UF UNIVERSITY of FLORIDA
The Foundation for The Gator Nation

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273- 9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

Women's Ischemia Trial to Reduce Events in Non-Obstructive CAD (WARRIOR)

3. Who is paying for this research study?

The sponsor of this study is the Department of Defense

4. In general, what do you need to know about this research study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

The purpose of this research study is to determine if intensive medical therapy provided as part of a directed protocol is better than usual medical care in women who have signs and symptoms of suspected ischemia with no evidence of significant blockages in their coronary arteries. Your participation in this study will last until the last patient enrolled has been followed for 36 months.

b) What is involved with your participation, and what are the procedures to be followed in the research?

At the initial visit, if you have not had a cardiac catheterization or a CT Angiogram in the last 5 years, you will be asked to have one done to confirm you do not have any significant blockages in your coronary arteries that would exclude you for this trial. You will be randomly assigned to usual care or intensive medical therapy. You will have a physical examination and vital signs will be recorded. You will be asked to complete several quality of life forms. You will be seen at 3 months then every 6 months for the duration of the study either in clinic or by telephone.

c) What are the likely risks or discomforts to you?

There is the potential that treatment of patients with intensive statin and ACE-I or ARB may result in lowering of blood pressure or other side effects. Risks of drawing blood; Risks of CTA scan; Risks of CT Angiogram with contrast; Risk of side effects from Beta Blocker, Calcium Channel Blocker and Nitroglycerin if used during CT Angiogram; and Reproductive risks.

d) What are the likely benefits to you or to others from the research?

Important knowledge to be gained in the study includes the impact of an intensive statin and ACE-I or ARB strategy vs usual care strategy in patients with signs and symptoms of ischemia with no evidence of significant blockages in their coronary arteries.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

Your provider will determine if you should or should not be treated with medications being used in this study based on your specific medical history.

You have been invited to participate in this research project because you have had symptoms of chest pain and are suspected of or have been found to have no obstructive disease in your coronary arteries.

A description of this clinical trial will be 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.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

5. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

Your provider will make recommendations for treatment based on your individual risk factors and medical conditions.

6. What will be done only because you are in this research study?

You will be one of 4,422 women who are being asked to participate in this study. If you meet the eligibility criteria and after learning about the study and reading this document you agree to provide written informed consent, the following activities will take place. Due to the impact of COVID-19 on social distancing/clinic/institutional policies/your comfort level you may be given the opportunity to do all or some of the study visits using telemedicine (phone or zoom). In order to do these visits virtually and provide the safest experience, the study staff will need you to have the ability to take your blood pressure at home or some other location within 3-5 days prior to the planned visit. In addition, you will be asked to come to the clinic or go to Quest Laboratories to have labs drawn. You will also need internet access to access the consent form and questionnaires, or arrangements will be made to mail these documents to you prior to the planned visits. The preferred type of visit for the yearly visit is to do that visit in person so your physical examination can be completed and your labs drawn, but local recommendations and your preferences will be discussed with you by the study staff.

At the initial visit, after providing written informed consent if you have already had a cardiac catheterization or coronary CT angiogram within the past 5 years you will be randomly assigned, (much like a flip of a coin) to usual care or intensive medical therapy.

If you have not had a cardiac catheterization or coronary CT angiogram within the last 5 years, you will be scheduled to have a coronary CT angiogram at the center you are enrolling at or a local imaging center that can perform the procedure.

A CT scan is an x-ray technique that uses a computer to create cross-sectional (or slice-like) pictures of the heart. The CT scanner is a large X-ray machine that has a short, open-ended tube in the middle (like a very short tunnel). The CT scanner takes x-ray pictures of thin slices of your heart. A computer then puts these images together to make one detailed picture. The CT angiogram consist of 2 scans for this study, one with and one without contrast and will be done at the Baseline visit.

On the day of the CT angiogram, you should continue to take your medications as usual, including any diabetes and blood pressure medications. You will have 2 scans, one with and one without the use of contrast. Contrast material is a dye which makes blood vessels and organs easier to see on x-rays. A CT scan with contrast can detect blockages (calcium build up) in the heart arteries. A CT scan with contrast is called a CT Angiogram.

CT Angiogram (CT Scan with Contrast)

You will have this CT scan immediately after the CT scan without contrast. You will remain on the CT scanning table and we will insert a tube into a vein in your arm (an IV catheter) in which we will inject the contrast. Then, you will have a CT scan of your heart (CT angiogram). A CT angiogram can detect (find) calcium in the heart arteries in more detail than the CT scan without contrast.

Lower heart rates (the speed with which the heart beats and pumps blood) allow the CT scan to take clearer pictures. Therefore, if necessary, we may give you either an oral (by mouth) and/or IV (injected into a vein) medication called a beta-blocker (metoprolol) that will lower your heart rate just before the scan. Beta-blockers are medications that are often used to treat high blood pressure or fast heart rhythms. You may receive more than one dose by pills or IV over about 60 minutes before the scan.

If your heart rate is not slow enough with the beta-blocker medication, or if you are not able to take beta blocker medications, you might receive a calcium channel blocker medication called diltiazem, which also slows the heart rate.

We also may give you the medicine, nitroglycerin during the CT scan to place under your tongue just before the pictures are taken. Nitroglycerin dilates (widens) the heart arteries. We will check your blood pressure and heart rate often during and after receiving these medications.

The CT scan procedure takes around 45 minutes. Since you will need to arrive earlier to have an IV catheter placed and to possibly receive medication to slow your heart rate, the entire procedure will take around 1 hour.

A cardiologist (doctor who is a heart specialist) will review your CT scans. We will give you and your primary physician (if you request) the results of the CT scans of the heart.

If the images reveal significant blockages in your coronary arteries, you will no longer eligible to participate in the study.

The CT scans will be provided to you and or your physician so that they can determine the need for further evaluations or additional testing as part of normal standard of care.

If an unexpected important result is found which does not involve the coronary arteries, the CT scans and findings from the CT angiogram will be made available to the you and your physician so it can determine if further evaluations or additional testing as part of normal standard of care.

If the CT results confirm your eligibility you will return to the clinic to be randomly assigned to usual care or intensive medical therapy. You will be asked questions about your medical and surgical history. Copies of recent cardiac evaluation tests will be collected and results recorded. You will be asked to fill out a release of medical record form in the event you are hospitalized at an outside facility the study staff can obtain those records so we can accurately record what happened and report that to the study. You will have a physical examination if it is an in person visit, and vital signs will be recorded at all visits. You will be asked to complete several quality of life forms on an electronic tablet during the clinic appointment or these will have been mailed to you. Approximately 3 tablespoons of blood (45 cc) will be drawn to store in the biorepository. Regardless of group assignment you will have blood drawn to test your fasting cholesterol profile and hemoglobin A1c (HbA1c). These labs will need to be drawn at the clinic and/or QUEST. If you are randomized to Intensive Medical Therapy (IMT) and if you have never taken a statin, a baseline liver panel (ALT) will be drawn, and if you are not currently taking an ACE/ARB a basic metabolic profile (BMP) will be drawn approximately 1 week after initiation of medication therapy. You may come to the clinic or go to QUEST to have this done.

If you are randomized to IMT and able to become pregnant (have not gone through menopause, had a hysterectomy, oophorectomy, or sterilization such as a tubal ligation procedure) a urine pregnancy test will be performed at the office/clinic or at your home (a pregnancy test will be mailed to you and you will have to provide the test via zoom to the study staff) at the baseline visit. You will be asked to come back to the clinic for your next evaluation at 3 months and every 6 months for up to 66 months either as an in person visit or by telemedicine.

