FOCUS - Pilot Study of Muscadine Grape Extract to Improve Fatigue Among Older Adult Cancer Survivors

NCT04495751

IRB Approval Date: 31JUL2024

Department/Section of *Department Of Hematology and Oncology*

Pilot study of muscadine grape extract to improve fatigue among older adult cancer survivors (FOCUS)

Informed Consent Form to Participate in Research
Heidi Klepin, MD, MS, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to see if muscadine grape extract improves fatigue in people age 65 and above who have a history of treated cancer and report the symptom of fatigue. You are invited to be in this study because you are 65 or older, have had cancer previously, and you have reported that you have fatigue. Your participation in this research will involve 2 in-person visits and 4 phone visits and last about 12 to 16 weeks.

Participation in this study will involve surveys, taking muscadine grape extract or placebo, donating blood, urine, and a stool sample. All research studies involve some risks. Risks to you during this study that you should be aware of are possible gas, indigestion, diarrhea, nausea, abdominal pain and constipation. There is the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include participating in another study. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remaining pages 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 person in charge of this study is Dr. Heidi Klepin. If you have questions, suggestions, or concerns regarding this study, or you want to withdraw from the study, her contact information is: [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].

Pilot study of muscadine grape extract to improve fatigue among older adult cancer survivors (FOCUS)

Informed Consent Form to Participate in Research
Heidi Klepin, MD, MS, Principal Investigator
CCCWFU #98320

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 be in this study because you are sixty-five years of age or older, have a history of being diagnosed with cancer, and report fatigue. 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 determine if muscadine grape extract improves fatigue in people age 65 and above who have a history of treated cancer and report the symptom of fatigue. Muscadine grape extract is a natural product. It can be purchased commercially, but not at the concentration we are testing in this study. To participate in this study, we require that you take the pills provided. Muscadine grape extract is 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.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 64 people at Wake Forest University will be in this study. In order to identify the 64 participants needed, we may need to screen as many as 180 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

If you take part in this study, you will be randomized to one of two study groups. Randomization means that you are put into a group by chance. You have a one in two (50%) chance of being placed into either group. Half of the people in this study will receive the muscadine grape extract, the other half will receive a placebo. A placebo is an inactive substance. Neither you nor the investigator will know which study drug (muscadine grape extract or placebo) you are receiving. This is done so that a fair evaluation of results can be made. This information would be available to the research team if needed in an emergency.

Regardless of which group you are assigned to, we will collect data from you and your medical record about your health and medicines, and will ask you survey questions about how you are feeling. This will include questions about your symptoms, fatigue, general well-being and quality of life. The surveys may take up to 30 minutes to complete. You will take four pills twice daily for the duration of your participation in the study. You will be asked to report any side effects that you feel. You will have 2 regular study appointments, one at the start of the study and one 12 weeks later at the completion of the study. We will also call you 3 times during the 12 weeks. You will be asked about concerns or symptoms at each in person visit and by phone every 2 weeks after your first visit. You will also be called to check on any symptom concerns 30 days after your last dose of study medication.

You may use other therapies prescribed to you to treat symptoms while participating in this study.

To measure your physical functioning, you will be asked to complete a short physical function performance battery (SPPB) and a 6 minute walk test. During the SPPB you will be asked to complete a balance test, to walk approximately 10 feet, and to attempt to stand up from a chair five times as quickly as possible. During the 6-minute walk test you will be asked to walk back and forth from one end of a long hallway to the other at your own pace while attempting to walk as long a distance as possible in six minutes. We will also measure your hand grip strength. You will be asked to squeeze as hard as you can for a few seconds with each hand on an instrument with handles that measures force. To measure cognitive speed, you will be given instructions to draw symbols on a chart while being timed. You will complete these tests at your baseline and 12 week visits.

You will have blood drawn (about 4 tablespoons) and give a urine sample at the first and last study visits (baseline and 12 weeks) to determine the amount of muscadine grape extract components in your blood and urine, as well as to measure inflammation or growth factors that might be affected by the grape extract. You will also be given a kit twice, to perform tests of your stool in your home. This will come with instructions on how to perform the test at home and a pre-paid, pre-addressed envelope to mail this sample to the lab. In the future, research on your specimen may involve whole genome sequencing.

STORAGE OF BIOLOGICAL TISSUE

If you agree to participate in this study, we will bank any unused blood to use for future research related to inflammation and prostate cancer. Your sample will be obtained in the Clinical Research Unit (CRU) at Wake Forest University Baptist Medical Center (WFUBMC). If you have another clinical appointment at WFUBMC on the same day, your sample might be drawn at that time and location instead of in the CRU. The sample will be stored in the Hypertension Core Laboratory to be used by researchers approved by Dr. Heidi Klepin.

The choice to let your blood sample be kept for future use is up to you. No matter what you decide to do, it will not affect your care in this study. If you decide now that your blood sample can be kept for research, you can change your mind at any time. Just contact the study investigator, Dr. Heidi Klepin at [redacted] and let her know that you do not want your blood sample used for future research. Otherwise, the blood sample may be kept until it is used or it is discarded.

In the future, people who do research may need to know more about your health. While the researcher may be given 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 being contacted in the future.

