Participant Informed Consent for Clinical Research

Study title for participants: Molecular Mechanisms of Clinical Resistance to Targeted Therapy Among Patients with Breast Cancer

Official study title for internet search on http://www.ClinicalTrials.gov: Molecular Mechanisms of Clinical Resistance to Targeted Therapy Among Patients with Breast Cancer

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If you are the parent or legal guardian of the person who is being asked to participate in this research study, you may give consent on his or her behalf. The word "you" in this document refers to your child, if the participant is a minor, or to a person with a cognitive impairment for whom you are the Legally Authorized Representative (LAR).

Overview and Key Information

Why is this study being done?

We are asking you to take part in a clinical research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

You are being asked to take part in this study specifically because you have breast cancer that has come back after treatment. We are trying to understand why the tumor came back or stopped responding to therapy.

Taking part in this study is your choice.

You can choose to take part or not to take part in this study, and you can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document presents important information to help you make your choice. Please take time to read it carefully. Talk with your doctor, family, or friends about the risks and benefits of taking part in this study. It's important that you have as much information as you need, and that all your questions are answered.

What is the usual approach to my breast cancer?

The usual approach includes standard of care treatment, with no participation in a specimen collection protocol.

What are my other choices if I decide not to take part in this study?

- You may choose to have the usual approach described above
- You may choose to take part in a different research study, if one is available

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get either a biopsy or removal of your tumor and a blood draw.

You will sign consent that you will take part in the study. You will discuss the biopsy with the surgeon and sign consent for it. You will then have a biopsy of your cancer. Later, if your cancer starts to grow again we may ask you to repeat this biopsy so that we have cancer from before and after your next treatment. If in the future, you have more biopsies during the course of your treatment, we will ask for an extra tissue sample. We will compare the biopsy to prior tumor biopsies you may have had.

In each case, we will send some of the biopsy tissue to be studied in the lab. The rest will be used in routine diagnostic studies for your further care.

We may ask you some questions after the study is complete.

The major goal of this program is to understand why some types of tumors are resistant to therapy. There are two basic types of tests that will be done, those that will be done in a clinically approved laboratory and those that will be done in a research laboratory. The results of testing that is done in a clinically approved laboratory will be told to you and entered into your medical record, which can be reviewed at any time with your doctor.

The results of testing done in a research laboratory may not be available to you and will not be placed in your medical record.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important to think carefully about these as you make your decision.

Risks

We want to make sure that you know about a few key risks right now. We will also give you more information in the What risks can I expect from taking part in this study? section of this consent form.

If you choose to take part in this study, you may have side effects related to the biopsy procedure or venipuncture. You may have:

- Pain at the biopsy or venipuncture site.
- Bleeding at the biopsy or venipuncture site.
- Infection at the biopsy site.

Benefits

There are no direct benefits to taking part in this study. We do know that the information from this study will help doctors learn more about how and why certain cancers are resistant to certain treatments. This information could help future patients both in preventing and treating cancer.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop participating in the study at any time.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

If you decide to stop, let the study doctor know as soon as possible.

If you stop, you can decide whether to let the study doctor or a member of the study team continue to contact you to ask questions about your health. We will not be able to withdraw information about you that has been used or shared with others before you informed us of your decision to stop.

Are there other reasons why I might stop being in the study?

- Yes. The study doctor may take you off the study if:
- Your health changes, and the study is no longer in your best interest
- New information becomes available, and the study is no longer in your best interest
- You do not follow the study rules
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA).

It is important that you understand the information in this informed consent document before you make a decision about participating in this clinical trial. Please read, or have someone read to you, the rest of this document. If there is anything that you don't understand, ask the study doctor or nurse for more information.

What is the purpose of this study?

The purpose of this study is to learn why certain drugs stop working in patients. In lab studies, tumors become resistant in several ways. Specific molecules seem to change and this may be why therapy stops working. However, we do not know if the same molecules change in patients. This study is being done to see if they do change. If we learn more about how patients become resistant, we may be able to offer better treatment in the future.

About 400 people will take part in this study at Memorial Sloan Kettering Cancer Center (MSK).

What are the study groups?

Most patients on this study will be patients who have breast cancers that are positive for Human Epidermal Growth Factor Receptor 2 (HER2) or Estrogen Receptor (ER). HER2 positive breast cancer expresses the protein HER2, which can be found on the surface of cancer cells, in large amounts. ER positive breast cancer expresses the protein ER, which can be found on the surface of cancer cells, in large amounts. For the patients with HER2 positive breast cancer, we are trying to understand why drugs that work against HER2 stop working. For the patients with ER positive breast cancer, we are trying to understand why hormonal therapies stop working. By doing so, we hope to develop new drugs that work against the resistant cancers.

