Study of Acarbose in Longevity (SAIL)

NCT Number: 02953093

Date: 2/8/2018

ALBERT EINSTEIN COLLEGE OF MEDICINE

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to participate in a research study called "**Study of Acarbose in Longevity" (SAIL)**. Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." Her name is Dr. Erika Brutsaert You can reach Dr. Brutsaert at:
Office Address: 1300 Morris Park Avenue, Block Building.
City, State Zip: Bronx, New York 10461
Telephone #: 718-839 7961
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

Support for this research study is provided by:
Glenn Foundation for Medical Research

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253 or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg Room 1002
Bronx, New York 10461

Why is this study being done?

The goal of this study is to find out if acarbose, a medicine commonly used to treat diabetes, may have other effects in the body that could slow the aging process. Laboratory experiments have shown that mice treated with acarbose live longer. Scientists believe that acarbose may have "anti-aging" effects and could protect people from conditions like heart disease and cancer. Acarbose might do this is by changing the way genes work in the body ("gene expression") or by changing the bacteria in the intestine. The purpose of this study is to find out whether acarbose treatment can change "gene expression" in the muscle and fat tissue and change the bacteria in the intestine of older adults who have pre-diabetes, making them more like healthy, younger people. We will also study whether acarbose improves blood sugar levels and several heart disease risk factors.

Why am I being asked to participate?

You are being asked to take part in this study because you may fit the following characteristics:

You are age 60 and older, male, and you may have impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), also called pre-diabetes. If you agree to take part in this study you will have tests and examinations to be sure that you qualify for the study.

For the purpose of this study, pre-diabetes means that you have blood sugar levels higher than normal, but not high enough to be considered diabetic. Currently, the medical standard of care is to treat pre-diabetes with healthy lifestyle changes. The U.S. Food and Drug Administration (FDA) has not approved acarbose for the treatment of pre-diabetes, or anti-aging effects. This means the use of acarbose in this study is experimental.

How many people will take part in the research study?

You will be one of about 30 people enrolled in this study.

How long will I take part in this research?

It will take you about 22 weeks to complete this research study. During this time, we will ask you to make 6 study visits to Einstein Clinical Research Center (CRC).

What will happen if I participate in the study?

- If you qualify for the study, you will be started on 10 weeks of acarbose and 10 weeks of placebo.
- The order of the treatment will be randomly assigned (like a flip of a coin). Half of the participants will receive placebo first (followed by acarbose), and the other half will receive acarbose first (followed by placebo)
- The acarbose and placebo capsules are taken three times daily for 10 weeks. The dose will start low (25mg acarbose or placebo) and be increased at two weeks. If you can take 2 capsules three times daily without side effects, you will be switched to a higher dose pill and will eventually take up to 2 tablets three times daily (100mg of acarbose 3 times daily, or placebo). After a 2 week "washout" with no medications, you will get the other treatment for another 10 weeks, increased in the same way.
- You and your doctor cannot choose the order in which you receive acarbose and placebo. You will not know the order of the treatments until the research study is completed.
- All study procedures are the same for both study groups.

Week 1/Visit 1: Screening (about 2½ hours)

As determined by the telephone interview and initial screening, you have been invited to a screening visit. If you agree to participate, we will:

- Ask you not to eat or drink anything (except water) for 10 hours before your screening appointment
- Measure your blood pressure, height, weight and waist size
- Ask you questions about your medical history
- Perform a fingerstick glucose using a blood glucose testing meter

The results of the fingerstick will show whether you are eligible to continue with the screening visit. If you are eligible to continue, we will:

- Draw blood (about 21/2 tablespoons) from a vein in your arm. The following tests will be done: glucose and routine studies, including cholesterol, kidney and liver function
- Begin the oral glucose tolerance test (OGTT) and ask you to drink 10 ounces of a sweet liquid (glucose)
- Two hours later, take a blood sample (about 1 teaspoon) to measure glucose

The total amount of blood taken at this visit will be approximately 3 tablespoons. If results of these tests show that you are eligible, you will be invited to continue in the study (see Visit 2 below).

If you have had an oral glucose tolerance test (OGTT) within the past year, these results may be used to decide if you are eligible to enroll in the study.

Week 2/Visit 2: Beginning of treatment period 1 (approximately ½ hour)

- For the next 10 weeks, you will take study medicine (acarbose or placebo) and will follow your usual diet and activity routine. You will be given a bottle of study medication (acarbose or placebo) and instructed on how to take it (one pill with breakfast, lunch and dinner the 1st week, two pills with each meal in 3rd week, then 2 pills per meal of the higher dose capsule in the 5th week).
- You will be given an appointment to return for your next visit in approximately 4weeks
- The study team will contact you by phone once a week to check on how you are doing and to answer any questions

Week 6/Visit 3: Safety visit (½ hour)

- You will come in for a safety visit
- Blood pressure and weight will be measured
- A brief medical history will be taken to assess for any changes in medications or new medical conditions.
- Study staff will discuss medication side effects and whether doses were adjusted.
- If you are tolerating 2 pills three times daily of the lower dose pill. you will receive a higher dose pill. Otherwise you will continue the lower dose.
- You will be given a collection kit for your stool sample.
- Blood will be collected from a vein in your arm. Less than 1 tablespoon will be collected for a liver function test.
- Home stool collection: If you qualify to continue in the study, we will give you a kit with a collection tube and spatula. We will also provide gloves and a container for stool collection that will sit on your toilet. When you have a bowel movement, you will collect about a half-teaspoon of stool with the spatula and scrape it onto the collection tube. After the tube is filled, you shake it and store at room temperature. You will then be asked to bring in the sample to study visit 4.

Week 12/Visit 4: End of treatment period 1/ muscle and fat biopsies. (4 ½ hours)

- You will be asked not to eat or drink anything (except water) for at least 10 hours before your appointment. If you are taking blood pressure medication you will be asked not to take it the morning of this visit but to bring the medicine with you.
- The study team will ask about any new medical problems or medications since your last visit.
- A brief physical examination will be performed by the study doctor or nurse, which will include measurement of blood pressure, heart rate, weight and height.
- An intravenous line (small plastic tube with saline solution going into a vein) will be inserted in your arm for blood sampling. Fasting blood samples will be taken and stored for future tests of cholesterol, kidney and liver function, as well as blood for glucose, insulin and inflammatory markers (about 3 tablespoons total).
- You will be asked to undergo a thigh area muscle biopsy (sampling). An area of the thigh skin will be cleaned with iodine solution and made numb using an injection of an anesthetic (1% lidocaine solution). A special biopsy needle will be used to obtain a sample of muscle tissue (about 100-200 mg, or less than 1/10 of an ounce) using 4-5 passes of the biopsy needle. The incision size for the thigh area sampling will be small (less than half an inch), and will be covered with a Band-Aid and a compression bandage to prevent bleeding. The procedure usually takes about 10 minutes and the expected blood loss is minor, less than half a teaspoon).
- You will also be asked to undergo a biopsy of fat tissue from the abdominal area. An area on the abdomen will be cleaned with iodine solution and made numb using an injection of an anesthetic (1% lidocaine) and a small amount of saline (salt water). A small incision (less than 1 inch) is made in the skin. The liposuction tube is inserted under the skin and approximately 2 grams (less than half an ounce) of fat tissue mixed with saline is removed. After the biopsy, the skin will be covered with a Band-Aid a compression bandage to prevent bleeding. The procedure usually takes 10-15 minutes and the expected blood loss is minor, less than half a teaspoon.
- People who take aspirin regularly may have a higher risk of bleeding from the biopsies. If your physician has prescribed aspirin for you, you should ask your doctor if it is safe for you to stop the aspirin for a week before the biopsy, which may reduce the chance of bleeding. If your doctor decides it is NOT safe for you to stop aspirin for a week before the biopsies, then you are not eligible to participate in the study.
- Following the biopsy procedure, you will be served breakfast and asked to eat all of it. You can take your blood pressure medications at this time. You will be asked to remain in the center for the next 3-4 hours for additional tests. During this time, you may sleep, read, watch television or engage in other quiet activities. You may drink only non-caffeinated, non-caloric beverages.
- At, 30, 60, 120 and 180 minutes following breakfast, additional blood samples will be taken (about 1 tablespoon each time, other than at 120 minutes, when about 2 tablespoons will be taken) from the intravenous line.
- You will be asked to give a urine sample for routine urinalysis and tests of inflammatory markers.
- After completion of these procedures, you will be offered lunch and you may return home.
- For the next 2 weeks you will be off of study medicine. You will then start the second treatment 2 weeks later. You will be given a bottle of study medication (acarbose or

placebo) and instructed on how to take it (one pill with breakfast, lunch and dinner the 1st week, two pills with each meal in 3rd week, until you return for the following visit.
- You will be given an appointment to return for your next visit in approximately 6 weeks
- The study team will contact you by phone once a week to check on how you are doing and to answer any questions

Week 14- phone call: Begin treatment period 2

- We will call you after 2-week washout period and remind you to begin your second set of capsules.
- We will ask you to increase the number of capsules in the same way as you did for treatment period 1.

Week 18/Visit 5: Safety visit 2

- Same procedures as visit 3

Week 24/Visit 6: End of treatment period 2/ Muscle and fat biopsies 2 (4 ½ hours) .

- Same procedures as visit 4.
- After this visit, your participation in the study is finished.

Genetic Testing

This study will not involve formal genetic testing. However, RNA (genetic information obtained from DNA) extracted from the muscle and fat tissue biopsies and from blood samples will be examined for changes in gene expression.

Specimen Banking (Future Use and Storage)

We will store your specimens and information about you in a "biobank", which is a library of information and specimens (tissue and blood) from many studies. These specimens and information can be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government. Your specimens and information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the consent or the IRB office at 718-430-2237. If you do, we will destroy remaining specimens and information but if these were already shared with other researchers, we cannot get them back.

You can choose not to participate in the biobank and still be part of the main study and this will not affect your treatment at this facility.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my specimens and information about me used for future research studies.

_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW

_____ I consent to be contacted in the future to learn about:
_____ New research protocols that I may wish to join.
_____ General information about research findings.
_____ I do not want to be contacted at all.

Will I be paid for being in this research study?

You may receive a total of **$460** for participation in the study. If you choose to withdraw from the study before all visits are completed, you will be paid only for the visits you completed.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens/data or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

There will be no cost to you to participate in the study.

Taking part in this study will not involve added costs to you. All study drugs will be given free of charge by the sponsor. You and/or your insurance company will have to pay for any costs that are part of your regular medical care.

What will happen if I am injured because I took part in this study?

If you are injured as a result of this research, only immediate, essential, short-term medical treatment as determined by the participating hospital, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.
- You are not waiving any of your legal rights by signing this informed consent document.

- If additional treatment is required as a result of a physical injury related to the research, necessary medical treatment will be provided to you and billed to your insurance company or to you as part of your medical expenses.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Erika Brutsaert MD at (718) 839-7961, Monday through Friday between 8 AM and 4 PM.

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- You must take your study drug as instructed, returning any unused study drug (including any empty bottles), at every visit.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- ***Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.***
- If you think you have become pregnant, contact your research study doctor immediately.
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor's name and phone number.
- You may carry out all your normal daily activities.

Confidentiality

We will keep your information confidential, however, a risk of taking part in this study is that your confidential information might be shared accidentally with someone who is not on the study team and is not supposed to see or know about your information. This is very unlikely, because the study team takes confidentiality of your information seriously. Your research records will be kept confidential and your name will not be used in any written or verbal reports. Your information will be given a code number and separated from your name or any other information that could identify you. The form that links your name to the code number will be kept in a locked file cabinet and only the investigator and study staff will have access to the file. All information will be kept in a secure manner and computer records will be password protected. Your study information will be kept as long as they are useful for this research.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

The only people who can see your research records are:

- the research team and Clinical Research Center staff who work with them
- the organization that funded the research: The Glenn Foundation for Medical Research
- groups that review research (The Albert Einstein College of Medicine and Montefiore Medical Center, the Einstein IRB, and the Office for Human Research Protections, and the US Food and Drug Administration)

These people who receive your health information, may not be required by privacy laws to protect it and may share your information with others without your permission, if permitted by laws governing them. All of these groups have been asked to keep your information confidential.

Are there any risks to me?

Blood Draw
Rarely, the vein where we inserted the needle will become sore or red. Sometimes, a temporary harmless "black and blue" may develop. Very rarely, fainting may occur.

Risks of Taking Acarbose:

Common side effects:

- Possible adverse effects may include bloating, gas, diarrhea or abdominal pain. In most cases, these symptoms become less and disappear after taking acarbose for 1-2 weeks. These symptoms may also improve if the dose of acarbose is temporarily reduced.
- Liver test abnormalities without symptoms can occur with treatment with acarbose.

Uncommon side effects:

- Acarbose is considered a very safe drug, but should not be used by people who have serious liver disease (if you have this, you are excluded from this study). Serious side effects are very rare (less than 1 in 10,000) and include: hepatitis (liver inflammation), intestinal blockage (ileus) and severe inflammation of the intestinal wall (pneumatosis coli).

There may be other risks of Acarbose that are currently unknown.

Fat and Muscle Biopsies:

- The risks of the fat and muscle sampling procedure are pain and discomfort, which should clear up in a few days. You may also experience stiffness (like a "Charlie Horse"), which should be present for only one or two days. You may also feel tightness where the fluid is injected for the fat biopsy and may see temporary black and blue marks. The muscle biopsy on the leg may leave a temporary hematoma, which is a small amount of blood which collects under the skin and feels like a bump. You will be advised to restrict your activities for a few days after the procedure. Rare complications, such as infection and bleeding at the site of the biopsy, will be minimized by applying pressure to the site and using a sterile technique. A small scar (about 1/3 inch) may remain on the abdomen and thigh. There is a possibility of a permanent loss of sensation in the skin at the site of the biopsy.
- The fat biopsy technique (liposuction) is used frequently by dermatologists and plastic surgeons, who remove 150 times as much fat as you will have removed. The risks of occasional infections, needle piercing of the abdomen, bleeding, and wound healing in studies done with large amounts of fat removal are less than 1 in 10,000.
- The small dose of lidocaine used for the muscle and fat biopsy is not associated with risks. However all drugs have the risk of an allergic reaction. If you are allergic to lidocaine you must inform the study staff and the biopsy will not be done.

Glucose drink:

- Some people have mild nausea or abdominal discomfort following the glucose drink which may last for 1-2 hours. There may also be headache, shaking, trembling, sweating or low blood sugar.

In addition to the risks listed above, the study drug and procedures may have unknown, unforeseen, or unanticipated side effects. There is always the possibility that you will have a reaction that is currently not known and not expected. All drugs may have the risk of causing an allergic reaction that, if not treated promptly, could be life-threatening. It is important that you report any and all symptoms or possible reactions to your doctor. You will be monitored for side effects by the study staff, and the study doctor may decide that you should be withdrawn from the study. You will be informed of any new and significant side effects, or any other information that may affect your willingness to continue in the study.

Fecal sample

There is a risk of spreading harmful bacteria or viruses from your stool to others with the stool collection, especially if you have an infection of your bowels (enteritis or colitis). This risk can be decreased if gloves the stool collection, including cleaning of hands and collection supplies is done instructed.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you will have a reaction that we do not know about yet and is not expected. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

Are there possible benefits to me?
You will not receive any personal direct benefit from taking part in this study. However, we hope you will participate because the study will generate important information about what changes occur in the body with aging.

What choices do I have other than participating in this study?

You can refuse to participate in the study. If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you.

Your other choices are not to participate in this study.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed.

If you decide to withdraw after receiving the study drug, you should talk with the research study doctor to see how best to complete the withdrawal process.

In addition, you may be asked to return to the research study doctor again for any final tests in order to close the record and tests or monitoring that are necessary for your health as a result of your participation. These results may be recorded.

Can the study end my participation early?

We will not let you participate in the study any more if

- You fail to follow instructions given to you by the research study doctor.
- New information about important medical risks and benefits become available.
- You develop unexpected side effects from the study medicine
- You take medications which are not allowed in the study
- You are unable to take study medicine
- You are unable to complete study procedures
- If the study doctor feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if this decision is made and the reason for it.
- In addition, your participation will end if the investigator or study sponsor stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time

Visit schedule

		Treat-ment A			Wash -out	Treat-ment b		
	Visit 1	Visit 2 0	Visit 3 4 wks	Visit 4 10 wks	2 wks	Phone call: 12wks	Visit 5 16 wks	Visit 6 22 wks
Informed consent	x							
OGTT & eligibility labs ($)	x	Dispense study meds (treat-ment A)		Dispense study meds (treat-ment B)		Start treatment B		
Safety monitoring (*)			x				X	
Plasma for miRNA				x				X
Stored samples for biomarkers,				x				x
Vital signs, height, weight	x	x	x	x			x	x
History & physical	x	Interim history	Interim history	Interim history			Interim history	Interim history
Standard meal test (#)				x				x
Muscle & adipose tissue biopsy				x				x
Fecal collection				x				x
Compensation		**20**	**20**	**200**			**20**	**200**