Protocol Title: A Phase 1, Dose Escalation, Open-Label Clinical Trial with Experimental Controlled Human Malaria Infections (CHMI) to Evaluate Safety and Protective Efficacy of an Anti-Malaria Human Monoclonal Antibody, VRC-MALMAB0100-00-AB (CIS43LS), in Healthy, Malaria-Naive Adults (VRC 612)

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UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

PRINCIPAL INVESTIGATOR: Kirsten E. Lyke, M.D.

STUDY TITLE: VRC 612 (20I0017): A Phase 1, Dose Escalation, Open-Label Clinical Trial with Experimental Controlled Human Malaria Infections (CHMI) to Evaluate Safety and Protective Efficacy of an Anti-Malaria Human Monoclonal Antibody, VRC-MALMAB0100-00-AB (CIS43LS), in Healthy, Malaria-Naive Adults

STUDY SITE: The Center for Vaccine Development and Global Health (CVD), University of Maryland School of Medicine, Baltimore, MD

Cohort: *Healthy Volunteer*

Consent Version: *Version 8.0, October 26, 2021*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Kirsten Lyke, MD, [redacted]

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study. This study is taking place at more than one site.

You are being asked to take part in a research study at the Center for Vaccine Development and Global Health (CVD), University of Maryland, Baltimore (UMB) sponsored by the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at UMB is your choice.

This is a study of an experimental drug called "CIS43LS". CIS43LS is a monoclonal antibody that targets malaria. CIS43LS has not been tested in humans before this study. However, in the first 2 parts of this study, 25 participants got 29 administrations of CIS43LS. We do not know if CIS43LS will protect you from malaria infection. You cannot get malaria from CIS43LS because there is no malaria in it.

The main purpose of this study is to see if CIS43LS is safe and how your body responds to it. Since this is the first time that CIS43LS will be given to people, we do not know how your body will respond. We will follow everyone who gets CIS43LS for about 24 weeks. If you have side effects from CIS43LS, we expect them to be like the side effects that occur with similar antibody products, which usually occur within the first 24 hours after the antibody is given. These include fever, chills, shaking, nausea, diarrhea, vomiting, pain, headache, dizziness, tiredness. The following side effects, although rare, may occur including trouble

breathing, itchiness, rash, hives, swelling, or chest pain. Some antibody products have a risk of serious allergic reactions that can be life threatening.

Another purpose of this study is to test if CIS43LS prevents you from getting malaria when you are bitten by mosquitoes that carry live malaria parasites. This is called a "malaria challenge" or a "Controlled Human Malaria Infection" (CHMI). We will follow everyone who gets CHMI for about 2 months. Each CHMI will include the participants who get a dose of CIS43LS and "control" participants who do not get CIS43LS. Everyone who takes part in the CHMI may get malaria infection. You will need to come to the clinic every day for 12 days starting 7 days after the CHMI to be checked for malaria infection.

At the first sign of malaria infection in your blood, we will treat you with a medication that will cure you. At Day 21 after CHMI, everyone will get treated with a malaria medication to make sure they are cured of malaria even if the test was never positive. The drugs that treat malaria may cause some side effects. The type of malaria used in the CHMI will not come back or re-infect you again after you are treated with the medication.

During the study, we will collect blood samples from you. Some of your blood will be stored for future research. You will be compensated for your time and inconvenience for taking part in this study.

The study will last about 2 to 6 months, depending on your study group. All clinical study visits and the CHMI will take place at the UMB. You must be available on the day of the CHMI and for at least 8 weeks afterwards for follow up so we can check your blood for malaria parasites. It is important that the level of malaria in your blood does not get to dangerous levels.

To be in this study, you must:

- have completed the screening process and be eligible,
- agree to take part in the CHMI and to comply with post-CHMI follow-up requirements,
- agree not to travel to a malaria endemic region during the entire course of the study,
- agree not to donate blood to a blood bank for 3 years after the CHMI,
- use an effective birth control method and try not to become pregnant during your time in the study if you are a woman who is able to get pregnant,
- agree to have your blood samples and data stored for future use.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with UMB staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either

case, you will not lose any benefits to which you are otherwise entitled. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Malaria is a disease that affects more than 250 million people throughout the world. The parasites that cause malaria are known as *Plasmodium*. They live in the mosquito saliva and are injected into the skin when a mosquito bites a human. This can cause malaria infection. Malaria occurs in most tropical parts of the world including Africa, Southeast Asia and South America. It is a serious threat to the local populations, to travelers and to military personnel stationed overseas. Although there are medicines to treat malaria, there is no vaccine that fully prevents infection and treatment is not easy to get in many areas of the world. If malaria is not treated right away, it can become a serious and sometimes deadly disease. If it is treated right away, it can be completely cured.

This is a research study. The purpose of this research study is to test a drug that could prevent malaria infection in humans called CIS43LS. CIS43LS is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to prevent malaria infection. It is a monoclonal antibody (MAb) that targets the parasites that cause malaria. Antibodies are naturally made by the immune system to fight infection by blocking germs (bacteria and parasites) like malaria. Monoclonal means that all the antibodies in CIS43LS are exactly the same.

CIS43LS was developed at the Vaccine Research Center (VRC) at NIH. It was made in a laboratory and looks like an antibody that your own body could make. It has shown promise for prevention of malaria in laboratory and animal studies but has not been studied in humans before this trial.

This is the first study to give CIS43LS to humans. We do not know if CIS43LS will protect you from malaria infection. You cannot get malaria from CIS43LS because there is no malaria in it.

The purpose of this research study is to see if CIS43LS is safe and how your body responds to it. We will give you a dose of CIS43LS and measure how much of it stays in your body over time. We will check to see if your immune system prevents CIS43LS from working. We also want to see the differences between getting CIS43LS as an infusion in a vein in your arm (intravenously, IV) or when injected under the skin (subcutaneously, SC).

In this study, you will be exposed to malaria through bites from mosquitos infected with malaria parasites. This is called a “malaria challenge” or a “Controlled Human Malaria Infection” (CHMI). We do this to find out if CIS43LS prevents you from getting malaria after you are bitten by the infected mosquitoes in a controlled setting. We will monitor you closely and test your blood over many days to see if you get infected with malaria. Even if your test is negative, we will give everyone malaria treatment by 21 days after CHMI.

We are asking you to join this research study because you are a healthy adult between the ages of 18 and 50 who has never been infected with malaria. You must be willing to take part in the CHMI and comply with follow-up requirements after CHMI to be in this study. You must also

agree not to travel to a malaria endemic region during the whole study and not to donate blood to a blood bank for 3 years after CHMI.

WHAT WILL HAPPEN DURING THE STUDY?

Most people who get CIS43LS on this study will get it by infusion into a vein (IV). Some people will get CIS43LS into the fat under the skin (SC). A group of people called "control" participants will not get the study product but will take part in the CHMI. This group helps us make sure the mosquitos can infect people.

This study has 3 parts, Part A, Part B, and Part C. Part A and Part B were completed in 2020 at the Vaccine Research Center, part of NIH, in Bethesda, MD. In Parts A and B, doses of CIS43LS were tested and a CHMI occurred in Part B.

Part C is being done at UMB. You are invited to participate in Part C of the study.

In **Part C**, CIS43LS doses are being tested to better understand how much CIS43LS is needed to protect participants from malaria infection after CHMI. The lowest IV dose being tested (1 mg/kg IV) and the highest SC dose (10 mg/kg SC) have not been given to humans before. All other doses given into the vein or under the skin have been tested in Parts A and B.

VRC 612 Part C Study Schema					
Site	**Group**	**Participants**	**CIS43LS Administration**		**CHMI**
			Dose (mg/kg)	**Route**	
UMB	11	7	1	IV	X
	12	4	5	IV	X
	13	4	5	SC	X
	14	4	10	IV	X
	15	4	10	SC	X
	16	6*	Control		X
	Total	29	*Group will include 2 backup controls		

If you decide to take part in this study, you will be asked to review and agree to this informed consent form and the procedures outlined within it. You will have completed the screening process which includes a physical exam and review of your medical history, vital signs and laboratory results. You must be healthy and qualify for enrollment before you can take part in Part C of the study.

Enrollment will begin at the lowest dose (Group 11) and will continue through to the higher doses. We will let you know the group you are in at the time of enrollment.

Participants can be enrolled in the control group (Group 16) at any time. If you are in the control group, you will not receive a dose of CIS43LS. After enrollment, we will check your health and draw blood before the CHMI.

