MCC-12-08248
NCT02332928
4/01/2020

RESEARCH PARTICIPANT INFORMED CONSENT

TITLE:	Melatonin supplementation for cancer-related fatigue in patients receiving radiotherapy: A double-blind placebo-controlled trial
PROTOCOL #:	MCC-12-08248
VCU IRB #:	HM20003275
SPONSOR/ INVESTIGATOR:	Egidio Del Fabbro, MD

OVERVIEW AND KEY INFORMATION

Taking part in this study is your choice

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

Why is this study being done?

Fatigue, or a sense of exhaustion, is commonly experienced by patients with cancer. When patients with breast cancer are treated with radiation therapy they often experience increased levels of fatigue. The purpose of this research study is to test the effectiveness of melatonin in lessening the fatigue that frequently occurs in patients receiving radiation therapy.

You are being asked to participate in this study because you have been diagnosed with breast cancer and because you may meet the study entry requirements.

Up to 142 individuals will participate in this study.

What will happen if I decide to take part in this study?

You will be randomly assigned (like the flip of a coin) to receive either melatonin or placebo. The melatonin and placebo treatments will involve taking a liquid syrup orally each night, beginning the night before radiation therapy begins and ending 2 weeks after the radiation therapy is completed.

We will ask you to keep a diary and write down when you take your study drugs.

We will ask to collect a blood sample for research purposes prior to beginning treatment, during treatment, and after your radiation treatment.

We will give you surveys to fill out with questions about how you're feeling prior to beginning treatment, during treatment, and after your radiation treatment.

We will also collect other information about you and your cancer treatment from your medical records.

How long will I be in this study?

Your participation in this study will last up to 16 weeks.

What are my other choices if I do not take part in this study?

If you decide not to enter this study, there may be other treatments for fatigue available. The study doctor will discuss these with you. You do not have to participate in this study to be treated for breast cancer.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the **Risks and Discomforts section**.

If you choose to take part in this study, there is a chance that you could have side effects from the melatonin.

Some of the most common side effects that the study doctors know about are:

- Sleepiness during the daytime, especially if combined with a sedative
- Headaches

Benefits

There is no guarantee that you will receive any medical benefits from being in this study. If you are receiving melatonin, and if melatonin can relieve the symptoms of fatigue, you may feel less tired during this study. If you are receiving the placebo, you may also feel less tired during the study. While you may not receive any direct benefit from receiving the study drug, the information from this research study may lead to a better treatment in the future for the fatigue associated with cancer and radiation therapy.

DETAILED RESEARCH CONSENT

Now that you have a general overview of the study, we want to provide the details about what your participation involves. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask the study staff.

DESCRIPTION OF THE STUDY

Melatonin is sold over-the-counter in the United States as a dietary supplement. Because melatonin is not regulated as a drug, the FDA does not require the manufacturer to demonstrate its safety or effectiveness. Nonetheless, this study is designed to test the effectiveness of melatonin in lessening the symptoms of fatigue that are associated with cancer and radiation therapy.

In this study, melatonin will be compared to a placebo (a look-alike inactive substance) for its ability to make patients with breast cancer feel less tired while undergoing treatment with radiation therapy. As determined by their treating physician, patients will receive one of three types of standard-of-care radiation therapy. The 3 types of radiation therapy include the following therapies:

- 1 week of accelerated partial breast irradiation (5 consecutive days of treatment)
- 3-4 weeks of an accelerated hypofractionated radiation therapy schedule (5 consecutive days of treatment per week)
- 6-8 weeks of a standard radiation therapy schedule (5 consecutive days of treatment per week)

One-half of the patients will be treated with melatonin and one-half of the patients will be treated with placebo. The dose of melatonin used in this study will be at least four times higher than is typically used as an over-the-counter dietary supplement. The melatonin and placebo treatments will involve taking a liquid syrup orally each night, beginning the night before radiation therapy begins and ending 2 weeks after the conclusion of radiation therapy.

Prior to beginning treatment, during treatment, and for approximately 8 weeks following treatment, patients will complete 2 surveys that will measure their fatigue and 1 survey that will measure their symptoms. The surveys should take less than 20 minutes to complete. A small amount of blood (about 1 teaspoon) will also be taken to measure how melatonin affects the levels of different biological molecules. This part of the study will not use your samples to sequence all or part of your DNA. If you choose to take part in the optional studies described in the **Additional Studies Section,** a small amount of blood (about 1 teaspoon) will also be taken.

Blood samples will continue to be used until they are used up. The individual results of the research using your samples will not be provided to you. The samples are collected only for the research study. There will be no benefit to you.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue participation.

