Soluble Epoxide Hydrolase Inhibition and Insulin Resistance

NCT03486223

Date 8/11/2021

Institutional Review Board
Informed Consent Document for Research

Principal Investigator: James M. Luther, M.D. **Revision Date: 7/26/21**
Study Title: Variation in Soluble Epoxide Hydrolase Activity and Insulin Sensitivity in Humans – Aim 2
Institution/Hospital: Vanderbilt University Medical Center

This informed consent applies to adults age 21-60 with pre-diabetes.

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study. Anyone you authorize to receive your medical record will also get this note.

1. What is the purpose of this study?

You are being asked to take part in this research study because you have been diagnosed with pre-diabetes. The purpose of this study is to test how a new medication (GSK2256294) may affect the activity of an enzyme the body produces, the sensitivity of your body to insulin, and blood flow in tissues in the body. This medication is not approved by the Food and Drug Administration (FDA). About 114 people will take part in this study.

2. What will happen and how long will you be in the study?

Screening Visit 1
If you decide to take part in the study, you will come to the Vanderbilt Clinical Research Center (CRC). You will have a complete physical, including height, weight, and waist measurement. We will ask you about your medical history. We will take your blood (about 1 tablespoon) and a urine specimen to check that you have no problems to keep you from being in the study. If you agree, part of this blood will be used for DNA (gene research.)

Screening Visit 2
If your bloodwork shows it is safe for you to be in the study, we will ask you to come back to the CRC for an oral glucose tolerance test.

You will come to the CRC in the morning, having had nothing to eat or drink since midnight. If you are a woman who could become pregnant, we will ask for a urine sample for a pregnancy test. If you are pregnant, you will not be allowed to be in the study.

We will measure your blood pressure and place a small tube in your vein to draw blood. We will take blood from your arm. We will then give you some liquid containing a measured amount of glucose to drink. We will take your blood again 30, 60, 90, and 120 minutes after you drink the liquid. The total amount of blood taken during the test day will be a little more than a tablespoon.

We will measure your body composition (the percent of your body that is fat, muscle, and bone) by giving you a DEXA (dual energy X-ray absorptiometry) scan. To have this scan, you will lie down on a table for about 10 minutes while the machine scans your whole body.

Study Medication 1
If you qualify to be in the study, we will give you a study drug to take for 7 days. You will be given either GSK2256294 or a placebo, a tablet with no active ingredient. Which one you are given will be decided at random, like the toss of a coin. Neither you nor the study doctors will know which you are given, but we can find out if there is a need. The study nurse or doctor will discuss how to take your medication.

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We will also give you a jug to collect the urine you produce the night before the study. You will bring the jug with you to the study day.

Study Day 1
On the 7th day of the study medication, you will come to the CRC in the morning, having had nothing to eat or drink after midnight.

If you are a woman who could become pregnant, you will have a pregnancy test. If you are pregnant, you will not be allowed to continue in the study.

We will place small tubes in the veins in your arms to give medication and to draw blood. We will place sticky patches on your chest to measure your heart rate and electrocardiogram (ECG, a measure of your heart's electrical activity).

During the study you will have an elastic band put loosely around your arm. This will be used to measure blood flow to your arm during the last 2 minutes of each study medicine infusion. Blood pressure cuffs will be placed on your upper arm and around your wrist. We will draw blood samples from the small tube in the vein in your arm several times during the day.

We will take a small piece of fat from your belly fat using liposuction. First we will clean the skin over your belly. Numbing medication will be applied on the area. A needle will be placed through the skin and into the fat pad under the skin. We will make a small incision, and a small piece of the fat will be removed for analysis.

After this, you will rest for at least 45 minutes. After the rest period, we will take a blood sample.

<u>Optional: Muscle Biopsy</u>
The muscle biopsy is for research purposes only and will give us more information on how your body handles nutrients. Before and after the metabolic clamp study, a muscle biopsy will be taken from the mid-thigh area. The first biopsy will use one thigh muscle, and the second biopsy will use the other thigh muscle. Lidocaine will be used to numb the area where the biopsy will be done. A small incision (about an inch) will be made in the skin. A special needle will be used to withdraw the muscle tissue. The amount will be about the size of a pencil eraser. Any bleeding will be stopped with a pressure dressing.

You may choose not to have the muscle biopsies and still continue in the study. Please indicate your choice below.

