Cilostazol for HFpEF Consent Form (includes HIPAA Authorization)

Title of Research Study:
Cilostazol for HFpEF (Heart Failure with a Preserved Ejection Fraction)

Investigator Team Contact Information*:*

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Markus Meyer MD Investigator Departmental Affiliation: Medicine Phone Number: (802) 922-0656	Study Co-Investigator: Tamas Alexy MD Phone Number: (612) 367-7883

Your doctor, who is also responsible for this research study, or if your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Supported By: *Department of Medicine*

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Why am I being asked to take part in this research study?

You are being asked to take part in this research study because you have heart failure with a normal pump function of the heart. This condition is also called heart failure with a preserved ejection fraction

or HFpEF in short. It is due to a stiff heart muscle that impairs filling of the heart chambers. This leads to shortness of breath. There is no known treatment for this disease.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

We have found that increasing the heart rate in patients with HFpEF makes them feel better, improves both breathing and a blood marker for heart failure. Cilostozol is an approved drug for the treatment for vascular disease and improves walk distance. It increases heart rate by up to 10 beats per minute. In related patient groups, such as patients with atrial fibrillation, cilostazol makes patients feel better and improves the heart failure blood test. In this one-month study we will compare a cilostazol pill to a dummy pill (placebo). Study participants will change between the two types of pills every week. Both cilastozol and placebo are taken twice a day (morning and evening).

We want to find out if cilostazol makes you feel better than the dummy pill and if the heart failure blood test improves with cilostazol.

We encourage you to ask questions and take the opportunity to discuss the study with anybody you think can help you make this decision

How long will the research last?

You will be in this research study for one month

What will I need to do to participate?

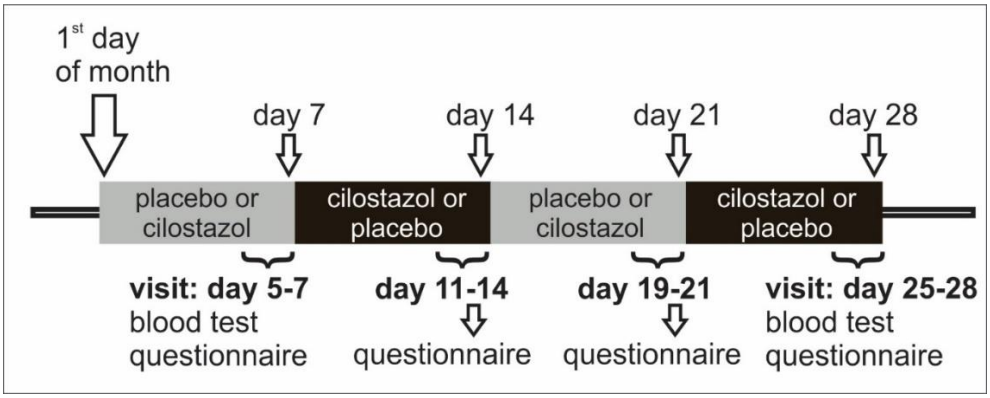
You will receive a 1 month pill box (see below) that is preloaded with cilostazol and placebo

Please take your study medications 30 minutes before or 2 hours after breakfast and dinner.

Each week you will called and asked to answer a questionnaire (12 questions) about the quality of your life (time commitment: 5 minutes). You are encouraged to raise any question.
Let us also know if you have been started on a new medication,

You are asked to come in twice at the beginning and the end of the month to have a blood test (1 Teaspoon of blood, 20 minutes) and have your blood pressure and heart rate checked.

This is a time line of the 1 month study:



More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

Cilostazol has the following known side effects when compared to placebo:

- Patients that use cilostazol are 20% more likely to have a headache.
- Patients that use cilostazol are 12% more likely to have abdominal symptoms and diarrhea.
- Patients that use cilostazol are 9% more likely to have palpitations (pounding heart)

There is a theoretical concern that cilostazol may worsen another type of heart failure due to strengthening the pump function of the heart. This concern which was raised for patients with heart failure with a reduced pump function was never confirmed in clinical studies. Please find the original text of the warning below. Another concern is that cilostazol could increase the bleeding risk due to it's effects of blood platelets. Cilostazol and may also interact with other drugs.

This is the original text of the warning: Cilostazol and metabolites are inhibitors of phosphodiesterase III; such activity has been shown to decrease survival of patients with class III-IV congestive heart failure; contraindicated in patients with congestive heart failure of any severity.

