

<b>Official Title</b>	Association of HSD3B1 genotype with response to preoperative letrozole therapy among postmenopausal women with estrogen-receptor positive (ER+) HER2/neu-negative (HER2-) invasive carcinomas of the breast.
<b>NCT Number</b>	NCT05183828
<b>Document Type</b>	Informed Consent Form
<b>Document Date</b>	8/14/2024

Fred Hutchinson Cancer Center  
University of Washington

**Consent to take part in a research study:**

**Association of HSD3B1 genotype with response to preoperative letrozole therapy among postmenopausal women with estrogen-receptor positive (ER+) HER2/neu-negative (HER2-) invasive carcinomas of the breast.**

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**Emergency number (24 hours): 206-598-6190 and ask for the oncology fellow who is on-call**

Call Breast Group Research Desk 206-606-6329 Monday through Friday, 9 am to 5 pm.  
At all other times, call the paging operator at UW Medical Center at 206-598-6190; ask the operator to page the on-call Oncology Fellow.

**Important things to know about this study.**

You are invited to participate in a research study. The purpose of this research study is to find out more about the anti-cancer effects of letrozole in post-menopausal women with invasive carcinoma of the breast that is estrogen-receptor positive (ER+) and HER2/neu-negative (HER2-). We are studying whether this medication will work better, worse or the same in women who do or do not have a mutation in a gene called HSD3B1. Letrozole will be given for 21 days before surgical resection.

People who agree to join the study will be asked to undergo a buccal swab (cheek swab), complete a quality-of-life questionnaire, and take letrozole (an anti-estrogen pill) for 21 days before surgery. This study involves testing your left-over tumor tissue from a previous biopsy and surgery to determine whether there is a mutation in the gene HSD3B1, and how this might affect the biology of the tumor (e.g. estrogen, progesterone, and androgen receptor status).

The side effects of letrozole are well known, it can cause hot flashes, night sweats, mood changes, sleep disturbance, vaginal dryness, or joint pain. You may also experience mild temporary discomfort associated with swabbing the inside of your mouth to obtain a DNA sample.

You do not have to join this study. You can choose to receive standard methods to treat your breast cancer instead of participating in this study. We will give you details about the purposes, procedures, and risks related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

### **We invite you to join this research study.**

We invite you to join this research study because you are a post-menopausal woman with ER+/HER2- breast cancer and are scheduled to have surgery to remove your cancer. Up to 68 people will join this study.

Research is not the same as treatment of medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say “yes” or “no”, or to drop out after joining. If you say “no,” you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

### **Why are we doing this study?**

In this study, we want to understand whether letrozole works better for post-menopausal women who have ER+ and HER2- invasive carcinoma of the breast with the HSD3B1 gene mutation. We are doing this study to examine if changes to the HSD3B1 gene affects hormones in a way that makes some medications for breast cancer more or less effective.

If you join this study, you would receive letrozole before surgery.

### **What research tests, procedures, and treatments are done in this study?**

If you agree to be in this study, we would do these tests and procedures:

- We will prescribe you letrozole to take daily for 21 days before surgery. Your doctor may also prescribe you letrozole or another anti-estrogen drug as treatment for your breast cancer after you have completed your surgical treatment. We will ask you to keep a diary indicating each time you took the medication.

- We will examine your previously collected tumor biopsy and surgical specimen for the gene mutation if there is enough tissue for analysis as determined by a pathologist.
- We will obtain a buccal sample. We will give you a plastic stick (similar to a lollipop stick) with a small soft fabric brush on the end. We will ask you to rinse your mouth with water, rub the swab gently on the inside of your cheek, and then place the swab in a test tube. We will either send you a buccal swab kit in the mail, or a study coordinator will help you obtain a sample during a clinic visit. We will test this sample to see whether you have the gene mutation in HSD3B1.
- We will examine your medical records.