I ___do ____do not want to have the muscle biopsies.
We will then begin to give you a solution of paraminohippurate (PAH), a drug approved by the FDA to measure kidney function, through the vein in your arm.

We will give you glucose (a solution of sugar in water) and insulin (a medication approved by the FDA to treat diabetes) through the vein in your arm for about 3 hours. We will then ask you to place your hand in a heated box or under a heating pad. We will take blood samples every 5 minutes for 3 hours. We will give you potassium chloride to make sure your blood potassium doesn't get too low.

At the end of the insulin infusion we will repeat the fat biopsy. We will ask you for a final urine sample. You will then be finished with Study Day 1. We will give you something to eat when you are finished.

Approximately 10 tablespoons of blood will be taken from you during this study day.

For the next 7 weeks, you will not take any study medication and you will eat your usual diet.

Study Medication 2
At the end of the 7 weeks, you will be given either GSK2256294 or a placebo, whichever you did not take the first time. Neither you nor the study doctors will know which you are given, but we can find out if there is a need. The study nurse or doctor will discuss how to take your medication.

We will also give you a jug to collect the urine you produce the night before the study. You will bring the jug with you to the study day.

Study Day 2

On the 7th day of the second study medication, you will come to the CRC in the morning, having not had anything to eat or drink after midnight. All procedures in Study Day 1 will be repeated.

At the end of this Study Day, you will be done with the study.

Part of this study will include testing your DNA. If we find changes related to how your body responds to the study medication or other changes, we may contact you to ask if you would like to participate in other studies.

May we contact you in the future regarding other studies for which you may be eligible?

☐ Yes ☐ No

3. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

4. Side effects and risks that you can expect if you take part in this study:

Inconveniences
Not eating or drinking after midnight on the night before each study day
Picking up your meals at the CRC.

Pregnancy Risks
The drugs used in this study may hurt an unborn child. If you take part in this study, you and any person you have sex with must use a barrier method of birth control, such as a diaphragm or condoms, while you are in this study. If you become pregnant while you are in this study, you must tell your doctor at once. Also, women must not breast feed while in this study. If you are a woman and are able to become pregnant, you will have a urine test to make sure that you are not pregnant before you receive treatment in this study.

Electrodes
Having sticky patches on your skin may make you itch, have reddened skin, or a rash.

Risks of the Catheters
Putting a catheter into your vein to give medications and draw blood may cause pain, redness, soreness, bruising, or infection at the needle stick site. Rarely some people faint. We will use careful and sterile techniques to minimize these side effects.

GSK2256294
GSK is an investigational drug. Some people have experienced irritation at the site of the sticky patches for the ECG while taking GSK. There have been no safety concerns based on early studies in humans. There is a theoretical risk that GSK could increase the spread of cancer if it were given to someone who had cancer and if it were taken for a long time. We will not study you if you have had a history of cancer or if you are not up to date on cancer screening. In addition, we will give you GSK for only one week. In animals, GSK has caused changes in the ECG, a measure of risk for certain heart rhythm problems. We will not study individuals who already have certain heart rhythm changes, and we will perform an ECG after you take the study drug.

Para-aminohippurate (PAH)
The side effects of PAH may include flushing, tingling, nausea, vomiting, warmth, desire to move your bowels or urinate (uncommon); or flushing and abdominal pain (rare).

Glucose
Glucose may cause high blood sugar. Symptoms of high blood sugar are hunger, thirst, frequent urination, dry mouth, and dry skin. Giving glucose through the vein may cause irritation of the vein, including redness and pain. We will give the glucose through a bigger vein to decrease this risk.

Insulin
Infusion of insulin may cause low blood sugar. Symptoms of low blood sugar are nausea, extreme hunger, feeling nervous or jittery, cold, clammy, wet skin and/or excessive sweating not caused by exercise, a rapid heartbeat, and numbness or tingling of the fingertips or lips, and trembling.

Biopsy
This procedure may cause pain, soreness, and infection at the biopsy site. You may feel some pressure or a tugging sensation during the procedure. We will use careful and sterile techniques to minimize these side effects. After the numbing wears off, the area may be sore for about a week. For the next 48 hours after your biopsy, we will ask that you do not take a bath, get in a swimming pool, or use a sauna.

Lidocaine
Lidocaine, a numbing drug, may burn or cause rash, redness or soreness where you get the shot. There is a risk that this drug may cause problems with heart rhythm.

Potassium chloride
Common side effects are diarrhea, flatulence (passing gas), nausea, and vomiting. Rare but serious side effects include hyperkalemia (high levels of potassium in the blood.) This can usually be treated, but if severe can cause the heart to stop beating. Other rare side effects are abdominal pain and stomach ulcers.

Muscle Biopsies

The muscle biopsy may cause muscle soreness, bruising, or infection. It may also result in a small blood-filled bump at the biopsy site. There is a small chance that some slight bleeding may also occur. The soreness may last as long as 48 hours.

5. Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

6. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

7. Good effects that might result from this study:

a) The benefits to science and humankind that <u>might</u> result from this study are that we may learn more about diabetes and how to treat it.
b) The benefits you might get from being in this study. None.

8. Other treatments you could get if you decide not to be in this study:

You may choose not to be in this study and nothing about your healthcare will change.

9. Payments for your time spent taking part in this study or expenses:

If you complete this study, including the muscle biopsy, you will be paid $600. If you do not complete the study, you will be paid for the parts you do complete as follows:
Screening day 2: $25
One full study day: $150
Muscle biopsy: $100

This amount may be taxable and will be reported to the Internal Revenue Service (IRS). We may ask you for your Social Security number and address before you are compensated for taking part in this study.

10. Reasons why the study doctor may take you out of this study:

You may be removed from this study without your consent if:
- Staying in the study would be harmful to you
- You no longer meet the requirements of the study
- The study is stopped.

If you are removed from the study, you will be told the reason.

11. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor.

12. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact the study nurse at [redacted]. If you cannot reach the research staff, please page the study nurse, [redacted]. If you cannot reach the study nurse, please page Dr. Luther at [redacted].

For additional information about giving consent or your rights as a person in this study, please feel free to call the Vanderbilt University Institutional Review Board Office at [redacted] or toll free at [redacted].

13. Clinical Trials Registry.

A description of this clinical trial will be available on 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.

14. Confidentiality:

All efforts, within reason, will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. Information that could identify you will be kept in a locked cabinet or a password-protected computer. Only members of Dr. Luther's study team will have access to this information.

Dr. Luther and Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Luther and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

15. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data

gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Luther and his study team may share the results of your study and/or non-study linked lab tests, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, or your treating physician. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

As part of the study, Dr. Luther and his study team may share the results of your study and/or non-study linked Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The sponsor and/or Vanderbilt may give or sell your health data, without identifiers, to others or use it for other research projects not listed in this form. The sponsor, Vanderbilt, Dr. Luther and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Luther in writing and let him know that you withdraw your consent. His mailing address is

Dr. James Luther
[redacted]
Vanderbilt University
Nashville, TN 37232-6602.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date Signature of patient/volunteer

Principal Investigator: James M. Luther, M.D. **Revision Date: 7/26/21**
Study Title: Variation in Soluble Epoxide Hydrolase Activity and Insulin Sensitivity in Humans – Aim 2
Institution/Hospital: Vanderbilt University Medical Center

Consent obtained by:

Date Signature

Printed Name and Title Time

Consent for Genetic Research

The purpose of part of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment.

You are being asked to give a blood sample for genetic research. What we learn about you from this sample will not be put in your health record. Your test results will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results.

A single blood sample will be taken at the time we are taking a screening sample. It will not take any extra time or require an extra needle stick.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only Dr. Luther and members of his study team will have access to your name.

Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that comes from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Your sample will be used to make DNA that will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

Your samples may be used to make new products, tests or findings. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Your samples and information about you may be shared with others to use for research. To protect your privacy, we will not release your name.

You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Giving samples for research is your free choice and you may be in the study even if you do not want your samples used or stored for gene research.

At any time, you may ask to have your sample destroyed. You should contact Dr. Luther at

Dr. James Luther
[redacted]
Vanderbilt University
Nashville, TN 37232-6602.
to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

Please check Yes or No to the questions below:

My blood/tissue sample may be used for gene research in this study.

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future gene research in diabetes.

☐ Yes ☐ No

My blood/tissue sample may be stored/shared for future gene research for other health problems (such as cancer, heart disease, etc).

☐ Yes ☐ No

Signature: _____ Date: _____