PRINCIPAL INVESTIGATOR: Alexandra Freeman, MD

STUDY TITLE: A Phase IIa Efficacy, Safety, Tolerability and Pharmacokinetic Study of Encochleated Amphotericin B (CAMB) in Patients with Mucocutaneous (Esophogeal, Oropharyngeal, Vaginal) Candidiasis Who are Refractory or Intolerant to Standard Non-Intravenous Therapies

STUDY SITE: NIH Clinical Center

Cohort: *Affected Patient*

Consent Version: *March 29, 2021*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Alexandra Freeman , MD *freemaal@mail.nih.gov* *301/594/9045*

Study Coordinator: Doris Swaim, RN *doris.swaim@nih.gov* *301/827/9716*

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.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

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. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. 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?

You are participating in a study of an experimental antifungal drug called encochleated amphotericin B (or CAMB) to see if it is safe and if it will help treat persistent fungal infections. CAMB is a special oral form of the antifungal drug amphotericin B, which is a commonly used antifungal treatment. However, the traditional form of amphotericin B can only be given

intravenously and also has been known to have some severe side effects. We want to see if this new oral form of amphotericin B will be safe for treating fungal infections without some of these side effects.

You already agreed to participate in this study and the optional extension period to receive CAMB for a total of 48 months. We are inviting you to continue the extension period for a total of 60 months of treatment with CAMB.

For this study, the NIH is partnering with the maker of CAMB, a company called Matinas Biopharma Nanotechnologies, Inc.. CAMB has not been approved by the US Food and Drug Administration (FDA) for use in humans, but the FDA has given us permission to use it in this study. CAMB has also been tested in 47 healthy human volunteers at the same doses we will use in this study, however those participants only received one single dose.

EXTENSION SCHEDULE

In the extension, you may continue taking CAMB for up to 60 months. During this period of time, we will see you at least every 12 weeks at the NIH Clinical Center (CC). We may see you more frequently if you are having any side effects. At these visits, we will do the following procedures:

- Blood and urine tests to look for any side effects.
- Pregnancy tests (if you are able to get pregnant).
- Swabs for fungal cultures.
- A clinical evaluation and physical exam (including a gynecologic exam if your infection is in your vagina).
- Optional collection of blood, urine, saliva, stool and vaginal secretions for research tests and storage for future research.
- Clinical photography of your infection, if applicable.

Between the 12-week visits to the NIH, we will have you get blood work checked every 2 weeks to look for side effects. The 2-week blood draws can be done at your community laboratory. Also, we will call you every 2 weeks in between the 12-week visits to ask about any new symptoms or medications.

Some visits can be replaced with phone or computer calls with the study doctors to discuss how CAMB is making you feel and if you have had any side effects. You can visit your local clinical laboratory (such as Quest Diagnostics or LabCorp) or your primary care doctor, who can collect your blood and urine samples and send the results of the tests to us. Your sample will be labeled with a coded study identifier (Matinas MB70004), gender and date of birth. The local clinical lab charges will be billed to the study sponsor. We will let you know which visits can be done this way.

You need to avoid becoming pregnant for the duration of your participation. If you become pregnant while on this study or during the 4 weeks after your last dose of the study medication, then you need to inform the study doctors as soon as possible. You will be asked to stop taking CAMB, but the study doctors will continue to follow up with you for safety and pregnancy outcome.

If during the study you engage in sexual activities that could cause pregnancy, the following forms of pregnancy prevention are acceptable:

- Have had a hysterectomy and/or had both tubes tied (bilateral tubal ligation) or both ovaries removed.
- Be in a monogamous relationship with a partner who has had a vasectomy at least 6 months ago.
- Have an intra-uterine device (IUD).
- Be on birth control pills, patch, ring, implant, or injection, and
- If you use the pill, patch, or ring then you must also use a condom, cap, or diaphragm with spermicide.

STUDY PROCEDURES

Clinical evaluation and physical exam

We will assess your infection to determine its severity and if it is responding to the investigational treatment. You will have a physical exam, which includes taking your temperature, blood pressure, respiratory rate, and pulse. We will ask you about how you're feeling, if you've had any illness recently, and about the medications you are taking now and have taken in the past, including non-prescription drugs. You must tell the study team about all of the medications you are taking because you cannot use amphotericin B while taking CAMB. We will discuss each drug with you and tell you if it is permitted on the study. For example, you cannot take azole antifungal drugs if you are using them to treat your mucocutaneous candidiasis. If you are using an azole antifungal drug for some other infections, you may be able to continue. Please also be sure to let the study team know about any new medications before you start taking them.

