Title: **Effects of eicosapentaenoic acid on endothelial function in diabetic subjects: a pilot trial**

NCT#: NCT02422446

Date: May 28, 2015

Partners HealthCare System
Research Consent Form

Subject Identification

General Template - Drug Clinical Trial
Version Date: October 2014

Protocol Title: Effects of eicosapentaenoic acid on endothelial function in diabetic subjects: a pilot trial

Principal Investigator: Luc Djousse, MD, ScD

Site Principal Investigator:

Description of Subject Population: Adults aged 30-75 with a diagnosis of type 2 diabetes and elevated triglycerides

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

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.

Why is this research study being done?

This is a pilot study. Pilot studies are done on a small group of subjects to learn if a larger study would be useful.

We are doing this research study to find out if Vascepa (icosapent ethyl), which is an omega-3 that occurs naturally in fish can improve the health of the blood vessels and other markers of

heart disease among people with type 2 diabetes and elevated triglycerides**.** We also want to find out if Vascepa is safe to take without causing too many side effects.

We are asking you to take part in this research study because you have been diagnosed with type 2 diabetes and have high levels of triglycerides. Abnormal changes in blood vessels are frequently seen in people with diabetes. Elevated triglycerides can increase the risk of heart disease, especially among people with diabetes who are already at higher risk of heart disease.

A total of 33 people enrolled at Brigham and Women's Hospital (BWH), will take part in this research study. The Amarin Pharma Inc is providing the drug and paying for this research study to be done.

Vascepa is approved by the U.S. Food and Drug Administration (FDA) to treat elevated triglycerides.

This research study will compare Vascepa to no Vascepa (control).

Amarin Pharma, Inc. is paying for this study to be done.

How long will I take part in this research study?

It will take you about 16 weeks to complete this research study. During this time, we will ask you to make 3 study visits to BWH. We will also call you once a month during the study.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Screening Visit (Visit 1)

The Screening Visit will take about 1 hour. At this visit, we will first obtain your consent to participate in this study. Then we will do some tests to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures (results for blood levels of triglycerides will take few days to arrive). If you don't qualify, the study doctor will tell you why.

We will ask you to fast and refrain from caffeine-containing beverages or tobacco consumption for 12 hours prior to this visit. Only clear liquids are permitted. You may take your morning medications before coming to this visit.

During this visit, we will also:

- Ask you about your medical history
- Draw a blood sample (1 tablespoon)
- Perform endothelial function testing to measure the health of your blood vessel using a digital pulse amplitude device with 2 rubber probes on the surface of your index fingers on both hands while you are lying down. This test will take about 20 minutes. We ask that you come to the visit with short nails on your fingers for this test because long finger nails could tear the rubber probe that we use for this test.
- Ask you about your current medications including any supplements you may be taking

Baseline Visit (Visit 2) – Assignment to a Study Group

We will ask you to fast and refrain from caffeine-containing beverages or tobacco consumption for 12 hours prior to this visit. Only clear liquids are permitted. You may take your morning medications before coming to this visit.

Visit 2 will take about two hours. At this visit, we will:

- Ask you about your medical history
- Draw a blood sample (3 tablespoons)
- Test your urine for pregnancy, if you are a women and able to become pregnant. Pregnant women cannot take part in this research study; if you had a surgical sterilization or are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test
- Perform endothelial function testing using a device to measure the health of your blood vessel using a digital pulse amplitude device with 2 rubber probes on the surface of your index fingers on both hands while you are lying down. This test will take about 20 minutes; We ask that you come to the visit will short nails on your fingers for this test because long finger nails could tear the rubber probe that we use for this test.
- Ask you about your current medications including any supplements you may be taking
- Measure your weight, height, blood pressure, and pulse
- Ask questions about your diet and ask you to complete a questionnaire about your diet

- We will give you a study diary to complete during the next 12 weeks

If you still qualify for the study, we will assign you by chance (like a coin toss) to the Vascepa group or the control group. You and the study doctor cannot choose your study group. You will have **an equal chance** of being assigned to the Vascepa group and control group.

Your study doctor won't know which study group you are in, but s/he can find out if necessary.