IMT participants will receive lifestyle recommendations based on the Patient-centered Assessment and Counseling for Exercise and nutrition (PACE) program. Study coordinators will provide specific behavioral counseling focusing on smoking cessation, diet, physical activity and weight management at baseline and each follow up visit. Assessment of your readiness to change will be done using several surveys.

Details of the visits are listed below.

If you are randomized to the intensive medical therapy, you will receive study medication unless you and your study doctor agree to continue with your current medications.

This therapy will consist of three classes of medications that are approved and used to treat cholesterol, lower blood pressure and reduce risk of cardiovascular events. One is a high potency cholesterol medication (statin), either atorvastatin at 40 or 80 mg or rosuvastatin at 20 or 40 mg to be taken once a day. In addition, you will be prescribed either lisinopril 10-80 mg or losartan 50-100 mg once daily or in divided doses depending on your blood pressure and other medical conditions. Any of these medications may be decreased or increased depending on your response to the medications. Your other medications may also be adjusted if you are currently on other medications that may lower your blood pressure. The third medication is low dose aspirin 81 mg taken daily.

If your study doctor is located in the state of Florida, all three of these medications (atorvastatin or rosuvastatin AND lisinopril or losartan AND Aspirin) will be prescribed and mailed to your home address. If your study doctor is located outside the state of Florida, two of the medications (atorvastatin or rosuvastatin AND lisinopril or losartan) will be available from a designated pharmacy. The site consent addendum will outline how you will be provided the $10 so that you can obtain a year's supply of aspirin 81 mg from a local retailer like Walmart, CVS, Target. You will receive standardized lifestyle instruction to target risk reduction.

If you are intolerant to statins or if your doctor has concerns regarding your cholesterol, it may be recommended that you take a PCSK9 inhibitor. This will not be provided by the study, however it is covered by most insurance plans.

If you are randomized to the Intensive Medical Therapy (IMT) arm, you will be given the choice to stay on your current medical regimen or switch to the IMT specific medications and dosages to receive study medication. However, if you choose to stay on your current medical regimen, these medications will not be provided by the study and the dosages may need to be modified so that you are taking high dose statin therapy and effective doses of the ACE or ARB.

If you are randomized to the Usual Care (UC) directed Medical Therapy arm, your medications will be reviewed by your provider and recommendations will be made based on an assessment of your risk status. You will receive standardized lifestyle instruction to target risk reduction.

Follow up Visit at 3 months followed by every 6 month visits

1. Medical status assessment.
2. For an in person visit, a physical exam and collection of vital signs will be performed. For telemedicine visits, you will need to take your blood pressure at home either 3-5 days before the visit or on the day of the visit.

3. Lifestyle assessment and counseling will be performed.
4. Quality of Life (QOL) assessment will be collected by logging into the data collection system or by sending you the surveys to complete on paper and return by mail if you do not have internet capability.
5. Hospitalization and health care utilization information will be collected.
6. Biorepository blood draw will be performed if not done previously at randomization.
7. Once per year, a fasting blood sample will be collected and processed at the clinic or an outside lab to measure your cholesterol profile and hemoglobin A1c.
8. At each 6-month appointment, if you are assigned to the IMT group, you will receive a refill of your medications. Your study medication will be sent to you by a mail order pharmacy or dispensed at the visit by the research pharmacy.

Close out visit (in addition to all assessments for the regularly scheduled visit)

1. Full QOL assessment will be collected
2. Endpoints will be collected

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 1 on the addendum.

Storing your medical information and contact information for future studies

We wish to store your excess blood samples and the medical information we collect as part of your participation in this study and potentially use it in future research. Many different kinds of research use blood samples and medical information to answer new research questions. We will also store your contact information so that we may contact you in the future regarding other research studies you might be interested in participating.

Your blood samples and medical information will be kept in a secure location at the University of Florida. There is no direct benefit to you by allowing us to keep your blood samples and medical information. Although every effort will be made to keep your information confidential, there is a small risk that an unauthorized person may obtain your information. Therefore, there is a very slight risk that a test result could be linked to your identity and inadvertently disclosed to a third party.