[ ] YES I am willing to have my blood stored for future research.
[ ] NO I do not want to have my blood stored for future 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 an assigned number and only the research team 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.

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/tissue 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 /tissue will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/tissue sample will not affect your care. Your blood/tissue 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.

How Long Will I Be in the Study?

You will participate in the study for 12-16 weeks depending upon when you take you last study medication.. 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. If you stop taking muscadine grape extract during the course of the study for any reason, we will ask you to continue with study visits if possible.

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. Potential risks and side effects related to taking muscadine grape extract may include

- Excess gas
- Indigestion
- Diarrhea
- Nausea
- Abdominal pain
- Constipation

Because muscadine grape extract use for treatment of fatigue is investigational, there may be other side effects that we cannot predict. Please tell the research team about all the medications, vitamins and supplements you are taking. This may help avoid or minimize additional side effects, interactions and other risks. It is unlikely but possible that you may experience an allergic reaction to the study drug. Allergic reactions may involve itching, rash, or in severe cases, difficulty breathing and changes in blood pressure or other symptoms. Alert the study team if you have any known allergies. Although very unlikely, there may be a risk of death from taking muscadine grape extract.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. 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.

Potential risk and side effects related to the SPPB and 6-Minute Walk Test may include muscle or joint soreness following the tests. These symptoms usually go away quickly and are typically not serious. There is also slight risk of falling during the walking portion of testing.

From blood draws, 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)

If you experience side effects that you think might be related to the muscadine grape pills that are intolerable, at

any point during the study you can call Dr. Klepin or her study team for assistance (336-716-5772 phone).

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 with fatigue in the future. The benefits of participating in this study may be a decrease in fatigue. Based on experience with muscadine grape extract in animals and other research studies, researchers believe the components of the muscadine grape may contain agents that benefit people with a history of cancer. Because individuals respond differently to therapy, no one knows in advance if it will be helpful in your particular case.

WHAT OTHER CHOICES ARE THERE?

This study is designed with the hope that the study drug may improve fatigue in older adults who have been previously treated for cancer. You should talk to your doctor about all the choices you have. Your alternative is to not participate in this study.

What about My Health Information?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information (**PHI**). The information we will collect for this research study includes: demographics, medical history, medicines used, vital signs, analysis of your blood, surveys about your quality of life, questions about the effects the study pills may have on you, and results from the physical performance tests.

As part of this study, we will need to know some information about your previous cancer diagnosis and treatment. To do so, we will need to obtain medical information concerning your cancer diagnosis and treatment from your medical record. If you receive treatment for your cancer at any other facility, with your authorization, we will need to request copies of information about your cancer diagnosis and treatment. At that time, we will be required by the hospital to submit a current medical record release form to obtain this information.

We will make every effort to keep your PHI private. We will store records of your PHI in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your PHI:

1) The study investigator and her staff; others at Wake Forest University Health Sciences (WFUHS) who oversee research
2) Other people or laboratories providing services for this research project on behalf of WFUHS and WFUMBC

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

Some of the people, agencies and businesses that may receive and use your PHI 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 WFUHS and North Carolina Baptist Hospital (NCBH); 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. Some

of these people, agencies and businesses may further disclose your health information. If disclosed by them, your PHI may no longer be covered by federal or state privacy regulations. Your PHI may be disclosed if required by law. Your PHI 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.

Any PHI collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your PHI in the research records until all activities in the study are completely finished.

You can tell Dr. Heidi Klepin that you want to take away your permission to use and share your PHI at any time by sending a letter to this address: Dr. Heidi D. Klepin [redacted]

However, if you take away permission to use your PHI, you will not be able to remain in the study. 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 PHI.

If you choose to participate in this study, your medical record at WFUBMC 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 medical reports created as a result of your participation in the research study may be entered into the computer systems of WFUHS and NCBH. 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.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study medications and procedures related directly to the study, will be paid by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility. Neither you nor your insurance company will be billed for the muscadine grape extract used in this study.

WILL MY 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 muscadine grape extract; the results will be provided to the sponsor, the FDA and other federal and regulatory agencies as required.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid a *$20.00* gift card at the completion of each study visit. If you complete both scheduled study visits, you will be paid a total of *$40.00* in gift cards. Thus, if you withdraw from the study for any reason prior to study completion, you will not receive further compensation. Additionally, parking validation will be provided for all study-related visits. The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the Clinical and Translational Science Institute (NIH CTSA UL1TR001420), and the Chronic Disease Research Fund of WFUHS. WFUHS has a financial interest in the muscadine grape extract. This means that WFUHS could financially profit from the results of the study if the extract is licensed for use related to this research.

WHAT HAPPENS IF YOU EXPERIENCE INJURY OR ILLNESS AS A RESULT OF BEING 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 (WFUSM) 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. WFUBMC 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 WFUSM, and the NCBH, 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. Heidi Klepin at [redacted].

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, new information becomes available, you have an unexpected reaction or the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study. Clinically relevant research results will/will not be disclosed to you. 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 other without additional consent.

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. Heidi Klepin 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].

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.

Participant Name (Printed):_____

Participant Signature:_____Date:_____Time:_____am / pm

Person Obtaining Consent:_____Date:_____Time:_____am / pm