If you are female and able to become pregnant, you must use an effective method of birth control for the entire study. You will be given a pregnancy test before you get any dose of CIS43LS and before the CHMI. If you are pregnant, we will not give you CIS43LS and you cannot take part in the CHMI.

CIS43LS Administration

You will be in the clinic for about 8 hours on the day CIS43LS is given.

- **IV Dosing (Groups 11, 12, 14):** We will place an IV line (thin tube) in a vein in your arm. The IV line will be attached to a bag that has CIS43LS mixed with a liquid called "normal saline" or salt water. It will flow into your vein for about 30 minutes. If you have side effects during the infusion, it may be slowed down or stopped as needed. At the end of your infusion, we will monitor you for any side effects for at least 2 hours afterwards.

  We will also place an IV line in your other arm for blood collection during this visit so that we do not have to perform multiple needle sticks. We will draw your blood before and right after the infusion, and then 3 more times during the 4-6 hours after the infusion. You will be allowed to go home about 4-6 hours after the infusion, as long as you do not have concerning side effects. If you have side effects, we will treat them. You will need to come back to the clinic 2 times during the same week for blood draws.

- **SC Dosing (Groups 13, 15):** We will use a small needle to inject CIS43LS into the fatty tissue of your belly. We may use your arm or thigh area instead of your belly if those areas are more appropriate for your body. You will get 1 to 4 injections to get the full dose of CIS43LS. You will be monitored for at least 2 hours after getting all injections of CIS43LS. If there are no safety concerns, you will be allowed to leave the clinic after the safety check. You will need to come back to the clinic 3 times during the same week for blood draws.

We will give you a thermometer so that you can check your temperature every day for 7 days after you get CIS43LS. You will need to record your highest temperature and tell us about any symptoms you have. We will also give you a measuring device so that you can measure any redness, swelling, or bruising you may have at the injection site. You will get a password to a secure website to record this information. If you do not have internet access, you may use a paper diary that we will provide to you instead.

If you have any side effects or feel unwell after you get CIS43LS, you should tell a UMB nurse or doctor as soon as possible. You can reach the clinic staff by phone 24 hours a day. If you have symptoms, you may be asked to come into the clinic for an examination before your next scheduled visit. You may also stay overnight in the hospital, if needed. It is very important that you follow the instructions from the clinic staff.

Follow-Up after CIS43LS Administration

Follow-up visits will last 30 minutes to 2 hours and allow us to check you for any health changes or problems. We will ask you how you are feeling and if you have taken any medications, check your vital signs, and may perform a targeted physical exam based on how you are feeling. We will take about 1–11 tubes of blood at each visit for safety and/or research tests. Blood draw volumes will be within the UMD Center for Vaccine Development and Global Health limits. We will tell you right away if any of your test results show a health problem. You might need to have extra clinic visits and laboratory tests if you have health changes that need to be checked.

Clinical studies follow a set schedule. This helps us answer the research questions. The visit schedule is a little flexible, but it is **important that you follow the schedule as closely as possible. You should try to not miss any visits.** You should contact the clinic staff as soon as possible if you need to change the date or time of any study visit. When you complete Part C of this study, we may invite you to take part in another study for follow-up sample collection.

Controlled Human Malaria Challenge (CHMI)

In order for us to learn if CIS43LS can prevent malaria infection, a CHMI will be conducted. The CHMI will be performed at UMB by experienced staff, with support from U.S. Military staff from the Walter Reed Army Institute of Research (WRAIR). The CHMI visit will last about 4 to 6 hours and will begin very early in the morning.

During the CHMI, we will put mosquitoes carrying the malaria parasite into a cup. The cup, which is covered with nylon tulle netting, allows the mosquitoes to bite you under controlled conditions. They cannot escape from the cup. No more than 5 mosquitoes are put in the cup at one time. You will hold the cup against your arm for 5 minutes, and then the mosquitos will be checked for blood feeding and presence of malaria parasites. If needed, more mosquitoes may be added until we are sure that a total of 5 infected mosquitoes have fed on your blood.

Follow up after the CHMI is very important so we can check your health. We know that it takes anywhere from 7-15 days to find malaria parasites in the blood. So, after the CHMI, we will call you by phone to check on you 2 times in the first week. Then, starting on day 7, you must come to the clinic every day for about 30-minute visits through day 18 so we can collect blood for diagnostic and research purposes. The visits may be longer if medical evaluation is needed. If you test positive for malaria parasites, you will be treated right away with antimalarial medication. We will also bring you back about 8 weeks after the CHMI to make sure you are cured. At day 21, anyone who still has a negative malaria test will be given antimalarial medication. This way we can make sure that anyone who might have malaria infection is treated, even if your tests are negative. If you are negative for malaria, we will call you by phone to check on you about 8 weeks after the CHMI.

