

CONSENT FORM

(Randomized Study)

CIRB NSABP B-42: A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer

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CIRB NSABP B-42: A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more information.

Why have I been asked to take part in this research study?

You are being asked to take part in this study because you had breast cancer with a positive estrogen and/or progesterone (ER/PgR) hormone receptor test *and* because you received 5 years of hormonal therapy to help prevent the cancer from returning. Some of your hormonal therapy was with a drug called an aromatase inhibitor (AI). Although you have no evidence of cancer now, it is still possible that your breast cancer may return. Therefore, you are being asked to take part in this research study to learn if receiving additional treatment after completing standard therapy will further reduce the chances of breast cancer returning.

Who is conducting the study?

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is conducting this study.

Why is this research study being done?

This study will look at the effects (good and bad) that letrozole has on you.

- The main purpose of the study is to learn whether or not continuing hormonal therapy with an AI called letrozole for 5 additional years after already taking 5 years of hormonal therapy (which included an AI) can further reduce the chance of breast cancer returning. Letrozole is investigational (still being researched) for use in patients who have already received an AI as part of their 5 years of hormonal therapy. Letrozole is considered “investigational” because it has not yet received approval from the Food and Drug Administration (FDA) or Health Canada for use after 5 years of hormonal therapy which included an AI.

An AI works by interfering with a substance called aromatase that helps to make estrogen. Estrogen is known to promote the growth of hormone receptor-positive breast cancers such as yours. An AI almost completely blocks out estrogen in postmenopausal women. By blocking out the estrogen levels, growth of tumors is blocked and the chance of breast cancer returning is smaller. In this study, you will be given letrozole or a placebo (a pill that looks like letrozole but does not contain any active drug) after 5 years of hormonal therapy. It is important to look at whether or not taking additional letrozole after already taking an AI affects how well letrozole works to continue to reduce the chances of cancer coming back.

- Another reason for doing this study is to find out whether or not taking the drug letrozole after taking 5 years of hormonal therapy that included letrozole (or other AI) causes more thinning of your bones (osteoporosis) which can cause your bones to break more easily. We also want to find out if letrozole increases the chance of heart attack, stroke, and other problems with blood vessels called arteries.

How many people will take part in the study?

About 3,840 women will take part in this study.

What will happen if I take part in this research study?

Before you begin the study: You will need to have the following exams, tests, and procedures to find out if you can be in the study. These exams, tests, and procedures are part of regular cancer care and may be done even if you do not join this study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- medical history and physical exam
- mammogram
- testing for bone mineral density (This is a test to measure the strength of bones.)
- blood tests to measure your cholesterol levels. These blood tests will be done because some patients in studies with letrozole have developed higher than normal cholesterol levels. Because studies have not confirmed if this is related to letrozole and because increased cholesterol levels are a common problem for postmenopausal women, your doctor will check your cholesterol before you join the study. Your doctor may also check these levels while you are receiving study therapy.

During the study: If the exams, tests and procedures show that you can be in the study and you choose to take part, then you will be “randomized” into one of the two treatment groups. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either of the two groups.

After you have joined the study, you will begin your study drug.

If you are in Group 1: You will take a placebo tablet that looks like the letrozole tablet but does not contain any active drug. You will take 1 tablet by mouth every day for 5 years.

If you are in Group 2: You will take a letrozole tablet (2.5 mg each day). You will take 1 tablet by mouth every day for 5 years.

Neither you nor your study doctor will know whether you are taking letrozole or placebo.

Summary of treatment:

Group 1	Group 2
<i>Placebo</i> <i>One tablet daily for 5 years</i>	<i>Letrozole 2.5 mg</i> <i>One tablet daily for 5 years</i>

During the study you will need to have the following tests and procedures. They are considered part of regular cancer care.

During your treatment with letrozole/placebo:

- history and a physical exam by your doctor about every 12 months. Also, every 6 months between your yearly exam by your doctor, your study doctor or other study personnel will check with you to see how you are doing on the study medication. This may or may not require an office visit or physical exam. This will be up to your study doctor.
- mammogram about every 12 months.
- bone mineral density testing about every 2 years. Your doctor may recommend this test be done more often, depending on the results of your previous bone mineral density tests.
- blood tests to check your cholesterol levels. How often these blood tests will be done depends on your cholesterol test results before you started taking the study drug. It also depends on whether or not you have any medical or family history that might mean you are at increased risk for developing heart problems in the future. You should discuss this with your study doctor.

