Informed Consent Form Main

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| **Official Title:** | Phase I/II Trial of Letrozole (Femara) and Sorafenib (Nexavar) in Postmenopausal Women With Hormone-Receptor Positive Locally Advanced or Metastatic Breast Cancer |
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[redacted]

CONSENT TO TAKE PART IN A RESEARCH STUDY [redacted]

**Title:** Phase I/II Trial of Letrozole [redacted] and Sorafenib [redacted] as First-Line Therapy in Postmenopausal Women with Hormone Receptor-Positive Locally Advanced or Metastatic Breast Cancer

**Principal Investigator:** [redacted]

**Introduction**

This form is part of an informed consent process for a research study and it will give you information that will make it possible for you to decide whether you wish to volunteer for this research study. "Volunteer" means you want to take part in the study; you do not have to. Once you understand what is involved and all of your questions have been answered, if you still wish to participate, you, along with the study doctor/principal investigator or a member of the study team, will be asked to sign this informed consent. You will receive a copy of the consent form to keep. If you have questions at any time during the research study you should feel free to ask them and obtain answers to your questions that you completely understand. You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

**Funding Companies of Study:**

[redacted] is the funder of this research protocol. The budget usually covers the cost of the research, such as the costs of collecting the information required by the study protocol. The study drug sorafenib [redacted] is available commercially and will not be provided. [redacted] will supply the drug letrozole [redacted]





[redacted]

**Financial Disclosure:**
One of the investigators (a study doctor on the research team) participating in this study owns stock in one of the funding companies. Please feel free to ask any further questions you might have about this matter.

**Why have I been asked to participate in this study?**
You are being asked to take part in this study because you have hormone receptor-positive advanced or metastatic (spread to other parts of the body) breast cancer. Cancer cells that are hormone receptor-positive grow and multiply when the estrogen hormone attaches to the hormone receptor. This type of cancer is usually treated with "hormonal therapy," sometimes called "anti-estrogen therapy," that starves the cancer cells of the estrogen they need to grow.

The purpose of this research study is to evaluate a new treatment for breast cancer, sorafenib, also called [redacted], in combination with an approved treatment called letrozole or [redacted], for treatment of hormone receptor-positive advanced or metastatic breast cancer. Letrozole is a type of drug that is called an aromatase inhibitor (AI), which blocks an enzyme that makes estrogen. AIs almost completely block out estrogen in postmenopausal women. Letrozole was approved by the U.S. Food and Drug Administration in January 2001 for the treatment of patients with locally advanced or metastatic breast cancer who have not had earlier treatment. It has been shown to be more effective than the present standard of care, tamoxifen, and to have fewer side effects than other drugs used in hormonal therapy.

Sorafenib is an approved medication by the U.S. Food and Drug Administration used to treat certain advanced kidney cancers and liver cancer. Sorafenib fights cancer by interfering with the ability of cancer cells to grow and divide. The drug blocks two different pathways that would normally help cancer cells to multiply; one way is by limiting the blood supply and nutrients to the cancer cells and the second way is to stop the signal that allows cancer cells to grow in number. Breast cancer cells are especially dependent on these two pathways to grow and we may be able slow down or stop them with sorafenib. There have been studies performed with sorafenib alone in patients with metastatic breast cancer; these studies showed that sorafenib by itself showed only a small effect on the cancer. However, there is a lot of potential for sorafenib to be combined with other medications.

This study is being conducted for the following reasons:

- To help to find the ideal dose of letrozole and sorafenib together.
- To find out how breast cancer tumors such as yours respond to the combination of letrozole and sorafenib.
- To learn more about the side effects of this combination of drugs.

**Who may or may not participate in this study?**

In order to take part in this study, you must meet the following conditions:

- You must have a diagnosis of advanced or metastatic breast cancer with estrogen receptors and/or progesterone receptors present.
- You must be 18 years or older.
- You must be postmenopausal (you are 56 years or older and have not had any menstrual bleeding in the past 12 months, you have had surgery to remove both ovaries, or production of estrogen from your ovaries has been stopped with medications, such as goserelin or leuprolide).
- You must not have received hormonal therapy for metastatic disease.
- You must not have received chemotherapy for metastatic disease.
- You must not have any other serious or significant medical problems, which, in your doctor's opinion, may make it dangerous for you to have hormonal therapy or chemotherapy (for example: history of a heart condition known as *congestive heart failure*, where your heart fails to pump blood effectively, an infection which is not resolved, or severe malnutrition).