This type of CHMI has been done for over 35 years for many malaria vaccine studies. The mosquitoes that will be used are raised in a laboratory for CHMIs. They are infected with a specific strain of the malaria parasite (*Plasmodium falciparum*) that is known to be treatable with the anti-malaria medication we will give you. While the mosquitos are being grown, they feed on transfusion quality human donor blood that has been screened following FDA requirements to make sure that the blood is not carrying any other infectious agents. This type of malaria does not cause recurrent infections after you are treated.

HOW LONG WILL THE STUDY TAKE?

The study will last for at least 24 to 32 weeks for those who receive CIS43LS. The study will last for up to 8 weeks for those who participate as controls for the CHMI. You will visit UMB for about 11 or 12 study visits based on if you get CIS43LS by IV or SC, respectively. You will also have up to 16 follow-up visits after the CHMI. We will discuss the exact schedule of these visits with you. If you participate in the CHMI, the study will last another 8 weeks after the CHMI.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

A total of 50 people were enrolled into Part A and Part B of this study. We plan to enroll about 30 people into Part C. This includes about 23 people who will get CIS43LS, 6 control participants and 2 backup control participants.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

Possible Risks of CIS43LS

This study is the first time that CIS43LS is given to people. As of February 15, 2021, 25 participants received 29 administrations of CIS43LS in Part A and Part B of the study. CIS43LS was given 25 times by IV and 4 times by SC administration. The limited experience collected in this study so far suggests CIS43LS is safe and well tolerated for further investigation.

The information described below is taken from studies with other antibodies that are like CIS43LS and may work the same. Some of those antibodies are approved for use in people. Like other drugs, monoclonal antibodies can cause side effects, some of which can be serious. Most side effects occur within the first 24 hours after an antibody is given.

- Side effects to antibodies given by IV may include: fever, chills, shaking, nausea, vomiting, pain, headache, dizziness. More serious but rare side effects may occur, including trouble breathing, high or low blood pressure, itchiness, rash, hives, lip or face swelling, diarrhea, racing heart, or chest pain. These symptoms usually go away within a few minutes to hours after the product is given. We are giving CIS43LS at a controlled rate. If you develop symptoms while getting CIS43LS, tell the nurse right away. Slowing or stopping the flow rate may help improve the symptoms.
- Side effects to antibodies given by SC may include: mild itchiness, redness and/or swelling at the site of injection. Tiredness, muscle pain, and headache have also been reported. These symptoms usually go away within 1 to 2 days.

Some antibodies have a risk of serious allergic reactions that can be life threatening including:

- Anaphylaxis is one type of allergic reaction that may happen soon after an antibody is given. This reaction can include difficulty breathing, low blood pressure, hives, rash, or swelling in the mouth and face. This reaction is rare but can be life threatening.
- Serum sickness is a type of allergic reaction that may happen several days to weeks after an antibody is given. This reaction may include hives, rash, fever, enlarged lymph nodes, muscle pains, joint pains, chest discomfort or shortness of breath.

Some antibody products can increase the risk of serious infections. CIS43LS is not expected to increase the risk of serious infections because it attacks a parasite instead of the human immune system.

CIS43LS may have other side effects that are not yet known. Taking part in this study may affect your eligibility for future monoclonal antibody or malaria studies. We will give you any new information about risks or other information that may affect your decision to continue in the study as it becomes available. You may not donate blood while taking part in this study and you may not donate blood for one year after the date of your last dose of CIS43LS or three years after your last CHMI.

Possible Risks of IV or SC Dosing

General risks of methods that use a needle include stinging, discomfort, pain, soreness, redness, bruising, swelling or a tiny cut at the needle insertion site.

Possible Risks of Blood Drawing

Blood drawing may cause pain, bruising, and may cause a feeling of lightheadedness or fainting. Rarely, it may cause infection at the site where the blood is taken. An IV line will be placed in your vein for a few hours on a day CIS43LS is given by IV. Problems at the IV site are usually mild and may include pain, bruising, minor swelling, or bleeding. Rarely, there may be an infection, vein irritation, nerve problem, or blood clot.