Other tests

Your doctor may schedule other blood tests, bone mineral density testing, and other tests or procedures which are not required for this study but which your doctor believes are a part of good medical care to monitor your health while you are on the study. Discuss this with your study doctor.

Other drugs your doctor may prescribe:

Your doctor may recommend treatment with bisphosphonates, drugs which strengthen bone, depending on the results of your bone mineral density test(s).

Your doctor may recommend drugs to lower your cholesterol levels if the results of your cholesterol tests show that these levels are higher than normal.

After you complete the letrozole/placebo, for the rest of your life:

- contact from your study doctor or nurse about every 12 months to collect information about your health. This contact may be by phone with study personnel or during an office visit with your doctor.
- mammogram about every 12 months

Optional tissue collection

We would also like to have tissue samples from the surgery you had when your cancer was first diagnosed. These samples will be sent to the NSABP only if you agree to the tissue collection described at the end of this consent form.

How long will I be on the study?

Therapy with letrozole or placebo will last a total of 5 years from the date you start taking the tablets. We would like to keep track of your health for the rest of your life.

Can I stop being in the study?

Yes, you can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study drug can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and tests will be most helpful for you.

You can choose to withdraw in one of two ways. In the first, you can stop your study treatment, but still allow the study doctor to report your health status to the NSABP. In the second, you can stop your study treatment and request that no new information be reported to the NSABP.

Can anyone else stop me from being in the study?

The study doctor may stop you from taking part in this study at any time if he or she believes it is in the best interest for your health, if you do not follow the study rules, or if the study is stopped by the NSABP.

What side effects or risks can I expect from being in the study?

You may have side effects while on this study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person. Everyone taking part in the study will be carefully watched for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medications to help lessen some of the side effects. Many side effects go away soon after you stop taking your study drugs. In some cases, side effects may be very serious, long-lasting, or may never go away. *There is also a risk of death.*

You should talk with your study doctor about any side effects that you may have while taking part in the study.

Risks and side effects related to therapy with letrozole/placebo include those which are:

Likely

These side effects occur in **25% or more** of patients receiving letrozole:

- Weakness or decreased energy
- Hot flashes/flushes

These side effects occur in **10-24%** of patients receiving letrozole:

- Increased cholesterol levels
- Increased sweating
- Swelling in hands or feet
- Constipation
- Dizziness
- Headache
- Joint pain/stiffness

Less likely

These side effects occur in **3-9%** of patients receiving letrozole:

- Difficulty sleeping
- Depression
- Hair loss or thinning
- Diarrhea
- Nausea
- Loss of appetite
- Bone fracture
- Osteoporosis, or bone thinning, a disease that can affect postmenopausal women. The study drug may increase your chance of developing osteoporosis. The study drug also may slightly increase your risk for bone fractures caused by osteoporosis. Talk with your doctor or nurse about your risk of developing osteoporosis, about tests that can detect osteoporosis, and about ways to prevent osteoporosis and fractures.
- Drowsiness
- Muscle aches
- Back pain
- Shortness of breath
- Vaginal bleeding
- Vaginal dryness

Rare but serious

These side effects occur in **less than 3%** of patients receiving letrozole:

- Heart problems, including narrowing of the blood vessels in the heart, chest pain, and heart attack have occurred in women receiving letrozole. However, the percentage of women developing these problems while taking letrozole was similar to the percentage of women receiving tamoxifen, which is an alternative hormonal therapy for breast cancer. In another study, the percentage was the same with women taking letrozole as with women taking a placebo (a pill that contains no active drug). This means that letrozole may not be associated with increasing the risk for heart problems, or it may be associated with a very small increase in risk. One of the aims of this study is to learn more about this risk.
- Blood clot in a blood vessel

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in this study?

Taking part in this study may or may not make your health better.

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

You have received standard therapy for your breast cancer. Currently, there is no approved therapy for cancer-free patients after 5 years of adjuvant hormonal therapy that included an AI. In breast cancer, adjuvant therapy is treatment that is given after breast surgery to lower the chance of cancer coming back. Although letrozole is available in the United States and Canada, it is not approved for use in patients who have already received 5 years of adjuvant hormonal therapy which included an AI. The FDA and Health Canada consider the use of letrozole in this setting to be investigational.

You may choose to receive no further treatment after already receiving 5 years of standard therapy. Please talk with your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure 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, for quality assurance, and data analysis include:

- the National Surgical Adjuvant Breast and Bowel Project (NSABP);
- the All Ireland Cooperative Research Group (ICORG);
- Novartis Pharmaceuticals Corporation, (the company that provides letrozole/placebo for this study);
- your local Institutional Review Board (IRB), a group of people who review the research study to protect your rights;
- the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials; and
- government agencies, including the NCI or its authorized representatives, the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), Health Canada, and the Irish Medicines Board. These agencies may review the research to see that it is being done safely and correctly.

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer during this study. Some health plans will not pay these costs for people taking part in studies. 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.

Tests, procedures, or drugs for which there is no charge in this study:

Novartis Pharmaceuticals Corporation, through the National Cancer Institute (NCI) will provide you with letrozole/placebo at no cost to you for this study.

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://www.cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him or her at the number listed on the cover page.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

The Data Monitoring Committee (DMC), an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. You may be asked to sign another consent form in response to new information.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor at the number listed on the cover page.

For questions about your rights while taking part in this study, call the MultiCare Health System Institutional Review Board (IRB) (a group of people who review the research to protect your rights) 253-403-3877.

You may also call the Operations Office of the NCI Central Institutional Review Board [CIRB] at 1-888-657-3711 [from the continental U.S. only].)

Additional Studies

The following section of the informed consent form is about additional research studies that may be done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be part of the main study even if you answer "no" to taking part in these additional studies.

What about the use of my tissue for research?

About using tissue for future research: The NSABP would like some of the tissue from the breast surgery you had when your cancer was first diagnosed. If you agree, the tissue samples will be sent to the NSABP Tissue Bank where the tissue will be kept and may be used in future research to learn more about cancer and other diseases. The tissue samples will be given only to researchers approved by the NSABP. Any research study using your samples must also be approved by an IRB. The research that is done with your tissue samples is not designed to specifically help you. It might help people who have cancer and other diseases in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your tissue samples will not affect your care.

Things to think about: The choice to let the NSABP keep the tissue samples for future research is up to you. No matter what you decide to do, it will not affect your care. If you decide now that your tissue samples can be kept for research, you can change your mind at any time. Just contact your study doctor and let him or her know that you do not want the NSABP to use your tissue samples, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until the NSABP decides to destroy them.

In the future, people who do research with your tissue samples and people who do other types of health-related research may need to know more about your health. While the NSABP may give them reports about your health, they will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue samples are used for genetic research (about diseases that are passed on in families). Even if your tissue samples are used for this kind of research, the results will not be told to you and will not be put in your health records.

Your tissue samples will only be used for research and will not be sold. The research done with your samples may help to develop new products in the future, but you will not get paid.

Benefits: The possible benefits of research from your tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them. The research that may be done with your tissue is not specifically designed to help you, but it may help people who have cancer or other diseases in the future.

Risks: The greatest risk to you is the release of information from your health records. The NSABP will protect your records so that your name, address, phone number, or any other information that may easily identify you will be kept private. The chance that this information will be given to someone else is very small.

There will be no cost to you for any tissue collected and stored by the NSABP.

Making your choices

Please read each question below and think about your choice. After reading each question, circle “yes” or “no.” If you have questions, please talk to your doctor or healthcare team member.

Participation in the optional collection and use of tissue samples: Remember, no matter what you decide about the **optional** collection and use of the tissue samples in this research study, you may still take part in the B-42 study.

1. My tissue samples may be kept by the NSABP for use in future research to learn about, prevent, or treat cancer.

YES

NO

2. My tissue samples may be kept by the NSABP for use in future research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

YES

NO

Contact in the future for other research: Remember, no matter what you decide, you may still take part in the B-42 study.

3. My study doctor (or someone he or she chooses) may contact me in the future to ask me to take part in more research.

YES

NO

Where can I get more information about cancer and its treatment?

- You may call the National Cancer Institute’s (NCI’s) Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615
- You may also visit the NCI Web site at <http://cancer.gov>
- For the NCI’s clinical trials information, go to: <http://cancer.gov/clinicaltrials>
- For the NCI’s general information about cancer, go to: <http://cancer.gov/cancerinfo>
- You may also visit the NSABP Web site at <http://www.nsabp.pitt.edu>

You will receive a copy of this form. If you want more information about this study, ask your study doctor.

Signatures

I have been given a copy of all ten pages of this form. I have read the consent form or it has been read to me. This information was explained to me and my questions were answered.

I agree to take part in this research study.

