APPROVED
AS MODIFIED
Sep 10, 2012
WIRB®

*Cardiovascular Institute of the South*
*20121250*

| RESEARCH SUBJECT INFORMATION AND CONSENT FORM | |
|---|---|
| **TITLE:** | The Effects of Ranolazine on CPET Parameters in Ischemic Cardiomyopathy Patients (ERIC) |

**This consent form contains important information to help you decide whether to participate in a research study.**

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You can take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – your choice.**
- **If you join this study, you can still stop at any time.**
- **No one can promise that a study will help you.**
- **Do not join this study unless all of your questions are answered.**

## After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

## Please read this consent form carefully.

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**RESEARCH SUBJECT INFORMATION AND CONSENT FORM**

| | |
|---|---|
| **TITLE:** | The Effects of Ranolazine on CPET Parameters in Ischemic Cardiomyopathy Patients (ERIC) |
| **PROTOCOL NO.:** | None<br>WIRB® Protocol #20121250 |
| **SPONSOR:** | Cardiovascular Institute of the South |
| **INVESTIGATOR:** | Agostino Gus Ingraldi, M.D.<br>2730 Ambassador Caffery Pkwy<br>Lafayette, Louisiana 70506<br>United States |
| **SITE(S):** | Cardiovascular Institute of the South<br>2730 Ambassador Caffery Parkway<br>Lafayette, Louisiana 70506<br>United States<br><br>Cardiovascular Institute of the South<br>Suite B<br>443 Heymann Blvd<br>Lafayette, Louisiana 70503<br>United States |
| **STUDY-RELATED PHONE NUMBER:** | Agostino Gus Ingraldi, M.D.<br>Cindy Landry, L.P.N., C.C.R.C.<br>337-988-1585 (24 hours) |

**Introduction to a research study**

We are asking you to be in a research study. Sometimes research studies are also called clinical trials.

The main goal of most research studies is to learn things to help people in the future.

A person who is in a research study is usually called a "subject" (or a "participant" or "volunteer"). A subject has to consent (agree) to be in a research study by signing a consent form.

This consent form will help you decide if you want to be a subject in this study. Please read this consent form carefully and completely. Ask us to explain any words or information that you don't understand.

You can take home an unsigned copy of the consent form so you can think about the study and talk to your family and friends before you decide if you want to be in the study.

**What you should know before you decide to be in this study**

- You will be in the study for about eight weeks (two months).
- We expect about 50 subjects to be in the study.
- You don't have to be in this study. You can also leave the study without giving a reason.
- This study might include standard medical treatment or care that is normally given for a condition or illness.
- This study might include an investigational drug or procedure. "Investigational" means that the United States Food and Drug Administration (FDA) hasn't approved the drug or procedure.
- Before you decide to be in this study, you should know what part of the study (if any) is investigational.
- Your medical or other records might become part of the research record for this study. If that happens, people and groups associated with the study might look at or copy your records.
- We might bill your health insurance for any standard medical care you receive in this study. Your health insurance might then have access to the research records.
  Your health insurance might not pay for treatment, care, or services that are part of a research study. Being a subject in a research study could also affect your current or future health insurance coverage.
- We will give you a signed and dated copy of this consent form if you decide to be in the study.

**Why are we doing this study?**

***Background***

Coronary heart disease (CHD) is a leading cause of death and disability in the United States and other developed countries. Close to 18 million people in the U.S. have CHD, and about 23 million people worldwide have heart failure. Heart failure has many causes, but the most common cause is ischemia from CHD. "Ischemia" means that a body part such as the heart or brain doesn't get an adequate supply of blood.

Ischemia in heart muscle causes a number of problems. Eventually the heart doesn't fill properly with blood during the relaxation phase of the heartbeat (called diastole), and this in turn means the heart does not have enough blood to pump to the rest of the body.

***Study Purpose***

We want to study the possible benefits of a drug called Ranexa® (ranolazine) in patients with ischemic heart disease by using cardiopulmonary exercise testing (CPET). CPET measures how your lungs and heart work while you exercise on a stationary bike or treadmill.

The United States Food and Drug Administration (FDA) has approved Ranexa® for use in patients with coronary artery disease (CAD). The drug is mainly used to reduce angina (chest pain).

Ranexa® is believed to improve relaxation during diastole. This may reduce the demand for oxygen and decrease the oxygen supply-demand mismatch that happens with ischemia. Improving this mismatch should make the heart work more efficiently, which in turn will allow exercise capacity to increase before symptoms develop.

