THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Multicenter Trial for Eliminating Breast Cancer Surgery or Radiotherapy in Exceptional Responders to Neoadjuvant Systemic Therapy
2016-0046

Subtitle: MD Anderson Texas Medical Center Consent

Study Chair: Henry Kuerer

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn how often breast cancer recurs (returns after treatment) in the breast in patients who have been treated with chemotherapy or endocrine therapy and have had follow-up radiation therapy (but not surgery) or surgery (but not radiation) and are in complete remission (no evidence of disease).

This is an investigational study. Radiation therapy is delivered using FDA-approved and commercially available methods. The possible endocrine therapy will be given using FDA approved and commercially available drugs. The study doctor can explain how radiation therapy and endocrine therapy are designed to work.

Future patients may benefit from what is learned in this research study. You may be able to avoid surgery or radiation. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

You will receive radiation therapy or surgery possibly followed by endocrine therapy for as long as your doctor thinks it is in your best interest. Your participation on this study will be over after the follow-up period (10 years after you complete radiation therapy or surgery).

You and/or your insurance provider will be responsible for the cost of the standard of care treatments in this study (radiation therapy, surgery, and endocrine therapy) and all standard of care tests and procedures.

You may choose not to take part in this study.

1. STUDY DETAILS

Study Groups

If you agree to take part in this study, depending on the type of breast cancer you have, you will be assigned to 1 of 6 arms.

If the disease is either triple negative (ER/PR negative and HER2 negative) or HER2 positive, with or without lymph node involvement, you may be in **Arm A1 or A2**. As of September 2023, Arm A1 has closed, and participants will only be enrolled into Arm A2. As described below, you will have a biopsy and if there is no sign of disease, you will receive radiation. If the biopsy shows disease, you will be taken off study after surgery.

If you have ER and/or PR positive, HER2 negative disease that does not involve the lymph nodes, you will be in **Arm B1 or B2**. As of September 2023, Arm B1 has closed, and participants will only be enrolled into Arm B2. You will have endocrine therapy first, followed by an ultrasound. If the tumor is under a certain size at that time, you will receive radiation followed by endocrine therapy, followed by a biopsy. If the ultrasound shows the tumor has increased above a certain size, you will be taken off study after surgery.

Arms C and D are both closed to enrollment. If the disease is either triple negative (ER/PR negative and HER2 negative) or HER2 positive, and does not involve the lymph nodes (nodal disease), you may have been enrolled in **Arm C or Arm D**. If you are in Arm C, you will have surgery (a lumpectomy) without radiation. If the results of the surgery show disease, you will be taken off the study after surgery and receive radiation therapy outside of this study. If you are in Arm D, you will receive radiation therapy.

No matter which arm you will be in, tumor tissue collected at the beginning of the study will be used for testing that will help the doctor decide which arm you will be in. If you are being considered for **Arm B only**, a part of this tissue sample will also be used to determine your Oncotype score. The Oncotype test may be able to predict how likely it is for your breast cancer to return or respond to chemotherapy. If your Oncotype score is too high, you will not continue in the study.

Arm A Study Treatment and Visits

At any point after you have completed chemotherapy and before you begin radiation therapy, you will have an image-guided biopsy of the breast to test for evidence of disease. To perform an image-guided biopsy, a needle is inserted into the affected area

using imaging such as, ultrasound, MRI, or mammography to collect cells or tissue from an organ, lymph node, or suspected tumor mass. The doctor will use the imaging to guide the needle into the area. The sample collected will be a core biopsy that collects a small piece of tissue.

If the biopsy shows evidence of the disease, you will be scheduled for standard of care surgery and will still receive radiation therapy but will not remain on this study. You would sign a separate consent form for the radiation therapy and surgery.

Within 12 weeks after you have completed chemotherapy, you will have radiation therapy to your breast. The doctor will discuss the dose amount and length of the radiation therapy period with you. During radiation therapy, you will have weekly visits with your doctor.

Before your first radiation therapy visit and at 6 months and 1 year after you complete radiation therapy:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn to check for circulating tumor cells (CTCs) at 6 months and 1 year after you complete radiation therapy. CTC testing checks how many tumor cells are in your blood.

Arm B Study Treatment and Visits

After completing 3 months of endocrine therapy, you will have an ultrasound.

If the tumor has increased above a certain size, you will be scheduled for standard of care surgery but will not remain on this study.

If the tumor size remained the same, decreased, or did not increase by a certain amount, then you will be scheduled to have radiation followed by 6-12 months of endocrine therapy. The doctor will discuss the dose amount and length of the radiation therapy period with you.

After radiation, you will have an image-guided biopsy of the breast to check the status of the disease.

If the biopsy shows no evidence of the disease, you will receive additional endocrine therapy.

If the biopsy shows disease, you will be scheduled for standard-of-care breast conserving surgery but will not remain on this study.

All participants being offered radiation therapy, surgery, and/or endocrine therapy will be asked to sign a separate consent for them. The procedures and therapy will be described in more detail.

