A Randomized, Placebo-controlled, Double-blinded Trial of the Safety and Efficacy of Tecovirimat for the Treatment of Adult and Pediatric Patients With Monkeypox Virus Disease

NCT05559099

Informed Consent Form
Version 4.0, dated 15Dec2023

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: PALM 007: A randomized, placebo-controlled, double-blinded trial of the safety and efficacy of tecovirimat for the treatment of adult and pediatric patients with monkeypox virus disease

Sponsors: United States National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)

Democratic Republic of the Congo (DRC) Institut National de la Recherche Biomédicale (INRB)

Study Agent Provided by: NIH/NIAID; SIGA Technologies, Inc.

Principal Investigators: Jean-Jacques Muyembe-Tamfum, MD, PhD
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Site: DRC, Central Africa

KEY INFORMATION

This consent form describes a clinical research study and is designed to help you decide if you would like to be a part of the study. A clinical research study helps doctors test new ways to treat a disease. One way to do this is by studying drugs that are used to treat other diseases. In a study, the drugs are 'experimental,' which means they have not been proven to work. That is why studies are needed to find out if the drugs are safe and work as treatments.

This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. More information that may help you make a decision can be found in other sections of the document.

What you should know about this study:

- You are being asked to join this clinical research study because you have monkeypox virus disease, which is also called mpox.
- You can take as much time as you need to review this form and discuss your study participation with your family, friends, and community as you feel comfortable and appropriate, in order to decide whether or not you would like to participate.
- Ask the study team to explain any words or information that you do not understand.
- You are a volunteer and you do not have to join this study.
- Your other option is to continue receiving any other care you have already been receiving, which would include the standard of care treatment for mpox.
- If you join the study, you can change your mind later. You can decide not to take part or you can quit at any time. There will be no penalty or loss of benefits if you decide not to join or to quit the study. Your care within your community will not be affected.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to be in the study.

- If you are signing for a person who cannot consent for themselves, such as a child or a person who is too sick to read and understand this, the word "you" in this consent form refers to that person. If you decide to participate in this study, you will review this document with a study staff and will be requested to sign and date at the end of this form to show that your questions have been answered and that you want to take part in the study. A copy of this signed/marked informed consent will be provided to you. This consent must be signed/marked before any study procedures are performed.
- If you are a man or woman of childbearing age, you must agree to use effective contraception when engaging in sexual activity that could lead to pregnancy from the time you enroll until the end of your participation in the study.

What is this study about?
We are looking for new treatments for mpox disease, which is caused by infection with the monkeypox virus. Mpox can make people very sick and some people can die from it. There are no medicines approved in Africa to treat mpox. There is one drug approved in Europe to treat mpox, but it has not been used in many people with the disease. We would like to collect more information about how well it works to treat mpox by testing it in a controlled way in this research study.

What drug is being studied?
We are studying a drug called tecovirimat (TPOXX). This drug is approved in the European Union to treat mpox and similar viral infections like smallpox. It is also approved in the United States (US) to treat smallpox and recommended by the US Centers for Disease Control and Prevention under an Investigational New Drug application (IND) to control mpox outbreaks.

To find out if tecovirimat (the study drug) works well to treat mpox, we will compare it to getting something that does not have the drug in it, so some people on this study will get a placebo. The placebo capsule looks like the study drug but does not have any drug in it, just inactive ingredients. Using a placebo is common in research studies. The study drug and placebo are swallowed as capsules or mixed with food.

Will you get the study drug or placebo?
There are 2 study groups. If you join the study, you will be randomly put into 1 of these groups. This is decided by chance, like rolling dice or flipping a coin. Out of every 2 people on this study, 1 will get the study drug and 1 will get placebo. You and the study staff will not know what group you are in and will therefore not know if you are getting the study drug or the placebo. Additionally, everyone will continue to receive the standard of care treatment regardless of what group they are in.

What will happen on this study that is different than if you were not on this study?
If you join this study, you will need to be in the hospital for at least 14 days. This may be a longer amount of time in the hospital than you normally would be in if you were not in this study. You will need to swallow several capsules two or three times a day for 14 days. After 14 days, you will stop taking the capsules, and you will be able to leave the hospital when you have recovered from the mpox. While you are in the hospital, you will receive standard care for mpox. For the research, we need to collect more information on your health and get more frequent urine and blood samples and swab samples from your throat and mpox lesions than you would have if you were not in this study. We will test these samples to

figure out when you have recovered from mpox. We will count the mpox skin lesions on targeted regions of the body every day until they are healed. After that, we will examine the rest of your body daily until all of the lesions have healed. We will also take pictures of the skin lesions.

One month after you started taking the study drug or placebo, you will come to the study clinic for a visit so we can collect more health information and samples. If you are still in the hospital, the visit will happen in the hospital. After that, there is an optional visit 1 month later that may be done in the hospital or by phone. Then you will be done with the study.

If you get new mpox symptoms after you have recovered from your first infection, we will take more swab and blood samples, count your new lesions, and offer you standard treatment. If you are still in the hospital, this will happen in the hospital. If you have already left the hospital, we will ask you to come back for an extra visit for this.

Your total amount of time on this study will be 1 to 2 months. You will be compensated for the time and inconvenience of taking part in the study.

What are the main study risks?
The most common side effects of the study drug include headache, nausea, stomach pain, and vomiting. Some people may have some of these or other side effects from the study drug. Other people may have no side effects. Most side effects are temporary and should not last more than a few days. The study drug may cause other changes that could hurt or bother you that we do not know about yet.

The study drug has not been studied in pregnant or breastfeeding women, so we do not know if it affects a fetus or nursing infant and women should avoid getting pregnant while they participate in this study. Mpox may be more severe in pregnant women and may be spread to the fetus or to the baby at birth. Therefore, pregnant women may enroll in this study since the study drug may help treat mpox.

The placebo should not cause any side effects, but it will not help treat your mpox because it does not contain any drug.

We will monitor you closely while you are taking the study drug or placebo, and short-term medical care will be provided if you have any side effects that can be treated.

When we collect blood, even though we may collect more blood than normally taken, it will be done the usual way and the risks do not differ in this study from when you normally get blood drawn.

Are there benefits to being in the study?
If the study drug works well to treat mpox and you receive it on this study, you may benefit by recovering more quickly, having less severe illness and fewer symptoms, and being less contagious. If you receive the placebo on this study, it will not help your mpox.

The rest of this document will describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document.

1. What will happen if you want to join this study?

If you think you may want to join this study, we will describe the study and answer any questions you may have. You can also talk to your friends and family about the study.

If you agree to be in the study, we will ask you to sign this consent form. When you sign your name or put your mark on the consent form, it means that you agree to be in the study. You can change your mind at any time and leave the study. If you decide not to join the study or to leave the study later, you will not lose any regular health care services you already are getting. Up to 600 people will be in this study in several different sites.

2. What does the study involve?

If you decide to join this study, you will be in the study for 1 to 2 months.

At the beginning of this study, you will stay at the hospital for treatment of your monkeypox virus infection. While you are in the hospital, you will get the supportive care that you would typically get for mpox. For this research study, we will ask you some questions about your medical history, age, sex, residence, current health, vaccination status, and risk for mox, and look through your medical history to collect information for this study. If you are able to get pregnant, you will have a pregnancy test, even if you are already pregnant. We will also do physical exams, take vital signs, check your health, and review your mpox symptoms frequently while you are in the hospital. We may also request the results of tests you have done as part of your medical care to review as part of this study. We will count your mpox skin lesions and take pictures of them. We will collect 1-2 tbs of blood every few days until discharge and swab samples from inside your throat and from your mpox skin lesions for the first 9 days and then every other day until they are fully healed. We will use these samples to monitor your health, see how your body responds to the study drug, and to test for the monkeypox virus. We may also test your blood for malaria. If you agree, we will test your blood for HIV (the virus that causes AIDS). This test may not be done until later, so we may not have a result to give you right away. A member of the study team will explain this test further. If you do not want your blood to be tested for HIV, you are still able to participate in this study. According to DRC guidelines, the study team will provide you HIV test counseling. If you have a positive test, meaning that you have HIV infection, the study staff/counselor or an official from the Health zone will attempt to contact you to tell you what that means and will refer you for treatment according to the national guidelines, as the treatment for HIV will not be provided as part of this study. The study team may also report positive results to the necessary authorities according to the guidelines of DRC.

While you are in the hospital, you will get the study drug or placebo two or three times a day every day for 14 days in a row. Several capsules may need to be swallowed each time, or the capsule ingredients can be mixed with food if you cannot swallow capsules. It is important to eat a certain amount of food when taking the medication to improve its absorption. You must remain in the hospital for all 14 days,

even if your mpox improves during this time. After 14 days, you will be allowed to go home once all of your mpox skin lesions have healed and 2 different blood tests show that you no longer have monkeypox virus.

You will come back to the clinic for a study visit about 1 month after you started taking the study drug or placebo. If you are still in the hospital at this time, the visit will happen in the hospital. If you are leaving the hospital very close to the 28 day visit, this may count as the 28 day visit. During this visit, we will ask how you are feeling and if you have been sick, check your health, and collect blood and urine samples.

About 1 month later, we will give you the option to come back to the study clinic or talk to us on the phone. The clinic staff may visit your home if they are unable to reach you by phone, in order to remind you of your scheduled visit or for follow up. We will ask you questions about your health and how you are feeling. If you come to the study clinic, we will do a physical exam and collect blood samples. You do not have to have this extra visit if you do not want to. You can still be in the study if you do not agree to have this visit.

If you get new mpox symptoms after you have recovered from your first infection, we will take more swab and blood samples, count your new lesions, and offer you standard treatment if you are still enrolled in the study. We will use the samples to check your health and to test for the monkeypox virus. If you are still in the hospital, this will happen in the hospital. If you have already left the hospital, we will ask you to come back for an extra visit for this.

As part of this study, we will do some routine medical tests on your samples. We will share the results of these tests with you, and your health information will go in your medical record. We will also store and use some of your samples for research tests, and you will not receive these results.

Optional blood sample for participants at least 18 years of age: In addition to the tests described above, we would like to collect an extra sample of blood from you 7 days after you start taking the study drug or placebo. We will use this sample to measure how much study drug is in the body. This is optional, so you can say no to this blood sample and still be in the study. If you agree, we will collect up to 4ml of blood about 4 hours after you take your first dose of study drug or placebo on day 7.

I give permission for an extra blood sample to be taken as described above (please check one option below):

___ Yes

___ No

3. What could be the side effects from the study drug?

The study drug was given to more than 300 healthy adults in a research study in the United States. Some of these people had side effects. The most common side effects were:

- headache;
- nausea;
- stomach pain;
- vomiting.

Less common side effects included dry mouth, chapped lips, heartburn, burping, fever, body pain, chills, feeling ill, thirst, joint pain or stiffness, migraine, loss of attention, taste changes, tingling of the skin or mouth, depression, uneasiness, irritability, panic attack, mouth or throat pain, skin rash that may be raised or itchy, redness or swelling of the face, itching, increased heart rate, changes in some laboratory tests of the blood, and abnormal tests of electrical activity of the brain.

None of the side effects were serious, but some people stopped taking the study drug because of their side effects.

Some people may have some side effects from the study drug. Other people may have no side effects. These side effects are temporary and should not last more than a few days.

Since this is a new drug that has not been given to many people, it may cause other changes that could hurt or bother you that we do not know about.

Short-term medical care will be provided if there are side effects from the study drug that can be treated. It is important that you always tell the study staff if you have any problems.

4. What are the other risks or discomforts of the study?

There are no risks or known side effects related to the placebo, but it is possible that your mpox may not get better or may even worsen while you are taking the placebo since it does not contain any drug. Since the placebo has no effect on mpox, this would not be different than if you were not participating in this study since you will also be receiving the standard of care that is normally given to treat mpox.