Unlike a treadmill test alone, CPET measures the exchange of oxygen and carbon dioxide and provides a direct assessment of the amount of energy used. CPET is recognized as the gold standard for heart function/exercise capacity testing because it directly measures the amount of oxygen inhaled and the amount of carbon dioxide exhaled during exercise.

CPET can accurately assess heart function and detect improvements in function more precisely than exercise studies that don't measure the exchange of oxygen and carbon dioxide.

With this study, we hope to show that:

- Ranexa® will improve heart function that can be objectively assessed with CPET
- improvement in CPET results with Ranexa® will translate into improved outcomes for patients, including improved quality of life

**What will happen in the study?**

If you decide to be in the study, you will have a CPET evaluation to verify that you have ischemia. This first CPET evaluation will also serve as a baseline for the study.

If this first CPET shows that you qualify for the study, we will start you on 500 mg of Ranexa® twice a day. The next week we will double the dose to 1000 mg twice a day.

After you take the higher dose for four weeks (one month), you will have a second CPET. We will compare the results of the two CPETs to assess any changes that happened while you took Ranexa®.

We will call you after you have taken 500 mg for one week and 1000 mg for one week to make sure you are tolerating Ranexa® and taking it as directed.

There will be no other changes in medication during the study and no heart procedures. You will have to stop being in the study if you need a medication change or a heart procedure.

At your study visit for the second CPET, we will count the number of Ranexa® tablets to make sure you have taken the correct amount. If you don't take Ranexa® as directed, you might have to stop being in the study.

In addition to measuring improvement in heart function and exercise tolerance, we also want to see if you think Ranexa® improves your quality of life. To do this, we will have you fill out a questionnaire.

***CPET***

During the CPET, you will exercise on either a stationary bike or treadmill.

We will put a number of sticky pads called electrodes on various areas of your chest so that we can do an electrocardiogram (EKG) while you exercise. An EKG measures the heart's electrical activity.

We will also monitor your blood pressure and oxygen with a blood pressure cuff on your arm and a small oxygen-measuring device called an oximeter clipped to your finger. You will also wear a mask over your mouth and nose to measure the exchange of oxygen and carbon dioxide.

We will monitor you during the entire exercise test, and emergency drugs and equipment are on hand if you have any trouble during the test.

**What are your responsibilities during the study?**

During the study, we expect you to

- Follow the instructions we give you
- Store your Ranexa® tablets at room temperature
- Take Ranexa® as directed (it can be taken with or without meals)
- Swallow the Ranexa® tablets whole—don't crush, break, or chew them
- Let us know if you can't keep a study appointment or won't be available for a phone call

For the CPETs

- Don't eat for two hours before the test
- Don't smoke or have caffeine before the test
- Wear comfortable clothes and shoes for the test

**Will being in this study involve risk to you?**

The risks for both CPET and Ranexa® are listed and discussed below.

***Risks from CPET***

The risks from CPET can include

- Irregular heart beat (arrhythmia)
- Chest pain (angina)
- Heart attack (myocardial infarction [MI])
- Orthopedic injury
- Death

These risks are generally rare when the test is properly monitored, and emergency equipment and drugs are available for problems.

***Risks from Ranexa®***

Ranexa® can prolong the heart's QT interval, which is a serious side effect that could lead to heart rhythm changes that might be fatal.

The most common side effects of Ranexa® are less serious and include

- Dizziness
- Headache
- Constipation
- Nausea

Other less common side effects reported with Ranexa® include the following:

- slow heart beat (bradycardia)
- heart palpitations
- ringing in the ears (tinnitus)
- vertigo
- blurred vision
- abdominal pain
- dry mouth
- vomiting
- indigestion (dyspepsia)
- weakness (asthenia)
- swelling in the arms and legs (peripheral edema)
- loss of appetite (anorexia)
- fainting (syncope)
- confusion
- blood in the urine (hematuria)
- trouble breathing; shortness of breath (dyspnea)
- excessive sweating, especially hands and feet (hyperhidrosis)
- low blood pressure (hypotension) and a drop in blood pressure when standing after either sitting or lying down (orthostatic hypotension), which can cause faintness or dizziness

***Other Risks***

In this study, we are using Ranexa® for a use other than its FDA-approved use, so there might be risks or side effects that we don't know about yet.

Ask us if you have any questions or want more information about possible risks and side effects.

**Will being in this study help you?**

Your heart function and exercise tolerance might improve while you are in this study. But we can't promise this. We can't promise that you will have any medical benefit from being in this study.

But what we learn from this study might help people with CHD in the future.

**Will it cost you to be in this study?**

You won't have any additional costs from being in this study. The study will pay for both Ranexa® and the CPET.

You might have unexpected expenses from being in this research study. These charges might be submitted to your health insurance. However, your health insurance might not pay these charges because you are in a research study.

In addition, if you are injured as a direct result of being in this study, your insurance company might not pay to treat these injuries.

Ask the study doctor to discuss the costs that will or will not be covered by the sponsor. We also encourage you to determine your health insurer's policy about paying for treatment in a research study.

**Will you be paid to be in this study?**

No, we won't pay you to be in this study.

**What if you are injured or get sick from being in this study?**

If you are injured or get sick from being in this study, we will either treat you or refer you for treatment.

You or your health insurance will be billed for the cost of any treatment for injury or illness. Cardiovascular Institute of the South does not plan to compensate you for any injury or illness or for lost time or earnings.

You don't give up any of your legal rights if you sign this consent form.

**What if we learn important new information while you're in the study?**

We will tell you about any new information that might change your decision to be in this study. We might ask you to sign a new consent form that includes this information.

**What are your options if you decide not to be in this study?**

You don't have to be in this study to receive treatment for CHD. You also don't have to be in the study to have CPET. You can have both standard care treatment and CPET for CHD outside of the study.

We will talk with you about your other treatment options.

**Do you have to be in this study?**

No, you don't have to be in this study. Being in this study is your choice. You can decide not to be in the study, or you can leave the study at any time. You don't have to give a reason. Whatever you decide, you won't be penalized or lose any benefits.

We can also take you out of the study at any time and for any reason without your agreement. We might do this if

- We think leaving the study is best for you
- You don't agree to stay in the study after we tell you about changes in the study that might affect you
- You don't take all of the prescribed Ranexa® or you don't take it as directed
- You need a change in medication or a heart procedure not allowed by the study

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.

**AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES**

**What information may be used and given to others?**
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

**Who might get this information?**
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

**Your information <u>may</u> be given to:**

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Cardiovascular Institute of the South
- Western Institutional Review Board® (WIRB®)

**Why will this information be used and/or given to others?**

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

**What if I decide not to give permission to use and give out my health information?**
Then you will not be able to be in this research study.

**May I review or copy my information?**
Yes, but only after the research is over.

**May I withdraw or revoke (cancel) my permission?**
Yes, but this permission will not stop automatically.
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

**Is my health information protected after it has been given to others?**
There is a risk that your information will be given to others without your permission.

**What if you have questions or want more information?**

You can ask questions about this study at any time.

You can also call us (Agostino Ingraldi, M.D., or Cindy Landry, L.P.N, C.C.R.C.) at 337-988-1585 (24 hours) if

- you have questions about this study or your part in it
- you think you have a research-related injury, problem, or reaction to Ranexa®
- you have concerns or complaints about this study

You can also contact the Western Institutional Review Board® (WIRB®) if

- you have questions about your rights as a research subject
- you have questions, concerns, or complaints about this study

WIRB is a group of people who independently reviews research studies in the United States and around the world.

WIRB won't be able to answer some types of questions, such as questions about study appointment times. But you can contact WIRB if you can't reach the study staff or if you want to talk to someone other than the staff.

WIRB's contact information is listed below:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

**Is there anything else you should know?**

- Don't sign this consent form unless you were able to ask questions and someone answered your questions to your satisfaction.

- We will give you a signed and dated copy of this consent form to keep.

**My consent to be in the study**

My signature on this consent form means that

- I read this consent form (or someone read it to me).
- The study doctor or study staff answered all my questions about the study and my part in it.
- I authorize the release of my study and/or medical records to the study doctor, Cardiovascular Institute of the South, the FDA, DHHS agencies, government agencies in other countries, and WIRB.
- I don't give up any of my legal rights by signing this consent form.
- I agree (consent) to be in this research study.

***Consent Instructions***
*Consent: Subjects able to provide consent must sign on the subject line below.*

_____
Subject Name (printed)

_____ _____
Signature of Subject Date

**---------- Use this witness section only if applicable ----------**

*If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:*

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject.

The subject freely consented to be in the research study.

_____ _____

Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for subjects who do not speak English.

**Attestation Statement**

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered his or her questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

| _____ | _____ |
|---|---|
| Printed Name of Person Conducting the Informed Consent Discussion | Position |
| _____ | _____ |
| Signature of Person Conducting the Informed Consent Discussion | Date |