mother and infant)*

Risks from blood draws

You will feel slight pain when we take blood from your finger or vein and your baby will feel slight pain if we take blood from the baby's heel. There will be no other risks to your new-born baby. Sometimes you may feel little dizzy or your head may feel light. There may be a small swelling of the skin where the needle went in. Those will go away in short time and the study personnel will examine you and your baby for those symptoms.

Risks from study drugs

Dihydroartemisinine-piperaquine is well tolerated when used to prevent malaria. Sometimes side effects are: headache, anaemia, fever, weakness, palpitations.

Benefits to you and your infant

By participating in the study, you may get better diagnosis of malaria because of increased number of tests for malaria. You and your baby will be regularly seen by clinical staff and in case of any symptoms or abnormal test results you and your baby will be either treated here or referred to another clinic for medical care.

Reasons for taking you out of the study without your consent

You may be removed from the study without your consent for the following reasons:

- You are found to not be eligible for the study

- The research study is stopped or cancelled
- The study staff feels that staying in the study would be harmful to you
- You are not able to attend visits or complete the study tests
- Other administrative reasons that will be made clear to you

Costs to you
There is no cost to you for participating in the study. Treatments available to you from the study for malaria will be given to you free of charge.

Your records will be private
Efforts will be made to keep your personal information as confidential as it is possible and allowed by the law. You and your baby will be identified by a study participant ID number and personal information from you and your baby records will not be released without your written permission. You and your baby will not be personally identified in any publication about this study. Your records may be reviewed by: study monitors, study staff, study auditors, sponsors, and Ethics Committees.

To ensure your medical safety, study staff may verify, from time to time, that you are not enrolled in any other research studies. In addition, if needed, we will request permission to access non-study medical records related to any of your illness. All copies of your records will be kept in a locked file cabinet. Only study staff will have access to this cabinet.

New findings
You will be told of any new information learned during the study that might cause you to change your mind about staying in the study.

Injury because of being in the study
Based upon what we know, it is unlikely that you will be injured as a result of being in this study. It is important that you tell the study staff if you feel that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the study clinic will give you immediate necessary treatment for your injuries. The cost of this treatment will not be charged to you. You will then be told where you may receive additional treatment for injuries.

When you sign this consent form, you do not give up your rights to care for injury caused by being in the study.

Contact information
You will be given a copy of this form to take with you.

If you ever have questions about this study or in case you are injured as a result of participation in this study, you should contact: **Principal Investigator**, ***[each site will provide name and phone number of their site PI]***

Your rights as a study participant
This research has been reviewed and approved by the Ethics Committee of the Hospital Clinic of Barcelona, Spain and the local IRB in your country. These committees have reviewed this study in order to help protect participants.

If you accept to participate in this study please answer to the following questions:

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1. What kind of treatments can you receive during the study?
2. In addition to the drugs, what else will you receive to prevent malaria?
3. Can you recall how many times we will ask you to give a blood sample? And how many times your child will be finger-pricked?
4. Can you recall how many times in the presence of study nurse you will take dihydroartemisinine-piperaquine or placebo to prevent malaria?
5. When do you have to bring your child to the study clinic after birth?
6. Can you get malaria even if you participate in the study? And your baby?
7. Where do you have to go if you or baby has fever?

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STATEMENT of CONSENT AND SIGNATURE

Participant and new-born approval:
The consent form has been explained to me and I agree to take part in this study. I also agree to let my new-born baby take part in this study. I understand that I am free to choose to be in the study and that saying "No" will not affect the treatment I get in this clinic, now and in future.
NOTE: You are not giving up any of your legal rights by signing this informed consent document.

If you agree circle YES

Volunteer's Name *(print)*	Volunteer's Signature or Thumbprint *(if cannot write)*	Date
Volunteer's Legal Guardian or Representative (as per country policy) *(print)*	Legal Guardian's Signature	Date
Witness's Name (if participant illiterate) *(print)*	Witness's Signature	Date

I have explained the purpose of this study to the volunteer. To the best of my knowledge, she understands the purpose, procedures, risks and benefits of this study.

Investigator/Designee Name *(print)*	Investigator/Designee Signature	Date

NOTE: This consent form with original signatures must be retained on file by the principal investigator. A copy must be given to the volunteer.

If the woman refuses to take her copy of the consent with her, she states so below and signs and dates her decline statement.

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