Taking the Study Drug
If you are assigned to Vascepa group, we will give you a supply of Vascepa to take home with you. You will take the study drug by mouth, two capsules in the morning with foods and two capsules in the evening with foods for 12 weeks. Use enough water to take the capsules. It is important for you to follow our instructions about how to take the study drug. Bring any unused study drug with you to your next study visit.

If you are assigned to the control group, we will ask you to continue your usual habits and complete all of the study procedures.

Your Study Drug Diary
We will give you a study diary to fill out at home each day. You will write down the date and time you take the 2 capsules of Vascepa, and any side effects you may have after taking those capsules. Bring this diary with you to each study visit, so we can track your progress.
If you are not assigned to Vascepa, we still ask you to write down the date and time of any side effect that you may have. **Example: <u>March 2, 2015 at 9 AM: stomach pain</u>**.

We will ask you to fill out the diary even if you are assigned to the control group.

We will call you once a month to find out if you are experiencing any side effects or health problems, and to remind you about your final study visit.

Final study visit (Visit 3)
Twelve weeks after the second study visit, you will come back to BWH for a final visit. If you were assigned to Vascepa, you will take the study drug for the entire 12 weeks. The third study visit will take about 2 hours.

We will ask you to fast and refrain from caffeine-containing beverages or tobacco consumption for 12 hours prior to this visit. Only clear liquids are permitted. You may take your morning medications before coming to this visit.

During this final study visit, we will:

- Draw a blood sample (3 tablespoons)
- Perform endothelial function testing using a device to measure the health of your blood vessel using a digital pulse amplitude device with 2 rubber probes on the surface of your index fingers on both hands while you are lying down. This test will take about 20 minutes; We ask that you come to the visit will short nails on your fingers for this test because long finger nails could tear the rubber probe that we use for this test.
- Ask you about your current medications including any supplements you may be taking
- Measure your weight, height, blood pressure, and pulse
- Ask questions about your diet and ask you to complete a questionnaire about your diet
- Ask you about any side effects or health problems since your last visit
- Collect any unused capsules of Vascepa if you were assigned to the Vascepa group
- Collect your study diary

After You Complete the Study

After you complete the study, we will refer you back to your own doctor for your ongoing medical care.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

What are the risks and possible discomforts from being in this research study?

Risks of Taking Vascepa

Taking Vascepa may cause you to have one or more of the side effects listed below.

Common side effects:

- Joint pain (2 out of 100 people reported this side effect)

Less common side effects:

- Nausea (3 out of 1000 people reported this side effect)
- Diarrhea (5 out of 1000 people reported this side effect)
- Pain (3 out of 1000 people reported this side effect)

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

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of Vascepa on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control **for the entire study period and six months** after your final visit.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal rings, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)

- abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

Risks of Taking Vascepa with Other Medications

Taking Vascepa with blood thinners together may increase the risk of bleeding and may cause serious side effects. You must stop Vascepa before starting your treatment with any blood thinners.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Pain during the test assessing the health of your blood vessels:
You may have pain on the testing upper arm during this test when the air is put into the blood pressure cuff (as if we were measuring your blood pressure). However, such pain usually goes away few minutes once the blood pressure cuff is released. You may have bruise where the blood pressure cuff was placed.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this research study. If you receive Vascepa, it is possible that your elevated triglycerides may improve while you are taking it.
Others with heart disease may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for my condition?

You do not have to take part in this research study to be treated for elevated triglycerides. Other treatments or procedures that are available to treat elevated triglycerides include: statins (rosuvastatin, artovastatin, fluvastatin, or pravastatin) and other drugs that lower lipids.

Talk with the study doctor if you have questions about any of these treatments or procedures.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

We will pay you $200 if you complete all three study visits. If you do not complete the study, you will not receive any payment.

We will pay for parking in the hospital garage during study visits.
We will pay for the cost of your parking up to $8 for each visit.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

What will I have to pay for if I take part in this research study?

Amarin Pharma Inc is providing the study drug at no cost.

Study funds will pay for study-related procedures (for example: test to examine the health of your vessel, blood levels of triglycerides, diet and health questionnaires), and blood pressure, weight, and height measured during the study visits that are done only for research.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Luc Djousse, MD, ScD is the person in charge of this research study. You can call him at 617-525-7591, M-F 9-5 with questions about this research study.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research

- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: May 28, 2015