Winship2563-13: Phase II study of everolimus beyond first progression in postmenopausal women with advanced, hormone receptor positive breast cancer

Informed consent date: January 30, 2018

NCT02269670

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University, Grady Health System and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Winship2563-13: Phase II study of everolimus beyond first progression in postmenopausal women with advanced, hormone receptor positive breast cancer

Principal Investigator: Elisavet Paplomata, MD

Study-Supporter: Novartis Pharmaceuticals

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this Web site at any time.

Study Overview

Breast cancers that express the receptor for estrogen and/or progesterone are initially sensitive to hormonal therapies, such as tamoxifen and aromatase inhibitors. Unfortunately, resistance to hormonal agents develops inevitably.

Everolimus targets a protein called mTOR, which appears to become more active in breast cancers that are no longer controlled by hormonal therapies. Everolimus is approved for the treatment of kidney cancers. It has been recently approved in combination with the aromatase inhibitor Exemestane for metastatic breast cancer, which does not respond to hormonal agents. Smaller studies have also shown that everolimus is active in combination with other hormonal agents.

Everolimus has been FDA approved in combination with the endocrine treatment Exemestane for these breast cancer patients, whose tumors express hormone receptors. The purpose of this study is to investigate if we can continue everolimus in combination with a different endocrine therapy in patients who progress after that combination. The alternative option for these patients would be treatment without everolimus or chemotherapy.

This study will enroll patients who are already on everolimus for metastatic breast cancer but have progression of their cancer; after getting on the study, the patients will continue to take everolimus at the same dose and will change their endocrine/hormonal therapy.

If you enroll in this study and your cancer gets worse, you will be taken off the study.

It is hoped that everolimus will help control the disease and stop the tumor from growing. This assessment will be based on imaging studies, which will be done regularly during the study or based on new complaints, which are suspicious for progression of the disease.

How Many People Will Take Part In The Study?
About 38 people will take part in this study, all of who will take everolimus with a hormonal therapy.

Procedures
At an initial "screening" visit, you will be asked about your current condition, your medical history, and any medications you may be taking. You will undergo a series of tests to evaluate your disease. These include:

- A physical examination
- Measurement of your blood pressure, heart rate, and temperature. An electrocardiogram (EKG) will also be done to check your heart rhythm.
- Obtaining your height and weight
- Approximately one tablespoon of blood for routine tests
- CT (computed tomography) scan will be done if you have not had one recently. The CT will find and measure the location of your disease.
- A bone scan may also be done if your study doctor finds it necessary.

We will perform a pregnancy test if you are a woman who could have children. You must not be pregnant, breastfeeding, or planning to have children (male patients included) in order to join the study.

If you meet the "entry criteria" from testing at your initial visit, we will give you a time to come back. At that next visit we will formally enter you in the study. If your screening visit was more than 14 days ago, we will have to repeat many of the same tests. These would include measuring your weight, temperature, blood pressure, and heart rate. If your imaging was done more than 4 weeks earlier, we will need to repeat them. We will also need samples of your blood for laboratory testing. We will use these results as your baseline readings.

If you are found to be eligible for the study, and agree to participate, you will continue to take everolimus but will change your hormonal treatment. Everolimus will be taken by mouth every day. Your endocrine treatment will either be a pill or an injection in the muscle. This will be explained to you in detail.

At the start of your study treatment (day 1 of cycle 1), your doctor will perform a physical exam and take your vital signs, weight, and temperature. You will have routine blood tests performed.

Each cycle will be 28 days (4 weeks). On Day 1 of each new cycle and before the next dose of study therapy can be given, a physical examination will be made. Blood pressure and heart rate (your "vital signs"), temperature, and weight will be measured. Standard blood tests will be carried out to check your blood counts, liver and kidney function and electrolytes. The dose and timing of your therapy may be changed based upon test results or due to any serious side effect you may be experiencing. If delays in treatment do occur, it may also result in you having to attend extra visits. If the side effects are severe and do not come under control, you may be withdrawn from the study if the study doctor feels this is in your best interests. If the study therapy is delayed by more than four weeks due to side effects, then you will be withdrawn from the study.

Throughout the study, the effect of the study treatment on your cancer (as judged by its change in size) will be assessed every 8 weeks initially, and then after 3 months every 12 weeks. Tumor assessments will be a CT scan, and maybe a bone-scan if your doctor finds it useful.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

Risks and Discomforts
While on study, you are at risk for these side effects. You should discuss these with the researcher and/or your regular doctor. There may also be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and uncomfortable. Many side effects go away shortly after the chemotherapy drugs are stopped, but in some cases side effects can be serious or permanent.

The risks involved in this study are the possible side effects of the study treatment and those of taking blood. Additional risks include those from medicine tests and CT scans and x-rays. There is a risk that the study drugs will not be effective in controlling your cancer. However, you will be closely monitored and should the drugs not be effective you will be removed from the study.

Everolimus:

Common side effects:

- Fatigue
- Diarrhea
- Nausea
- Abdominal pain
- Mouth sores
- Constipation
- Anemia
- Low platelet counts
- Low white blood cell count

Less frequent side effects:

- Vomiting
- Neuropathy
- Anorexia
- Fever
- Shortness of breath
- Back pain

- Coughing
- Edema
- Headache
- Hand-foot syndrome
- Heartburn
- Difficulty sleeping
- Rash
- Sore throat
- Dizziness
- Flushing
- Increased tearing of eyes
- Elevated cholesterol and/or triglycerides

Other side effects:

- Low potassium
- Chest pain
- Infection
- Change in taste
- Allergic reaction
- Hair loss
- Blood in urine
- Non-infectious pneumonitis (inflammation of the lung)
- Muscle weakness
- Gallstones and gall bladder damage
- The development of gout (painful joints due to an increase in a protein called uric acid in your blood) which may require therapy
- Decreased heart function
- Elevated liver tests

Other risks and inconveniences:
Obtaining blood samples may cause some discomfort, bruising, bleeding from the site of sampling, formation of a blood clot, and in rare cases, infection, dizziness and fainting. The blood pressure cuff may also cause discomfort or bruising to the upper arm.

Risks and side effects of endocrine therapy:

If your doctor chooses a endocrine therapy that is a pill, then you will be asked to take a pill by mouth, usually once a day the same time, however some endocrine treatments may be given at a more frequent schedule, which will be explained to you in detail.
The most common side effects of endocrine therapy are:

- Risk of stroke and cardiovascular disease
- Risk of uterine cancer
- Hot flushes
- Vaginal discharge
- Sexual dysfunction which may include decreased libido, decrease in orgasmic response, vaginal dryness, pelvic pain, infertility, and/or changes in the labia or perineum.
- Menstrual abnormalities
- Risk of osteoporosis and fractures

- High cholesterol
- Fatigue
- Poor sleep
- Bone or joint aches and stiffness

If your doctor chooses to give you an injection, it will be in the muscle and may be associated with the following complications:

- Abscess
- Hematoma
- Injury to blood vessels and peripheral nerves
- Pain at the injection site
- Tingling or numbness
- Infection
- Bleeding
- Allergic reaction

Radiation-Related Risks:
You will be exposed to radiation from nuclear medicine and CT scans. These procedures are necessary for your medical care and will occur even if you do not participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 3 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

Reproductive risks:
The risks to an unborn fetus or nursing child from everolimus are not known. These medications may damage sperm and may harm the baby if you become pregnant.

Therefore, women who are pregnant or nursing (breastfeeding) a child may not participate in this trial. You must confirm that, to the best of your knowledge, you are not now pregnant, and that you (or your partner) do not intend to become pregnant during the trial. A negative pregnancy test at the screening for all women of childbearing potential is a requirement for study entry.

If there is any possibility that you (or your partner) may become pregnant during the study, the study doctor will discuss appropriate birth control measures with you. If you are pregnant, you will be withdrawn from the trial without your consent.

If you will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you.

Benefits
Information from this study may help you and/or other people with metastatic breast cancer that is no longer controlled by hormonal therapies.

You may receive no direct benefit from being in this study. However, your taking part may help breast cancer patients get better care in the future.

Other Treatment outside this Study
Instead of being in this study, you have these options:

1. Supportive care (care to help you feel more comfortable, including hospice care)
2. Treatment with other drugs (chemotherapy, anti-angiogenic therapies).
3. Radiation therapy
4. Surgery
5. Other hormonal therapies
6. Other experimental therapy

New Information
It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Compensation
You will not be offered payment for being in this study.

How will you protect my private information that you collect in this study?
Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information
Your samples, genomic data and health information will be stored and shared with other researchers. The samples and information will be available for any research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from.

Medical Record
If you have been an Emory, Grady Health System and Saint Joseph's Hospital patient before, then you already have an Emory, Grady Health System and Saint Joseph's Hospital medical record. If you have never been an Emory, Grady Health System and Saint Joseph's Hospital patient, you do not have one. An Emory, Grady Health System and Saint Joseph's Hospital medical record will be made for you if an Emory, Grady Health System and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory, Grady Health System and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory, Grady Health System and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory, Grady Health System and Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: None

Tests and procedures done at non-Emory, Grady Health System and Saint Joseph's Hospital places may not become part of your Emory, Grady Health System and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury
If you get ill or injured from being in the study, Emory, Grady Health System and Saint Joseph's Hospital will help you to get medical treatment. Emory, Grady Health System and Saint Joseph's Hospital and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory, Grady Health System and Saint Joseph's Hospital or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Elisavet Paplomata at telephone number 404-778-1900. You should also let any health care provider who treats you know that you are in a research study.

Costs
Everolimus (RAD001) will be provided by Novartis Pharmaceuticals, the company who makes this medication. There will be no cost to you for the everolimus or the serum pregnancy test you receive as part of this study.

You will have to pay for the items or services for which the study sponsor does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory and Saint Joseph's Hospital will submit claims to your insurance for items and services that the sponsor does not cover. Emory and Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory, Grady Health System and Saint Joseph's Hospital and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory, Grady Health System and Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study
You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest;

- You were to object to any future changes that may be made in the study plan;
- Staying in the study would be harmful;
- You need treatment not allowed in this study;
- You fail to follow instructions;
- You become pregnant;
- The study is cancelled;
- Your cancer progresses;
- or for any other reason.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory, Grady Health System and Saint Joseph's Hospital may use and disclose your PHI to get payment for study related treatment and to run normal business operations. c
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Winship Cancer Institute is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory, Grady Health System and Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: [Office for Human Research Protections; Food and Drug Administration].
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Pharmaceutical Collaborators, the manufacturers of Everolimus, and their authorized agents

- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
This authorization will not expire because it is a research study.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Elisavet Paplomata, MD, Winship Cancer Institute, Emory University, 1365-C Clifton Road NE, Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to

do so by the laws that cover them. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Elisavet Paplomata at 404-778-1900:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

If you are a patient receiving care at Saint Joseph's Hospital of Atlanta and have a question about your rights, please contact Kristi McGinnis at the Emory Saint Joseph's Hospital Research Committee via phone at 678-843-7767.

If you are a patient receiving care from the Grady Health System and have a question about your rights, you may contact the Office of Research Administration at research@gmh.edu.

Consent and Authorization

Consent and HIPAA Authorization for Optional Study/Studies:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional study/studies previously described:

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____ **am / pm**

Signature of Subject (18 or older and able to consent) **Date** **Time** **(please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____ **am / pm**

Signature of Person Conducting Informed Consent Discussion **Date** **Time** **(please circle)**