Consent to Participate in a Research Study

NIAID Protocol #: 16-I-N042

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Sponsors: Centre de Recherche sur les Filarioses et Autres Maladies Tropicales (CRFilMT)
Yaoundé, Cameroon

National Institute of Allergy and Infectious Diseases (NIAID),
National Institutes of Health (NIH),
Bethesda, MD, USA

Site: Mbalmayo, Cameroon

GENERAL INFORMATION

We invite you to participate in a research study called "A double-blinded, randomized, placebo-controlled dose escalation study to examine the efficacy and microfilaricidal kinetics of imatinib for the treatment of *Loa loa* (A pilot study)." The study is sponsored by the Centre de Recherche sur les Filarioses et Autres Maladies Tropicales in Cameroon and the National Institutes of Health of the United States of America. Participation in this study is voluntary. Before you decide to participate, please take as much time as you need to ask any questions and discuss this study with anyone, including your family and friends.

BACKGROUND/PURPOSE OF STUDY

Many people who live in west or central Africa are at risk for infection from a very small worm called *Loa loa*. This parasite is also called an African eye worm. The adult worms produce baby worms called microfilariae, which live in the blood. *Loa loa* infection can cause itching, swelling, and extremely rarely problems with the kidneys, eyes, and heart. Because this infection is usually not serious, patients in Cameroon usually do not seek treatment. However, infection with *Loa loa* can cause serious problems in people

who are being treated for infections with other parasites. Therefore, we are looking to make a new safe and effective way to treat *Loa loa* infection.

The purpose of this research study is to find out if a drug called imatinib can treat *Loa loa* infection. We want to see if imatinib, an orally administered pill, is effective at slowly killing the *Loa loa* worms because killing the worms too quickly may cause severe side effects. Imatinib is an approved drug to treat certain types of cancer. This study will be the first time that it is being tested for *Loa loa* infection. We will test three different doses of imatinib in people with non-severe *Loa loa* infections (microfilarial counts less than 2500/mL). It is important to know that you will only be given one dose of either imatinib or an inactive agent called a placebo. Because we cannot predict ahead of time how *Loa loa* infections will respond to imatinib, we need to study several doses to learn how much might be needed to safely help treat infection with *Loa loa*.

STUDY PARTICIPANTS

If you are between 18 and 65 years old and have a non-severe *Loa loa* infection but are otherwise healthy then you can take part in this study. Women of childbearing potential are not eligible to participate. We will recruit 20 people for this study.

PROCEDURES EXPLAINED

You will be in this study for 12 months. There are a total of 15 study visits to the clinic site. Each visit should take approximately 2 hours. The first visit is called the screening visit, and the purpose is to make sure that you are eligible to take part in this study. We will give you a physical exam and evaluate the severity of your infection. We will ask you about how you are feeling and if you have had any illness recently. We will collect blood from a vein in your arm to count your blood cells, see if your organs are working well, measure your *Loa loa* infection, and make sure that you are not infected by certain other parasites. A blood sample will also be drawn so we can do laboratory tests on it in the future. Because imatinib may be harmful to the developing fetus, you cannot participate in this study if you are of childbearing age or breastfeeding.

Within 14 days after your screening visit if you are eligible for the study, you will return to the clinic for your baseline visit. You will have another physical and we will ask you about how you are feeling and if you have had any medical problems since we last saw you. We will collect blood and urine for laboratory tests. You also have the option to provide samples of blood, urine, and stool so we can do laboratory tests on them in the future. This is voluntary so you may decline to provide these samples and still participate in the study. If you had a pregnancy test more than 2 days before this visit, then you will have another at this visit to confirm that you are not pregnant.

You will then receive a single dose pill of either imatinib or a placebo. The placebo will be a vitamin pill that looks like imatinib but does not contain any drug. Researchers use a placebo to see if a study drug is more or less safe or effective than not taking anything. Whether you receive imatinib or placebo will be decided randomly. This is like

deciding by drawing lots. Fifteen people will receive imatinib and five people will receive placebo. Until the end of the study, neither you nor the study team will know if you are receiving imatinib or placebo. Which dose of imatinib you get will depend on when you join the study. If you join earlier then you will get the lower doses or placebo, and if you join later then you will receive the higher doses or placebo. About 2 to 4 hours after you take imatinib or placebo, we will collect another sample of blood for more laboratory tests.

You will return to the clinic every day for the next week, and then once per week for the 3 weeks after that. At all visits, you will have a physical and we will ask you how you are feeling. We will collect blood for laboratory tests at all visits, and we will collect urine for laboratory tests during the first week. You will also have the option to provide blood samples so we can do laboratory tests on them in the future.

You will return to the clinic for follow-up visits at 3, 6, and 12 months after you have taken imatinib or placebo. As with the previous visits, you will have a physical exam, we will ask you how you are feeling, and we will collect blood for laboratory tests. At the 6 and 12-month visits, you also have the option to provide samples of blood, urine, and stool so we can do laboratory tests on them in the future.

If you develop side effects from taking imatinib, then we will treat you for those side effects according to the standard of care in Cameroon. You will be finished with the study after your 12-month visit.

RISKS/DISCOMFORTS EXPLAINED

The drug that we are testing in this study, imatinib, is approved by the United States Food and Drug Administration for the treatment of some types of cancer. Side effects of imatinib that have been reported by healthy volunteers who took a single dose of the drug are headache, nausea, vomiting, and diarrhea.

Cancer patients who take imatinib every day for an extended period of time have side effects that include rashes, swelling, and lowered blood cell counts. Some have had more severe side effects that include death. Because you will only take imatinib one time, it is thought to be unlikely that you will have these same side effects.

