Study Title: Carnitine Consumption and Augmentation in PAH
Version Date: 5/27/2021
PI: Anna R. Hemnes, MD.

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
The goal of this clinical research study is to evaluate how much of a naturally occurring nutrient, known as carnitine, is gained through a person's diet, and to determine if using a supplement in the form of tablets can increase a person's blood levels of carnitine. As with all dietary supplements, the FDA has no oversight over Carnitine tablets. The study will be conducted over the course of 14 weeks and will include 4 visits to the Clinical Research Center at Vanderbilt University Medical Center. During the last 2 weeks of the study, you will be asked to take approximately 3 pills twice a day. Side effects of the supplement are uncommon but do include gastrointestinal symptoms such as nausea, vomiting, abdominal cramps, and diarrhea, as well a "fishy" body odor. Very rare cases of seizures have occurred with carnitine supplements. Compensation for your time will be provided in the form of money. A total of $400 can be earned upon completion of all study procedures and visits.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you are over 18 years of age with pulmonary arterial hypertension (PAH) on existing standard of care therapy for PAH. The purpose of this study is to determine whether the supplementation of a naturally occurring nutrient called carnitine might be helpful in treating your disease.

Lower than usual levels of carnitine have been observed in several chronic or long-term illnesses. These observations tell us the carnitine that is gained from a person's typical diet may not be enough to meet

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the body's needs. The use of supplemental carnitine has been studied extensively and been found to be safe and effective. We propose to test whether patients with PAH have low levels of carnitine by their natural diets, and if the use of a daily carnitine supplement will increase the carnitine levels in their blood. We propose a single-center study of 10 subjects with PAH at Vanderbilt University Medical Center. All subjects will also be treated with background standard of care therapy at the discretion of their PAH care physician.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
Medical and family history data: No physical risk, but it is possible your private health information could be revealed. However, we are very careful to keep your data as confidential as we possibly can. All data is stored in a password protected computer file. Only the study team has access to your data.

ASA24 Food diary: the diary is of no risk, but you might find it inconvenient and will take a small amount of time to complete

Blood collection: pain, redness, soreness, bruising, or very rarely infection may occur at the needle stick site. Rarely some people faint

6-minute walk test: low risk, but you may feel tired and breathless during this test

Echocardiogram: low risk, the gel used may feel cool

Carnitine: Given its safety and role in energy production, carnitine has been studied extensively and is widely available. Side effects related to taking carnitine supplements are largely associated with long-term use. These include: nausea, vomiting, abdominal cramps, diarrhea, and a "fishy" body odor. There have been rare cases of reported seizure activity in patients with pre-existing conditions as well as without.

Good effects that might result from this study:

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a) The benefits to science and humankind that might result from this study. It is possible that a new beneficial supplement therapy may become available for a targeted group of responsive patients
b) The benefits you might get form being in this study. If you are a "responder". Then future clinical trials may lead to specialized treatment plans that could help you.

Procedures to be followed:
If eligible, we will ask you to come to the Clinical Research Center (CRC) for 4 study visits over a period of 14 weeks. This study will consist of 4 study visits: Visit 1, Visit 2 (12 Weeks), Visit 3 (12 weeks + 1 day), and Visit 4 (14 weeks). Visit 1 and Visit 3 visits are both estimated to take approximately 2 hours each. Visit 2 and Visit 4 are both estimated to take approximately 4 hours each. The study staff will also call you one week prior to the Visit 2 and Visit 4.

Visit 1:
You will need to be fasting, meaning no food for 8 hours before you come into the clinic. For your convenience, we will schedule your visit as early in the morning as possible. This visit will last approximately 2 hours.

The following procedures will be performed:

- Review of inclusion/exclusion criteria
- Review medical history
- Review current medications
- Determine WHO functional class (measurement of health and disability)
- Physical exam
- Vital signs
- Height and weight
- Blood draw
- Six-minute walk test
- Orientation to food and supplement diary (ASA24)

After fasting research labs have been drawn, you will have the opportunity to eat a snack. The investigator or research nurse will take a medical history, perform a physical examination including checking vital signs, and review current medications. You will then perform the six-minute walk test.

