COVER PAGE

Informed Consent/Parental Permission

ClinicalTrials.gov
NCT04009343

PharCide

Pharmacokinetics and Pharmacodynamics of the Gametocytocidal and Post-treatment Chemoprotective Effects of Antimalarials

Document Date: 16 Dec 2022

IRB Informed Consent Date: 8 Apr 2019

Cover page with official title, NCT number, and document date must be included.

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

INFORMED CONSENT DOCUMENT

Parents/legal guardian of study participants

Study Title: The Pharmacology of Gametocytocides (PharCide)

Principal Investigator: William Moss, MD

IRB No.: 7663

PI Version Date: Version 1.6 (8 Apr 2019)

History of Revisions

Version 1.1 (1 Feb 2017)
- Added section, “Alternative Treatment Outside the Research Study”
- Added paragraph detailing blood volumes of blood collections

Version 1.2 (14 Feb 2017)
- Added section, “Common Side Effects of Study Drugs”

Version 1.3 (8 Mar 2017)
- Added parental permission and witness lines and removed the “LAR” label on the signature lines

Version 1.4 (5 Sep 2018)
- Expanded “Purpose of research project” to include information about all aims
- Amended paragraph about screening procedure and pre-screening consent
- Removed HIV testing
- Added information about health insurance for clinical trial participants, required by local regulatory bodies
- Amended “Procedures” to describe updated sampling strategy and blood volumes to account for intensive PK subgroup

Version 1.5 (7 Sep 2018)
- Expanded “Purpose of research project” to include information about the malaria-microbiome study aim.
- Expanded “Procedures” to describe stool collections.

Version 1.6 (8 Apr 2019)
- Replaced Eurartesim™ with D-ARTEPP™ including side effect profile

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What you should know about this study

- You are being asked to allow your child to join a research study.
- This consent form explains the research study and your child’s part in the study.
- Please read it carefully and take as much time as you need.

- You and your child are volunteers. You can choose not to allow your child take part and if you allow your child to join, you may quit at any time. There will be no penalty if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to allow your child to continue to be in the study.

Purpose of research project

Malaria is a common disease in Nchelenge District. It is caused by the bite of infected mosquitoes. We have very effective drugs for curing malaria. However, some drugs are better than others for stopping malaria from going on to infect other mosquitoes and people, even though they are equally good for curing malaria. The malaria parasite can take many forms. One of those forms, called “gametocyte”, is responsible for transmitting malaria between mosquitoes and people. Our research is being done to understand which drugs are better for killing the gametocyte, and therefore stopping malaria transmission. To do this, We are comparing two drugs that the Ministry of Health in Zambia have approved to treat malaria: *Coartem*™ and *D-ARTEPP*™. Both medications are equally good at curing malaria, but they have different effects on gametocytes.

The main goal of the study is to figure out the effects of the medicines on gametocytes, but we will study other issues about the drugs and about malaria. We will research three other things. One, we will compare the ability of the drugs to protect children against malaria again, after they have already been treated for it once. To do this, we will continue to monitor participating children for 9 weeks (63 days) to test them weekly for malaria and to test the amount of medicine that remains in their body. Two, we will research whether the parasites can become tolerant to the medicines, meaning that the medicine no longer works as well against the malaria parasite. We will do this by researching the parasite using genetic tests. Three, we will test whether the bacteria and other microbes in your child’s intestine are related to how your child processes or “digests” the medicine and how your child responds to malaria infection. To do this, we will collect three very small amounts of your child’s stool to test in the laboratory for bacteria and other microbes.

Why you are being asked to participate

You are being asked to allow your child to participate in this research study because your child has malaria. This research study is being done by the Tropical Disease Research Center and Macha Research Trust in Zambia, and the Johns Hopkins University Bloomberg School of Public Health (JHSPH) in the USA. It is sponsored by the Malaria Research Institute at JHSPH. While your child is in the study, your child will receive standard of care medical treatment for malaria and receive an antimalarial medication.

This is a consent form. It gives information about this study. The study staff is available to talk more about the study. You can ask questions about this study at any time. If you agree to allow your sick child to participate, we will ask you to sign the consent form. You will get a copy of this form to keep. Participation in this study is voluntary.

Before you decide if you want your child to participate in this study, we want you to know as much as possible about the study. This consent form will explain the purpose of this study, how the study will be done, any risks and benefits to your child and what is expected of you and your child.

The study includes a screening procedure. Your child should have already completed the screening procedure at this point. If not, then even if you provide consent, we may screen your child and find out that your child is not eligible for this study. In any case, your child will still receive the standard of care for her or his malaria.

Alternative treatment outside the research study
If your child does not participate in the research study, your child will be treated by the health center staff as they normally treat children with malaria.

Procedures
If you allow your child to join this study, we will ask your child to do the follow things.

- We will assign your child to receive one of two antimalarial drugs: *Coartem*™ or *D-ARTEPP*™ both of which are recommended for the treatment of malaria by the Ministry of Health in Zambia.
- Your child will be admitted to the clinic to receive her or his antimalarial drugs, and for both standard and research tests.
- To test the drugs and malaria parasites in your child's body, we will take very small amounts of blood on several occasions over three days, so that we can tell what the drugs and the parasite are doing over time.
- We will collect blood using an intravenous (IV) catheter. Our nurse will place an IV catheter that will stay in your child's vein until it is time to leave the health center.
- In addition to blood samples, we will take three stool samples: one during the first 3 days, another after 1-2 weeks, and the third one 5-9 weeks later.
- After you take your child home on the third day, we will ask you to come back on the following (fourth) day, and then once a week for 9 weeks.
- At each of the weekly visits, we will ask you questions about your child's health, we will examine your child, and we will test your child for malaria including taking a small amount of blood from the vein using a small needle.

The amount of blood we will take from your child is a safe amount for a child that weighs at least 10 kilograms. For the first day of the study, we will take less than 4 teaspoons total (13 mL) and not more than ½ teaspoon (2 mL) at one time. After the first day, the amount will decrease. On the second and third days, we will take between ½ to 2 ½ teaspoons (2-11 mL). For the other visits, we will take less than ½ teaspoon (<2 mL). Some children will have more blood taken than other children depending on how much they weigh, and which drug they are receiving.

Risks/discomforts

When the IV catheter is placed, or when your child's blood is drawn, they may feel some mild local discomfort. Redness, pain, swelling, bruising, or an infection may occur where the blood is drawn. This is the same risk as in any routine placement of an IV catheter.

There is also the inconvenience for you and your child staying at the clinic for three days. Typically, for this kind of malaria disease, we would give you the medicines to take home, but instead we are asking you and your child to stay in the clinic for three days to receive the medicine and have blood tests.

Finally, there is also the inconvenience of coming back to the clinic 10 times for check-up visits: one time on the fourth day, and then once a week for 9 weeks. We will reimburse you for the cost of transportation, and can help locate a place for one family member to spend the nights if needed, and offset the cost of any lodging.

Common side effects of study drugs
Both antimalarial drugs are approved for use in patients with malaria by the Government of Zambia. For *Coartem*™, common side effects in children include vomiting, loss of appetite, headache, cough and fever. For *D-ARTEPP*™, common side effects (affecting less than 1 in 10 but more than 1 in 100) include anemia, headache, heart rhythm disturbances, fever, and general weakness. Your child would be treated for malaria with one of these drugs regardless of participation in this study.

Benefits
Research is designed to benefit society by gaining new knowledge. Your child may get no direct benefit from the screening tests. However, the weekly visits to clinic will allow us to find out early on if your child gets malaria again, because we will be checking for malaria every time, so that he or she can get treatment as soon as possible.

Payment
We will be giving you money for transport to and from your home to the study clinic for all study visits and other visits needed if your child is sick. You or your child will not be paid for participation in the study. We will also provide snacks and hydration while your child is in the clinic. If the caregiver needs local lodging, we will help arrange and cover the costs of food and accommodations.

Health insurance
If your child is enrolled in this study, your child will be covered by health insurance for activities related to the clinical trial as required by the Government of Zambia.

Protecting data confidentiality
There is always some risk that information about your child may become to known to people outside of a study. We will minimize this risk as much as possible in the following ways. Your child's information—both personal and medical—we will be kept secret from people not involved in the study, and stored in a secured area and on secured computers. All papers or computer files that have information about your child will use a unique number instead of your child's actual name. The code that links your child's

name and number will be kept in a secured area. The computer files will be kept on secure computers that are password-protected.

Protecting subject privacy during data collection
We will protect yours and your child's privacy by using the same approach as we would otherwise use in the Kabuta Rural Health Clinic. That is, we will conduct interviews and physical examinations in a semi-private setting as is typical for this health center.

Biological specimens
The blood specimens and data collected from your child during this study are important to science. You will not own the blood specimens or data after you give it to the study. We cannot provide any financial benefit to you from any product or idea created by the investigators using the data or materials collected from you.

Cost of participation in the study
There is no financial cost to you or your child for participating in the study—only the time that you and your child volunteer.

What happens if you leave the study early?
Deciding to leave the study before it is done will not affect yours or your child's relationship with the doctors, nurses, researchers, or anybody else. Your child does not have to be in the study to receive health care. You can withdraw your child from the study at any time, without any penalty. The investigators might also stop your child's participation at any time if they think it is not in your child's best interest to continue.

Sharing your health information with others
Other people at Tropical Disease Research Center, Macha Research Trust, or Johns Hopkins and its partners who work on this study or who need to make sure the study is being done correctly may see the answers to your questions and other information.

In addition, if we find something concerning when we do our tests, we will inform your child's doctors and nurses so that they can take care of your child as needed.

Payment of treatment costs for injury or illness from study participation
If you have questions about injuries as a result of being in the study, contact the doctors at the study clinic. You can get health care services at Kabuta Rural Health Center in case of such injuries. If funds provided by the study investigators to carry out this research project are available, you will not have to pay for care for study-related injuries.

Clinical Trial Registration
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by United States law. This website will not include information that can identify your child. At most, the website will include a summary of the results. You can search this website at any time.

Who do I call if I have questions or problems?

- Call the local principal investigator, Dr. Modest Mulenga, at 212620737 if you have questions, concerns, or if your child gets sick or injured as a result of being in this study.
- Call or contact the Tropical Disease Research Center IRB Office if you have questions about your rights as a study participant. Contact the IRB if you feel you have not been treated fairly or if you have other concerns. The IRB contact information is:

Name:	Institutional Review Board of the Tropical Disease Research Center
Address:	6th floor Ndola Central Hospital, P.O Box 71769, Ndola, Zambia
Telephone:	(+260) 212-620-737

What does your signature (or thumbprint/mark) on this consent form mean?

Your signature (or thumbprint/mark) on this form means:

- You have been informed about this study's purpose, procedures, possible benefits and risks.
- You have been given the chance to ask questions before you sign.
- You have voluntarily agreed to allow your child to be in this study.

_____	_____	_____
Print name of Parent or Guardian Providing Permission	Signature of Parent or Guardian	Date/Time
_____	_____	_____
Print name of Witness	Signature of Witness	Date/Time

_____

Name and Study ID of Participant

Ask the participant's parent to mark a thumb impression in this box if the participant's parent is unable to provide a signature above.

Future Use of Specimens

We also ask your permission to retain your child's blood specimen beyond the duration of the study to allow us to run additional tests for malaria parasites, including tests to identify different kinds ("clones") of malaria parasites, tests to detect whether certain drugs can work against the parasite, and tests to measure how good the parasite is at being transmitted to mosquitoes.

_____ *Please initial here or mark your thumbprint if you grant permission for these additional tests.*

Give one copy to the participant and keep one copy in study records