More detailed information about the risks of this study can be found under sections:
"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)" and "What happens to the information collected for the research?"

Will being in this study help me in any way?

There may be no benefit to you by participating in this study.

More detailed information about the benefits of this study can be found under
"Will being in this study help me in any way? (Detailed Benefits)"

What happens if I do not want to be in this research?

There are no known alternatives, other than deciding not to participate in this research study.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect 25 participants in this research study.

What happens if I say "*Yes, I want to be in this research*"?

You would receive the pill box with cilostazol and placebo and start the study on the 1st of the next month. We would be in contact with you by telephone every week to ask you questions. This will also be an opportunity for you to ask questions or raise concerns. You will not be told if you are getting placebo or cilostazol, however your study doctor will know.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for: answering the questionnaire and come in twice for a blood draw

What happens if I say "Yes", but I change my mind later?

If you take part in this research study, and want to leave, you should tell us. Your choice not to be in this study will not negatively affect your right to any present or future medical care. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you stop being in the research, information about you that has already been collected will be removed from the study database.

Can I be removed from the research?

It's possible that we will have to ask you to leave the study. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

We will exclude patients unable to follow up or answer follow up phone calls, we are providing two reliable contact phone numbers for patients to call at any time.

What are the risks of being in this study?
Is there any way being in this study could be bad for me? (Detailed Risks)

This research may hurt you in the following ways:

Risks from Blood Draws:

Discomfort/pain, minor bruising/bleeding and fainting due to blood draws.

Risks from Research Questionnaires:

Inconvenience at having to answer questions and follow-up phone calls.
Emotional discomfort when answering some question items. If any question makes you uncomfortable, you may discuss the need to answer it with the study nurse or doctor. You may choose not to answer questions that make you feel uncomfortable.

Risks from cilostazol:

Patients that use cilostazol are 20% more likely to have a headache.
In 20% of patients cilostozol can lead to abdominal symptoms and diarrhea.
Cilostazol, can lead to palpitations in 10% of the patients.
There is a theoretical concern that cilostazol may worsen another type of heart failure. This concern was never confirmed in clinical studies.

Other risks:

There is a theoretical concern that cilostazol may worsen another type of heart failure due to strengthening the pump function of the heart. This concern which was raised for patients with heart failure with a reduced pump function was never confirmed in clinical studies. Another concern is that cilostazol could increase the bleeding risk due to it's effects of blood platelets. Cilostazol and may also interact with other drugs.

Rare or unknown side effects could possibly occur, including life-threatening reactions or

death. Your condition may not improve or may even worsen while participating in this study.

Rarely, loss of confidentiality of your medical records.

If you notice swelling of the legs, trouble breathing, weight gain, worsening energy level, worsening exercise tolerance, headaches, palpitations, diarrhea and other symptoms or if your physician feels that you are having side effects, you can call Dr. Meyer or Dr. Alexy.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Women of childbearing age have to be on a reliable birth control agent for the duration of study participation. Pregnant women and those not taking a reliable birth control agent will be excluded from the study. Your sexual activity is not affected.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. Your insurance will not pay for services ordinarily covered because these services are performed in a research study. The research study will pay for the blood test.

Will being in this study help me in any way? (Detailed Benefits)

We cannot promise any benefits to you or others from your taking part in this research.

What happens to the information collected for the research, including my health information?

We try to limit the use and sharing of your information, including research study records, any medical records and any other information about you, to people who have a need for this information. But we cannot promise complete confidentiality.

Overview

If you participate in this study, your information, including your health information, will be used and shared for purposes of conducting this research. As described later in this Consent Form, your information may also be used and shared for publishing and presenting the research results, future research, and any optional elements of the research you agree to in this Consent Form, which may include creating audio and video recordings of you. If you sign this Consent Form, you are giving us permission to use and share your health information for these purposes, and if we are using your

medical records, you are giving permission to any health care providers who are treating you to share your medical records with us.

What health information will be made available?

Health information about you to be used and shared for the research includes those items checked by the research team below:

☒ Your medical records, which may include records from hospital and clinic visits, emergency room visits, immunizations, medical history and physical exams, medications, images and imaging reports, progress notes, psychological tests, EEG/EKG/ECHO reports, lab and pathology reports, dental records and/or financial records. These records may be used and shared for as long as this research continues.

☒ Information collected as part of this research study, including research procedures, research visits, and any optional elements of the research you agree to, all as described in this Consent Form. This information might not be part of your medical record, and may include things like responses to surveys and questionnaires, and information collected during research visits described in this Consent Form.

What about more sensitive health information?

Some health information is so sensitive that it requires your specific permission. If this research study requires any of this sensitive information, the boxes below will be marked and you will be asked to initial to permit this information to be made available to the research team to use and share as described in this Consent Form.

☐ My drug & alcohol abuse, diagnosis & treatment records _____ (initial)

☐ My HIV/AIDS testing records _____ (initial)

☐ My genetic testing records _____ (initial)

☐ My mental health diagnosis/treatment records ____ (initial)

☐ My sickle cell anemia records _____ (initial)

Who will access and use my health information?

If you agree to participate in this study, your information will be shared with:

- The University of Minnesota research team and any institutions or individuals collaborating on the research with us;

- Others at the University of Minnesota and M Health/Fairview who provide support for the research or who oversee research (such as the Institutional Review Board or IRB which is the committee that provides ethical and regulatory oversight of research at the University, systems administrators and other technical and/or administrative support personnel, compliance and

audit professionals (Such as the Quality Assurance Program of the Human Research Protection Program (HRPP)) , individuals involved in processing any compensation you may receive for your participation, and others);

- The research sponsor(s), any affiliates, partners or agents of the sponsor(s) involved in the research, organizations funding the research, and any affiliates, partners or agents of the funding organization(s) involved in the research;

- Organizations who provide accreditation and oversight for research and the research team, and others authorized by law to review the quality and safety of the research (such as U.S. government agencies like the Food and Drug Administration, the Office of Human Research Protections, the Office of Research Integrity, or government agencies in other countries); and

- Organizations that process any payments that may be made to you for participating in this study, and any other individuals or organizations specifically identified in this Consent Form.

Additional sharing of your information for mandatory reporting

If we learn about any of the following, we may be required or permitted by law or policy to report this information to authorities:

- Current or ongoing child or vulnerable adult abuse or neglect;
- Communicable, infectious or other diseases required to be reported under Minnesota's Reportable Disease Rule;
- Certain wounds or conditions required to be reported under other state or federal law; or
- Excessive use of alcohol or use of controlled substances for non-medical reasons during pregnancy.

How will my information be used in publications and presentations?

We may publish the results of this research in scientific, medical, academic or other journals or reports, or present the results at conferences. Information that makes it easy to identify you (such as your name and contact information, SSN and medical records number) will not be part of any publication or presentation. If you have an extremely unique or rare condition that is not shared by many others, it is possible that some people may be able to determine your identity even without these identifiers.

What will be done with my data when this study is over?

We will use and may share data for future research. They may be shared with researchers/institutions outside of University of Minnesota. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

Do I have to sign this Consent Form and give my permission to make my information, including my health information, available for use and sharing?

No, you do not have to sign this Consent Form. But if you do not sign, you will not be able to participate in this research study. Treatment available outside of the study, payment for such treatment, enrollment in health insurance plans and eligibility for benefits will not be impacted by your decision about signing this Consent Form.

Does my permission for making my health information available for use and sharing ever expire?

No, there is no expiration date.

May I cancel my permission for making my health information available for use and sharing?

Yes. You may cancel your permission at any time by writing to the researcher at the address on the first page of this Consent Form. If you cancel your permission, you will no longer be in the research study. You may also want to ask someone on the research team if canceling will affect any research related medical treatment. If you cancel your permission, any health information about you that was already used and shared may continue to be used and shared for the research study and any optional elements of the study to which you agree in this Consent Form.

What happens to my health information after it is shared with others?

When we share your information with others as described in this Consent Form, privacy laws may no longer protect your information and there may be further sharing of your information.

Will I be able to look at my records?

It is possible that the research team may not allow you to see the information collected for this study. However, you may access any information placed in your medical records after the study is complete.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include your name or any other direct identifiers such as your contact information. The Web site may include a summary of the results of this research. You can search this Web site at any time.

Will I receive research test results?

Most tests done in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the investigators will contact you to let you know what they have found.

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, we will not pay you for your time and effort.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is illiterate

☐ The participant is visually impaired

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____