



**CEDARS-SINAI MEDICAL CENTER**  
**CONSENT FORM FOR RESEARCH**

**Title: Preoperative Combination of Pembrolizumab and Radiation Therapy in Patients with Operable Breast Cancer**

**SPONSOR: CEDARS SINAI MEDICAL CENTER; DEPARTMENT OF DEFENSE (TNBC COHORT ONLY)**

**STEPHEN SHIAO, MD, PHD, PRINCIPAL INVESTIGATOR**

**STUDY CONTACT PHONE NUMBER AT CSMC: 310-423-2836**

**AFTER HOURS CONTACT (24 HOURS): 310-423-2836**

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**Study Contact Phone Number at CSMC: 832-423-8255**

**KEY INFORMATION ABOUT THIS RESEARCH STUDY**

We are seeking your consent to take part in this research study. Your participation in this research is voluntary. If you choose to participate, you can stop at any time. Please consider the following summary, along with the more detailed information provided throughout this consent form.

- The purpose of this study is to assess the feasibility of pembrolizumab (study drug) combined with standard radiation to the tumor (tumor boost) before patients undergo standard treatment. An important purpose of this study is to see if by combining the radiation therapy with the study drug will increase the ability of the immune system to control or destroy cancer cells without delaying your planned standard cancer treatment
- The main procedures of this study include the administration of study drug in combination with standard radiation prior to undergoing standard treatment that may consist of one or more of the following: breast-conserving surgery, radiation to the entire breast/chest wall after surgery, and chemotherapy. If you choose to take part in this study, it will last about 1 year.
- All research studies involve some risks. Risks or discomforts from this study may include side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal
- If you agree to take part in this research study, there may or may not be direct medical benefit to you. The possible benefit of taking part in the research study is the

improvement of your condition. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

- We hope the information learned from this research study will benefit other individuals with breast cancer in the future by helping us to learn more about the combination of the study drug, pembrolizumab, with tumor boost radiation therapy.
- If you choose not to participate, there may be other choices available to you. Some other choices may include choosing to be treated following the sequence of treatments (radiation after surgery), receive the tumor boost by radiation or not receive a boost at all, choose to take part in a different study at CSMC or elsewhere if available, or you could decide not to be treated. You will not lose any services, benefits or rights you would normally have if you choose not to participate.

Please take time to read this entire form and ask questions before deciding whether to participate in this study. You are encouraged to talk with family members, close friends, trusted advisors and/or healthcare providers before you make your decision.

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## **1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?**

We are doing this study to assess the feasibility of pembrolizumab (study drug) combined with standard radiation to the tumor (tumor boost) before patients undergo standard treatment that can consist of one or more of the following: breast-conserving surgery, radiation to the entire breast/chest wall after surgery, and chemotherapy. We will give pembrolizumab and a radiation tumor boost to research participants and watch carefully for any side effects.

You have been asked to participate in a research study because you have a specific subtype of breast cancer for which breast surgery, possibly chemotherapy and radiation to the tumor is planned as part of standard treatment.

The study will enroll up to 60 people in total at Cedars Sinai Medical Center.

This research study is designed to test the investigational use of pembrolizumab. This drug is approved by the U.S. Food and Drug Administration (FDA) for the treatment of some skin and lung cancers. However, it is not approved by the FDA for breast cancer patients.

Pembrolizumab is a type of medication called an antibody. Antibodies are normal proteins in your body that help fight infections and possibly cancer. Pembrolizumab is a special type of an antibody produced in a laboratory. Pembrolizumab works by blocking a specific protein called Programmed Death-1 (PD-1), located on white blood cells, to strengthen the immune system. When PD-1 is blocked, the immune system may be “released” to target your tumor cells.

An important purpose of this study is to see if by combining the radiation therapy with the study drug will increase the ability of the immune system to control or destroy cancer cells without delaying your planned standard cancer treatment.

## 2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures which will be given to you as a separate handout.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care (routine)** procedures would be performed both as part of this study and if you do not participate in this study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as Appendix B to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart.

### Overview of study

If you choose to participate in this study, you will receive two doses of the study drug intravenously (through the vein) before your planned breast surgery or chemotherapy. The study drug will be administered three weeks apart. At the time of your second dose, you will receive radiation to the tumor in the affected breast. This type of radiation treatment is called a “tumor boost”, which is a standard part of radiation therapy for breast cancer that may occur either before or after planned breast-conserving surgery. The tumor boost that you will receive will be delivered in 3 consecutive treatments, rather than the conventional schedule of 4-5 treatments. You will receive breast surgery or begin chemotherapy approximately eight weeks after your first dose of the study drug.

Research blood will be collected at four separate times, once before you receive the study drug, at the second dose, when you begin breast surgery or chemotherapy, and after your standard of care treatment ends. You will also be required to donate tumor tissue three times, once before you begin the study drug, again at the second dose, and at the time of standard treatment. You may be required to donate tumor tissue a total of four times if you proceed to breast surgery after receiving chemotherapy as standard treatment (described below). If you have a Hormone Receptor positive (HR+) tumor, the pre-treatment tumor tissue can be obtained from an earlier procedure, but if archival tissue is not available, then a standard tumor biopsy will be performed. If you have a triple negative (ER-PR-HER2-) tumor, the pre-treatment and second tumor tissue sample must be obtained from a research tumor biopsy. For both HR+ or triple negative cohorts, the third sample will come from your planned breast surgery or another research biopsy. However, if you receive chemotherapy prior to your breast surgery, the fourth sample will be obtained with a research biopsy which could be from fresh surgical tissue or archival. Your treating physician will determine whether or not a fourth sample will be necessary for this study.

These research samples will be collected in order to evaluate tumor biomarkers (made of DNA, RNA, proteins, cells or components of cells). A biomarker is a biological molecule found in blood, other body fluids, or tissues that may be a sign of a condition or disease. Biomarkers also involve studies of your genes (DNA) and studies will be done to see whether differences in genes

are associated with activity of the study drug or if genes change over time. These samples will not be used to make decisions about your eligibility, treatment assignment, or other clinical management. They will only be used for research to learn more about the disease and how it responds to treatment.

A mandatory cosmesis evaluation including digital photographs of both your treated and untreated breast will be conducted at 3 times during the study: 1) before you begin the study drug, 2) 4 weeks after you begin standard treatment and 3) 6 months after you started standard treatment. The purpose of the cosmesis evaluation is to compare the cosmetic difference between your treated and untreated breast.

#### Optional Sub-study

Details of optional sub-studies are described in separate consent forms. You are not required to participate in the sub-studies in order to take part in this research study.

#### How long will you be in the study?

It is estimated that your participation will be up to 1 year. However, your participation may be shorter than 1 year, as it may vary for each participant. The total time includes screening, a six-week study treatment, and a 10-month follow-up phase. Follow-up includes your standard clinic visits every 3 weeks for up to 12 weeks and one visit at 6 months and 12 months post treatment.

In this study, testing of your specimens may go on for long periods of time. Therefore, while your direct participation in this study will be over once you have completed the procedures/visits described above and in the flowchart of procedures, your specimen(s) may be studied for many years.

We would like to review your medical records to see how you are doing for several years after you complete the study treatment. Keeping in touch with you and checking on your condition every so often helps us look at long-term effects.

### **3. WHAT ARE THE POSSIBLE RISKS?**

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as Appendix B. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

#### **Risks of Pembrolizumab (Study Drug)**

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

**Very common, some may be serious (i.e. causing hospitalization, life-threatening or where noted, may cause death). Out of 100 people who received pembrolizumab, 20 or more people may have the following:**

- Itching of skin
- Loose or watery stools
- Cough

**Common, some may be serious (i.e. causing hospitalization, life-threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:**

- Joint pain
- Back pain
- Rash
- Fever
- Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or upset stomach
- Stomach pain
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools

**Uncommon, some may be serious (i.e. causing hospitalization, life-threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:**

- Inflammation of the lungs so you may feel short of breath and cough.
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure, at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection.

**Rare, some may be serious (i.e. causing hospitalization, life-threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, less than 1 person may have the following:**

- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting. Sometimes this condition can lead to death.
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not

eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine

- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and abdominal aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the muscles so you may feel weak or pain in the muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe upper abdominal pain that may move to your back, sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots.
- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy.
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma.

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

**Risks of Radiation to the Tumor (Tumor Boost):**

<b><u>COMMON, SOME MAY BE SERIOUS</u></b> (occurs in greater than 20% of people)
<ul style="list-style-type: none"><li>• Skin reaction (redness, possible skin weeping)</li><li>• Tenderness in the area of the tumor boost in the affected breast</li></ul>
<b><u>OCCASIONAL, SOME MAY BE SERIOUS</u></b> (occurs in 4- 20% of people)
<ul style="list-style-type: none"><li>• Cough that may or may not bring up mucous</li><li>• Shortness of breath</li></ul>
<b><u>POSSIBLE, SOME MAY BE SERIOUS</u></b> (occurs in <3% of people):
<ul style="list-style-type: none"><li>• Inflammation of the lungs requiring steroid medications and oxygen therapy</li><li>• Pain, weakness or decreased sensation in the arm</li></ul>
<b><u>RARE, AND SERIOUS</u></b> (occurs in 1-3% of people):
<ul style="list-style-type: none"><li>• Development of another cancer many years later due to radiation therapy</li></ul>

It is possible that there are overlapping side effects from giving pembrolizumab (study drug) and radiation therapy together. When given pembrolizumab (study drug), pneumonitis (inflammation of the lungs) occurred more frequently in patients with a history of prior chest radiation (6.9%) than in patients who did not receive prior chest radiation (2.9%).

**Unknown Risks**

There also may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal.

*Risks of a Tumor Biopsy*

The type of biopsy you will receive will depend on the type of tumor you have. Please see the separate and attached Appendix C detailing the possible risks associated with the biopsy to be performed. Possible side effects from the collection of any tumor biopsies include:

- Pain

- Inflammation
- Bleeding
- Swelling
- Infection
- There is a rare possibility of tumor cells spreading from the tumor into the nearby area

Depending on the location of your tumor (s) your physician will decide whether the biopsy will be guided by MRI scan or ultrasound. MRI and ultrasound do not use radiation and are noninvasive techniques used to guide the radiologist during the biopsy.

#### Genetic Testing

Genetic studies have raised concern as to whether the studies would place research subjects at risk for discrimination based on genetics. The federal Genetic Information Nondiscrimination Act (GINA) was passed to address this concern. GINA makes it illegal for medical insurance companies and most employers to discriminate based on genetic information. The protections of GINA do not apply to life, disability, or long-term-care insurance. Although there are substantial protections against the risk of discrimination, you should be aware of this general concern.

#### Reproductive and Lactation Risks

Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant while on this study. If you are capable of becoming pregnant you will need to use 2 methods of birth control. Check with the researcher about approved birth control methods to use while participating in this study.

Women should not breastfeed a baby while on this study.

#### Unknown Risks to the Developing Embryo or Fetus (an unborn baby)

If you are pregnant, or become pregnant during participation in this research, the study drug might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact the researcher immediately if you believe you might be pregnant.

#### Collection of Pregnancy Outcomes

If you become pregnant during the study, we will collect information on the outcome of your pregnancy including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications, and the health status of your child. By signing this consent, you are agreeing to have this information about you and your child collected from your medical records in the rare case that you become pregnant during your participation in this research study, however, you are always free to withdraw your consent to participate in any research procedure.

#### Incidental Findings

It is possible that the research procedures could uncover information related to your health that you did not know about before and that is unrelated to the Study. Some of these findings may be too preliminary to share. Cedars-Sinai will carefully consider the research findings and determine if they should be shared with you. Research findings would only be shared with you if such sharing is approved by the Cedars-Sinai IRB and is permitted by applicable law. In some

cases, additional clinical testing may be required. The cost of any additional testing and any related treatment will be your responsibility.

#### **4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?**

If you agree to take part in this research study, there may or may not be direct medical benefit to you. The possible benefit of taking part in the research study is the improvement of your condition. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study will benefit other individuals with breast cancer in the future by helping us to learn more about the combination of the study drug, pembrolizumab, with tumor boost radiation therapy.

#### **5. WILL I BE INFORMED OF RESEARCH RESULTS?**

Some of the research tests done in this study follow standard clinical procedures and are performed in certified clinical labs. These test results may be shared with you and may be placed in your Cedars-Sinai medical record. Other research tests done in this study are for research purposes only and are performed in a research only lab where the results are not intended for clinical use. These research-only results will not be shared with you or included in your Cedars-Sinai medical record.

##### Unanticipated Incidental Findings

If, unexpectedly, we find that results of your research procedures could suggest important medical information and we determine there is something you or your doctors can do in response to this finding, we will contact you using the last contact information provided by you. If necessary, we may recommend additional clinical testing to confirm the research finding. The cost of any additional testing and any related treatment will be your responsibility.

#### **6. WHY WOULD MY PARTICIPATION BE STOPPED?**

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended
- Funding for the study is reduced, stopped or withdrawn
- If it is in your best interest
- Your condition gets worse
- You have a confirmed pregnancy
- You do not consent to continue in the study after being told of changes in the research that may affect you
- You do not follow the study procedures.

You may choose (or you may be required) to withdraw from certain parts of the study, but invited to continue with other parts. For example, you might stop taking a study drug, but continue with follow-up visits or allow us to continue to collect data from your medical records. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form.

**7. ARE THERE ANY OTHER OPTIONS?**

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- You may choose to be treated following the sequence of treatments (radiation therapy following surgery).
- You may choose to receive the tumor boost by radiation using conventional 4-5 fractions, or not receive a boost at all.
- You may choose to take part in a different study at CSMC or elsewhere, if one is available.
- You could decide not to be treated.

The researcher will discuss these options and their risks and benefits with you.

**8. WILL MY INFORMATION BE KEPT CONFIDENTIAL?**

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

You may, depending on the circumstances of the study and applicable law, be asked to sign a separate “Authorization Form” that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

We might share your information and/or research samples collected in this study with other researchers at Cedars-Sinai, other academic institutions, or third party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

**9. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?**

Contact your researcher at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your researcher of your situation at the phone number listed on page 1 of this consent form.

**Who pays for my research related illness or injury?**

Cedars-Sinai has no plans to pay for costs associated with the treatment of research-related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783.

**10. FINANCIAL CONSIDERATIONS**

**Costs of Participation**

Please review the flowchart for a listing of items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor (Cedars Sinai Medical Center).

Only items, drugs and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

**Compensation for Participating**

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

You will not be paid for providing samples for this study. Once you provide the samples for the research, you no longer have access to them. The donated samples become the property of CSMC or the study sponsor. Researchers might use your samples (even if identifiers are removed) to develop new products, tests or discoveries. Sometimes, these inventions may result in commercial profit for the researchers, CSMC, and/or other organizations. If this happens, you will not receive any financial benefits.

*Financial Interest in the Research*

The PI and institution have no potential financial conflict of interest with respect to this study.

**11. WHAT IF I HAVE QUESTIONS OR PROBLEMS?**

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783  
Email: [ResearchConcerns@cshs.org](mailto:ResearchConcerns@cshs.org)

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

## 12. CONSENT PROVISIONS

If you sign this form below, it means that:

- (1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
- (2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
- (3) You have received and understand all of the information you desire regarding your participation in the research study;
- (4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
- (5) You are voluntarily agreeing to participate in this research study;
- (6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights;
- (7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
- (8) You have been provided with a copy of the “Experimental Subject’s Bill of Rights”, if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and a copy of the Experimental Subject’s Bill of Rights.

**SIGNATURE BY THE PARTICIPANT:**

\_\_\_\_\_  
Name of Participant (Print)

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

\_\_\_\_\_  
Date of Signature

**SIGNATURE BY THE INVESTIGATOR:**

I have personally explained the research to the participant in non-technical terms, answered all questions, and attest that he/she freely consents to participate. The participant has been provided with the Experimental Subject's Bill of Rights.

\_\_\_\_\_  
Signature of the Investigator Who Obtained Consent

\_\_\_\_\_  
Date of Signature

**SIGNATURE BY THE INTERPRETER/WITNESS**

*(Signature of an interpreter is only required when a non-English speaking subject is consented with the assistance of an interpreter. The witness may be any person who is conversant in both English and the language of the Non-English speaking subject, such as the interpreter (the certified hospital interpreter), study staff, a family member, or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.)*

\_\_\_\_\_  
Signature of Interpreter/Witness

\_\_\_\_\_  
Date of Signature



## CEDARS-SINAI MEDICAL CENTER

### EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of any signed and dated written consent form used in relation to the experiment.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

**APPENDIX B: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks**

*The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.*

Study Procedure	Related Risks
<p><b>Blood draw:</b> A needle is placed in the vein in your arm to draw blood</p>	<p>Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting.</p>
<p><b>Infusion Procedure:</b> Infusion is the administration of drugs directly into your bloodstream using intravenous (IV) lines. The risks associated with IV lines are described separately below.</p>	<p>Occasionally, people have allergic reactions (including life-threatening reactions) when taking any medication. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death. If you experience any difficulty breathing, closing of the throat, swelling of the lips, tongue or face, or hives, you should stop taking your study drug and immediately seek emergency medical attention.</p> <p>In general, allergic reactions to medicines are more likely to occur in people who have allergies to other drugs, foods, or things in the environment, such as dust or grass. If you have allergies to other medicines, foods, or other things in the environment, or if you have asthma, you should let your researcher know.</p>
<p><b>Intravenous (IV) lines:</b> You will receive the study drug or other medications or contrast agent through an intravenous (IV) line. An IV line is a small tube that is attached to a catheter and inserted by needle into a vein usually in your hand or arm. Qualified medical professionals will place IV lines for use in this study.</p>	<p>IV lines are usually safe and well tolerated and complications are rare, but can include phlebitis (swelling of the vein) and infection. The IV may come out accidentally or blood may leak around the line. If the IV is not in the vein, medication or fluid can enter the surrounding soft tissues, and can be associated with swelling, discomfort, bruising and irritation. Rarely, a clot can develop in the IV line itself. If this happens, the staff may remove the old IV line and start a new IV line. There is also a small risk of feeling lightheaded and fainting.</p>
<p><b>Biopsy:</b> A biopsy is the removal of a sample of body tissue for examination under a microscope, by the doctor or scientist, to determine the state of health or disease in the tissue. The type of biopsy you will require is</p>	<p>There are some risks associated with biopsies. A small amount of bleeding, pain and skin bruising may occur. There is a potential for injury to internal organs from this procedure. These risks will be discussed with you further by the physician doing the</p>

<p>dependent upon the disease/condition for which you are being treated.</p>	<p>biopsy. A separate summary of the risks associated with the type of biopsy you will require is included as an appendix to this consent form. The appendix describes the biopsy procedure and its risks in more detail, specific to the type of biopsy you will have.</p> <p>If you have a bleeding tendency, you need to disclose this to the investigator and his or her staff. If you are taking aspirin, you will be advised to temporarily discontinue it. Infection is also a risk. Any additional specific risks will be disclosed prior to any procedure.</p>
<p><b>Archival Tissue:</b> If you previously had a biopsy sample taken from you and it is still available, a portion of that sample will be collected and used for the tissue sample required at Screening. You will not need to undergo a biopsy at Screening if existing tissue is available.</p>	<p>There are no physical risks associated with these procedures.</p>
<p><b>Electrocardiogram (EKG):</b> abbreviated as EKG or ECG – is a test that measures the electrical activity of the heartbeat using electrodes (disposable adhesive discs placed on the skin).</p>	<p>There’s no pain or risk associated with having an electrocardiogram. When the disposable adhesive discs are removed from your skin, there may be some minor skin discomfort or irritation. You may experience temporary discomfort (pulling on the skin/skin hair) during removal of the patches. This hair may be shaved for patch placement.</p>
<p><b>Cosmesis Evaluation:</b> Your treated and non-treated breast will be evaluated for physical difference and assigned a score. Photographs of just your breasts will be taken.</p>	<p>There are no physical risks associated with these procedures. No identifying images of you will be taken.</p>
<p><b>Pregnancy Test:</b> If you are a woman who is able to become pregnant, [blood/urine] samples will also be used to do a pregnancy test</p>	<p>If your test is positive, you will be told and at that point you should discuss options available with your primary physician.</p>
<p><b>Concomitant Medications:</b> You will be asked about your previous and current medications that you take.</p>	<p>There are no physical risks associated with these procedures.</p>
<p><b>Physical Exam:</b> Includes height, weight, vital signs (heart rate and blood pressure)</p>	<p>There are no physical risks associated with these procedures.</p>
<p><b>Medical History Review:</b> You will be asked about your medical and surgical history with attention to history of current disease, other pertinent history, current medication use, and information regarding underlying diseases]</p>	<p>There are no physical risks associated with this procedure.</p>
<p><b>Demographic Information:</b> You will be asked about your age, gender, race, ethnicity</p>	<p>There are no physical risks associated with these procedures.</p>

**APPENDIX C: BREAST CORE NEEDLE BIOPSY**



**CEDARS-SINAI MEDICAL CENTER®**

**RESEARCH BIOPSY APPENDIX:**  
**CORE NEEDLE BIOPSY**

**INTRODUCTION**

This information sheet is provided to you as a supplement to the consent form for a research biopsy presented to you today. This document is intended to summarize the known risks specific to the type of biopsy you will have. This appendix will always be provided together with a consent form, which you will be asked to sign if you agree to undergo a research biopsy.

It is important that you understand that the research biopsies are NOT required for your ongoing care.

**WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?**

Depending on the location of your tumor(s) your physician will decide whether the biopsy will be guided by MRI scan or ultrasound. The level of risk will depend upon which procedure is used and where in your body the biopsy is taken. Complications are rare but can include:

- Bleeding from the biopsy site. People with bleeding problems or low platelet counts have a higher chance for this.
- Infection at the biopsy site. This is more of a risk in people with weakened immune systems.
- Long-lasting discomfort/pain at the biopsy site
- Bruising at the biopsy site
- Complications related to sedation, such as an allergic reaction, nausea or irregular heartbeats.

The specific risks associated with the procedure will be further discussed with the physician who will perform the procedure. Your doctor will provide you with a separate surgical consent form for this hospital procedure. In addition to the risks described above, there may be other discomforts or risks to you which are presently not foreseeable. You should discuss possible risks with your doctor before making a decision to take part in this optional procedure.