At your first visit and at 3 months after you complete endocrine therapy and then at 3-8 weeks, and 6 months after you complete radiation therapy:

- You will have a physical exam (this exam will not be required at the 3-month visit).

- Blood (about 2 ½ tablespoons) will be drawn for CTC and DNA and/or RNA sequencing. This test may not be done at your first visit if you are not at the clinic that day.
- At the 6 month visit, you will have an ultrasound.

These procedures will be repeated 1 year after you complete radiation therapy if you have a biopsy scheduled at that time point.

Arm C Study Treatment and Visits
You will have surgery to remove the tumor(s). If the surgery shows no evidence of disease, you will continue on the study. If the surgery shows evidence of the disease, you will be scheduled for standard-of-care radiation therapy but will not remain on this study. You would sign a separate consent form for the radiation therapy and surgery.

Before your surgery and at 6 months and 1 year after you complete surgery:
- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for CTC testing before your first radiation therapy visit, and at 6 months and 1 year after you complete radiation therapy.

Arm D Study Treatment and Visits
You will have surgery to remove the tumor(s). If the surgery shows no evidence of disease, you will continue on the study. You will sign a separate consent form for the radiation therapy and surgery.

Before your surgery, you will have a physical exam.

Questionnaires (All Arms)
You will be asked to complete 3 questionnaires about your quality of life and symptoms when you first agree to take part in this study, and again at 6 months, 1, 3, and 5, 7, and 10 years after your radiation treatment or surgery. The questionnaires can be completed by mail, email, or during a phone call. The questionnaires should take about 15 minutes to complete each time. If you are in Arm B, your first questionnaire can be completed at either your first or second visit.

Follow-Up
Every 6 months for 2 years (Cohort A2) or 5 years (all other patients) after you finish radiation therapy or surgery and then yearly for an additional 8 years (Cohort A2) or 5 years (all other patients), you will have a physical exam and mammogram. If the doctor thinks it is needed, you will have an MRI instead of a mammogram at every other 6-month visit.

About 220 participants will be enrolled on this multicenter study (about 50 in Arms A1 and A2, 20 in Arms B1 and B2, 50 in Arm C, and 30 in Arm D).

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The known side effects are listed in this form, but they will vary from person to person.

Tell the study staff about any side effects you may have, even if you do not think they are related to the procedure.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

There is a chance that the biopsy and/or surgery may miss a small amount of cancer. This information may impact your doctor's decision to recommend you additional or different therapy.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel "closed in" and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

There are no expected physical risks related to an **ultrasound**

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

You should discuss the risks of **questionnaires** with the study chair. The known risks are listed in this form, but they will vary from person to person. Some questions may make you feel upset or uncomfortable. You may refuse to answer any question. If you have concerns after completing the questionnaire(s), you are encouraged to contact your doctor or the study chair.

While you are in this research study, **mammograms** will be used to evaluate your disease. The frequency of these exams is the same as what you would receive as standard care. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer. Certain types of drugs or combinations of these drugs with radiation may further slightly

increase the risk of developing a new cancer.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study. Only authorized study staff will have access to study data.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Ask your doctor about acceptable methods of birth control.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may or may not result in your removal from this study, depending on when the pregnancy occurs. Please discuss this with the study team.

OPTIONAL PROCEDURES FOR THE STUDY—COHORT C and D PATIENTS ONLY

Optional Procedure #1: If you are assigned to Arm C or D and you agree, you will have an optional image-guided biopsy of the breast before surgery for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.

To perform an image-guided biopsy, a needle is inserted into the affected area using imaging such as ultrasound, MRI, or mammography to collect cells or tissue from an organ, lymph node, or suspected tumor mass. The doctor will use the imaging to guide the needle into the area. The sample collected will be a core biopsy that collects a small piece of tissue.

Optional Procedure #2: If you are assigned to Arm C or D and you agree, you will have an optional biopsy of the area where the tumor was removed for biomarker testing. This testing may be performed before the sample is sent to the pathology lab to check for disease. This testing will not compromise the sample or the ability of the pathologist to review the sample.

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure.

Optional Procedure Risks

Having **biopsies and bone marrow biopsies/aspirates** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have a tissue biopsy before surgery for biomarker testing? (If you are in Arms A or B, please select NO.)

YES NO

Optional Procedure #2: Do you agree to have your surgical sample used for biomarker testing before review by the pathology team? (If you are in Arms A or B, please select NO.)

YES NO

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care.

MD Anderson does not know at this time what you may be reimbursed for. A financial counselor will be made available to you after the injury or illness is reported. If the sponsor pays any of your medical expenses, they may need to be given your name, date of birth, and Medicare ID or social security number. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Henry Kuerer, at 713-745-5043) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can continue to collect data from your routine medical care. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health 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 that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

To protect your identity, the samples collected from you will be labeled a unique number instead of your name or other identifying information. Only the study doctor or study staff will have access to the code that can link you to your samples.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under this protocol.

_____
_____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT
I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT