Official Title: Metformin for Older Patients with Heart Failure with Preserved Ejection Fraction (MET-PEF-Pilot)

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Wake Forest®
School of Medicine

Department/Section of Internal Medicine/Cardiology

MET-PEF:
METFORMIN FOR OLDER PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

Informed Consent Form to Participate in Research

Dalane W. Kitzman, MD, Principal Investigator (Atrium Health Wake Forest Baptist)
Nicole Cyrille-Superville, MD (Atrium Health Sanger Heart and Vascular Institute)

SUMMARY

You are invited to participate in a research study. The purpose of this research is to study the effect of a medication called metformin XR extended release (XR) on physical function, gut health, inflammation, and quality of life in people with heart failure. You are invited to be in this study because you have heart failure. Your participation in this research will involve 6 study visits and last about 5 months.

Participation in this study will involve taking study medications and attending study visits at which there will be assessments and tests. All research studies involve some risks. A risk to this study that you should be aware of are the side effects reported during the use of the study medication, metformin XR, including diarrhea, nausea, and vomiting.

You may or may not benefit from participation in this study. Your participation, however, may help other patients in the future by improving the knowledge of diseases and improving medical care.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. If you do not join the study, you will continue to receive care for your heart failure. Your study doctor will talk to you about other possible treatments, their risks, and benefits. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The people in charge of this study is Dr. Dalane Kitzman and Dr. Nicole Cyrille-Superville. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: [redacted] (or [redacted] after hours and ask for the cardiology fellow on call) and [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have heart failure. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out what effects (good and bad) the medication metformin XR has on you and your condition. In this study, the effects of metformin XR will be compared to placebo to see which is better.

Metformin XR is an FDA approved medication to treat type 2 diabetic patients worldwide, but it has not been approved for this condition. In this study, Metformin XR is considered an investigational drug. This means it has not been approved by the U.S. Food and Drug Administration (FDA). Drugs and devices that do not have approval by the FDA cannot be sold or prescribed by your physician.

Previous research shows that metformin XR can improve gut health and reduce inflammation in your body. These beneficial effects could potentially improve exercise performance and quality of life in patients with heart failure.

This research study will help answer the question whether metformin XR can improve your exercise performance, increase mucin in your gut (a protein marker of your gut health), reduce markers of inflammation in your gut, and improve your physical function and quality of life.

In this study metformin XR will be compared to placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study you will either receive the active study medication, metformin XR or placebo which is not active. Placebos are used in research studies to see if the drug being studied really does have an effect.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 86 people at 2 research sites will take part in this study, including approximately 60 people at this research site. In order to identify the 86 subjects needed, we may need to screen as many as 150 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

You will be enrolled in the study for approximately 20 weeks, or 5 months, during which you will visit the clinic 6 times and receive phone calls every 2 weeks. You are responsible to attend all study visits scheduled by the study team. If you need to reschedule any visits, please contact the study team.

Screening Visit

At the Screening visit, you will undergo a series of screening tests to evaluate your eligibility for the study. The screening assessments include:

- Recording of demography (date of birth, race, gender) and relevant medical history
- Recording of your current medications
- A physical exam by the study doctor
- A measurement of your weight, height, and waist circumference
- An echocardiogram, a test that uses sound waves to produce a picture of your heart. If an echocardiogram has been performed in the last 3 months, you may not have the procedure
- Surveys to evaluate your quality of life
- A 6 minute walking test, a test to measure your current functional status. During this test, you will walk as far as you can in 6 minutes
- A Short Physical Performance Battery test, a test to measure your current functional status. The SPPB is a short test that measures your ability to balance, your normal walking speed, and your ability to stand up unassisted from a chair.
- Assessment of your heart failure symptoms
- Blood samples for routine blood tests to examine your health as well as your eligibility for the study, including:
    - Comprehensive Metabolic Panel to evaluate your kidney function
    - A complete blood count to evaluate your hemoglobin
    - Vitamin B12
    - Hemoglobin A1c (a marker of the amount of blood sugar (glucose) attached to hemoglobin)
    - Ferritin (a measure of the iron in your blood)
    - Blood for biomarkers of leaky gut and inflammation
    - For participants enrolled at Wake Forest site: blood for biomarkers of your mitochondrial function (how your cells produce energy)

  Approximately 4 tablespoons of blood will be drawn.
- At this visit you will be dispensed a kit to collect a stool sample in. You will collect the stool sample at home and mail it to the lab. The stool sample is used to evaluate proteins that indicate the health of your gut.

Randomization Visit

After a review of your Screening Visit assessments, if you are eligible to continue in the study, you will be scheduled for a Randomization Visit. The following assessments and procedures will be conducted at the Randomization Visit:

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- A cardiopulmonary exercise test (CPET): A CPET is designed to find out how efficient your heart, lungs, and blood are during exercise. We will ask you to exercise on a treadmill while you are attached to machines that will record your breathing and heart function. We will ask you to walk on the treadmill for as long as you are able to do so. While you are walking, you will breathe into a tube that will collect and measure the air

you breathe in and out. Your heart rate and blood pressure will be monitored throughout this activity. We will monitor your heart using an electrocardiogram by placing small stick-on pads to your skin and attaching sensors (electrodes) that can detect the electrical activity of your heart. This test takes approximately 45 minutes in total, with about 10-15 minutes spent exercising.

- Study Drug Assignment: If you meet all the eligibility requirements and this research study is right for you, you will be randomized into one of the study groups. Randomization means that you are put into a group by chance. It is like flipping a coin. You have an equal chance of being assigned to either the metformin XR or placebo group. Neither you nor the investigator will know which study drug, device, procedure, treatment, etc. you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency. Your study doctor will explain what you have to do and the tests that you will have during the study. You will only be given the study medication while the study is going on but not after it has ended.

Study Drug Titration Period (Randomization-Week 3)

You will be given the study medication for the entire study. In order to minimize side effects, you will gradually increase your dose over the first 3 weeks, starting with 500mg (1 tablet) and increasing to 1500 mg (3 tablets). Once you reach week 3, you will be at "target dose"

Treatment Arm	Week 1	Week 2	Week 3-20
Placebo	Metformin XR placebo	Metformin XR placebo	Metformin XR placebo
Metformin XR	500 mg metformin XR	1000 mg metformin XR	1500 mg metformin XR

Phone Calls

Every 2 weeks, you will receive a call from study staff to inquire about symptoms and adverse events during your participation in the study. You should report any changes in your health status and medications during this time. Study staff will also ask you about your compliance with taking the study medication. These phone calls will occur during weeks 1, 2, 6, 8, 10, 14, 16, and 18. After week 1 and 2, the study staff will also instruct you to increase your medication dose by 1 pill.

Week 4 Visit

At Week 4, you will visit the clinic in order for a check in with the study staff and a count of your medication. You should report any changes in your health status and medications during this time. The following assessments and procedures will be conducted:

- A review of your medications
- A check of any problems taking the study medication
- A Comprehensive Metabolic Panel to assess your blood sugar and kidney function and other markers to see how well you are tolerating the medication. Approximately 1 tablespoon of blood will be drawn.

Week 12 Visit

At Week 12, you will visit the clinic in order for a check in with the study staff and a count of your medication. You should report any changes in your health status and medications during this time. The following assessments and procedures will be conducted:

- A review of your medications
- A check of any problems taking the study medication

Follow-up Visit 1

At week 20, you will come to the clinic for the first of 2 follow-up visits to repeat assessments. The assessments will include:

- Changes in your medical history
- Recording of your current medications
- A physical exam by the study doctor
- A measurement of your weight, height, and waist circumference
- An echocardiogram
- A 6 minute walking test
- A Short Physical Performance Battery test
- Surveys to evaluate your quality of life
- Blood samples for routine blood tests to examine your health, including:
    - Comprehensive Metabolic Panel to evaluate your kidney function
    - Vitamin B12
    - Blood for biomarkers of leaky gut and inflammation
    - For participants enrolled at Wake Forest site: blood for biomarkers of your mitochondrial function

  Approximately 4 tablespoons of blood will be drawn.
- At this visit you will be dispensed a kit to collect a stool sample in. You will collect the stool sample at home and mail it to the lab. The stool sample is used to evaluate proteins that indicate the health of your gut.
- A check of any problems taking the study medication

Follow-up Visit 2

The assessments at Follow-up Visit 2 will include:

- A cardiopulmonary exercise test (CPET)
- You will return all unused study medication to study staff

You will have approximately 4 tablespoons of blood withdrawn from a vein at Screening and Follow-up Visit 1. You will have approximately 1 tablespoons of blood drawn from a vein at the Week 4 visit. The total amount of blood withdrawn during the study will be approximately 9 tablespoons.

We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests/exams to your personal physician?

[ ] Yes [ ] No _____ Initials

Storage of Biological Specimens

If you agree to participate in this study, the blood collected at the Screening Visit and Follow-up Visit 1 will be stored to use for future research. This sample will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained in the Clinical Research Unit (CRU) at Wake Forest University Baptist Medical Center. The sample will be stored in the CRU and it will be given only to researchers approved by Dr. Kitzman. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES you many contact for future research studies
____NO I do not want to be contacted regarding future research studies.

How Long Will I Be in the Study?