Phone Call (Week 11):
The research coordinator will call you to remind you to complete the food and supplement diary for the 3 days prior to Visit 2. Any questions you have will be answered.

Visit 2 (Week 12):

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You will need to be fasting, meaning no food for 8 hours before you come into the clinic. For your convenience, we will schedule your visit as early in the morning as possible. This visit will last approximately 4 hours.

The following procedures will be performed:

- Review of interim medical history
- Review of current medications
- WHO functional class (measurement of health and disability)
- Physical exam
- Vital signs
- Blood draw
- Urine pregnancy test (as necessary)
- Six-minute walk test
- Transthoracic Echocardiogaphy
- Dispense carnitine supplement
- Review of food and supplement diary (ASA24)

After fasting research labs have been drawn, you will have the opportunity to eat a snack. The investigator or research nurse will take a medical history, perform a physical examination including checking vital signs, and review current medications. The subject will perform the six-minute walk test. An experienced research sonographer will perform the transthoracic echography.

Visit 3 (Week 12+1 day):
You will need to be fasting, meaning no food for 8 hours before you come into the clinic. For your convenience, we will schedule your visit as early in the morning as possible. This visit will last approximately 2 hours.

The following procedures will be performed:

- Vital signs
- Symptom assessment
- Blood draw
- Review of ASA24 and supplement diary
- Dispense 2 weeks supply of carnitine supplement

Phone Call (Week 13):
The research coordinator will call you to assess symptoms and potential side effects as well as review medication changes. Supplement compliance will be assessed and reinforced. Any questions you have will be answered.

Visit 4 (Week 14):

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You will need to be fasting, meaning no food for 8 hours before you come into the clinic. For your convenience, we will schedule your visit as early in the morning as possible. This visit will last approximately 4 hours.

The following procedures will be performed:

- Review of interim medical history
- Review of current medications
- WHO functional class (measurement of health and disability)
- Physical exam
- Vital signs
- Symptom assessment
- Blood draw
- Six-minute walk test
- Transthoracic Echocardiography

Turn in supplement diary and any remaining supplements

Payments for your time spent taking part in this study or expenses:
Subjects will be reimbursed for time at the clinic for research procedures and reasonable travel expenses necessary for their participation in the study. The reimbursements will be distributed as follows:
Visit 1: $75
Visit 2: $75
Visit 3: $100
Visit 4: $150

Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator or the NIH that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt or the NIH to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt or the NIH to give you money for the injury.

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Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being in this study, please feel free to contact Alisha Lindsey (937) 638- 2416. If you cannot reach the study staff, please contact Dr. Anna R. Hemnes, MD at (615) 343- 8227.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
Your study doctor will take you out of the study, if you request, in writing your wish to withdraw.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. The contact information may be found above. We will destroy your stored blood sample and stop any further research. However, data collected before your request will still be used.

Clinical Trials Registry:
A description of this clinical trial will be available on 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 Web site at any time.

Confidentiality:
All samples will be coded. Only the key study personnel will know what patient is linked to a particular code number. Samples will not have your name or other identifying information on the labeling. Medical history data will be stored in a password protected database that only key study personnel may access.

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosure that you make yourself are also not protected.

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Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Vanderbilt University Medical Center may share the results of your study and/or non-study linked laboratory tests, six-minute walk tests, echocardiograms, medical history, medical assessments, medications, questionnaires, and study diary results, as well as parts of your medical record, to the groups names below. These groups may include people from the Federal Government Office for Human Research Protections, the VUMC Institutional Review Board, Vanderbilt University, the Food & Drug Administration, the National Institute of Health (NIH). Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Hemnes in writing and let her know that you withdraw your consent. Her mailing address is VUMC, Division of Pulmonary Medicine, T1218 MCN, Nashville, TN, 37232-2650. At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

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STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date _____ Signature of patient/volunteer _____

Consent obtained by:

Date _____ Signature _____

Printed Name and Title _____