Patient's name (printed or typed)

Patient's Signature Date

Physician name (printed or typed)

Physician Signature Date

Signature of person conducting the
Informed consent discussion

Date

Authorization (Permission) to Use or Disclose (Release) Identifiable Health Information for Research

CIRB NSABP B-42: A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer

Patient's Name: _____ Birth Date: _____

1. What is the purpose of this form?

The NSABP is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your personal health information, you must sign and date this form to give them your permission.

2. What personal health information do the researchers want to use?

The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter an NSABP research study, information that will be used and/or released may include the following:

- the history and diagnosis of your disease;
- specific information about the treatments you received, including previous treatment(s) you may have had;
- information about other medical conditions that may affect your treatment;
- medical data, such as laboratory test results; pathology results; and reports of physical exams, diagnostic tests, x-rays, and tumor measurements;
- information on side effects (adverse events) you may experience, and how these were treated;
- long-term information about your general health status and the status of your disease;
- data that may be related to tissue and/or blood samples that may be collected from you; and
- numbers or codes that will identify you, such as your social security number and medical record number.

You may request a blank copy of the NSABP data forms from the study doctor or his/her research staff to learn what information will be shared.

3. Why do the researchers want my personal health information?

The Northwest CCOP will collect your health information and share it with the NSABP Biostatistical Center and the NSABP Operations Center if you enter a cooperative group research study. The NSABP centers will use your information in their cancer research study. You are being asked to take part in a study known as: CIRB NSABP B-42: A Clinical Trial to Determine the Efficacy of Five Years of Letrozole Compared to Placebo in Patients Completing Five Years of Hormonal Therapy Consisting of an Aromatase Inhibitor (AI) or Tamoxifen Followed by an AI in Prolonging Disease-Free Survival in Postmenopausal Women with Hormone Receptor Positive Breast Cancer

NSABP THIS RESEARCH STUDY. To be in the study you must have had some previous treatment with a class of drugs called aromatase inhibitors (AI). This study will look at the effects (good and bad) that the drug letrozole, which is an AI, has on you.

- The main purpose of the study is to learn whether or not continuing hormonal therapy with an AI called letrozole for 5 additional years after already taking 5 years of hormonal therapy (which included an AI) can further reduce the chance of breast cancer returning.
- Another reason for doing this study is to find out whether or not taking the drug letrozole after taking 5 years of hormonal therapy that included letrozole (or other AI) causes more thinning of your bones (osteoporosis) which can cause your bones to break more easily. We also want to find out if letrozole increases the chance of heart attack, stroke, and other problems with blood vessels called arteries.

4. Who will be able to use my personal health information?

The Northwest CCOP will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. The Northwest CCOP may also permit these groups to come in to review your original records that are kept by The Northwest CCOP so that they can monitor their research study.

- the NSABP Operations Center;
- the NSABP Biostatistical Center;
- the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute that supports the research of the NSABP;
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law;
- other people or organizations assisting with NSABP research efforts (including other groups who review the research to protect the rights and ensure the safety of patients);
- Novartis (the company providing letrozole); and

- central laboratories, central review centers, and central reviewers. The central laboratories, centers, and review agencies may also give your health information to those groups listed above.

5. *How will information about me be kept private?*

The NSABP will keep all patient information private to the extent possible, even though the NSABP is not required to follow the federal privacy laws. Only researchers working together with the NSABP will have access to your information. The information will only be shared in a manner that will protect your identity.

The NSABP will not release personal health information about you to others except as authorized or required by law. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

6. *What happens if I do not sign this permission form?*

If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

7. *If I sign this form, will I automatically be entered into the research study?*

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a specific research consent form.

8. *What happens if I want to withdraw my permission?*

You can change your mind at any time and withdraw your permission to allow your personal health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new personal health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the person below. He/she will make sure your written request to withdraw your permission is processed correctly.

Karyn Hart, RHIT, CCRP
Program Coordinator
Northwest CCOP
315 Martin Luther King, Jr., Way
Tacoma, WA 98405
(253) 403-1461

8. How long will this permission last?

If you agree by signing this form that researchers can use your personal health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

9. What are my rights regarding access to my personal health information?

You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your personal health information kept by the Northwest CCOP. You do not have the right to review and/or copy records kept by the NSABP or other researchers associated with the research study.

Signatures

I agree that my personal health information may be used for the research purposes described in this form.

Signature of Patient
or Patient's Legal Representative: _____ Date: _____

Printed Name of Legal Representative (if any): _____

Representative's Authority to Act for Patient: _____

Signature of Person Obtaining Permission: _____ Date: _____

Printed Name of Person Obtaining Permission: _____