You will be in the study for about 20 weeks or 5 months. You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. **Risks and side effects related to the study medication include the following**:

Common side effects (occurring in greater than 1 out 20) of using metformin XR include:

- Nausea
- Vomiting
- Diarrhea

Less common side effects (occurring in 1 to 5 out of 100) of using metformin XR include:

- Abdominal pain
- Constipation
- Distended abdomen
- Heartburn
- Flatulence
- Dizziness
- Headache
- Upper respiratory infection
- Taste disturbance

Vitamin B12 deficiency: Metformin has been associated with impaired absorption of Vitamin B12, which can lead to a small risk (5-10%) in a deficiency after long term use. This study will monitor your Vitamin B12 levels. Symptoms of Vitamin B12 deficiency include weakness, tiredness, heart palpitations and shortness of breath, pale or clammy skin, constipation and diarrhea, and numbness, tingling, and muscle weakness. If you experience symptoms of vitamin B12 deficiency, you should report these to the study doctor.

Lactic acidosis: A very rare (occurring in less than 10 per 100,000 patients), but serious risk of metformin is lactic acidosis, which is a buildup of lactic acid in the body, and can be fatal if not treated. Symptoms of lactic acidosis include exhaustion and extreme fatigue, muscle cramps, body weakness, rapid heart rate, abdominal pain, diarrhea, and general malaise. Lactic acidosis associated with metformin use appears to be limited to people with diabetes. If you experience symptoms of lactic acidosis, you should contact your doctor immediately.

Risks of the study procedures and assessments include the following:

Blood draw: You may experience discomfort, bruising and/or bleeding where the needle is

inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

Echocardiogram: The adhesive electrodes used during this test may cause slight discomfort when they are removed from your skin. This may feel similar to pulling off a Band-Aid.

6-minute walk test and Short Physical Performance Battery: There is a rare chance you could lose your balance, trip, or fall. To minimize this risk, we will make sure you have a clear walking path and that trained staff is always nearby. You may also become tired and short of breath.

CPET: As during any moderate exercise, you will become tired and short of breath; this is normal. It is likely that your heart rate and blood pressure will increase during exercise. In rare instances, abnormal changes may occur such as fainting, irregular heartbeat, and low blood pressure. In very rare instances, a heart attack may occur as in any other strenuous activity. Every effort will be made to minimize any possible problem. The medical personnel will constantly monitor you during testing and you have the ability to stop the tests at any time. Trained medical personnel and equipment are available to deal with unusual situations, should they arise.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other risks that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be include improvements in your gut health, physical function, and/or quality of life.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have.

Other healthcare choices may include, but are not limited to increasing the dose of medications you are already receiving to treat your heart failure, or adding new treatment to your existing treatment.

The benefit of these therapies is that they have been shown to be effective in the treatment of heart failure. There may be risks associated with these other therapies that the study doctor or your personal doctor can discuss with you.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the effectiveness of Metformin XR. The results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $300 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid $50 for each complete study visit.

If you have difficulty with transportation for study visits, please talk with the study coordinator.

Greenphire is a company working together with Atrium Health (AH) to manage the study participant payment process. You will be issued a Greenphire ClinCard, which is a debit card that your funds are loaded onto at the completion of each study visit. When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 2 business days and can be used at your discretion. You will be issued one card for the duration of your participation.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

In order for Greenphire to be able to reimburse you via the ClinCard, Greenphire needs to collect certain information about you, including: name address date of birth email address (optional) W9 or W8 SSN.

This information will be collected from you by AH teammates.

All information is stored in a secure fashion on Greenphire's system. Your information will not be shared with any third parties and will be kept completely confidential. By signing this consent form, you consent to providing all the before mentioned personal information that is needed to set up the ClinCard payments. You agree that the information you provide is used by Greenphire to perform payments to you.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institute of Health and by Wake Forest University Health Sciences. The sponsor is providing money or other support to the researchers to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of

such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Dalane Kitzman at [redacted] (after hours call [redacted] and ask to speak to the cardiology fellow on call) or Dr. Nicole Cyrille-Superville at [redacted]4.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** contact information, medical history and current health information directly related to study eligibility and participation, and the results of tests and procedures.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries. This includes researchers at Atrium Health Sanger Heart and Vascular Institute and the University of South Florida Microbiome Lab.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Dalane Kitzman or Dr. Nicole Cyrille-Superville that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Dalane W. Kitzman
[redacted]

Dr. Nicole Cyrille-Superville
[redacted]

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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.

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may

be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Dalane Kitzman at [redacted] (after hours call [redacted] and ask to speak to the cardiology fellow on call) or Dr. Nicole Cyrille-Superville at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm