Lefamulin for *Mycoplasma genitalium* treatment failures in the US

NCT05111002

8/24/2022

UNIVERSITY OF WASHINGTON
CONSENT FORM

Lefamulin for *Mycoplasma genitalium* treatment failures in the US

Researchers:

Lisa E. Manhart, MPH, PhD	Professor	Epidemiology	(206) 744-3646
Lindley A. Barbee, MD, MPH	Assoc. Professor	Medicine/Infectious Dis.	(206) 744-2595
Meena S. Ramchandani, MD, MPH	Assoc. Professor	Medicine/Infectious Dis.	(206) 744-2484
Julie C. Dombrowski, MD, MPH	Assoc. Professor	Medicine/Infectious Dis.	(206) 744-5640
Anika Parker	Research Coordinator	Epidemiology	(206) 744-0382
24-hour emergency number	Harborview Paging Operator	Infectious Diseases Fellow on call	(206) 744-3000

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully. You may ask any questions about the study. Then you can decide whether or not you want to be in the study.

KEY INFORMATION ABOUT THIS STUDY

This research study will test whether a new antibiotic that is used to treat pneumonia can cure *M. genitalium* when other antibiotics have failed. We are inviting you to take part in the study because your doctor diagnosed you with *M. genitalium* and other antibiotics have not been able to cure it. This page is to give you key information to help you decide whether or not to participate. Ask the research team questions. If you have questions later, the contact information for the research investigators in charge of the study is above.

WHY ARE WE DOING THIS STUDY?

M. genitalium causes symptoms in the reproductive tract and is often resistant to antibiotics. Lefamulin might cure *M. genitalium*, but no one has tested this. In some cases, antibiotics used to treat *M. genitalium* work better if another antibiotic (doxycycline) is taken first. By doing this study, we hope to learn whether lefamulin is effective against antibiotic-resistant *M. genitalium a*nd to learn whether taking doxycycline first makes it work better.

WHAT WILL YOU BE ASKED TO DO IF YOU PARTICIPATE?

If you agree to participate:

- You will receive 14 lefamulin pills or 14 lefamulin pills and 14 doxycycline pills in the mail. We will randomly choose which persons get only lefamulin and which get both doxycycline and lefamulin. You will not be able to change which antibiotics you get.
- You will take the study medicine(s) as directed for one week (each).
- You will collect one culture sample and one sample to confirm *M. genitalium* infection the same day you take your first dose of study medicine (doxycycline if you receive both doxycycline and lefamulin; lefamulin if you only receive lefamulin) and mail this to our laboratory.
- You will answer questions about your symptoms, any side effects, and your behavior with your sex partners.
- You will collect samples two more times (three weeks and six weeks after you take your last lefamulin pill) during the study. You will also answer questions three more times if you only receive lefamulin (when you take your last lefamulin pill and three weeks and six weeks after you take your last lefamulin pill) or four more times if you receive both doxycycline and lefamulin (when you take your last doxycycline pill, when you take your last lefamulin pill, and three weeks and six weeks after you take your last lefamulin pill) during the study.
- The risks of lefamulin during pregnancy are unknown and doxycycline can cause problems to the developing baby in pregnant persons, so you and/or your partners must be on highly effective contraception during the study.

WHY MIGHT YOU **NOT** WANT TO BE IN THIS STUDY?

If you are in this study, you will receive treatment for your *M. genitalium* infection with a new antibiotic (lefamulin). We do not know if this antibiotic works, and it might not cure your infection. You may have side effects from lefamulin (and doxycycline if you are randomly chosen to receive both antibiotics). You do not have to participate in the study to receive these antibiotics. Your regular doctor could prescribe them for you.

WHY MIGHT YOU WANT TO BE IN THIS STUDY?

When lefamulin was tested in the laboratory, it was effective against *M. genitalium,* and we do not know of other antibiotics that cure antibiotic-resistant *M. genitalium* infections. You will receive lefamulin or lefamulin and doxycycline and three tests for *M. genitalium* at no cost to you. If you are in this study, you will contribute to our understanding of how to treat *M. genitalium* infections better in the future.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. If you decide not to take part, you will not lose any services, benefits, or rights you would normally have. Your doctor will still keep trying to treat your infection. You can choose to withdraw at any time during the study.

WHAT IF YOU WANT MORE INFORMATION?

The rest of this document gives you more information about the study, like:

- What kinds of samples to take and when
- The risks (side effects) of lefamulin and doxycycline
- Who will pay for treatment if you are injured from the study procedures
- How we will protect your privacy
- Who to talk to if you have problems, suggestions, or concerns

PURPOSE OF THE STUDY

We are doing this study to find out whether an antibiotic called lefamulin (trade name Xenleta) cures *Mycoplasma genitalium* when other antibiotics have failed. Lefamulin is approved by the FDA to treat pneumonia, but it has not been tested to see if it can successfully treat *M. genitalium* infections. We also want to find out whether lefamulin works better if doxycycline is taken first.

STUDY PROCEDURES

You will go over the information that your doctor shared with the study doctor when they referred you in a Zoom meeting. This will include demographics, your symptoms, your previous *M. genitalium* test results, antibiotics that you have already taken, and information about your sex partners (sex, gender, any treatment for *M. genitalium)*. This information will become part of your study record. This information will also be shared with the Centers for Disease Control and Prevention (CDC), which is keeping a registry of *M. genitalium* treatment failures. The information that we share with the CDC will only have a patient unique identifier, or code, on it. It will not include your name. The Zoom meeting will take about 20-30 minutes.

You will receive 14 lefamulin tablets (600 mg each) or 14 lefamulin tablets (600mg each) and 14 doxycycline tablets (100mg each) in the mail. If you are randomly chosen (like the toss of a coin) to take only lefamulin, you will take one lefamulin pill in the morning and one lefamulin pill in the evening every day for 7 days.

If you are randomly chosen to take doxycycline followed by lefamulin, you will take one doxycycline pill in the morning and one doxycycline pill in the evening every day for 7 days. After you finish taking the doxycycline, you will take one lefamulin pill in the morning and one lefamulin pill in the evening every day for 7 days.

You will answer some questions on a website about your symptoms, any side effects from the antibiotics, and your behaviors with your sex partners. Examples of the most personal and sensitive questions include how many sexual partners you have had, what kinds of sexual behaviors you have practiced, and whether you used condoms. You do not have to answer any questions you do not wish to. These questions will take about 10 minutes.

You will also collect a “culture” sample and collect a sample to confirm *M. genitalium* infection from the area of your body where you have symptoms before taking the first pill. If you have urethritis, you will swab the tip of your penis and urinate into a collection cup. If you have cervicitis or pelvic inflammatory disease, you will swab the inside of your vagina. You will mail the two samples to our laboratory at the University of Washington using pre-paid shipping materials. We will culture *M. genitalium* and do a

test to find out whether it is resistant to 3 antibiotics: azithromycin, moxifloxacin, and lefamulin. We will test for *M. genitalium* to confirm whether you have an infection.

Three weeks after you finish taking the lefamulin pills, you will be mailed a sample collection kit. You will collect a culture sample that we will test for resistance to the same 3 antibiotics and a "test of cure" sample from the area of your body where you had symptoms. We will test for *M. genitalium* to see if lefamulin cured your infection. You will answer questions on a website about whether you still have symptoms and about your behaviors with your sex partners to see if you could have been reinfected. These questions will take 5-10 minutes.

Six weeks after you finish taking the lefamulin, you will be mailed another sample collection kit. You will collect another culture sample and another "test of cure" sample and mail these back to our laboratory for testing. You will answer the same questions on a website about symptoms and about your behaviors with your sex partners. These questions will also take 5-10 minutes.

Because we do not know the risks of taking lefamulin during pregnancy and because doxycycline can cause problems to the developing baby in pregnant persons, you must be on highly effective contraception during the study if you are capable of becoming pregnant. You must also avoid getting pregnant for at least 30 days after completing lefamulin.

RISKS, STRESS, OR DISCOMFORT

You may have side effects such as diarrhea, nausea, and vomiting when taking the lefamulin. If you are randomly chosen to take doxycycline before lefamulin, you may have side effects such as diarrhea, nausea, vomiting, excess vaginal yeast with itching, and reactions to sunlight (photosensitivity) when taking the doxycycline. You could have an allergic reaction to the medications with rash, itching, swelling in your mouth and throat, and shortness of breath. Rarely an allergic reaction can be severe and life-threatening. You may also have other side effects that we do not yet know about. The study doctor will talk with you if you have any serious side effects, and we will give you any information we learn about lefamulin during the study that might affect your willingness to participate. We will report side effects to Nabriva Therapeutics, the company that makes lefamulin.

There is a risk of heart problems (cardiac arrhythmia) with certain drugs. While you are taking lefamulin you should talk with your regular health care provider or the study physician before you take any new drugs. This applies to prescribed drugs and to drugs that you can purchase without a prescription.

We do not know if lefamulin is safe during pregnancy. If you learn you are pregnant while taking lefamulin you should stop taking it immediately and contact the study team. We will be required to report this to Nabriva Therapeutics' pregnancy pharmacovigilance program, and they may contact you.

Doxycycline can cause problems to the developing baby in pregnant persons. If you learn you are pregnant while taking doxycycline, you should stop taking it immediately and contact the study team.

Providing the samples may be uncomfortable or embarrassing. You are free to decline to provide the samples, but if you decide not to do this, you cannot participate in the study. You may feel uncomfortable answering the questions about sexual behavior and symptoms. You are free to decline to answer any questions.

Although we will make every effort to keep your information confidential, no system for protecting your confidentiality can be completely secure. It is still possible that someone could find out you were in this study and could find out information about you. The research team will contact you if you have persisting symptoms or unusual side effects. If we cannot reach you by telephone or email and we send a letter to your home, it is possible that someone might see the letter. However, the letter will only ask you to contact the research team about a study that you are participating in and include a telephone number.

ALTERNATIVES TO TAKING PART IN THIS STUDY

Your regular doctor can prescribe lefamulin and/or doxycycline, so you do not need to participate in this research study to get these antibiotics. However, you or your insurance will have to pay for them if you are not in this study.

BENEFITS OF THE STUDY

You will benefit from participating in this study by receiving a new antibiotic at no cost to you. Your participation in this study may benefit others by helping us find out whether lefamulin can cure *M. genitalium* when other antibiotics have not worked.

SOURCE OF FUNDING

The University of Washington is receiving financial support and the lefamulin from Nabriva Therapeutics, Ltd. to do this study.

CONFIDENTIALITY OF RESEARCH INFORMATION

All of the information you provide will be confidential. However, if we learn that you intend to harm yourself or others, we must report that to the authorities. We will use your name and contact information to identify you while you are in the study.

The web questionnaires are hosted on secure servers by the ITHS in Seattle, Washington. You will answer the questions using a coded (encrypted) connection, so you can submit your answers without it being broken into or changed. Information in questionnaires will not be written to the hard drive of your computer or stored on your mobile phone. All information submitted online is sent to a password-protected directory accessible only by the website administrator and research staff.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. Nabriva Therapeutics may also examine your study records. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

The U.S. Food and Drug Administration (FDA) has provided an exemption to regulations for investigational new drug (IND) regulations because lefamulin is already

approved to treat pneumonia. The U.S. Food and Drug Administration (FDA) reserves the right to review study data that may contain identifying information.

