

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

Cover page

Title: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

NCT number: NCT03747042
Document date: 12/20/2021

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

**Consent to be part of a Research Study
To be conducted at**

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

General Information – “Who is conducting this research?”

Principal Investigator

The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Nisha Unni, M.D., Department of Internal Medicine at UT Southwestern Medical Center.

Funding

The Cancer Prevention and Research Institute of Texas (CPRIT) is funding this study. CPRIT is providing money to UT Southwestern Medical Center to fund cancer research and prevention programs.

Purpose – “Why is this study being done?”

You are asked to participate in this research study because you have breast cancer that is treatable with surgery. Your cancer has special proteins on it that allow it to grow when exposed to estrogen, called estrogen receptors (ER).

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

In addition to surgery, your type of cancer is often treated with a drug called an aromatase inhibitor (AI). These are drugs approved by the Federal Drug Administration (FDA). These drugs prevent testosterone from being converted to estrogen. This decreases the level of estrogen in the body. Thus the cancer is prevented from growing. By not operating immediately, but treating with an endocrine drug for a few months before surgery, patients with larger tumors can often avoid mastectomy. This is considered a standard of care.

This study will use the aromatase inhibitor, Letrozole. Letrozole inhibits tumor growth by reducing the levels of estrogen and has been approved by the Food and Drug Administration (FDA) of the United States for use after surgery for postmenopausal women with estrogen receptor positive breast cancer. It is also considered a standard of care to give letrozole for a few months before surgery to shrink the tumor.

However, some cancers seem to be resistant or develop a resistance to this drug. In this situation, cancers may grow despite taking the pill.

This study will try to determine a method to find out which cancers are resistant or will become resistant to this type of treatment. This will allow us to tell which patients will benefit from the drug and which patients will not. This will allow doctors to better customize treatments for breast cancer. In addition, this study will analyze other molecules that may contribute to the treatment. If these can be identified, better drugs may be developed for the future.

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.

Information about Study Participants – “Who is participating in this research?”

As stated earlier, you are being asked to take part in this research study because you have breast cancer that is treatable with surgery. Your cancer has special proteins on it that allow it to grow when exposed to estrogen, called estrogen receptors (ER).

How many people are expected to take part in this study?
This study will enroll approximately 300 study participants.

Information about Study Procedures – “What will be done if you decide to be in the research?”

While you are taking part in this study, a piece of the original biopsy and a blood sample (about 2 teaspoons) will be sent for special study tests. Your blood may be drawn at any time during the study. You will then be given a pill called Letrozole for 7-30 days. This is an aromatase inhibitor (AI) that will likely be used even after your surgery for treatment of your breast cancer. You will take this once a day until 24 hours before your operation. You will then undergo routine surgery as planned by your surgeon. A piece of the tumor removed during the operation will be sent for a second set of study tests.

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. Many of the procedures are described below as **“standard care”** and would be done even if you do not take part in this research study. You will be told which ones are for **“research only”**.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer
--

In order to be a candidate for this study, you must have early stage breast cancer. This means that the cancer is fairly small, has not spread beyond the lymph nodes and can be treated with an operation such as a mastectomy or lumpectomy. You must also have entered and/or completed menopause.

The biopsy of your cancer will be or already has been tested for special proteins. These proteins are estrogen receptors (ER), progesterone receptors (PR) and Her2/neu (Her2). These are routine tests performed on all breast cancers. It helps doctors determine prognosis and customize treatments.

You may be eligible for the study if your cancer has estrogen receptors (ER+) and does not have Her2/neu (Her2-). ER+ cancers are stimulated by estrogen in your body to grow.

Most of the tests and procedures in the study are considered routine or standard of care. This means that these tests would be done before your surgery to learn about your current health even if you did not take part in this study.

Before treatment begins, you will undergo a screening process. This will involve routine procedures done on all surgical cancer patients. These procedures are: a medical history, a complete physical examination, and routine blood tests. You will also have a chest x-ray before your surgery. Your doctor may also order a bone scan, CT scan of your chest, abdomen and pelvis if indicated. Your doctor may order a PET scan if there is suspicion that the breast cancer has spread to your bones, lungs, and/or liver. These tests are all done as routine care.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you as well as other possible options.

Study Procedures - as a participant, you will undergo the following procedures:

As part of the study, we will obtain tumor sections from the initial diagnostic core biopsy that you had. This biopsy is done as standard of care to establish the diagnosis. The biopsy is a procedure that involves cleaning the skin with soap and numbing the skin and breast tissue with a numbing medicine (Lidocaine). A needle is placed into the breast tumor and pieces of tumor tissue are removed. This is called a core biopsy. To get enough tumor tissue for the study, 1-6 cores will be removed. This is often done with the help of an ultrasound. This is a painless device that uses sound waves to see the cancer tissue underneath the surface of the skin and can direct the biopsy to the right place.

About 7-30 days prior to your operation, you will be asked to take the drug called letrozole. It is a drug called an aromatase inhibitor (AI). This drug is a pill that you take once a day by mouth. Letrozole is FDA approved for the treatment of breast cancer. Letrozole is a drug that you will likely continue for your breast cancer treatment after your surgical procedure. Even if you did not participate in the study, your doctor would likely prescribe letrozole or another anti-estrogen or AI for the treatment of your breast cancer after surgery. Letrozole drug is used for your breast cancer type (ER+) because it prevents estrogen from stimulating cancer growth.

As with all drugs, there is the chance that some foods or medicines can affect how the study drugs work such as estrogen and progesterone hormones. We will ask you to give us a detailed list of all the medicines (including over the counter medicines) that you are taking before taking the study drug. You should tell your doctor about all the medications (over the counter herbal, and prescription) you are currently taking and check with your study doctor before beginning any new medicines.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

Pill Diary: We will ask you to complete a simple pill diary. In this diary you will write down the times you take your medicine every day. This record keeping should take about 1-2 minutes each day. You will also write how the pills made you feel. This diary will help us track if you missed any pills and also if you had any side effects.

You will take one letrozole pill each day until 24 hours before your cancer surgery. You will only need to complete the pill diary during the time you are taking letrozole before your surgery.

Surgery: Your operation to remove your cancer will not be changed because you take part in the study. Once the tumor is removed, it will be sent for routine analysis by the pathologist. A small part of the tumor will be used for research. Studies may be performed on the original biopsy to see if the letrozole caused any changes. This will not interfere with the routine analysis of your cancer.

Your doctor will decide whether to continue the letrozole following completion of the study. This will be based on your current health condition and the findings of the routine analysis of your surgically removed cancer.

Blood Draw: You will have a one-time blood draw (about 2 teaspoons) at any time point while you are in the study. If you are having blood drawn for other reasons, we will try to obtain this sample at the same time, so you do not have an additional needle stick. This blood will be looked at for certain factors (DNA) that may cause or relate to breast cancer or other conditions or illnesses.

Follow Up: After you have completed taking letrozole and have had your surgery, you will be followed about every six months for up to ten years to see how you are doing after being in the study. The research team may look in your medical record to obtain information on how you are doing. Or a research team member may call you.

If during this follow up period, your disease comes back we will collect the data that results from the routine biopsy.

We may want to contact you in the future for participation in other research studies or clinical trials. If you do not agree to be contacted in the future, you may still take part in the main study as described above.

Permission for future contact:

I agree to allow my study doctor, or someone approved by my study doctor, to contact me in the future.

___ Yes _____ Initial

___ No _____ Initial

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

Risks – “What are the risks of participation in the research?”

Letrozole – Letrozole side effects can be reversed, if they occur, when you stop taking the drug. This drug may cause some, all, or none of the side effects listed here. You should talk to your doctor about these side

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer
--

effects. You may also have side effects we have never seen before. We cannot predict whether this will happen. Your doctor will check you closely to see whether you are having any side effects.

Common side effects you might have include:

- Joint pain
- Tiredness
- Headache
- Dizziness
- Swelling in your hands, feet, or lower legs
- Hot flashes
- A rise in the amount of cholesterol in your blood if you take the drug for a long period of time
- Nausea

Uncommon side effects seen are:

- Pain in your muscles
- Loss of bone density and the danger of getting brittle bones (osteoporosis) if you take the drug for a long period of time
- Change in sleep (more sleep or less sleep)
- Rash
- Constipation
- Shortness of breath
- Cough
- Diarrhea
- Vomiting
- Liver inflammation
- Loss of appetite

Serious and/or life-threatening side effects that may occur with long term use of this drug are bone fractures and heart attack. In this study, you will take Letrozole every day for 7-30 days. This means the chance of you getting these long-term effects is very small.

Tumor biopsy (core breast biopsy) – You will have mild to moderate pain during the injection of the anesthetic. This will last for a few minutes afterward. There is a chance that you will have mild pain and tenderness or bruising around the biopsy site. This may last for up to 1 to 2 weeks after the biopsy. There is small chance of having significant bleeding or infection at the site of the biopsy.

A rare but serious side effect of pneumothorax (collapsed lung) can occur which may require additional treatment.

Lidocaine - a numbing drug, may burn or cause a rash, redness or soreness where you get the shot. There is a risk that this drug may cause problems with heart rhythm.

Pill Diary – this may be inconvenient for you.

Blood Draw- Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer
--

Risks that are not known:

Aromatase inhibitors have been used to treat breast cancer for many years. The risks are fairly well understood. However, there may be some risks that are not known that may become evident in the future. If you have side effects from this treatment, please tell your doctor or nurse about them as soon as possible.

Genetic Informational risks

This research study includes genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Releasing this information to you could cause psychological distress, anxiety or family problems. Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information is released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study at any time, please discuss your decision with the principal investigator. The researcher will discuss with you other options for your routine care.

Are there risks if you also participate in other research studies?

Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?

The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – “How could you or others benefit from your taking part in this study?”

There is no guarantee or promise that you will receive any benefit from this study. We hope the information learned in this study will help other patients being treated for breast cancer in the future.

Alternative procedures or course of treatment – “What other options are there to participation in this study?”

You may have an operation to remove your cancer without taking the study drugs prior to it.

Costs – Will taking part in this study cost anything?

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as: physical examinations, routine blood tests, x-rays, CT scans, PET scans, tumor biopsies, medications. It is important to understand that some insurance companies do not cover some costs (for example, approved drugs used in a way different from the package instructions). If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?

Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include: the results of your study and/or non-study linked laboratory tests, x-rays, etc. as well as parts of your medical record and medical history.

We will get this information by gathering information from you, your medical record, and the results of your tumor and blood testing for research.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer
--

How will your PHI be shared?

Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- the members of the local research team.
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- the Research offices at the University of Texas Southwestern Medical Center, and Parkland Health and Hospital System.
- Novartis, Inc., the company that makes Letrozole (in case of an adverse reaction)
- the Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

How will your PHI be protected?

In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of the UT Southwestern Medical Center or Parkland Health and Hospital System for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?

You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Dr. Nisha Unni, UT Southwestern Medical

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

Center, Dallas TX 75390-9179. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?

The federal rules say that you can see the health information that we collect about you and use in this study.

How long will your PHI be used?

By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends and all required study monitoring is over.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:

Nisha Unni, MD at 214-648-4180 during business hours and 214-645-4673 (HOPE) at other times.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at 214-648-3060.

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

			AM PM
Printed Name of Participant	Signature of Participant	Date	Time
			AM PM
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time

Witness / Interpreter Signature Section

Interpreter/witness (Interpreter signature required per hospital policies when physically present.)

I attest that I have interpreted the information in this consent form and it was explained to, and apparently understood by the subject or the subject's legal authorized representative, and that informed consent was freely given by the subject or the subject's legally authorized representative as indicated by their signature on the associated **short form**.

			AM PM
Printed Name of Interpreter	Signature of Interpreter	Date	Time

Title of Study: Pre-Surgical Trial of Letrozole in Post-Menopausal Patients with Operable Hormone-Sensitive Breast Cancer

Witness Signature (required when interpreter is not physically present-e.g., Language Line is used):

By signing below:

I attest that the information in the consent form was accurately explained to, and apparently understood by the subject or the subject's legal authorized representative, and that informed consent was freely given by the subject or the subject's legally authorized representative as indicated by their signature on the associated **short form**.

_____	_____	_____	_____	AM PM
Printed Name of witness	Signature of witness	Date	Time	

Blind or Illiterate Signature Section *At the time of consent, also complete this section if consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English (e.g., blind, physically unable to write, etc.)*

Declaration of witness:

By signing below, I confirm I was present for the entire consent process. The method used for communication (e.g., verbal, written, etc.) with the subject was: _____.

The specific means (e.g., verbal, written, etc.) by which the subject communicated agreement to participate was: _____.

_____	_____	_____	_____	AM PM
Printed Name of Witness	Signature of Witness	Date	Time	