Possible Risks of CHMI

During the CHMI, you will be bitten by mosquitoes that carry live malaria parasites which cause malaria infection. We do not know if CIS43LS will protect people from malaria. If you did not receive any CIS43LS, you are expected to get malaria. If you get malaria, you may experience the following symptoms:

- Fever, chills, headache, dizziness, muscle aches, sweats, fatigue, insomnia
- Nausea, vomiting, stomach cramps, diarrhea
- Decrease in numbers of red blood cells, white blood cells, and platelets
- Enlarged liver or spleen

Symptoms are usually mild to moderate but you may have some severe symptoms. You may have fevers for 1 to 3 days. You may miss time from work or school due to your illness. You will not be compensated for any loss of income for missing work. If malaria is not treated right away, it can lead to kidney, liver, heart or brain damage and death. The CHMI is considered to be safe because people are closely monitored and treated as soon as they are found to have malaria infection, but they must remain in close contact with the study team.

After the CHMI, it is important that you come to the clinic for your scheduled visits so that the level of malaria parasites in your blood does not increase to dangerous levels. From past studies we know that malaria parasites can be found in the blood anywhere from about 7 to 15 days. About half of the people infected with malaria parasites develop fever that usually lasts less than 12 hours. Once treatment for malaria is started, the fever does not last longer than 48 hours.

Other symptoms of headache, nausea, vomiting, and loss of appetite may occur. These symptoms may last an average of 3 days, with a range of 1 to 6 days when treatment is started soon after malaria parasites are identified by blood tests. **Failure to return for testing or treatment after a CHMI can result in a serious case of malaria that is life-threatening**. For this reason, you must give the names and phone numbers of at least two emergency contacts to the study staff. We will contact them before the CHMI to confirm communication with them in case we are not able to reach you by phone, text, or email after CHMI.

Among the over 2,700 participants who have taken part in a CHMI since 1971, two serious events have been reported. Both were cardiac events (chest pain) and occurred in people who got an investigational malaria vaccine. The pain was thought to be due to myocarditis (inflammation of the heart muscle). Myocarditis is a reported complication from vaccinations. Rarely, myocarditis has also been reported in association with naturally-acquired malaria infection.

These are the only two cases we know about in which a cardiac event occurred after CHMI. In the unlikely event that you develop myocarditis, you will be evaluated and followed by a cardiologist until resolution.

If you feel unwell at any time after the CHMI, you may be asked to remain in the clinic until you are checked by a study doctor. You might stay in the hospital overnight if needed.

Possible Risks from Treatment for Malaria

Standard treatment for malaria takes 72 hours to complete. We will give you the medication at the first detection of infection in your blood. You should expect to have malaria symptoms for about 3 days. Only drugs approved by the U.S. FDA will be used for treatment of malaria. We will treat you with Malarone unless you have a known allergy. In that case, we would treat you with chloroquine. Both drugs are effective in treating the type of malaria parasite used for the CHMI.

The drugs that treat malaria may also cause some side effects. Treatments and their side effects are described below:

1. The first line of treatment will be Malarone. If you get Malarone, you may have the following side effects:
    - Nausea, vomiting, abdominal pain, loss of appetite, diarrhea
    - Temporary elevation of liver function tests
    - Headache and coughing
    - Rarely, low blood count, oral irritation or ulcers, insomnia, fever, swelling, rash and hair loss
2. Another backup treatment option will be chloroquine. If you get chloroquine, you may have the following side effects:
    - Nausea, vomiting, abdominal pain, diarrhea, dizziness, sleep disturbances and photosensitivity
    - Headache, blurred vision, ringing in ears
    - Itching, skin rash, and make conditions of psoriasis (itchy skin rash) and porphyria (rare disturbance of metabolism that can be seen as disorders of the skin or other organs) worse

- Long term use can cause permanent eye damage or deafness, but you will only be receiving a short course of treatment
- Rarely, there may be changes in electrocardiograms (test of heart's electrical activity) and low blood pressure

If you need treatment with any other antimalarial drug, we will give you information about the side effects of that drug. You can also take over-the-counter medicine, like acetaminophen (Tylenol) and/or ibuprofen for fever, headache or other symptoms of malaria.

Mosquito Bite Site Reactions

Local, allergic reactions are common after mosquito bites. You may have itching and raised, red swelling at the sites of the bites. These reactions usually develop quickly, go away 1 to 4 days after a mosquito bite, and do not need treatment. So far, no severe allergic reactions to mosquito bites have been reported in prior CHMI studies. You will be observed for 30 minutes after the last mosquito bite. We will check the bite area and watch for any severe allergic signs. We may give you a steroid cream to use on the skin reactions.

Possible Risks from Stored Samples

There is a small chance that information from your medical records could be given to someone who should not get it without your permission. It is possible for someone to use that information to discriminate against you when you apply for insurance or employment. Similar problems may occur if you give information about yourself or agree to have your medical records released.

What are the risks related to pregnancy?

If you are able to become pregnant, we will do a pregnancy test before beginning this study. We will also give you a pregnancy test before you get CIS43LS and before CHMI. You must use effective birth control methods and try not to become pregnant while taking part in this study. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of CIS43LS that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant while taking part in this research study, please contact the research team member identified at the top of this document as soon as possible. You should not plan to become pregnant until you have completed participation in this study.

Safety Measures You Should Use as a Participant in the Study

You should not expect CIS43LS to protect you from malaria in the future. You should assume that you are not protected from malaria. After leaving the study, you should follow your physician's instructions to prevent malaria infection. We also ask that you follow our instructions below:

- Travel: Do not travel outside the local area from the CHMI through 28 days after. Before or after this point, please let the study staff know about planned travels so we can schedule your visits and have contact information before you travel. We ask that you not

travel to any areas with malaria during the entire period of the study. Country-specific information can be provided.

- Use of Antibiotics: Avoid taking antibiotics 4 weeks before the CHMI unless prescribed by a physician. Please notify the study team immediately if an antibiotic is prescribed for you or if you consider taking an antibiotic during the course of the study.
- Blood Donation: You will not be permitted to donate blood for transfusion purposes while in the study, for 1 year after the CIS43LS administration and for 3 years after the CHMI. To make sure that blood is safe for donation, blood banks will not accept blood donations for 3 years from anyone who is infected with or treated for malaria and for 1 year after exposure to an investigational product (CIS43LS).

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because the information may help us learn more about preventing and treating malaria infection. Results from this study may also be used to help develop new products that target malaria or other infectious diseases in the future.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Instead of being in this study, you could choose not to take part. You may be eligible for other studies taking place at UMB or at the NIH.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study at the NIH and UMB, or information we have learned from other scientists doing similar research in other places.

Return of research results

At each visit you will be checked for any health changes or problems. Blood will be drawn at almost every study visit to check on your health. You will be told right away by phone call, text, or in person in the clinic if any of your test results show a health problem.
After the CHMI, we will draw your blood to test for malaria parasites. You will be told right away by phone call, text, or in person in the clinic if we find that you have malaria infection.

We will use some of the blood samples to study how long CIS43LS remains in your body and if your body develops an immune response to CIS43LS and to the CHMI. We will also study the malaria parasites that we may find in your bloodstream after a CHMI if you get malaria infection. These tests are for research purposes only and are not for checking on your health. We will not give you these results.

The results of this study may be reported in medical journals, on the internet or at scientific meetings. We will give you information about how to find the study results once they are available.

EARLY WITHDRAWAL FROM THE STUDY

You may be removed from the research study by the researcher for any of the following reasons:

- You don't keep appointments or follow study procedures;
- You get a serious illness that needs ongoing medical care;
- You enroll in another research study at the same time you are in this study;
- You become pregnant;
- The study is stopped or cancelled;
- If the researcher believes that it is in your best interest to remove you from the study.
- The study is stopped by regulatory agencies, the study sponsor or study investigators. If this happens, we will tell you why.

You can stop taking part in the study at any time. However, if you decide to stop taking part in this study, you will be asked to keep follow up visits so we can check your health, especially if you got a dose of CIS43LS or take part in the CHMI. We may stop collecting samples that are for research purposes only.

We don’t know if you will get malaria after the CHMI. If you choose to stop the study after the CHMI and before we finish checking you for malaria infection, you will need to be treated for malaria by the study doctor regardless of whether you develop symptoms of malaria or parasites in your blood.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding malaria, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, devices, or that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

By agreeing to participate in this study, you are agreeing to have your specimens and data stored indefinitely and be used for future research. We will label them with a special code or number. Only the study team can link this number to you. Any identifying information about you (like name or date of birth) will be kept as confidential as allowed by the law.

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

How Long Will Your Specimens and Data be Stored by the NIH or UMB?

Your specimens and data may be stored by UMB and the NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

PAYMENT

Will you receive any type of payment for taking part in this study?

Some studies, including when taking part at a non-NIH site, offer compensation for participation in research. The amount of compensation, if any, is guided by both NIH and UMB policies and guidelines.

You will be compensated for your time and inconvenience. It is possible that you may have some expenses that are not covered by the compensation provided.

The compensation for specific study visits is as follows:

- $400 for a study visit that includes IV administration of CIS43LS with blood draws on the same day
- $175 for a study visit that includes SC administration of CIS43LS with no blood draw
- $325 for the malaria challenge visit with blood draws the day before
- $70 total for the timely completion of all 7 days of the daily diary
- $75 for a scheduled follow-up visit that includes a research blood draw
- $75 for all other clinic visits that do not include research blood draws

Total compensation for completion of all study visits is about $1,445 if you get CIS43LS by IV, $1,295 if you get CIS43LS by SC, and between about $720 and $1,630 if you take part in the CHMI. The total compensation you get is based on the number and type of study visits you complete.

If you are unable to finish the study, you will receive compensation only for the parts you completed.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year.

If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by UMB as part of your participation?

Some UMB clinical studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by UMB policies and guidelines.

This study does not offer reimbursement for, or payment of, travel, lodging or meals.

COSTS

Will taking part in this research study cost you anything?

UMB does not bill health insurance companies or participants for any research or related clinical care that you receive at UMB.

CONFLICT OF INTEREST

The UMB has a Financial Conflict of Interest Policy to make sure that studies funded under U.S. Public Health Service (PHS) grants are conducted fairly without influence from investigator Conflicts of Interest. UMB seeks to provide an environment where the design, conduct, and reporting of such PHS-Funded Research are free from financial bias and ensure fair and impartial results.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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 Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

The study doctor will take the following measures to protect the confidentiality of your research and/or medical records, such as coding your study record by study subject number, limiting access to the study records, and avoiding any individual identifiers (e.g. name, initials, exact date of birth) in publication or reports resulting from this study. Also, there will be a limited number of people who have access to your study records.

All study files are labeled with a code identifying you only by study subject number, and do not contain your name, initials, exact date of birth, or other items that could identify you personally. Specimens (e.g. blood samples) will not be labeled with your name or initials.

The monitors, auditors, the IRB, the Food and Drug Administration (FDA), representatives of the University of Maryland School of Medicine, the National Institutes of Health and the Department of Defense (DOD) will be granted direct access to your medical records for verification of the research procedures and date. By signing this document, you are authorizing this access.

The FDA may choose to inspect your records since you are a participant in this research study. When a study is submitted to FDA, the study doctor agrees to allow FDA access to the study records. The FDA will treat the information as confidential, but on rare occasions disclosure to third parties may be required by law. Therefore, absolute protection of confidentiality cannot be promised.

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

The authority to collect this information is under 42 USC 285f.

You may be registered in the University of Maryland School of Medicine computer system as a research subject, which may be informative for future clinical care.

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 Web site at any time.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, VRC or their agent(s)
- University of Maryland, Baltimore
- Department of Defense (DOD)

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the UMB and NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

When results of an UMB and NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the UMB and NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH and UMB researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to

those disclosures. Other permissions for release may be made by signing NIH or UMB forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

WHAT HAPPENS IF YOU ARE INJURED BECAUSE YOU TOOK PART IN THIS STUDY?

The UMB is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the site Principal Investigator, Kirsten Lyke, [redacted]. Other research team members you may call are: [redacted]. For questions

about your rights while in this study, call the National Institutes of Health Intramural Institutional Review Board at [redacted].

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

Study Title: VRC 612: A Phase 1, Dose Escalation, Open-Label Clinical Trial with Experimental Controlled Human Malaria Infections (CHMI) to Evaluate Safety and Protective Efficacy of an Anti-Malaria Human Monoclonal Antibody, VRC-MALMAB0100-00-AB (CIS43LS), in Healthy, Malaria-Naive Adults

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

Printed Name of Participant	
Signature of Participant	Date
Signature of Investigator or Designee Obtaining Consent	Date/Time