A description of this study is available on http://www.clinicaltrials.gov, as required by U.S. Law. 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.

USE OF INFORMATION AND SPECIMENS

Commercial Profit

The specimens we collect as part of this research may be used for commercial profit. There is no plan to share this profit with you.

Genetic Sequencing

The specimens that we collect as part of this research will not be used for whole genome sequencing of human DNA. We may perform whole genome sequencing of bacterial genomes in the future.

Returning Results to You

You will be informed of your *M. genitalium* test results. If the lefamulin does not cure your *M. genitalium* infection, the study doctor will consult with your doctor and your regular doctor will continue to treat your infection. You will not be informed of your culture and antibiotic resistance test results. The culture and antibiotic resistance test will not affect how the study doctor takes care of you: this testing may be done a long time after your participation is complete, and results will not be available in real-time.

Using Your Data in Future Research

The information and/or specimens that we obtain from you for this study might be used for future studies. We may remove anything that might identify you from the information and specimens. If we do so, that information and specimens may then be used for future research studies or given to another investigator without getting additional permission from you. It is also possible that in the future we may want to use or share study information that might identify you. If we do, a review board will decide whether or not we need to get additional permission from you. You do not have to agree to have your specimens and data stored for future use. If you do not wish to allow this, there is a place at the end of this form to indicate that.

You will be able to withdraw your data from the study database before analyses and/or publication and sharing. You will not be able to withdraw your data after they have been released or published.

OTHER INFORMATION

You may refuse to participate and the care you receive from your own doctor will not be affected in any way if you decide not to participate. You are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw, please contact the researcher listed on page 1 of this consent form.

You will receive the lefamulin (and the doxycycline if you are randomly chosen to take doxycycline before lefamulin) and additional *M. genitalium* tests free of charge if you participate in this study.

A copy of the consent form will be emailed to you at an email address that you provide. It will be a "PDF" document. Most computers already have PDF viewer software installed, which will allow you to open, read, or print the consent form. The email we send you will include a link to PDF viewer software such as Adobe Acrobat Reader in case your computer doesn't already have it. If you would prefer to receive a paper copy of the consent form at no cost to you, please contact the researcher listed on page 1 of this consent form.

Although not currently planned, we may contact participants in the future to request additional information and/or specimens.

RESEARCH-RELATED INJURY

It is important that you promptly tell the researchers if you believe that you have an injury or illness because of participating in this study. You can call the researchers at the number(s) listed at the top of this form during business hours. After business hours you can call the Harborview Medical Center Infectious Disease Fellow, who is available 24 hours a day. They will treat you or refer you for treatment. For a life-threatening problem, call 911 right away or seek help immediately. Contact Lisa Manhart at 206-744-3646 when the medical emergency is over or as soon as you can.

The costs of the treatment may be billed to you or your health insurance just like other medical costs, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. The researcher may request HSAP coverage by following established procedures. If you wish to request HSAP coverage yourself, contact one of the researchers or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. You may also call collect to the UW Human Subjects Division at 206-221-5940 if you do not otherwise have access to a telephone. Ask one of the researchers if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of compensation for injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form. We will bill your health insurance for treating problems that result from your *M. genitalium* infection or from standard clinical care. If you have no health insurance or your insurance refuses to pay, we will bill you. Nabriva Therapeutics will not provide any compensation for any research-related injuries.

Printed name of study staff obtaining consent: _____ Signature of study staff obtaining consent: _____ Date: _____

Participant's Statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research or if I have been harmed by participating in this study, I can contact one of the researchers listed on

the first page of this consent form. If I have questions about my rights as a research participant, I can call the Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of participant: _____ Signature of participant: _____ Date: _____

Telephone number (include area code and number): _____

__ I agree to have my specimens and data stored for potential future use. _____ _____

Initials Date

__ I do **not** agree to have my specimens and data stored for potential future use. _____ _____

Initials Date

Copies to: Participant
Researcher