The University of Florida will be allowed to collect, use and/or share your blood samples and medical information with other researchers whose research is approved by an Institutional Review Board (IRB) (An IRB is the oversight organization responsible for looking after the rights and welfare of people taking part in research).

Investigators may also share your blood samples and medical information with the study sponsor, the Food and Drug Administration, the Department of Health and Human Services, the Office of Human Research Protections, or other Government agencies.

Your blood samples and medical information may be shared with other research centers or private companies, in which case the University of Florida may charge the research center or private company a fee in order to recover the University of Florida's costs of sharing your blood samples and medical information. There is a risk that information received by these authorized persons or agencies could then be passed on to others beyond your authorization and not covered by the law.

There is a Federal law, called the Genetic Information Nondiscrimination Act (GINA), that makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

Research Monitor

The Research Monitor, Puja Mehta, MD, FACC, FAHA is responsible for overseeing the safety of the research and reporting observations/findings to the IRB or a designated institutional official. The Research Monitor will review all unanticipated events involving risks to subjects or others associated with the protocol and provide an independent report of the event to the IRB.

The Research Monitor may discuss the research protocol with the investigators; shall have the authority to stop a research protocol in progress, may remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report; and shall have the responsibility to promptly report their observations and findings to the IRB or other designated official and the Human Research Protection Office (HRPO) . Dr. Mehta may be reached by calling (352) 273-7901.

7. How long will you be in this research study?

Your participation in this study will last until the last patient enrolled has been followed for 36 months. Women enrolled early in this study may be followed up to 5.5 years.

8. How many people are expected to take part in this research study?

It is anticipated that up to 4,422 women will participate in this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

9. What are the possible discomforts and risks from taking part in this research study?

Screening Coronary CT Scan and Angiogram:

You will be asked to sign a clinical procedure consent form prior to this procedure. You'll be exposed to some radiation during the test. The amount varies depending on the type of machine used. For most people the dose from each set of CT scans will be about twice the amount you get from natural background radiation (sun and earth) each year. Your dose may be higher or lower based on your size, your heartbeat and the CT scanner. To put the total dose from a set of CT scans in further context, it is similar to the radiation dose from a cardiac imaging stress test (another test commonly used to detect heart disease) and much less (about 10%) of the maximum allowed exposure for radiation workers such as x-ray technicians, radiologists and nuclear plan technicians. The lifetime risk of lung cancer for men and women is 7%. The lifetime risk of breast cancer in women is 12%. Each set of CT scans add a very small theoretical risk of 0.05% IV contrast is given during the CT angiogram procedure and has some risks. Often people will feel a sensation of warmth and mild discomfort during the injection.

Other possible risks that occur infrequently (occur in about 3 in 100 people) include irregular heart rhythms, chest pain, low blood pressure, dizziness, temporary vision changes, headache, nausea and vomiting, itching, hives or flushing.

Severe reactions to contrast dye are uncommon and occur in less than 1 in 1,000 people. Serious reactions can include difficulty breathing and anaphylactic shock (low blood pressure and severe problems with breathing). Anaphylactic shock is extremely rare but can result in death. To minimize this risk, you will not be allowed to join this study if you have a known allergy to CT contrast dye. In the event that you experience an allergic reaction to CT contrast, a physician will be present during the scan to give you medical treatment. Talk to your Doctor if you're concerned of having an allergic reaction.

There is also a small risk of kidney damage occurring as a result of the contrast dye. Such damage is also rare and is usually, but not always, reversible. Since the risk of kidney damage is higher among persons with abnormal kidney function, the doctor will review the result of the blood test of your kidney function to determine if it is safe for you to undergo a CT with contrast.

To reduce the risk of kidney damage, we will ask you to drink one liter of water the night before your CT scan to prevent dehydration.