Blood draw

We will draw blood from a vein in your arm to count your blood cells, see if your organs are working well, and determine how your body is processing the drug. At some of the study visits, we will insert an IV line into a vein in your arm so blood can safely and comfortably be drawn throughout the day.

The amount of blood drawn at each visit to the NIH will be about 2 tablespoons (27 milliliters). The amount drawn every 2 weeks between NIH visits will be about half a tablespoon (7 milliliters). The total amount at all visits is within the limits allowed by the NIH CC for research purposes. While in the study, let the study team know if you are participating in other studies or have blood drawn for any other reason. Some of your blood will be stored for possible future testing.

Urine Collection

Urine will be collected into cups for routine medical tests and to determine how CAMB is eliminated through urine.

Saliva Collection

You will spit into a tube to collect saliva samples. This is optional, so you may decline this procedure and still remain in the study. We will use these samples to see how your body is processing CAMB.

Stool Collection

Collection of your stool is optional so you may decline this procedure and still remain in the study. You will pass stool into a plastic container that fits in the toilet under the seat, and then we will scoop a little bit into a special tube. We will use your stool to look at how your body is processing CAMB.

Vaginal Fluid Collection

If you have an infection in the vaginal area we will ask to take samples of vaginal fluid. This is optional, so you may decline this procedure and still remain in the study. Vaginal fluid will be collected using a menstrual cup. The study staff will instruct you how and when to insert and remove the cup during your study visits. Patients who have an IUD, are on their menstrual period, or have had a hysterectomy with removal of the cervix will not need to undergo this procedure. We will use your vaginal fluid to look at how your body is processing CAMB.

Gynecological Examination

If your infection is in your vagina, gynecological examinations will be done. We will evaluate the skin surrounding the vaginal and pubic area. We will insert a speculum into your vagina and gently rub a sterile cotton swab (like a Q-tip) on the infected area so we can look closely at your infection in the laboratory.

Fungal Culture Swab

We will gently rub a sterile cotton swab (like a Q-tip) on the infected area of your body so we can look closely at your infection in the laboratory. This will help us to better understand how CAMB is affecting your infection.

Pregnancy Test

You will have routine blood pregnancy tests during the length of your treatment.

Clinical Photography

We may take pictures of your infection. You will be asked to sign a standard NIH photography consent form if you are willing to let us take pictures.

RISKS AND DISCOMFORTS

The likelihood and severity of risks with this study are partially determined by your age, fungal infection, overall health, and the medications you use.

CAMB

A single dose of CAMB was given to healthy volunteers in another research study. In that study, commonly reported side effects were nausea and abdominal pain. Other less common side effects were vomiting and diarrhea. These side effects were likely the result of volunteers drinking a large volume of CAMB to get the full dose. To try to avoid this problem, you will take half of your dose twice per day so that each day you get the full dose, but in smaller volumes. There was also one case of a moderate respiratory infection that was determined to not be related to CAMB.

Amphotericin B that is injected into the blood and not given orally like CAMB has its own risks. These risks include allergic reactions, changes to blood clotting, anemia, gastrointestinal distress, and kidney damage. These effects have not been seen in people given one oral dose of CAMB, but taking the drug twice a day for several weeks will potentially increase the risk of events that have not been seen in other studies.

It is possible that the exposure to CAMB may cause resistance of the Candida to amphotericin. This could potentially make intravenous amphotericin less effective as a treatment option if needed in the future. After the study, there are other possible treatments that could be used for most Candida species if there is amphotericin resistance and an antifungal is needed, and these can be discussed with your physician or the study physician.

There are likely to be other risks to oral CAMB that are unknown, and that is why we will be following you closely throughout this study.

Blood Draw

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

Vaginal Fluid Collection

The only risk associated with the use of a menstrual cup is the possibility of dislodging an IUD. Therefore, if you have an IUD then we will not collect vaginal fluid from you.

Clinical Digital Photography

Taking pictures of the face and body may be embarrassing to some people. These photographs may be published in medical journals, without identifying the participant. We will attempt to preserve the anonymity of the participant as much as possible, while providing the information

needed to support the research being published. You may decline photographs or place restrictions on their use. We invite you to talk with us about any concerns you have related to photography.

Urine, Swab, Saliva and Stool Collection

There are no risks associated with collection of urine, swabs, saliva or stool.

