

**University of Wisconsin
Research Subject Information and Consent Form**

**A Randomized, Double-Blind, Placebo-Controlled Trial of
Spironolactone versus Eplerenone in Patients with Mild to
Moderate Heart Failure**

Investigator:

[name and contact information]

INVITATION/SUMMARY

You are invited to participate in a research study about medications used to treat heart failure. You are invited because you have mild or moderate heart failure. Your participation is voluntary. Approximately 4869 subjects will participate in this study, and ___ will be enrolled at this institution.

You are invited to participate in a research study. Participation in this study is voluntary, so you do not have to participate if you do not want to. In this study, we are testing two drugs used to treat heart failure called spironolactone and eplerenone to see if they help people with mild or moderate heart failure. Both spironolactone and eplerenone are approved by the Food and Drug Administration for the treatment of people with high blood pressure, but we do not know whether these drugs would help people with mild or moderate heart failure. If you are eligible to participate and agree to participate in this study, you will be assigned by chance (like the flip of a coin) to either spironolactone or eplerenone or an inactive substance called a placebo (a sugar pill). Neither you nor your study doctor will know which of these you receive until the end of the study. We would like to follow your progress on the study medication for about three years. This study will have no more than 12 visits to the cardiology clinic, unless your doctor thinks your medical condition needs to be checked more often. The first visit will last about 2-3 hours, but all of the others will be about 1 hour.

Everyone in the study will have physical examinations, procedures to check the functioning of your heart, and needlesticks for blood tests during the study. The main risk of spironolactone is breast pain or sexual side effects. Eplerenone has the same side effects, but they happen less often. We also don't know if these drugs are dangerous for fetuses (unborn babies) so pregnant women can not be in the study.

There are other drugs that work in the treatment of heart failure, so most people don't need to be in the study to get treatment. If you decide to join the study, you can change your mind or stop at any time. If you do not participate or stop participating, it will not affect your medical care at this [hospital or clinic]. If you join the study, there will be no charge to you for any of the study drugs, tests, or clinic visits related to the study.

There is more detailed information about this study on the following pages. If you have any questions, please call [phone number].

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to determine which of two drugs, spironolactone or eplerenone or an inactive substance (placebo) works better in people with mild to moderate heart failure.

WHAT WILL MY PARTICIPATION INVOLVE?

If you decide to participate in this research study, you will be assigned by chance (like the flip of a coin) to receive either spironolactone or eplerenone or a placebo. Neither you nor your doctor will know what you receive. This study will last about three years, and will involve about 12 visits to the cardiology clinic.

If you are interested in joining this study, we will find out if you are eligible to participate. We will ask you questions about your medical history and perform some tests on your heart. You will have a physical examination by one of the study doctors. You will have a needlestick to take about two teaspoons of blood. We will use the blood to test your liver and kidney function. If you have not had a procedure called an echocardiogram or “echo” in the last six months, we will do this procedure to test how well your heart pumps blood. This test does not hurt.

After these procedures, if you are eligible to participate and agree to participate, you will be given a pill which you should take once every day. You will have to come to the cardiology clinic regularly. When you come to the clinic, we will check your vital signs, like weight and blood pressure, and do blood tests (needlesticks) to monitor your progress. This visit will last about 1 hour. Every three months, we will also ask you to fill out a questionnaire about how your heart failure affects your daily life. If you are not coming to clinic for blood tests, we will send you the questionnaire by mail. The study schedule is outlined in the table below.

Study Schedule	Time
<ul style="list-style-type: none">• Visit to see if you are eligible to participate	
<ul style="list-style-type: none">• Assignment to one of the drugs• Quality of life Questionnaire	Day 1 of participation
<ul style="list-style-type: none">• Weight, Blood Pressure, Blood tests	Week 4 of participation
<ul style="list-style-type: none">• Weight, Blood Pressure, Blood tests	Week 8 of participation
<ul style="list-style-type: none">• Weight, Blood Pressure, Blood tests• Quality of life questionnaire	Week 12 of participation
<ul style="list-style-type: none">• Weight, Blood Pressure, Blood tests• Quality of life questionnaire	Month 6 of participation
<ul style="list-style-type: none">• Weight, Blood Pressure, Blood tests• Quality of life questionnaire	Month 9 of participation

<ul style="list-style-type: none"> • Weight, Blood Pressure, Blood tests 	Month 12 and every six months after that, unless your doctor thinks your medical condition should be checked more often
<ul style="list-style-type: none"> • Quality of life questionnaire 	Month 12 and every three months after that (On the months when you do not come to clinic for blood tests, we will send you the questionnaire by mail)

In the case of an emergency, we can find out which study medication you have been receiving. However, even if this happens, we would like your permission to continue to follow your progress with your heart by looking at your medical records.

ARE THERE ANY RISKS?