PROCEDURES

If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered. You will also be asked to sign a separate HIPAA authorization form that gives the research team permission to use your private health information for the purposes of this research study. This information will be used to determine if patients receiving melatonin, in comparison to patients receiving placebo, have fewer hospital admissions, emergency center visits, and medical days off work.

At your first study visit, your medical history will be taken and a physical exam will be performed. This exam will include measurements of your weight and vital signs (pulse, blood pressure and temperature). A blood sample will be collected for routine lab tests. Approximately 2 to 3 tablespoons of blood will be collected. This information will be used to make sure that you qualify to participate on the study. You must begin the study within 28 days of your examination and any of the lab tests that are done.

If you qualify for the study, you will be randomly assigned (like the flip of a coin) to receive either melatonin or placebo. You have an equal chance of being assigned to either one of these groups.

Neither you nor the study doctor will know if you are receiving melatonin or placebo. This information is available to the study doctor if needed in an emergency. This is called double blinding, and it is done so that a fair evaluation of results may be made.

You will have a physical exam and a blood sample will be collected (about 1 teaspoon) to measure if and how different cells and molecules change when you take the study drug. You will be asked a series of questions using the ESAS numerical scale, FACIT-F scale, and PROMIS scale. This examination and the tests will be repeated at the conclusion of your radiation therapy, and they will be repeated at 2 weeks and 8 weeks following your last radiation treatment. If your radiation therapy lasts for 3 weeks or longer, this examination and the tests will be repeated approximately every 2 weeks while you remain on radiation therapy.

The melatonin is suspended in liquid syrup that has a citrus-berry flavoring. The placebo is the same liquid syrup, but does not contain melatonin. Both the melatonin and placebo are light sensitive and you should store them in the light-resistant amber bottle in which you receive them. Each product should be stored at room temperature and shaken well before use.

You will begin taking your study drug (melatonin or placebo) by mouth starting the night before you begin radiation therapy. You should use the measuring cup provided to you to measure 10 mL for each dose that you take. You will keep a study diary to record the time each dose is taken and any side effects you are having. You should continue taking the study drug every night while you are receiving radiation therapy and for an additional 2 weeks after your radiation therapy has ended.

At each visit, you should bring all of your remaining study drug supply to the research clinic. At each visit, you should also bring your study diary.

RISKS AND DISCOMFORTS

Possible side effects associated with the use of melatonin include:

Likely (10% or more of patients)

- Sleepiness during the daytime, especially if combined with a sedative
- Headaches

Less Likely (1-9% of patients)

- Abdominal discomfort
- Mild anxiety
- Irritability
- Confusion
- Short-lasting depression
- Dizziness

Any drug may cause allergic reactions; these may be serious, even life-threatening.

Possible side effects associated with treating breast cancer with radiation therapy:

Likely (10% or more of patients)

- Reddening of the skin during treatment and for several weeks following treatment
- Tanning of the skin lasting months and may be permanent
- Slightly smaller breast size or change in the way the breast looks
- Tiredness and weakness during treatment and for several weeks following treatment
- Swelling of breast
- Peeling of the skin in the area treated with radiation
- Mild pain at the site of radiation treatment requiring over-the-counter pain relievers

Less Likely (3-9% of patients)

- Soreness or tightness in muscles of the chest wall under the treated breast
- Severe pain at the site of radiation requiring prescription pain relievers

Rare But Serious (less than 3% of patients)

- Cough
- Difficulty breathing
- Inflammation of the heart muscle
- Rib fracture
- Slight increase in risk for heart disease for patients with cancer in the left breast
- Risk of developing another cancer

Reproductive risks:

As the study procedures might injure an unborn child, pregnant women may not participate. Women who might become pregnant should use a medically accepted form of birth control such as total abstinence, an IUD, diaphragm, or condoms plus a spermicide. Because of a possible interaction with melatonin, hormonal forms of birth control should not be used. Methods of birth control other than total abstinence are not 100% effective, and should a woman become pregnant there is a risk of injury to an unborn child. You will be asked to sign an agreement that confirms that you will use an adequate form of birth control during your participation on the study and for 3 months following completion of the study.

Risks associated with blood draws:

The collection of your blood may cause pain, swelling, bruising, irritation or redness at the needle site. You may feel faint during or after a blood draw. It is also possible to get an infection at the site of the needle puncture, but this is extremely rare.

Risks of completing surveys:

Some of the questions about physical, emotional, or social difficulties may be upsetting to you. You may skip any questions that you do not wish to answer.

Risks associated with breach of confidentiality:

Although it is unlikely, it is possible that your private health information could be discovered by someone who is unauthorized to have access to it. See the forthcoming “Confidentiality” section for more information on safeguards in place to prevent a breach in confidentiality.

COSTS

You will not be charged for the study drug, the two-month follow-up, and blood tests that are performed only for this study (extra blood draws). You and/or your health plan/insurance company will need to pay for the radiation therapy, physical exams, and associated lab tests that are part of your regular cancer treatment. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The study will not pay for medical treatment.

CONFIDENTIALITY

Your research information and your personal identifying information will be kept private through the use of password-protected electronic files, locked research areas, and study identification numbers. Blood samples obtained for research purposes will be stored with the same safeguards.

In the future, identifiers might be removed from the information and samples you provide in this study, and after that removal, the information and samples could be used for other research studies by this study team or another researcher without asking you for additional consent.

Every effort will be made to ensure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies like the Food and Drug Administration (FDA) involved in keeping research safe for people.
- Virginia Commonwealth University and its Institutional Review Board (VCU IRB).

There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

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.

COMPENSATION FOR INJURY or ILLNESS

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study.

To help avoid research-related injury or illness, it is very important to follow all study directions.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide to not participate in this study. Your decision not to take part will involve no penalty or loss of benefits to which you are otherwise entitled. If you do participate, you may freely withdraw from the study at any time.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

QUESTIONS

In the future, you may have questions about your study participation. You may also have questions about a possible research-related injury. If you have any questions, complaints, or concerns about your participation in this research, contact:

Principal Investigator:
Egidio Del Fabbro, MD
Department of Internal Medicine
Virginia Commonwealth University
1101 E. Marshall Street
Box 980230
Richmond, VA 23298
Phone: 804-628-0617
Email: egidio.delfabbro@vcuhealth.org

Responsible Research Nurse:
Gwendolyn Parker, MS, FNP-C
Massey Cancer Center
Virginia Commonwealth University
401 College Street
Box 980037
Richmond, VA 23298
Phone: 804-828-5090
Email: ggparker@vcu.edu

The principal investigator and the responsible research nurse named above are the best people to call for questions about your participation in this study.

If you have general questions about your rights as a participant in this or any other research, you may contact:

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number for general questions, concerns, or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

ADDITIONAL STUDIES SECTION

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

You will not be billed for these optional studies. You can still take part in the main study even if you say “no” to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Initial your choice of “yes” or “no” at the end of this section.

Background information:

This study might use your samples to sequence part of your DNA. Deoxyribonucleic acid (DNA) is the “blueprint” or “recipe” that gives the body’s cells instructions on how to do their jobs. Scientists can use a test called whole genome sequencing to determine the order of all or part of the molecules that make up your DNA, like reading all the letters in a book. Sequencing is usually done to look for changes in the molecules of DNA that may cause health problems.

The optional studies involve genes, a form of DNA. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

We will study your DNA sequences, or genes, that code for three proteins called IL-1B, IL-6, and TNF. The genes that code for IL-1B, IL-6, and TNF sometimes differ slightly among different individuals and these differences might be important in causing the fatigue that sometimes occurs with radiation therapy. By studying your IL-1B, IL-6, and TNF genes we hope to determine if there is such an association.

What is involved: If you agree to take part, the study doctor for the main study would like to collect 1 additional blood sample (about 1 teaspoon) before your study treatment begins for the optional laboratory study.

Future contact concerning genetic testing results:

Sometimes samples are used for genetic research (about diseases that are passed on in families). Even if your samples are used for this kind of research, the results will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Withdrawal of genetic testing consent:

If you decide now that your specimens can be kept for genetic testing and later change your mind, just contact us and let us know that you do not want us to use your specimens. The specimens that remain will no longer be used for research. You may contact the investigator and/or responsible research nurse at the number listed on this form.

Confidentiality:

The results of genetic research on your specimens will not be put in your health record.

While this study has safeguards in place to protect your confidential genetic information and to make it extremely unlikely that your identity would be connected with any special studies that are performed on your tissue, it is possible that this information could be discovered by someone who is unauthorized to have access to it.

Your specimens will be used only for research and will not be sold. The research done with your specimens may help to develop new products in the future.

Samples for the Optional Laboratory Studies:

My blood samples may be stored and used for the research described above about fatigue in cancer patients.

YES_____ NO_____
initial initial

Future contact concerning further research:

I agree to allow my study doctor or someone approved by my study doctor, to contact me regarding future research involving my participation in this or related research.

YES_____ NO_____
initial initial

My Signature Agreeing to Take Part in the Main Study

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not waived any of the legal rights or benefits, to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form once I have agreed to participate.

_____
Participant Name, printed

_____ _____
Participant Signature Date

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

_____ _____
Investigator Signature (if different from above) Date