**How long will the study take and how many subjects will participate?**

It is expected that between six to twelve patients will take part in the Phase I (first) part of this study and once the first part of the study is complete, the next set of patients will be added to the Phase II (second) portion of the study. A total of 55 patients have been enrolled on the study. The study is now closed to any new patients. If you are already enrolled on the study, your study treatment is expected to last as long as your cancer does not get worse or until you are no longer receiving benefit from the treatment. You may stop taking part at any time for any reason.

**What will I be asked to do if I participate in this research study?**

Before you may take part in this study, you will need to answer questions and have the following tests and examinations to see if you are eligible. This is called screening. It is important that you answer all questions honestly and completely. Depending on the answers to these questions and the results of tests and examinations, it is possible that you may not be able to take part in the study.

In some instances, certain tests or procedures conducted during the study may have to be repeated. This can happen if some or all of the results are unusable. Also, you may be asked to have additional tests or examinations. This can happen if an unexpected medical event occurs during the study.

Before you begin treatment, you will need to have the following tests and procedures done:

- A history and physical exam.
- You will be asked about the extent of your physical activity and how you are generally feeling.
- Your weight and height will be taken.
- You will have blood drawn using a small needle or plastic tube, to check your blood counts, your blood chemistry, and how your liver and kidneys are working.

- You will have an electrocardiogram done (also known as "ECG" or "EKG"). This is a painless paper tracing of your heart's normal electrical activity.
- If your doctor feels you need it, you may have to have a CAT scan or MRI (special tests which look at the organs in your body).
- If available, a sample of the tissue taken from the biopsy of your tumor taken at the time of your original diagnosis will be requested from the doctor who performed the biopsy. The tumor will be studied to see the make-up of certain cells, which may make some cancers respond to this treatment. You may not directly benefit from these tests. **(Part of Research)**
- If you are a patient at [redacted] you will also be asked to have blood drawn using a small needle or plastic tube, to store for future testing. It is not known at this time what these tests may be. About 2 tablespoons of your blood will be used for these tests. These samples are optional, if you do not agree to these additional samples, you may still take part in the study. **(Part of Research)**
- You may be asked to have biopsies (removal of small tissue sample from the area where your disease is) taken before and during your first cycle of treatment. If you are a patient at [redacted] affiliate hospital, you have the option of traveling to [redacted] to have the biopsies performed at no cost to you. These biopsies may only be done at [redacted] These samples are optional. If you do not agree to these additional samples, you may still take part in this study. **(Part of Research)**
- You will have blood drawn using a small needle or plastic tube to check circulating tumor cells (CTCs) prior to beginning the trial and after 2 cycles of treatment (at 8 weeks). CTCs can be found in the blood of patients with a variety of metastatic carcinomas and recent research has shown that the presence of CTCs can potentially be used to predict how patients with metastatic breast cancer will do with certain medications. **(Part of Research)**

**Treatment Plan:**

If you decide to take part in this study and are able to join based on the above criteria, you will have the following treatment:

You will have hormone therapy (drugs used to target the cancer cells) known as letrozole (also known as [redacted] and sorafenib (also known as [redacted] A treatment period will be 28 days long. This period is known as a "cycle." These medications are taken by mouth.

You will take letrozole and sorafenib for 4 straight weeks (Days 1-28). If you are premenopausal, you have estrogen production from your ovaries. Many premenopausal women will still be menstruating, although that may not always be the case for each woman. Your doctor will help to decide if you are still premenopausal. To join this study you will need to become postmenopausal to decrease the estrogen production from your ovaries. Decreasing your estrogen may help to treat your breast cancer. This can be done with surgery to remove your ovaries or with a monthly injection into fat or muscle of goserelin or leuprolide, medications that stop your ovaries from producing estrogen. The injection to decrease estrogen production from your ovaries can start at any time, including the day you start study treatment.

