Title: PRE-OPERATIVE WINDOW OF ADJUVANT ENDOCRINE THERAPY TO INFORM RADIATION THERAPY DECISIONS
IN OLDER WOMEN WITH EARLY-STAGE BREAST CANCER (POWER)

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Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____
Medical Record # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a copy of this form.

Who is funding this study?

This study is being funded through grants from the National Institute of Health and the American Cancer Society to the University of Virginia (UVA) Cancer Center.

Key Information About This Research Study

Principal Investigator:	Trish Millard, MD University of Virginia Health System West Complex, Multistory Building 1300 Jefferson Park Avenue Box 800716 Charlottesville, VA 22908 Phone: 434-924-9333
Sponsor	University of Virginia Cancer Center

You are being asked to take part in a research study. You do not have to take part in this study.
You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

Historically, treatment for women over 65 years old with early stage ER+ breast cancer was surgery with or without radiation followed by endocrine pill therapy for 5-10 years after surgery. Many patients may also choose to have endocrine therapy before surgery as part of their clinical care. This is called neoadjuvant endocrine therapy and is also within breast cancer care guidelines.

Most women are treated with a type of surgery called a lumpectomy, which removes the cancer but leaves as much breast tissue as possible. ER+ breast cancer means that the cancer needs estrogen to grow. Endocrine therapy blocks or stops the production of estrogen to help treat ER+ breast cancer.

Radiation therapy can be used after surgery to treat early stage breast cancer. Radiation therapy uses high energy rays to kill cancer cells. Patients and doctors have to make a decision about radiation therapy immediately after their lumpectomy. Breast cancer treatment guidelines indicate that for women 70 years and older with early stage ER+ breast cancer, radiation is not needed if patients take endocrine therapy following surgery. Recent information from clinical trials in women age 65 or older with early stage ER+ breast cancer suggests that not doing radiation treatment following lumpectomy does not affect lifespan. However, at the time they make the decision about radiation therapy, most patients and doctors do not know how well the patients will tolerate and take the prescribed endocrine therapy. If a patient does not get radiation and also ends up not taking endocrine therapy, they may have a higher risk of breast cancer coming back.

This study is trying to find out if receiving endocrine therapy before the lumpectomy would change participants and doctors decisions regarding radiation treatment after surgery.

You are being asked to take part in this study because you were recently diagnosed with stage I ER+ breast cancer, are 65 years of age or older, and plan to have a lumpectomy.

Why would you want to take part in this study?
You might like to take part in this study because investigators think that it would be helpful to determine how well you tolerate endocrine therapy and follow prescribing directions before they have to decide whether you need radiation therapy.

Why would you NOT want to take part in this study?
Receiving endocrine therapy before surgery could delay surgery up to 3 months. You may want to have surgery as soon as possible and you may not want to take the endocrine therapy before your surgery. You might not want to take part in this study because you would be asked to come to clinic for 2-3 additional visits before your surgery. You may not want to complete questionnaires involved with the study.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form.
If you take part in this study you will:

- Take endocrine therapy for up to 3 months before your surgery
- Have 2-3 additional clinic visits before surgery to check on you while on the endocrine therapy before surgery
- Complete questionnaires at the visits before surgery and at 4 clinic visits after surgery

What is the difference between being in this study and getting usual care?
If you agree to be in this study, you will take endocrine therapy before your surgery. Your usual care options, outside of research, may or may not include taking endocrine therapy before surgery. If you were not in this study, you would have up to 3 fewer clinic visits and would not complete the questionnaires.

What other treatments may I receive if I decide to not take part in this study?
Treatment options include surgery, radiation, and endocrine therapy. Most commonly, surgery would be completed first, but you could receive endocrine therapy before surgery outside of this study.

Up to 105 people will sign consent to be in this study. Up to 83 people may receive study treatment in this study. Up to 70 people will sign consent to be in this study at UVA. People will be in this study at the University of Virginia and at Virginia Commonwealth University.

How long will this study take?

Your participation in this study will require 2-3 clinic visits over 3 months. Each visit will last about **1-2 hours**. In addition, after surgery you will be asked to completed questionnaires at 4 regular clinic visits which will add **about 30 minutes** over the procedures you are already having at those visits.

What will happen if you are in the study?

SCREENING (visit will last about 1 hour)

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start the study, there will be a screening period.

The following screening procedures will be performed for **clinical care** (which means as part of your routine medical care). The study team may access these results from your medical record and use the information for research purposes:

- Physical exam and vital signs (blood pressure, heart rate, respiration (breathing) rate, weight, height, and temperature).
- Review of your medical history and demographics (age, race, ethnicity) information, results from prior physical exams or laboratory tests, pathology reports, notes your clinicians may have made about your care

If review of these records and procedures show you are eligible, you may begin study treatment.

STUDY TREATMENT (each visit will last about 1-2 hours)

You will have clinic visits when you first are prescribed endocrine therapy (which may occur at the same time as screening), 1 month after you start endocrine therapy, and at the end of the 3 months of endocrine therapy.

The following tests may be performed as part of your clinical care and the results will be recorded for research purposes:

- Physical exam and vital signs.
- Review of side effects

You will be asked to take endocrine therapy for **research purposes** as directed by your physician for up to 3 months before your surgery.

You will be asked to fill out some questionnaires for **research purposes** at the 3 visits before surgery and at 4 clinic visits after surgery. These questionnaires will take about 30 minutes to complete and ask about:

- how cancer affects your life
- your beliefs about medicines and sensitivity to medicine
- your symptoms
- how frequently you take endocrine therapy
- general health and well being
- depression and anxiety

You will also be asked your preference about radiation therapy before starting endocrine therapy, as well as why you decide or not decide to participate in certain therapies to treat your cancer.

As part of your clinical care, you will have a pre-operative visit, which will include a physical exam and vitals. At this visit, you will be asked about side effects from the endocrine therapy and about your preference about radiation therapy **for research purposes**.

As part of your clinical care, you will have a surgery called a lumpectomy.

Depending on your decision with your medical team, you may or may not have radiation therapy as part of your regular clinical care.

After your surgery and radiation therapy, if you choose to receive it, you will receive endocrine therapy as part of your regular clinical care.

FOLLOW UP:

You may remain in study follow-up for up to 2 years after surgery or radiation therapy. We would like to collect information for the study at four times during the 2 year follow up: within the first 90 days post treatment, 6 months, 1 year and 2 years. These visits are when you would normally follow up with your breast cancer doctor(s) as part of your clinical care. The research procedures will add about 30 minutes to your regular clinic visits.

The following tests may be performed as part of your routine clinical care and the results will be recorded for research purposes:

- Physical exam and vital signs.
- Review of cancer status.

At each of the visits during the follow up period, you will be asked to fill out some questionnaires for **research purposes**. These questionnaires ask about:

- your symptoms
- general health and well being
- depression and anxiety

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Study Calendar

	Screening	Pre-Endocrine Therapy Period			Pre-Op	Surgery	Radiation	Follow Up			
		Day 1	Day 30	Day 90				FU 1 1-90 days after chemotherapy completion, RT completion, or Surgery	FU 2 6 months after FU 1	FU 3 12 months after FU 1	FU 4 24 months after FU 1
Informed consent	x										
Review eligibility	x										
Physical exam/ vitals	x		**x**	**x**	x			x	x	x	x
Endocrine Therapy		**--Taken daily as directed--**						--Taken daily as directed^--			
Lumpectomy						x					
Radiation Therapy*							x*				
Side effects review			**x**	**x**	**x**						
Questionnaires		**x**	**x**	**x**				**x**	**x**	**x**	**x**
RT preference		**x**			**x**						
Recurrence								x	x	x	x

Research procedures shown in **bold** text.
*Only for those that decide to receive radiation therapy.
^You may refuse adjuvant endocrine therapy after surgery, but will continue to be followed as indicated in the schedule above. Endocrine therapy may continue beyond 24 months as directed by your oncologist based on standard of care recommendations; however, the study will only collect information up to 24 months after surgery.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You must come to each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Ensure that the study drug is taken as instructed, keep the study drug in a safe place away from other children, return any unused study drug at each visit, and report any lost or missed tablets.
- Ensure that your endocrine therapy is taken only by you, the person for whom it has been prescribed.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks and side effects related to the endocrine therapy include:

Likely

- Hot flashes or flushing or sweats
- Muscle, bone, or joint pains
- Vaginal irritation, dryness, or discharge
- Muscle cramps

Less Likely

- Liver injury
- Rash
- Weight gain
- Hair thinning
- Dizziness
- Headache
- GI upset including nausea, vomiting, diarrhea, abdominal pain

- Forgetfulness or difficulty concentrating
- Difficulty sleeping

Rare but serious

- Decreased bone density or Osteoporosis with risk of fracture if on an aromatase inhibitor.
- Blood clot if on Tamoxifen. Call your doctor for any swelling, shortness of breath, or chest pain.
- Uterine cancer if on Tamoxifen. Call your doctor for any vaginal bleeding.

Risks of Sharing the Drug

Do not share your endocrine therapy with anyone. It is prescribed only for you and could hurt someone else. Keep it out of reach of children and people not able to read or understand the label.

Delay in time to surgery from diagnosis

Your cancer will be treated first with endocrine therapy before you have surgery. We do not anticipate any negative effects by having to delay surgery by 3 months as you will be on treatment with the endocrine pill therapy in this time.

Other unexpected risks:

You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Risks from Completing Questionnaires

Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and move to the next question.

During the research, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include: working with you to contact your doctor or therapist, referral to a therapist to discuss your thoughts, contact a trusted family member, significant other or clergy or work with you on a plan that may include getting you to a hospital for safety and treatment.

Could you be helped by being in this study?

You may or may not benefit from being in this study. Possible benefits include an awareness of how well you tolerate endocrine therapy, which could help you decide whether to receive radiation therapy. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- clinical care surgery followed by possible radiation therapy and endocrine therapy without participating in the study procedures

If you are an employee of UVa your job will not be affected if you decide not to participate in this study. If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: study questionnaires and radiation preference questions.

You and/or your insurance company will be responsible for costs of your endocrine therapy and all clinic visits during the study, as well as all procedures being performed as part of your clinical care, which includes, but is not limited to, surgery and radiation therapy.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health

b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part at the end of this form and return it to the researchers.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

Information obtained from you during this study will not be used in future research.

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.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Trish Millard, MD
University of Virginia Health System
West Complex, Multistory Building
1300 Jefferson Park Avenue
Box 800716
Charlottesville, VA 22908 Phone: 434-924-9333

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22903 Phone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

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Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

If an interpreter is involved in the consent process because the potential subject does not speak English well or at all, the participant should NOT sign on the line above – leave this line blank. Instead, the participant should sign the Short Form or full consent written in the language they can understand.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Signature of Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

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Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.
The follow up information will be collected by:

- Obtaining information from my medical records
- Phone call within the first 90 days post treatment, 6 months, 1 year and 2 years after surgery or radiation therapy
- Sending me questionnaires within the first 90 days post treatment, 6 months, 1 year and 2 years after surgery or radiation therapy

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Acknowledging Withdrawal

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study withdrawal section has been fully explained to the subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this withdrawal section to the subject the interpreter must sign and date the line above.