Physical Risks of Spironolactone:

The most common side effects (10% of patients or less) associated with spironolactone include the following:

- Breast pain or tenderness
- Breast swelling in men, which will go away if the drug is stopped
- Decreased sexual interest
- Irregular menstrual periods in women
- Decreased sexual function
- Mildly elevated potassium in your blood, which does not cause any symptoms

The following are less frequent:

- Moderately elevated potassium in your blood, which may cause symptoms such as nausea or irregular heartbeat

These side effects are rare:

- Very elevated potassium in your blood, which may cause life-threatening irregular heartbeats
- Allergic reaction, which may be life-threatening
- Other drug reaction, which may be life-threatening

There may be other side effects of this drug which we do not know about.

Physical Risks of Eplerenone:

The following are infrequent (2% of patients or less) side effects of eplerenone:

- Breast pain/tenderness
- Breast swelling in men, which will go away if the drug is stopped
- Irregular menstrual periods in women
- Decreased sexual function
- Very small increases in blood cholesterol and triglycerides (bad cholesterol)

- Moderately elevated potassium in your blood, which may cause symptoms such as nausea or irregular heartbeats

These side effects are rare:

- Very elevated potassium in your blood, which may cause life-threatening irregular heartbeats
- Allergic reaction, which may be life-threatening
- Other drug reaction, which may be life-threatening

There may be other risks of this drug which we do not know about.

Other Risks:

We do not know how these drugs affect unborn babies or babies who are breastfeeding. Therefore, all women who might be able to get pregnant must be using an effective form of birth control, such as birth control pills. Pregnant women or women who are breastfeeding babies cannot participate. If you become pregnant while on this study, tell your study doctor immediately.

You will have regular blood draws while in this study. The risk of serious harm from needlesticks is very low. The main risk is infection at the site of the needlestick, which is very rare. You might also get redness, swelling, or bruising at the site of the needlestick. Most people think that needlesticks hurt, and you may feel dizzy for a short period of time when blood is taken.

The quality of life questionnaires ask you about how your heart failure affects your life. The questionnaires ask things like whether you are not able to do things you enjoy because of your heart failure, or whether having heart failure makes you feel sad. There is the possibility that some of these questions might make you feel uncomfortable. You do not have to answer any question that makes you too uncomfortable.

If you have side effects from the study, your study doctor will discuss alternatives with you. Your study doctor can refer you to other medical services or counseling if you need them.

We will make every effort to make sure your confidentiality is protected. There is a small risk that other people may find out your private health or medical information. If your insurance company or employer does not know about your heart failure and they find out, it might mean that you could lose your insurance or your job.

ARE THERE ANY BENEFITS?

No benefit is guaranteed to you from participating in this study. However, the drug you receive may help your heart function better. Your participation in this research will

benefit other people in the future by helping us learn more about drugs to treat heart failure.

ARE THERE ANY COSTS?

All study medications, blood tests, heart function tests, and doctors' visits related to the study will be provided to you at no cost. Costs of hospital stays or doctors' visits which are not part of this study must be paid by you or your insurance company, even if they are for your heart failure.

ARE THERE ANY ALTERNATIVES?

You do not have to participate in this study to receive treatment for your heart failure. Alternatives to participating in this study include taking other medications for your heart. You can receive the medications in this study from other doctors without participating in this study. The study researchers can discuss your alternatives with you.

WILL I BE PAID FOR MY PARTICIPATING IN THE STUDY?

No, you will not be paid for participating in this study.

WILL THERE BE COMPENSATION FOR INJURY?

In the event that you are physically injured as a result of participating in this research, emergency care will be available. You will, however, be responsible for the charges for the emergency care. There is no commitment to provide any compensation for research-related injury. You should realize, however, that you have not released this institution from liability for negligence. Please contact the investigator, (name) at (phone number) if you are injured or for further information.

IF I DECIDE TO START THE STUDY, CAN I CHANGE MY MIND?

Your decision to participate in this research is entirely voluntary. You may choose not to participate. If you do decide to participate, you may change your mind at any time without penalty or loss of benefits that you had prior to the study. However, if you change your mind after starting the study, we will continue to monitor your progress with your heart by looking at your medical records. Your decision of whether or not to participate in this study will not affect the quality of medical care you receive at this institution.

Your participation may end even if you don't want it to if the study investigators, the Food and Drug Administration, or the study sponsors decide to stop the study early. This may happen if the risks or benefits of one of the drugs are too great, or if we find that the study will not help us determine which treatment is best.

WILL MY CONFIDENTIALITY BE PROTECTED?

The researchers might use information learned from this study in scientific journal articles or in presentations. None of this information will identify you personally. The researchers will make every effort to protect your confidentiality. All of the study data will be stored in locked filing cabinets or on a secure computer.

WHAT IF I HAVE QUESTIONS?

If you have questions about this research, please contact the study investigator. If you have any questions about your rights as a research subject, contact UWHC Patient Relations Representative at 608-263-8009.

Authorization to participate in the research study:

I have read the information in this consent form, reviewed any questions, and I voluntarily agree to participate in this study. I understand that if I start taking the study medication but later decide not to participate, the study doctors will continue to follow my heart failure by looking at my medical records. I have received a copy of this consent form.

Signature of Subject

Date

Signature of Investigator or Person Obtaining Consent

Date