Imatinib can harm the developing fetus if you take it when you are pregnant. There have been patients who took imatinib while pregnant who lost their pregnancies or had children with birth defects. To be safe, you cannot participate if you are a woman of childbearing potential (younger than age 45 or menstrual period in the last year) or are breastfeeding.

If imatinib kills the worms in your body too quickly, then you may get rashes, itching, swelling, problems with breathing, low blood pressure, and extremely rarely, complications with the nervous system or death. However, because you have a non-

severe infection, we expect that these side effects are very unlikely to happen in this study.

There are no risks associated with the placebo.

It is possible that your Loa loa may get worse while you are participating in this study.

Blood draws may cause pain and bruising and, rarely, infection. Sometimes drawing blood causes people to feel lightheaded or even to faint.

There may be additional risks to participating in this study that are currently unknown. You will be told about new findings that develop during the course of the study that may change your willingness to participate.

EXPLANATION OF POTENTIAL BENEFITS

You may not directly benefit from this study. If you do receive imatinib instead of placebo, then imatinib may help to treat your *Loa loa* infection, but it might not. Even if it treats your *Loa loa* infection you may not feel any different or better (often people do not have symptoms of infection). You may also benefit from having medical examinations during the course of the study. Additionally, the knowledge gained from this study may help other individuals in the future.

COMPENSATION

You will receive 10000 cfa for each visit as compensation for your time. The initial screening visit will not be compensated.

STORED SAMPLES

We would like to store samples of blood, urine, and stool in case there are additional tests we wish to perform in the future. These stored samples will be used only for studies related to parasite infection or your immune system. Samples will be stored at either the NIH in the United States or CRFilMT in Cameroon. All future studies must first be approved by ethics committees at the NIH in the United States and at CRFilMT in Cameroon. Ethics committees oversee medical research studies to protect participants' rights and welfare.

Samples will be labeled with a code that will link you to your blood, urine, and/or stool sample and will be accessed by study investigators only. We will keep any information that can be traced back to you as private as possible. Other investigators may want to study your stored samples. If so, then the study team may send your samples to them

without any information that can identify you. The study team may also share information such as your gender, age, health history, or ethnicity.

Investigators will use your samples *only* for research. We will not sell them. Future research that uses your samples may lead to new products, but you will not receive payment for these products. Some future studies may need health information (such as smoking history or present health status) that we do not already have. If so, the study team will contact you for this information.

In general, future research that uses your samples will not help you, but it may help us learn about parasite infections or related conditions. This research may also help us learn how to prevent or treat these conditions.

The greatest risk is that someone may take information from your medical records without your permission. The chances of this happening are very low.

By agreeing to participate in this study, you do not waive any rights that you have regarding access to and disclosure of your records. Whether or not you agree to let us store your samples, you may still participate in other studies conducted by the NIH or CRFilMT. Even if you agree now to let us store your samples, you can change your mind later. If you do, please contact us and say that you do not want us to use your samples for future research.

ALTERNATIVES TO PARTICIPATING IN STUDY

If you do not wish to participate in this study then you are free to decline.

MAKING YOUR CHOICE

You are free not to take part in this study if you do not want to. If you wish to withdraw from the study, then you may do so at any time. Refusing to take part will not affect your current or future medical care in any way at the study site clinic in Mbalmayo. If you decide to withdraw from the study later, then please inform any member of the study team. You will otherwise be a part of the study until you complete the 12-month study period.

CONDITIONS FOR REMOVAL FROM STUDY

You may be removed from the study without your consent if you are unable or unwilling to keep scheduled study visit appointments, or if for any reason that study investigators determine that participation in the study is placing you at undue risk.

CONFIDENTIALITY

We will keep the study information private. All files with information that could identify you will be kept in locked cabinets. Samples of blood, urine, and stool that are collected from you will be marked with a number that tells the study team that it is your blood, urine, or stool. These samples will not be marked with your name. However, we cannot guarantee absolute confidentiality. People responsible for making sure that the research is done properly may look at your study records. These might include people or their representatives from CRFilMT or the NIH. All of these people or their representatives will also keep your identity private. A description of this clinical trial will be available on http://www.Clinicaltrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this website at any time.

NEW FINDINGS WILL BE DISCUSSED

The findings of this study may be reported at meetings or in medical journals, but your name will not be used in the report. Although the specific information we learn about you will not be shared with anyone except the study investigators, the NIH, and its authorized representatives, absolute confidentiality cannot be guaranteed. A member of the study team will discuss any new findings related to your health or that may affect your willingness to participate in this study. If you have any concerns about your participation in the study, please feel free to discuss it with a member of the study team at any time.

LIST OF CONTACTS

If you want to speak to anyone about this research study or you think you have been hurt by taking part in this study, you should tell the study team (a member of the team will be present at the clinic each day during the study). They will ask the Principal Investigators, Dr. Elise O'Connell or Dr. Joseph Kamgno, to talk to you. You can also ask questions in the future, if you do not understand something that is being done.

DO YOU HAVE ANY QUESTIONS ABOUT PARTICIPATION IN THIS STUDY?

If you have questions or concerns at a later date, you may speak with one of our staff or you can call Dr. Joseph Kamgno of CRFilMT at 00237-22-20-24-42.

If you agree to participate in this study, then please sign or put your thumb or fingerprint below.

_____ _____

Subject Signature, Finger or Thumb Print **Date**

_____

Subject Name

_____ _____ _____

Witness Signature **Date** **Name**

_____ _____ _____

Physician Signature **Date**