BENEFITS OF PARTICIPATION IN THIS STUDY

You may not benefit directly from participating in this study, or your condition could worsen. CAMB may help to improve your mucocutaneous candidiasis infection, but it may not, and any improvement may end when the study is over. The information we obtain in this study will help us learn more about the use of CAMB in treating people with persistent fungal infections.

You will not receive any more CAMB after you have taken your final dose. Because CAMB is still under investigation, further approval from the FDA and the NIH Institutional Review Board are needed before CAMB can be provided outside of this study.

ALTERNATIVES TO PARTICIPATION IN THIS STUDY

You can choose not to continue to participate in this study and to remain on your current treatment plan. This decision will not affect any ongoing care or evaluations you may be receiving at the NIH. Your eligibility to participate in other research studies at the NIH will not be affected by your decision to enroll or not enroll in this protocol. You may also discuss alternative treatment options with your care provider.

WITHDRAWAL FROM THE STUDY

You can stop participating in this study at any time. Tell a member of the study team if you no longer want to participate. This decision will not affect any ongoing care or evaluations you may be receiving at the NIH.

Samples and data collected prior to this request will be stored for the duration of the protocol unless you specifically request the removal of all your samples from the study.

REASONS FOR ENDING YOUR PARTICIPATION EARLY

You may be removed from the study without your consent if the study doctor feels it is in your best interest or if the study is cancelled or stopped early.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

You will not receive any payment for taking part in this extension study.

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

For inpatient visits NIH will directly cover travel to and from the CC within the U.S., lodging and meals. For outpatient visits NIH will directly cover travel to and from the CC within the U.S. and lodging. The agency making the reservations and their representatives will have access to your identifiable information. You will receive a $10 meal *voucher for the day of your visit.*

When NIH studies offer reimbursement or direct payment for travel and meals related to participation in research, your social security number (SSN) is usually collected for the purpose of providing payment. Should you choose not to provide your SSN, you may be able to participate in the study, but you would not receive any eligible payment. Please note that when sharing your SSN, you should not provide your SSN via unsecure methods (regular, unencrypted email is an unsecure method) – it is best to provide your SSN in person or to a known person via telephone.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH CC. The costs for any other medical care provided outside the NIH during this period will not be covered. The local clinical lab charges for this study will be billed to the study sponsor.

STORED SAMPLES AND FUTURE RESEARCH

If you agree to participate in this study, then you also agree to let us store some of your blood, stool, saliva and vaginal secretions samples for future research. These stored samples may help us learn more about mucocutaneous candidiasis. Genetic testing will not be performed. We will label your stored samples with a code that only the study team can link to you. We will keep any information that can be traced back to you as private as possible. If you change your mind and decide you do not want us to store your samples, then please contact us. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy all of your samples.

We might send your samples to other investigators for their research, along with the coded label. We might also share information such as your sex, age, health history, or ethnicity. We will not sell your samples and you will not be paid for any products that result from the research. Some future studies may need health information (such as smoking history or present health status) that we don't already have. If so, then our study team will contact you. Future research that uses your samples will probably not help you, but it may help us learn more about how to treat mucocutaneous candidiasis. In general, the research tests we perform are not like routine medical tests, and may not relate directly to your medical care. The greatest risk of allowing us to store your samples is an unplanned release of your identification from the samples due to release of this information from the stored sample database. The chances of this happening are very low.

NEW FINDINGS

Any new findings discovered during this study that are considered relevant to your health or to your decision to continue in the study will be fully discussed with you.

CONFLICT OF INTEREST

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study are using CAMB, a drug developed by Matinas Biopharma Nanotechnologies, Inc. through a collaboration between your study team and the company. The company also provides financial support for this study. Matinas Biopharma Nanotechnologies, Inc. plans to use the results, and may get patents, or sell the drug in the future, or make profits other ways. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of CAMB.

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

We will keep your study information private. All files with information that could identify you will be kept in locked cabinets or password-protected, encrypted, and secure computers. In the future, some of your information may continue to be stored with a code and not your name. Only the study investigator can link that information together.

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 Matinas Biopharma Nanotechnologies, Inc.
- Qualified representatives from Matinas Biopharma Nanotechnologies, Inc.

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 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.

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

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 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 forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH 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.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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 Principal Investigator**,** Dr. Alexandra Freeman, Building 10, Room 11N234, Telephone (301) 594-9045. Other researchers you may call are: Study Coordinator, Doris Swaim, RN Building 10, Room 2C 132B, Telephone (301) 827-9716.

You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date