Another group of patients who have recurrent breast cancer that does not express HER2 or ER will also be asked to take part in the study. Their tumor cells will be compared to the tumor cells from before treatment to understand other ways in which breast tumors become resistant.

What extra tests and procedures will I have if I take part in this study?

Some exams, tests, and procedures are a necessary part of this research study, but they would not be part of the usual care for your condition. The procedures that will be done only for research purposes, or that may be done more often because you are participating in this study, are listed below.

- A biopsy or removal of the tumor

- A tube of blood

A single 10ml tube blood samples will be collected to test against your tumor sample. The samples are being taken for research testing and will be collected by drawing blood out of a vein in your arm.
Later, if your cancer starts to grow again we may ask you to repeat this biopsy so that we have cancer from before and after your next treatment. If in the future, you have more biopsies during the course of your treatment, we will ask for an extra tissue sample.

After your samples have been analyzed, if any part of them is left over, the material will be banked for use in future research. The samples will be stored for 15 years and, if they have not been used by the end of that period of time, they will be destroyed. You will have the option to choose to donate your leftover research blood samples for future use by the sponsor. This will be explained in the "Optional Studies" section on this consent form.

If your doctor identified an alteration in your tumor, it may help your doctor manage your cancer. If an alteration is found that increases your risk or the risk of your family members for disease, there may be steps you or your family members can take. None of these benefits are guaranteed. In some cases, the results of these tests may not work or come back for months or even years. In most cases, we find no relevant alterations that we can act upon today. However, all the information will be analyzed and is likely to be important for our understanding of the disease and development of new therapies.

As part of testing for tumor mutations, occasionally mutations are found in normal cells in addition to the tumor. These may be mutations you inherit from your parents and may be linked to an increased risk of cancer or other disease in your family members. The results will not be placed in your medical record. If you have given us your permission, we may contact you or your designated family member to discuss research findings related to your samples. If you wish to learn more about your genes and the potential for inherited risks of cancer and/or other diseases, please speak to your doctor who can assist you with contacting the MSKCC Clinical Genetics Service to discuss clinical genetic testing and counseling.

Will I receive the results of my research tests?

Neither you nor your doctor will receive the results of any tests done for research purposes during this study.

What risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- Pain at the venipuncture site.
- Bleeding at the venipuncture site.

Risks associated with biopsies include pain, redness, swelling, bleeding, bruising, infection and, rarely, death. [Include the following text in the list of risks if only lung biopsies will be done: Inflammation of the lungs (pneumonitis); symptoms include coughing, difficulty breathing, shortness of breath, and chest pain. This condition can be life-threatening; tell the study doctor right away if you have any of these symptoms.] The doctor performing the biopsy will explain the details and risks of the procedure, which may vary, depending on how the biopsy sample will be obtained.

Important information about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it difficult for you to have children.
- Some side effects may be mild. Others may be very serious, and may even result in death.

Important information about how you and the study doctor can make side effects less of a problem for you:

- If you notice or feel anything different, tell the study doctor. He or she can check to see if you are having a side effect.
- The study doctor may be able to treat some side effects.

Let the study doctor know about any questions you may have about possible side effects. You can ask the study doctor questions about side effects at any time.

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments
- Tell the study doctor about:
  - All medications and any supplements you are taking
  - Any side effects from these medications or supplements
  - Any doctor visits or hospital stays outside of this study
  - Whether you have been or are currently in another research study

Is there a conflict of interest for this study?

No conflicts of interest have been identified for either the institution or the investigator(s) in this study.

What are the costs of taking part in this study?

You will not have to pay for the biopsy or for tests and procedures done only for research purposes, including:

- Pathology costs
- Research tests on the biopsy tissue
- Research blood work

If you need to stay in the hospital or need any other medical care as a result of the biopsy, your health insurance company will be charged for this care. In some individual cases, the biopsy or surgery is being done for medical reasons. If you are one of these patients, your insurance company will be charged for the costs of biopsy, anesthesia, and pathology as usual. Any tests done in the clinically certified laboratory will be billed to insurance as usual. None of the research tests will be charged to your insurance company.

You and/or your health plan/insurance company will have to pay for all the other costs of treating your cancer while you are in this study. These charges include the costs of insurance co-pays and deductibles, as well as tests, procedures, or drugs that you get during the study to monitor your safety, and to prevent or manage any side effects.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this clinical trial. Also find out if you need approval from your health plan before you can take part in this study.

The study doctor or nurse can help you find the right person to talk to if you are not sure which costs will be billed to you or your insurance provider.

Will I receive payment for taking part in this study?

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

Your biospecimens (blood, tissue,) may be used in the development of new tests, drugs, or other products for sale. If they are, you will not receive any payment from the sale of these products.

What happens if I am injured or hurt because I took part in this study?

You will get medical treatment if you are injured as a result of taking part in this study.