Less common risk includes extravasations or “leaking” of the X-ray contrast material outside the vein during injection. This may result in painful soft tissue (skin or just under the skin) swelling and bruising.

If you're pregnant it is recommended that you do not undergo this test because of possible harm to your unborn child.

Beta-blocker (metoprolol): Beta-blocker medication (metoprolol) may be necessary if you undergo a cardiac CT scan with contrast, and there is a need to lower your heart rate. Side effects from beta-blockers used for CT scans are rare, and may include abnormally low heart rates, low blood pressure, dizziness, breathing problems, or an allergic reaction. We will observe you closely for any of these effects. If you have a history of severe lung or breathing problems or asthma, we will not give you a beta-blocker medication.

Calcium channel blocker (Diltiazem): If your heart rate is not slow enough with the beta-blocker medication or you are not able to take beta blocker medications, you might receive a calcium channel blocker medication called diltiazem, which also slows the heart rate but is less likely to cause breathing problems in people with lung disease. Side effects of diltiazem include slow heart rate and rarely dizziness.

Nitroglycerin: Nitroglycerin may be given if you have a cardiac CT scan with contrast. Nitroglycerin dilates (widens) the heart arteries. Nitroglycerin can sometimes cause a headache or low blood pressure, but if either of these occurs, it is usually brief in duration. Again, we will observe you closely for any of these effects.

Reproductive Risks: Because the medicines in this study could harm an unborn baby, you should not become pregnant while on this study. You should not nurse your baby while in this study. Ask about counseling and more information about preventing pregnancy.

A urine pregnancy test is not as sensitive as a blood pregnancy test and a negative urine test does not completely rule out an early pregnancy in progress.

If you have any questions about these or other risks, please ask the study staff.

Risks of Blood Draw: Your blood will be drawn by venipuncture (putting a needle into a vein), the same method used for regular lab blood draws. However, your blood will be used for research and you will not get any results. The risks of drawing blood from a vein include: discomfort where the needle was inserted; infection (rare); and feeling faint from the blood draw (uncommon).

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information

can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

Intensive therapy of potent statin plus ACE-I or ARB: There is the potential that treatment of patients with intensive statin and ACE-I or ARB may result in lowering of blood pressure or other side effects associated with each individual medication. These medications will be clinically indicated and close follow up should minimize potential risks.

Atorvastatin: Common side effects are diarrhea, upset stomach, muscle and joint pain, and fatigue. Allergic reactions can occur including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing, which may require treatment right away. Elevation in liver enzymes may result in brown or dark-colored urine, more fatigue than usual, yellow coloring of eyes. There is the potential of statin-induced myalgias, which are benign, or rarely statin-induced rhabdomyolysis which can be fatal, with the use of fixed dose potent statin therapy.

Rosuvastatin: Common side effects are headache, depression, muscle aches or pains, joint pain, sleep problems, constipation, nausea, stomach pain, indigestion or diarrhea. Infrequent but serious side effects include rhabdomyolysis (muscle damage or destruction) that can lead to acute renal failure and liver damage.

Lisinopril or Losartan: Common side effects are dry cough, headache, dizziness, nausea, excessive fatigue, or weakness. More severe, but less common are swelling of the face, throat, tongue, lips, feet, ankles or lower legs, hoarseness, difficulty breathing or swallowing. Women should not take if trying to become pregnant.

Aspirin: Common side effects are rash, gastrointestinal ulcerations, abdominal pain, upset stomach, heartburn, drowsiness, headache, cramping, nausea, gastritis, and bleeding.

Quality of Life Questionnaires: Some of the questions in the quality of life questionnaires may ask you to consider areas of your life about which you may not commonly think about. There are no physical risks from completing the survey, but the questions could cause you concern or emotional distress.

Personal Information: Taking part in this research may involve providing information that you consider confidential or private. Efforts such as coding research records, secure passwords, encrypted electronic storage, and allowing only authorized people to have access to research records, will be made to keep your information safe. Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 13- 17 in this form discuss what information about you will be collected, used, protected, and shared.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 1 of the addendum or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may

become available and might affect your decision to remain in the study. If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 1 of the addendum form.