You will continue to receive these medications unless:

- You have severe, serious and/or excessive side effects.
- Your cancer becomes worse.
- You wish to stop taking part in this study.
- Your doctor feels it is not in your best interest to continue this treatment, even if you wish to continue treatment.

After you start treatment you will have the following tests and procedures done:

Before Each Cycle of Treatment:

- Physical exam
- You will be asked questions to check how you are tolerating the drugs.
- You will be asked the extent of your physical activity and how you are generally feeling.
- Your weight and height will be taken.
- Your blood pressure will be taken weekly during the first 4 weeks of treatment.
- You will have blood drawn using a small needle or plastic tube, to check your blood counts, your blood chemistry and how well your kidneys and liver are working.
- You will be given a medication diary and asked to fill it out daily.

At Eight (8) Weeks:

- You will have blood drawn using a small needle or plastic tube to check the levels of circulating tumor cells (CTCs).

Every Twelve (12) Weeks:

- If your doctor feels it is necessary, you may need a CT scan or MRI (special tests which look at the organs in your body) to check the progress of your cancer.

End of Treatment
(this means these tests and procedures will be done after your last dose of sorafenib/letrozole treatment, at the end of the study and/or if your cancer worsens):

- Physical exam
- You will be asked questions to see how you are tolerating the drugs.
- You will be asked the extent of your physical activity and how you are generally feeling.
- You will have blood drawn using a small needle or plastic tube, to check your blood counts, your blood chemistry and how well your kidneys and liver are working.
- Your medication diary will be checked and collected.

**A table of tests and procedures you will have done for this study is included at the end of this consent.**

**What are the risks and/or discomforts if I chose to participate in this study?**

**General Risks:**

If you decide to take part in this study, you understand that you may take the risk of this treatment not being effective against your cancer. The drugs used in this study may cause all, none, or some of the following side effects listed. Also, there is always the risk of developing very uncommon or previously unknown side effects. The risk of using these drugs in combination is not known at this time.

**Specific Side Effects of Each Drug:**

**Sorafenib**

Sorafenib is an investigational drug studied for use in hormone receptor-positive advanced or metastatic breast cancer.

The **most common side effects** are:

- Redness and/or swelling of the hands and/or feet
- Skin rash
- Fatigue (a sensation of feeling overly tired or sleepy and lacking in energy)
  **CAUTION NOTE:** do not drive or operate any machinery if you are feeling overly tired or sleepy.
- Diarrhea – increased frequency of bowel movements with loose, watery stools

Other **less common side effects** are:

- An increase in blood pressure
- A decrease in appetite
- Weight loss
- Chills
- Fever
- Pain in your joints
- Pain in your muscles
- Allergic reactions to the medication
- Flu-like symptoms
- Flushing of your face and/or neck
- High blood sugar (diabetes)
- A decrease in the protein levels in your blood that can cause fluid retention
- A decrease in the phosphate levels in your blood that can affect your bones, muscles, heart and nervous system
- Hair thinning or patchy hair loss
- Cracking or peeling of skin on hands or feet
- Dry skin

- Itching
- Acne
- Changes in the nails of your fingers and/or toes
- Changes in the color-tone of your skin with development of uneven patches of various size that are lacking in color
- Non-life threatening skin cancer
- Abdominal pain
- Upset stomach/difficulty digesting food
- Heartburn
- Nausea (feeling as if you're about to throw-up)
- Vomiting (throwing-up)
- Gassiness (increase in belching and/or passing gas)
- Constipation (difficulty having bowel movements)
- Abdominal swelling due to a build up of fluid in your belly
- Intestinal bleeding
- Dehydration
- Sores in the lining of your mouth and/or throat that can make it difficult to swallow
- A decrease in the number of red blood cells. This can make you feel tired or weak, or you may have some difficulty breathing. If the decrease is severe, you may need a transfusion of red blood cells.
- A decrease in the number of white blood cells. This may cause an infection since while blood cells help to fight infections.
- A decrease in the number of platelets. This can cause you to bruise easily or to bleed more easily as platelets are important for making blood clots. If the decrease is severe, or you have bleeding, you may need a transfusion of platelets.
- Damage to your nerves that causes the feeling of pins and needles in your hands, fingers, feet and toes.
- Damage to your pancreas (this can cause pain, nausea and vomiting)
- Damage to the liver with abnormalities in blood tests that measure the liver's normal function
- Cough
- A build up of fluid of your chest cavity that can make you feel short of breath
- An inflammation of your lungs that can make you feel short of breath
- Lung collapse or rupture that can be life threatening.
- Bleeding from your urinary tract/blood in your urine
- Kidney damage and/or failure
- Depression

**Rare but serious side effects** are:

- Gastrointestinal (GI) perforation which is the development of an opening or hole in the wall of the bowel or stomach (gastrointestinal tract) that may require surgery to repair and can be life threatening (you may have severe stomach pain)
- Bleeding into the brain or spinal cord (you may have nausea, vomiting; headache; loss of consciousness, slurred speech, paralysis)

If any of these symptoms occur, please call your study doctor immediately at ([redacted]

The following medical problems have been reported on trials with sorafenib but it is not known if sorafenib causes them:

- Joint swelling and redness
- Arm or leg swelling
- Increased risk of gout
- Intestinal blockage
- Back pain
- Bone pain
- Chest or rib pain
- Headache
- Arm or leg pain
- Blood clots
- Changes in your immune system that can put you at risk of infection
- Stroke
- Changes in blood clotting properties; may increase risk of harmful bleeding or clotting
- Dizziness
- Feeling lightheaded or fainting
- Anxiety, nervousness
- Loss of memory
- Mental impairment (confusion)
- Irregular or fast heart beat
- Heart attack
- Heart failure
- Bleeding in the lungs and the chest
- Severe lung injury
- Eye redness with pain
- Double vision
- Spleen damage
- Peeling of the skin
- Low levels of sodium in your blood

- Voice changes
- Erectile dysfunction

**Letrozole**

Letrozole is an approved treatment for hormone receptor-positive advanced or metastatic breast cancer.

The **most common side effects** are:

- Weakness or decreased energy
- Hot flashes/flushes
- Increased cholesterol levels
- Increased sweating
- Swelling in the hands or feet
- Constipation
- Dizziness
- Headache
- Chest pain
- Joint pain/stiffness
- Hair loss or thinning
- Bone pain
- Back pain
- Shortness of breath
- Cough

Other **less common side effects** are:

- Difficulty sleeping
- Depression
- Increased blood pressure
- Diarrhea
- Constipation
- Nausea
- Loss of appetite
- Abdominal pain
- Bone fracture
- Osteoporosis, or bone thinning, a disease that can affect postmenopausal women. The study drug may increase your chance of developing osteoporosis and 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

- Vaginal bleeding
- Vaginal dryness

**Rare but serious side effects** are:

- 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 treatment 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 drugs). 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.
- Blood clot in a blood vessel

**Leuprolide or Goserelin**

Leuprolide and goserelin are drugs (monthly injections) that cause you to become postmenopausal to decrease the estrogen production from your ovaries, which may help to treat your breast cancer.

The **most common side effects** are:

- Hot flashes
- Decrease in sex drive
- Vaginal dryness and/or dyspareunia (painful intercourse)

Stopping of menstrual periods and the inability to have children while receiving the injections are desired effects of these medications

Other **less common side effects** are:

- Headache
- Tiredness
- Dizziness
- Mood changes
- Sleep disturbance
- Nausea
- Vomiting
- Loss of appetite
- Back or joint pain
- Local irritation where the shots are given
- Loss of bone mineral density (osteoporosis) may occur and may lead to broken bones

**Rare but serious side effects** are:

- Allergic reactions, including swelling
- Anaphylactic shock, a very severe allergic reaction that can cause death is quite rare, but has occurred.

If any of these symptoms occur, please call your study doctor immediately at [redacted]

**The risks associated with a CT scan** (a computerized picture to locate and measure your tumor):

- Discomfort or anxiety when lying inside the CT scanner
- The contrast material (dye) is injected and may cause you to get a metallic taste in your mouth
- You may feel warm and rarely cause nausea or vomiting
- You will be exposed to some radiation through this procedure. There is always a slight risk of damage from being exposed to any radiation, including the low amounts of x-rays used for the CT scan. If you are especially concerned with radiation exposure, please discuss this with your doctor.

**Possible Side Effects of Drawing Blood**

When your blood is drawn there is a possibility that there may be slight pain, a bruise, bleeding, discoloration, or (rarely) infection at the place where your blood is drawn.

**Other Medications or Supplements**

You should not take any over the counter medicines, herbal products, "natural" products, vitamins or food supplements or any other types of special products while participating in this study, unless you tell the study doctor/investigator and permission is given to continue taking these medicines.

Your study doctor will review the list of medications you are currently taking to determine if any of these medications cannot be taken in combination with the study drugs. If you require any of these medications and a suitable substitute is not found, you will not be eligible to participate in this study. You will not be asked to stop taking any medications that you need. You must also tell your doctor about all medications other doctors have prescribed for you.

There are many medications (prescription and non-prescription), which may interact with the study drugs.

**Sorafenib is not to be taken with grapefruit or grapefruit juice. Also, grapefruit or grapefruit juice should not be taken at anytime during the study.** Taking grapefruit or grapefruit juice is not allowed because it may affect how your body absorbs the medication. This could let too little or too much of the medication into your body and not allow the medication to work as it is supposed to.

**Are there any benefits if I choose to participate in this research study?**
It is not possible to predict (know in advance) how much benefit you will get from taking part in this study. If this treatment is successful, it is hoped that your cancer will shrink or become smaller in size. You may also experience improvements of your symptoms or increase the amount of time you live with your disease. In addition, the knowledge gained from your participation in this study will help patients with hormone receptor-positive breast cancer in the future. The information from this study will also help doctors learn more about letrozole when given with sorafenib for hormone receptor-positive breast cancer.

**What are my alternatives if I don't want to participate in this study?**
Your doctor is willing to discuss the benefits and side effects of other forms of treatments other than this study that are available. These include:

- Other usual hormonal therapy for your type of cancer, which may include the same hormonal therapy that is used in this study or other drugs such as tamoxifen.
- Other experimental studies with chemotherapy, hormones, radiation therapy, or new anti-cancer agents that may be available for your disease.
- You may also choose no further treatment, with care and medicines to help you feel more comfortable.

Please feel free to discuss these other options with your doctor and ask any questions you may have. Take as much time as you need to make your decision.

**How will I know if there is information learned that might affect my willingness to participate in this research study?**
During the course of the study you will be updated about any new information that may affect your willingness to remain in the study. If new information is learned that may affect you after the study has completed, you will be contacted.

**Who will have access to my research records from this study?**
By participating in this study, you should understand that we would be collecting your personal health information. This includes, but is not limited to, demographic data (name, date of birth, etc.) and data on your health (your history, physical findings, laboratory results, study-related findings, etc.). During the course of the trial, study visitors (known as monitors) will review your medical and research record to make sure we collected your study information properly. These monitors are employed by The [redacted] Sometimes, they will need to take notes or photocopy parts of your medical record. We will replace your name on these pages with your assigned study number. This data will be reported to other staff at [redacted] on a regular basis, as required by the study. The [redacted] of [redacted] will analyze, process and store your data with electronic data processing systems. The authorization for use of your research data has no expiration date and may be subject to redisclosure by The [redacted] and may no longer be protected. Your personal identity however, that is your name, address, and other identifiers, will remain confidential (a study number will be used for your name).

Only the study doctor, research team and study monitor will be able to link the study number to your name. Your data may also be forwarded to domestic and foreign drug regulatory agencies if you have an adverse (bad) reaction.

The following groups of people may also be allowed to inspect sections of your medical and research records related to this study:

- Representatives from the Institutional Review Board (a committee that reviews research studies to protect human subjects participating in research)
- [redacted]

Your information may also be submitted to domestic (within the United States) and foreign drug regulatory agencies in applications for marketing authorization and may be used in scientific publications (journals, articles). If the findings from the study are published, you will not be identified by name. Your identity will remain confidential unless the law requires disclosure such as in the case of reporting people who have diseases that others can catch. In this case, you will be informed of the intent to disclose (give out) such information to the authorized state agency. Such a law has already existed in New Jersey for several years.

You have the right to access your personal data at your study doctor's office and to request any corrections of your personal data that are wrong.

You must sign this consent form to be able to take part in this study.

**Will there be any costs to me to participate in this study?**

Your health insurance carrier or third party payer will be billed for the cost of routine blood tests, x-rays, scans and other routine tests that would be part of your standard medical care even if you were not taking part in this study. Whatever costs your insurance company does not pay will be your responsibility. All doctor's or hospital costs will be charged to you in the same way as if you were not part of this study. The tests for measuring biomarkers in the blood and the optional biopsies will not be billed to you or your insurance company. All other tests are considered routine. The drug sorafenib [redacted] will not be supplied. Your study doctor will discuss with you how to obtain sorafenib [redacted] from the manufacturer and you may be asked to pay for it or you may be responsible for any co-pays associated with obtaining it. [redacted] will supply the drug letrozole [redacted] You or your insurance will not be charged for letrozole [redacted]

If you have any questions about insurance coverage, including any out of pocket expenses you might incur, or which laboratory or facilities you are allowed to have tests at, a financial counselor will be made available to you upon request.

**Will I be paid to participate in this study?**
You understand that you will not be paid for taking part in this study.

**What will happen if I become injured during the study?**
If you participate in this study, you will be exposed to certain risks of physical injury in addition to those that you may have with standard therapy. Please refer to Risks/Discomforts section. Medical and/or dental treatment will be arranged by [redacted] for participants who suffer physical injuries or illnesses as a direct consequence of participation in this research. Your health insurance carrier or other third party payor will be billed for the cost of this treatment. No additional financial payment is available. You are not giving up any of your legal rights by signing this form or by taking part in this research study.

**What will happen if I do not wish to participate or decide not to continue in the study?**
You may choose not to be in the study. If you do choose to take part, it is voluntary, meaning you do want to take part. You do not have to. You may also refuse to participate, or change your mind at any time. If you do not want to enter the study or decide to withdraw from the study, your relationship with the study staff will not change, and you may do so without penalty or loss of benefits to which you are otherwise entitled. If you do not want us to continue using the data that has been about you, you must withdraw your permission in writing to Dr. Tan. Even if you withdraw your permission to use the data about you, we cannot retrieve any of the information previously submitted. In addition, the US Food and Drug Administration require us to continue to report anything that relates to the safety of these drugs.

At any time, the study doctor can decide to withdraw you from this study because further participation would not be in your best interest. Your study doctor can stop treatment even if you are willing to continue. If you, or your study doctor, decide to withdraw your participation from the study you may be asked to return for a final visit for safety reasons, or to return study medication(s).

**Who may I contact if I have any questions?**
If you have any questions about your participation in this study, you can contact the study doctor:

[redacted]

If you have any questions about your rights as a research subject, you can contact:
Director, Institutional Review Board
[redacted]

## ADDITIONAL RESEARCH TESTING, FUTURE USE OF BLOOD/TISSUES SAMPLES OR THE INTENT TO STORE SAMPLES

**Optional Future Research Samples**

Blood and tissue samples collected from you may be stored and used in the future to study scientific questions. It is not known at this time what those studies may be. It is unlikely that what we learn from these studies will have a direct benefit to you. These studies may benefit patients in the future. If there are any risks to you or your family associated with these scientific studies, which are not covered in this consent form, your consent will be obtained before such studies are performed. The results of blood/tissue (specimen) bank research may help find new ways to learn about, prevent, or treat cancer and other diseases.

**Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. If you have any questions, please talk to your study doctor or nurse.**

1. My blood may be taken and analyzed to help identify differences in patients' responses to the same drug (pharmacogenomics).

   Yes No Initials _____

2. My blood/tissue (specimen) may be kept for use in research to learn about, prevent or treat cancer.

   Yes No Initials _____

3. My blood/tissue (specimen) may be kept for use in research to learn about, prevent or treat other health problems (for example: Alzheimer's disease or heart disease).

   Yes No Initials _____

4. My blood/tissue (specimen) may be kept for use in genetic studies.

   Yes No Initials _____

5. Someone may contact me in the future to ask me to take part in more research.

   Yes No Initials _____

If you do not want your samples used for additional research testing, future research or for genetic testing, this will not affect your ability to take part in this study or in future studies.

Patient Name: _____

Patient Signature: _____

Date: _____

**What do I do if I do not want my samples to be used?**

[redacted] may keep records linking your identity with your blood/tissue sample(s) indefinitely. You may ask that your blood/tissue sample(s) and materials obtained from your sample(s) be destroyed. In such case, you should notify the study doctor in writing that you wish to have your sample(s) destroyed [redacted] will destroy any of your sample(s) that are still available after your request is received.

**How will my information be kept private and confidential?**

Information obtained from material from your sample(s) will be kept confidential so that only [redacted] or the [redacted] group will be able to link your individual research results with your identity.

Your sample(s) and materials derived from your sample(s) will be given a code number and stored in a password-protected secured database. These password-protected databases are located on secured servers with limited access by key study personnel. Only information related to your diagnosis will be linked with the sample's code number. Your name, date of birth, address, or other personal identifying information will not be accessible to anyone besides [redacted] group.

This basic research is not intended to give you clinical information. You understand and agree that you will not be told about your individual research results. Information resulting from this research will not be entered into your medical record. Neither you, nor your family members, nor outside parties or the study doctor will be able to look at your individual research results. It is possible, however, that members of regulatory authorities, such as the U.S. Food and Drug Administration, [redacted] Institutional Review Board, NCI, or other persons required by law may be allowed to look at this information. Because we are not sure of the significance of the laboratory research, we will not use these results to manage your medical care.

**What are my rights if I agree to the use of my blood/tissue for other types of research or for genetic testing for future research?**

You understand that you have the right to ask questions about your blood/tissue samples at any time.

**Who may give consent to participate in this study?**

The investigator is interested in finding out if you can fully understand the information that has been given so you can enter into this study. You will be told if your illness has affected your ability to give consent for

this study. If so, then the study doctor will also discuss your ability to enter into this research study with your legally authorized person who may make this decision for you.

You have the opportunity to agree or object to the study doctors talking to your legally authorized person, and agree or object to entering into the research study. The study doctor will check your ability to consent to being into the study, and your continued willingness to agree to participate in this study until you have completed your participation in the study.

The study doctor's assessment of your capacity to consent to enter into this research study only applies to you volunteering for this research study. It does not assess your capacity to make decisions for other purposes such as financial, legal, and/or medical decisions.

**What are my rights if I decide to participate in this research study?**
You have the right to ask questions concerning any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and receive answers to all of your questions.

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions regarding this form or this study have been answered. I agree to participate in this research study and have been given a copy of this consent.

Patient Name: _____

Patient Signature: _____

Date: _____

**Text continued on next page**

**SIGNATURE OF READER/TRANSLATOR IF THE SUBJECT DOES NOT READ ENGLISH**

The person who has signed above, _____, does not read English well. I read English well and am fluent in _____, a language the patient understands well. I understand the content of this consent form and have translated for the patient the entire content of this form. To the best of my knowledge, the patient understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered.

Reader/ Translator: Name: _____

Signature: _____ Date: _____

Witness: Name: _____

Signature: _____ Date: _____

**SIGNATURE OF INVESTIGATOR OR RESPONSIBLE INDIVIDUAL**

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research patient have been accurately answered and the patient has been given a copy of the consent.

Name of Investigator/Person Obtaining Consent: _____

Signature: _____ Date: _____

**Text continued on next page**

**Table of Tests and Procedures:**

| Evaluations | Pre-Study | Every 4 weeks (prior to each cycle after Cycle 1) | At 8 weeks | End of Treatment |
|---|---|---|---|---|
| Informed consent | X | | | |
| History and Physical | X | X | | X |
| Blood tests | X[1] | X[2] | X[3] | X |
| EKG | X | | | |
| Imaging studies and/or tumor assessments | X | | X[3] | |
| Archived tumor tissue[4] | X | | | |
| Tumor biopsy (if accessible) | X | X[5] | | |
| Review of side effects | | X | | X |
| Medication diary[6] | | X | | X |

1. Within 14 days prior to treatment.
2. Within 7 days prior to re-treatment.
3. CTC blood sample
4. A piece of your biopsy tissue from when you were originally diagnosed.
5. If biopsy is done, it should be done before Cycle 1 treatment begins and before cycle 2.
6. You will be asked to keep a log of your medications throughout the study.