If you think that you have been injured as a result of taking part in this research study, tell the study doctor or the person in charge of the study as soon as possible. The name and telephone number of the person in charge of this research are listed on the first page of this consent form.

If you think that your injury was a result of medical error, you keep all your legal rights to receive payment for treating the injury, even though you are in a study.

Who will see my medical information?

Your privacy is very important to us, and the researchers will make every effort to protect it. Trained staff at Memorial Hospital may review your records, if necessary.

Access to your protected health information will be limited to those listed in the Research Authorization form, which is a part of the informed consent process.

The study doctors have a Certificate of Confidentiality from the National Institutes of Health for this study. This gives MSK an additional way to protect sensitive information that identifies you in your records if it is requested as part of a legal proceeding. However, MSK may still be required to share some of your medical information if required by law.
Your information may be given out, if required by law. For example, some states require doctors to make a report to the state health board if they find that a participant in a research study has a contagious disease like tuberculosis. However, the researchers will do their best to make sure that any information about you that may be released will not identify you.

In the future, your information (data) and biospecimens may be de-identified, which means that your data and/or biospecimens will be assigned a unique code, and the list that links the code to your name will be stored separately from your biospecimens and data. Your de-identified information and biospecimens may be used for research that has not been described in this consent form, and they may be shared with another investigator for future research. You will not be asked if you agree to take part in future research studies.

If your information from this study is used in any reports or publications, your name and anything else that could identify you will not be used. It is possible that your de-identified information from this study will be shared with other researchers outside of MSK, and may be stored in public databases. All requests for data sharing will be reviewed by the study sponsor, and if individual results are included in the data, they will not contain any identifiable information about you, such as your name, address, telephone number, or social security number. Your privacy is very important to us and we use many safety procedures to protect your privacy. However, we cannot guarantee that no one will ever be able to use your information to identify you.

A Federal law, the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: o Health insurance companies and group health plans may not request your genetic information that we get from this research. o Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. o Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you, or when setting the terms of your employment. 32 Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, long-term care insurance, or if you are a member of the military.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about research studies, or for general information about cancer. You may also call the NCI Cancer Information Service to get the same information at 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns that you may have about this study, or to report side effects or injuries. You may also contact the lead researcher listed on the first page of this consent.

For questions about your rights while you are participating in this study, call the MSK Institutional Review Board (IRB) at 212-639-7592. If you have concerns, complaints, or input on research, or if you would like more information about the informed consent process, please contact the MSK Patient Representative Department at 212-639-7202.

Optional studies:

Please review each sentence below and think about your choice. After reading each sentence, check “YES” or “NO.” No matter what you decide to do, it will not affect your care. You will still be allowed to participate in this research study even if you don’t want to be contacted in the future. If you have any questions, please talk to your doctor.

1. I agree that researchers may contact me in the future to discuss findings which may come from my sample.

   Please check one: ☐ YES
   ☐ NO

2. In the event that I am unavailable to discuss new research findings, I agree to have a family member contacted to discuss new findings related to my participation in this study.

   Please check one: ☐ YES
   ☐ NO

If YES, please list the designated family member and contact information:

Name: _____

Relationship: _____

Address: _____

City: _____

State: _____ Zip _____

Telephone: _____

E-mail: _____

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

[Molecular Mechanisms of Clinical Resistance to Targeted Therapy Among Patients with Breast Cancer]

Federal law requires Memorial Sloan Kettering Cancer Center (MSK) to protect the privacy of information that identifies you and relates to your past, present, and future medical conditions (protected health information; PHI). We are committed to protecting the privacy of your information.

If you enroll in this research study, your protected health information will be used and shared with others, as explained below. MSK must obtain your permission before using or sharing your protected health information for research purposes. This form helps to make sure that you are informed of the ways in which your information will be used or shared in the future.

Carefully read the information below before you sign this form. By signing this form, you agree to the use and disclosure of your information for this research study.

1. What protected health information about me will be used or shared with others during this research?

- Your medical records
- Your research records, including new health information created from study-related tests, procedures, visits, and/or questionnaires
- Any health information or clinical data associated with your biospecimens, if the information or data could be reasonably used to identify you. This information or data will be shared only if you have agreed to it by signing this informed consent document.
- HIV-related information, including any information indicating that you have had an HIV-related test; or that you have HIV infection, HIV-related illness, or AIDS; or any information that could indicate that you may have been exposed to HIV. (New York State requires us to obtain your consent to use or share this information.)