We will insert a new, clean needle into a vein in your arm to take blood. You may feel a pinch when the needle goes through your skin. A bruise may appear where it was put in. You may also have swelling and redness, and the area may be sore. These things are common and should go away in a couple of days. Some people faint when they have blood drawn. There is a very small chance of an infection where the needle goes into your vein. An infection could be treated with antibiotics.

Collection of the swab samples may be uncomfortable, but should not hurt.

The pictures that we take of your mpox lesions may include any part of your body, including your face and eyes. This may be embarrassing. We will do our best to keep your identity as private as possible. These photographs may be published in medical

journals, without identifying the participant. They may also be used for teaching or education purposes, and for future research projects by the study team or other researchers. We invite you to talk with us about any concerns you have related to photography.

We will be careful to keep your study information confidential, but there is a small risk that someone not involved in the study could get this information.

5. What do I need to know about pregnancy or breastfeeding during the study?

Women: We do not know the effects of the study drug during pregnancy. If you are pregnant or become pregnant around the time you receive the study drug, there may be risks to you, the embryo, or fetus. These risks are not yet known. However, mpox can also have serious effects during pregnancy. Therefore, if you are pregnant you may join this study. The study doctor will discuss your options and the risks and benefits of the study with you. If you are not pregnant but are able to get pregnant, you must agree to use an effective method of birth control from the beginning of the study through the last study visit. We will discuss the options with you. If you think that you have gotten pregnant during the study, tell the study team right away and seek medical care for your pregnancy. If you are or become pregnant during the study, we may ask to follow up with you until delivery to collect information about your health and your baby's health.

We do not know if the study drugs can pass through in breast milk, and the risks to a nursing infant are not yet known. If you are breastfeeding or plan to breastfeed an infant, the study doctor will discuss your options and the risks and benefits of the study with you.

Men: The effects of the study drug on sperm are not known. To protect against possible side effects, you should not get a sexual partner pregnant while taking part in this study. You must agree to use an effective method of birth control, such as condoms, from the beginning of the study through the last study visit.

6. Are there benefits to being in the study?

If the study drug works and you receive it in this study, you may benefit by recovering more quickly from mpox, having fewer and less severe symptoms, or being less contagious. If you receive placebo, it will not help your mpox disease or symptoms.

Your participation in this study is important to learn more about how the study drug works to treat mpox. It will help in the development of treatments for mpox and may in the future help people all over the world.

7. What will happen to your samples and personal information?

We will store your samples and data (information) for a very long time to use for future research on mpox or other similar types of diseases after this study is over. This is in addition to them being used and stored for research testing under this current study. Your samples will be stored in a secure location, and your data will be placed

in a secure electronic system. Your stored samples and data will be marked with a code and not with your name. Only researchers linked to this study can get the codes.

In addition to our own use, we may share your samples and data with other researchers for future research with or without information that could identify you. If we include information that could identify you, we must get approval from the DRC ethics board. Other information, such as your sex, age, or health history might also be shared. Results from future research will not be shared with you. Your samples will not be sold. You will not be paid for any products that result from this research.

The only risk of allowing us to store your samples would be an accidental release of your identity.

I give permission for my samples and data to be stored and used for future studies as described above (please check one option below):

___ Yes

___ No

In addition, we might remove any information from your specimens and data that could identify you, and then share them with other researchers for future studies. If we do this, there will be no way to know that they came from you. We would not be able to remove your specimens or data from these studies or prevent their use in future studies because we would not be able to tell which specimens or data belong to you. We want to make sure that you understand that this is a possibility if you participate in this study.

If you agree to the storage of your samples and data now but you change your mind later and decide you do not want us to store your samples or data, please let us know. We will do our best to follow your wishes but cannot promise that we will always be able to destroy your samples or data.

8. Will it cost you anything to be in this study?

It will not cost you anything to be in this study. Hospitalization and standard care will be given for free to everyone participating in this study. You and up to 2 people who are with you will receive meals each day that you are in the hospital.

9. Will you be paid if you join this study?

As part of this study, you and up to two people who accompany you will receive an inconvenience allowance for your study visits. You and up to two others will receive $15, equivalent in local currency to 30,000 Congolese francs (CDF) for study visits at 1 and 2 months after the treatment initiation (if you attend the visit) for the time and inconvenience during the study period. Travel will be provided for you and up to 2 people who accompany you to and from these 2 visits. While you are still in the study, travel will also be provided for at least one extra visit, to you and up to 2 individuals accompanying you, if you develop new mpox symptoms after you recover from your first infection.

If you did not sign a screening consent, you and up to two others will receive $15, equivalent in local currency to 30,000 Congolese francs (CDF), for your first study visit. Travel will be provided for you and up to 2 people who accompany you to and from this visit.

An additional stipend of $4, equivalent in local currency to 8,000 CDF will be provided daily to you and up to two people who are with you during the hospitalization period.

10. Who is watching over this study?

In addition to the investigators and sponsors who are overseeing this study, a Data and Safety Monitoring Board (DSMB) will be looking at the study information very closely. The DSMB is made up of doctors and other people who are not directly involved in the study and who have a good understanding of mpox and research studies. The DSMB may recommend stopping the study earlier than planned if they think it is not safe to continue or if they find that the study drug is working well. The DRC ethics board will also be watching over this study and has the authority to stop it at any time.

11. How will your privacy be protected?

We will keep your study information private. All files with information that could identify you will be kept in locked cabinets or secure computers. People responsible for making sure that the research is done properly may look at your study records. This might include people from the DRC and the US including the NIH and their designees, and the drug company that makes the study drug (SIGA Technologies, Inc.). All of these people will also keep your identity private. Results from this study, but not your identity, may be shared with other researchers, local medical providers, or government health organizations to help them better understand monkeypox virus infection and treatment.

12. Could you be removed from the study early?

You could be taken out of the study early if you do not or cannot follow the study requirements, if the study doctors feel it is better for you to be removed from the study, or if the study is stopped early. If you are removed from the study early, we will still use your stored samples and data for research unless you ask us not to.

13. What if the researchers learn new information during this study?

Results of this study or other scientific research may affect your willingness to continue to take part in this study. During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

14. What other things should you know about this research study?

a. ClinicalTrials.gov
A description of this study is on the internet at http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

b. Conflict of Interest
Any potential conflict of interest will be resolved according to the guidelines of the local ethics review committee of DRC.

c. What is the Ethical Review Committee and how does it protect you?
Your government's ethics committee will review this study. It protects the rights and welfare of the people taking part in research studies. You can contact Paul Samson Lusamba Dikassa, President of the Kinshasa School of Public Health ethics committee (KSPH EC) (Tel: [redacted]) or Mbongo Pasi Moke Sangol, Vice-President of the KSPH EC in DRC (Tel: [redacted]) to answer questions you may have about being part of this study and your rights as someone who is in a study.

d. What do you do if you have questions about the study?
If you have questions about the study, you may contact the principal investigators. Prof. Jean-Jacques Muyembe-Tamfum can be reached by phone: [redacted], or by email: [redacted]. Dr. Placide Mbala-Kingebeni can be reached by phone: [redacted], or by email: [redacted].

e. What should you do if you are injured or ill as a result of being in this study?
We do not expect any harm from participating in this study. However, unforeseeable risks may be present. The study doctors will give you short-term medical care if you are hurt by being in this study.

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

_____ Date: _____/_____/_____ Time: _____
Signature or fingerprint of participant or guardian dd mm yy

_____
Printed name of participant or guardian

_____ Date: _____/_____/_____
Signature of investigator/designee dd mm yy

_____
Printed name of investigator/designee

Complete if participant is illiterate:

Witness to Consent Interview

On the date given next to my signature, I witnessed the consent interview for the research study named above in this document. I attest that the information in this consent form was explained to the subject, and the subject indicated that his/her questions and concerns were adequately addressed.

_____ Date: _____/_____/_____
Signature of witness dd mm yy

_____
Printed name of witness