If you wish to discuss the information above, please ask questions by email or call the study coordinator listed in question 1 of the addendum.

Certificate of Confidentiality: To help us protect your privacy, we have requested a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

10a. What are the potential benefits to you for taking part in this research study?

All patients will receive lifestyle counseling which may improve overall health.

10b. How could others possibly benefit from this study?

Important knowledge to be gained in the study includes the impact of an intensive statin and ACE-I or ARB strategy vs a primary risk factor strategy in subjects with signs and symptoms of ischemia but non-obstructive CAD.

11. What other choices do you have if you do not want to be in this study?

If you do not want to participate in this study, your care will be managed as it normally

would by your doctor. You can get these medications without participating in this study.

Your participation in this study is voluntary and any decision to take part or not to participate in the study will in no way affect the quality of your care.

12a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you request to be withdrawn the study staff will ask you if you are willing to allow for limited follow up so that the study can check in to see your general health status on an annual basis even if you choose not to continue with study visits.

The status of all patients who entered into the study is important to help the researcher answer the questions posed in this study.

In order to improve their ability to answer the questions, all patients who agreed to participate but withdrew or who were lost to follow up will have their health status assessed by searching the National Death Index at the end of the study.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 1 of the addendum. If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office listed on the "Consent Addendum" attached.

12b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from this study, no further information will be collected. Any information already collected during your participation may still be used.

12c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- At the discretion of the Principal Investigator or study physician based on what is best for your health and safety.
- New information suggests that taking part in the research study may not be in your best interests.
- The sponsor or the Principal Investigator has decided to stop the study for any other reason.
- You may also be withdrawn from the study if you do not follow the instructions given to you by the study team.

13. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization. The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study.

This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests.

This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information, obtained at each clinic visit during the study, may be collected, used, and shared with others:

- Diagnosis codes
- Complete medical history
- Medical Record Identifiers
- First and last name
- Address
- Contact information
- Date of birth
- Laboratory test results
- Cardiac evaluation tests (CT angiogram, cardiac catheterization)
- Social history (smoking/alcohol/drug use)
- Medication name and dose lists
- Data regarding any adverse effects reported during the study
- Collection of Social Security Number
- Information regarding emergency room visits
- Information regarding unscheduled office visits
- Medical Record Number
- Quality of Life Questionnaires

This information will be stored in locked filing cabinets or on computer servers with secure passwords or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set.

If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

14. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study.

More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- To determine if you are eligible for the study.
- To evaluate the safety and effectiveness of intensive medical therapy versus usual medical care in women with non-obstructive disease in coronary arteries.

Once this information is collected, it becomes part of the research record for this study.

15. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows.

These people include:

- the study Principal Investigator (listed in question 1 of the addendum) and research staff associated with this project.
- other professionals at the institution where you are participating in this research study.
- Your institution's IRB (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research) and the University of Florida Institutional Review Board which is responsible for the approval of this research study.

16. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- The study sponsor (listed in Question 3 of this form).
- University of Florida Division of Cardiology Coordinating Center
- The OneFlorida Consortium Staff
- Investigators at Cedars Sinai Hospital in Los Angeles CA

- Pharmacy at the University of Florida or the local Research Pharmacy
- United States governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections.
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- The Department of Defense representatives
- The Data Safety and Monitoring Committee and/or Designated, Independent Research Monitor
- The Clinical Endpoints Committee

Otherwise, your research records will not be released without your permission unless required by law or a court order.

It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

17. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until the end of this study.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study.

However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study.

If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

Since this research study is being conducted at several institutions, there is an Institution Specific "Addendum" to this consent form. Please read this addendum prior to agreeing to participate in this research study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study:

Signature of Person Obtaining Consent and Authorization _____ Date _____

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing _____ Date _____