We will also conduct genetic testing on your tissue. Your tissue contains DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests. This study will only test whether you have a mutation in a gene called HSD3B1. We will test both the cheek swab sample and the tumor tissue to see if the mutation is in either, or both, samples.

Within the week prior to your scheduled surgery, we will call you to complete a quality-of-life questionnaire, which should not take more than five minutes of your time. This questionnaire consists of five sections. For each section, you will be asked to rate (0-4) a number of statements based on your well-being over the past-7 days.

After you have finished taking letrozole and had your surgery, you would no longer be on the study and resume your standard medical care.

### **How long would you stay in this study?**

If you join this study, you would stay in this study for about 5 weeks. You would receive letrozole for 21 days prior to your tumor resection surgery. In case the tumor resection surgery occurs before or after day 22, you would need to be able to receive letrozole for a minimum of 14 days and can take letrozole for up to 70 days. This would mean you would be in this study for up to 12 weeks.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The entire study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

## What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study.

If you join this study, we would tell you if we discover new side effects that could affect you. You should talk with your study doctor about any side effects that you may have while taking part in the study.

### Side effects of letrozole:

Likely (more than 20% of patients)	Less likely (4-20%)	Rare but serious (less than 3%)
<ul style="list-style-type: none"><li>• Fatigue</li><li>• Increased sweating, night sweats</li><li>• Hot flashes, flushing</li><li>• Mood changes</li><li>• Difficulty sleeping</li><li>• Vaginal dryness</li><li>• Joint pain (arthralgias)</li><li>• Muscle pain (myalgias)</li><li>• Loss of bone density (osteopenia), which may lead to decreased height</li><li>• Bones becoming weak and brittle (osteoporosis)</li></ul>	<ul style="list-style-type: none"><li>• Fluid around lungs</li><li>• Swelling of the liver which may cause belly pain</li><li>• Constipation, diarrhea, nausea, vomiting, loss of appetite, heartburn</li><li>• Swelling of the body</li><li>• Dizziness, headache</li><li>• Worry, depression</li><li>• Hair thinning</li></ul>	<ul style="list-style-type: none"><li>• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness</li><li>• Stroke which may cause weakness, paralysis</li><li>• Blood clot which may cause swelling, pain, shortness of breath</li><li>• Liver damage which may cause yellow eyes and skin</li><li>• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat</li><li>• Vaginal bleeding</li></ul>

You are at risk for any of these side effects as long as you are taking letrozole. Also, your risk of some of the serious but rare side effects, such as stroke liver damage, and blood clots, may continue for several years after you stop taking letrozole. There may be other side effects that we cannot predict. You should discuss risks and side effects with the study doctor or with your regular doctor.

### Buccal sample (cheek swab) risks:

- The oral swab may briefly cause some discomfort on the inside of your cheek during the swabbing process.

## **Non-physical risks**

If you join this study, non-physical risks are:

- Results of genetic tests might be released by accident. This risk is very low, because we keep personal information private. If these results became known, you could have problems from others knowing about your genetic test results. For example, the results could cause stress or anxiety in family members who learn about their own risk of developing disease, or you could have problems with insurance because of your health status. There is also a risk that these test results could be combined with other information to identify you. If this happens, we will notify you and make every attempt to retrieve the information from parties to which it was released.

## **What are the benefits?**

Although the study will not benefit you directly, we hope the information we learn will help people with breast cancer in the future.

## **You have other choices besides this study.**

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Other choices include: standard treatment, participating in another research study, or no treatment.

Enrollment in this study may exclude you from other research studies.

## **Protecting your Privacy as an Individual and the Confidentiality of Your Personal Information**

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutch IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and University of Washington

- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.
- Veterans Affairs Seattle Institute for Biomedical and Clinical Research (VA SIBCR)

We will do our best to keep your personal information confidential. We will keep all study related data on encrypted devices with password protected servers. Once your tumor or cell sample results are analyzed we will separate this data from your identifiable information using a unique code.

But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, we are required to report certain sexually transmitted diseases and HIV infection. We also have to report suspected abuse or neglect of children and vulnerable adults. Workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.

We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.

This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To the funding agency and groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by the FDA.
- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.

- To authorities, if we learn of child abuse, elder abuse, or if participants might harm themselves or others.

### **How is my genetic information protected?**

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

### **Would we pay you if you join this study?**

There is no payment for being in this study.

### **Would you have extra costs if you join this study?**

There are no costs for being in this study. Letrozole will be charged to your insurance because letrozole is a part of standard breast cancer treatment for your type of estrogen-sensitive breast cancer.

### **What if you get sick or hurt after you join this study?**

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems, distress or illness related to this research, immediately contact Dr. Flanagan at 206-667-6736. You will be treated or referred for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

If there are concerns about loss of confidentiality, please contact Dr. Flanagan at 206-667-6736.

### **What will my information and/or buccal and tissue samples be used for?**

Your information, tumor samples, and buccal samples will be used for the purposes of this study.

Your tumor and buccal samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your samples.

During this study, we do not expect any test results that would affect your care, so we do not plan to return results to you.

### **Will my information and/or buccal and tissue samples ever be used for future research?**

After we do tests on tissue in this study, some tissue may be left over. We invite you to donate this leftover tissue for future research. This may include genetic research. We also would like to use your information for future research.

If you join this study, you would not have to donate tissue or information for future research. You would be free to say “yes” or “no.” Regular medical care would not change if you say “no.”

If you say “no,” your tissue and information (even if made anonymous) will not be used in future research.

If you donate tissue and information, it would be stored in a secure location. If we want to use your tissue for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated tissue and information would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with tissue and information might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the tissue.

If you donate tissue and information for research, you could withdraw the donation at any time by calling Dr. Flanagan at 206-667-6746. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated tissue to you or your doctor, but we might be able to destroy the donated tissue. We could not destroy tissue if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

## **Your rights**

- You do not have to join this study. You are free to say “yes” or “no”.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.

## **Your responsibilities**

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take letrozole as directed.
- Tell us about side effects.

### For more information

If you have questions or concerns about this study, you may talk to a member of the study team anytime. Other people you can talk to are listed below.

<b>If you have questions about:</b>	<b>Call:</b>
This study (including complaints and requests for information)	206-667-6736 (Dr. Flanagan) 206-606-6329 (Breast Group Research Desk)
If you get sick or hurt in this study	206-667-6736 (Dr. Flanagan)
Your rights as a research participant	206-667-5900 or email <a href="mailto:irodirector@fredhutch.org">irodirector@fredhutch.org</a> (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-1113 (Fred Hutchinson Cancer Center, Patient Financial Services) 866-245-4373 (UWMC, Patient Financial Services)

Emergency number (24 hours): 206-598-6190 and  
ask for the oncology fellow who is on-call

Read the question below and think about your choice. When you decide, please circle  
**YES** or **NO**.

Do you agree to donate your tissue and information for future research to study cancer?

(circle one)

**YES**

**NO**

## Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent;  
and
- agree to participate in this study.

\_\_\_\_\_  
Participant Name (printed)

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Date

## Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

\_\_\_\_\_  
Name of Person Conducting the  
Informed Consent Discussion

\_\_\_\_\_  
Signature of Person Conducting the  
Informed Consent Discussion

\_\_\_\_\_  
Date

## Impartial Witness

If you were a witness for a participant who was not able to read this written consent form, sign below to indicate (1) you were present at the consent discussion in person, (2) you witnessed the verbal presentation of the written consent form, and (3) the participant had the opportunity to ask questions and agreed to take part in the study.

Impartial Witness:

\_\_\_\_\_  
Name of Impartial Witness

\_\_\_\_\_  
Signature of Impartial Witness

\_\_\_\_\_  
Date

Protocol: RG1121659/IR10794  
Current consent version date: 08-19-2024  
Previous consent version date: 09-12-2023  
Copies to: Researcher's file, Participant, Participant's medical record