

UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT FORM

Protocol Title: *AN OPEN LABEL TRIAL OF MECASERMIN FOR HIV ASSOCIATED METABOLIC DISEASE*

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Why am I being asked to volunteer?

You are being invited to participate in a research study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this study is to test whether mecaseimerin (also called Increlex) improves lipids, glucose, and body fat in adults with HIV infection and lipodystrophy syndrome. Lipodystrophy is a condition in which a person loses fat from one or more body areas with or without gaining fat in other body areas. We will also assess the safety of the drug for this condition.

The use of mecaseimerin for this purpose is investigational. Mecaesimerin is approved by the FDA for use in children with short stature but not for adults with HIV and lipodystrophy syndrome.

Mecasermin is a clear sterile liquid that must be injected under the skin twice a day to be effective. The medicine is a manufactured version of a hormone found in the body called insulin like growth factor I.

How long will I be in the study? How many other people will be in the study?

Your participation in the study will be 24 weeks.

The study will last 48 weeks.

Ten subjects at the University of Pennsylvania will be enrolled in this study.

What am I being asked to do?

- Take the medicine. You are being asked to take mecaseimerin for 24 weeks, and also have several blood tests, x-rays, and 2 fat biopsies so we can monitor the effects of the medicine.
 - The medicine is given twice daily by injection under the skin. We will teach you how to give it. The medicine can be given under the skin of the arm, leg, abdomen, or buttocks.
 - The needles must be disposed of according to the laws in your city or township. In most communities, this means they can be disposed of in hard plastic containers with a hard cap (such as an empty bleach bottle or laundry detergent bottle) and placed with the household trash. You must check with your local community for proper disposal requirements.
- Fat Biopsy. Before you begin the medicine and after 24 weeks of treatment, a fat biopsy will be performed. This is done to determine the effect of mecaseimerin on fat cells. The biopsy will be performed by a physician study team member. It involves making a 1-2 cm (less than 1 inch) incision over the buttocks after numbing the skin. A small marble-sized sample of fat will be removed. The wound will be closed with a stitch or a bandage. These fat biopsies are for research purposes only.
- Body scans. You will have imaging studies to assess your body fat. These will be performed at week 0 and at week 24. The studies will include a body scan called a DEXA scan, and a brief CT (or CAT scan) of your abdomen and thighs. These imaging tests use x-rays. These tests are for research purposes only.
 - A CT scan is the term used to describe a radiological test known as computed tomography. The CT scanner is a doughnut-shaped device that takes pictures of the inside of your body using X-rays as the "light source". It is used routinely in the diagnosis of many diseases. CT can see inside the body into areas that cannot be seen on regular X-ray examinations. The test itself is painless. You will be asked to lie quietly on the CT scanning table. The technologist may ask you to hold your breath for some of images. While the study is in progress it is very important that you lie still. This will ensure quality images.
- Blood samples. You will also provide 4 blood samples of 10 mL each (about 2 teaspoons). This will be done at week 0, week 4, week 12, and week 24. You will need to be fasting for the blood samples at week 0, week 12, and week 24.

- **Body Shape Surveys.** You will complete a survey at week 0 and week 24. The surveys will assess your perception of your body shape.
- **Physical exam.** You will be asked to return to clinic for a physical exam at week 0, week 12, and week 24.
- **Review of medical records.** We will access your medical and laboratory records to gather the data we need to complete the study and monitor safety.
- We will call you weekly for the first 4 weeks to check for side effects or other problems, and answer questions. We will call you 4 weeks after the study ends to follow-up on any problems which may have arisen during the study.
- During the study we will ask you not to start any new lipid/cholesterol or glucose lowering medications or change the ones you are on. This is so we can more accurately estimate the effects of the medicine. You or your doctor should contact the study team if a change in these medicines is desired. However, your doctor can change your HIV medications in whatever way she or he feels is necessary.
- The schedule of tests are shown in the following table:

week	0	4	8	12	16	20	24	28
Blood Test for CD4, HIV mRNA, lipids, glucose, insulin, fatty acids, fat secreted hormones, growth factors, blood count, chemistry panel	x	x		x			x	
DEXA scan, abdominal and thigh CT scan, skinfold measurements	x						x	
Fat biopsy	x						x	
Body shape survey	x						x	
Clinic visit and physical exam	x			x			x	
Safety monitoring phone calls (weekly for 1 st 4 weeks, then at week 28)	x	x						x

What are the possible risks or discomforts?

There is no information of the risks of mecaseermin in patients with HIV infection and the lipodystrophy syndrome. Because mecaseermin has never been studied in patients with your condition, this research study may involve risks that we do not know exist at this time. Mecasermin has been used in other patient groups including patients with HIV infection and a condition called wasting syndrome, children with short stature, and patients with diabetes. From these other studies, we believe the major risks of mecaseermin are the following:

- **Hypoglycemia or low blood sugar.** This occurred in studies of mecaseermin in children treated for short stature and adults on insulin therapy for diabetes. The risk is higher for younger children and for those on insulin or glucose lowering medicines. It occurs most commonly in the first month of treatment. The symptoms can include dizziness, sweatiness, increased heart rate, and seizure. The risk is lowered if you take the medicine with a meal. You should carry a glucose source with you at all times (glucose tablets, candies, sugar-containing drink, etc.).
- **Increased fluid pressure in the brain** (also called benign intracranial hypertension or pseudotumor cerebri). This can cause symptoms of headache and dizziness. It was reported in 3 children who took the medicine for short stature. In all cases this resolved with stopping the medicine or reducing the dose.

- Joint pain and jaw pain. This is more common in doses higher than the one used in this study, but could occur in this study.
- Edema (swelling) of the face and extremities. This is one of the more common complications but is generally mild.
- Tonsillar enlargement. The symptoms could include new onset of snoring or sleep apnea. Sleep apnea is a condition in which breathing stops briefly during sleep. Several patients receiving mecasermin in other studies have had a tonsillectomy/adenoidectomy to remove the tissue.
- Allergic reactions and local irritation. As with any medicine, allergic reactions to the medicine or components of the medication can occur. Symptoms of a serious allergic reaction include a rash (hives), swelling of the lips or tongue, trouble breathing. Symptoms of local irritation could include pain, swelling, or redness.
- The DEXA scan and CT scans of the abdomen and thighs. This research study involves exposure to radiation from the DEXA scans and the brief CT scans of the abdomen and thighs. Therefore you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.
- The risks of fat biopsy include pain and discomfort, bleeding, scarring, and infection. The use of local numbing medicine, sterile technique, and steps to stop bleeding and promote healing will reduce the risks of these happening.
- The risks of blood drawing include pain, discomfort, bleeding, and infection. Our standard technique for drawing blood reduces the risk of these.
- If you are female, we will ask you to use a birth control method to prevent pregnancy while you are taking this medication.
- Reproductive risks: Because of the effects of this drug, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a pregnancy test before entry into the study and after 12 weeks of treatment. You are asked to use a medically accepted method of birth control while you participate in the study. These can include condoms, oral contraceptives, intrauterine devices, injected progesterone (Depot Provera), or other method recommended by your primary care provider. Some of these methods do not prevent transmission of sexually transmitted diseases so check with your doctor for recommendations. You should not become pregnant while you are taking this drug. If you do become pregnant, you must discontinue the drug, tell the investigator and consult an obstetrician or maternal-fetal specialist.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You may not get any direct benefit from being in this research study. You may benefit from use of the medication in the following ways:

- Your lipids may improve.
- Your glucose and insulin levels may improve.
- You may have an increase in body fat in the face and limbs.

Society may benefit by learning more about the cause of HIV lipodystrophy and whether mecasecamin is a potentially useful treatment for it.

What other choices do I have if I do not participate?

The alternative to entering the study is to not participate and continue your routine care with your doctor. Alternative treatments for HIV lipodystrophy and its problems (abnormal lipids, abnormal glucose control, and body fat abnormalities) can be discussed with your doctor.

Will I be paid for being in this study?

You will be paid \$200 after each evaluation at week 0 and week 24. The total is \$400. This is to compensate for time, travel, and the testing required by the study. If you leave the study early, the compensation will be provided on a prorated basis.

Will I have to pay for anything?

The blood tests for your CD4 count, viral load, lipids, glucose and insulin will be covered by your insurance as part of your routine care. We will do additional tests on the blood for research purposes that will be done at no charge to you or your insurance. The DEXA, CT scans, and fat biopsies will be done at no charge to you or your insurance. The medication and syringes to give it will be supplied to you at no charge.

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

What happens if I am injured or hurt during the study?

If you have a research-related injury contact the Principal Investigator, Dr. Roy Kim at 215-590-3174.

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask

them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

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. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records. Please refer to the separate "HIPAA Privacy Authorization" document that explains more specifically how your personal information will be protected.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

Name of Subject (Please Print)

Signature of Subject

Date

Name of Person Obtaining
Consent (Please Print)

Signature of Person Obtaining
Consent

Date