2. Who will use or share my protected health information?

MSK will use and share your protected health information. People and offices that deal with research oversight, quality assurance, and/or billing will be able to use and share your protected health information, including:

- The study's Principal Investigator and Co-Principal Investigator(s): [Sarat Chandarlapaty, MD, PhD, Pedram Razavi, MD]
- Your research team at MSK, including the participating investigators, research staff, research nurses, fellows/residents, and clerical support staff
- Any healthcare personnel who provide services to you in connection with this study
- Members and staff of MSK's Institutional Review Board (IRB) and Privacy Board (PB)
- Staff of MSK's Clinical Research Administration, which oversees clinical studies, and Clinical Research Information Technology Group, which manages research databases

- Members of MSK's Data Safety Monitoring Board/Committee and the Quality Assurance Committee

3. With whom outside of MSK may my protected health information be shared?

Although all reasonable efforts will be made to maintain the confidentiality of your protected health information, it may be shared with and used by the following:

- MSK's research collaborators, business partners, subcontractors and agent(s), in the United States or in other countries, working to conduct the study, to monitor the study, or to analyze the study information for this study or for other research about the study biopsy.
- The sponsor's research collaborators, business partners, subcontractors and agent(s), in the United States or in other countries, working with the sponsor to conduct the study, to monitor the study, or to analyze the study information for this study or for other research about the study biopsy.
- Other research doctors and medical centers participating in this research.
- Federal and state agencies, and other domestic or foreign government bodies, if required by law and/or necessary for oversight purposes, including:
    - Office for Human Research Protections (OHRP) of the US Department of Health and Human Services (HHS)
    - US Food and Drug Administration (FDA) and other regulatory agencies responsible for oversight of research
    - National Cancer Institute (NCI)/National Institutes of Health (NIH)
- Other qualified researchers, approved by Memorial Sloan Kettering Cancer Center, who may receive individual research results that do not identify you.

Some of the organizations that may receive your protected health information may not have to satisfy the privacy rules and requirements; they may share your information with others without your permission.

4. Why will my protected health information be used by or shared by MSK or others?

The main reasons for the use or sharing of your information include the following:

- To conduct the study, to monitor your health status, to measure the effects of the drug(s)/device(s)/procedure(s) being studied, and to determine the research results
- To ensure that the research meets legal and institutional requirements
- To develop new tests, procedures, and commercial products
- To enhance research databases, so that scientists can design better research studies to develop new therapies for patients and to gain a better understanding of disease
- To assist with MSK medical treatment, billing, or healthcare operations. For example, medical information produced by this research study will become part of your hospital medical record.

5. For how long will my protected health information be used or shared with others?

There is no set date at which your protected health information that is being used or shared for this research study will be destroyed or no longer used. The information used and created during the study may be analyzed for many years, and it is not possible to know when this analysis will be completed.

6. Statement of privacy rights:

- It is your right to refuse to sign this authorization form. If you do not sign this form, you will not be able to participate in this research study. However, if you do not sign, it will not affect your ongoing medical treatment or healthcare coverage.

- You have the right to withdraw your permission for MSK to use or share your protected health information. Please note that we will not be able to withdraw all the information about you that already has been used or shared with others to carry out research-related activities such as oversight, or information that is needed to ensure the quality of the study. To withdraw your permission, write to the study doctor listed on the first page of this consent form at: Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065. If you withdraw permission for us to use or share your protected health information, you will not be able to continue to participate in this research study.

- You have the right to request access to your protected health information that is being used or shared during this research and that is related to the research or to payment for the research. However, you may access this information only after the study is completed. You may have access to your medical record at any time. To request this information, please contact the study doctor whose name and telephone number are listed on the first page of this consent form. You may also ask the study doctor to correct any study-related information about you that is wrong.

Notice concerning HIV-related information

Individuals/organizations are prohibited from sharing any HIV-related information about you without your approval, unless they are permitted to do so under federal or state law. You have a right to request the list of people who may receive or use your HIV-related information without your authorization.

If you experience discrimination because of the release or disclosure of your HIV-related information, you may contact the New York State Division of Human Rights at 888-392-3644 or the New York City Commission on Human Rights at 212-306-7500. These agencies are responsible for protecting your rights.

Participant Informed Consent/Research Authorization for Clinical Research

Statement of professional obtaining consent
I have fully explained this clinical research study to the participant or to his/her Legally Authorized Representative (LAR). In my judgment, and in that of the participant or his/her LAR, sufficient information, including risks and benefits, was provided for the participant or his/her LAR to make an informed decision. The consent discussion will be documented in the participant's EMR.

Consenting professional must personally sign and date		
Consenting professional's signature		**Date:**
Consenting professional's name (Print)		

Participant's (or Legally Authorized Representative's [LAR's)]) statement
I have read this form that describes the clinical research study. I have also talked it over to my satisfaction with the consenting professional. By signing below, I agree to the following: (1) to voluntarily participate in this clinical research study; (2) to authorize the use and disclosure of my/the participant's protected health information (data about myself/the participant); and (3) to state that I have received a signed and dated copy of this consent form.

Participant/LAR must personally sign and date		
Participant/LAR signature		**Date:**
Participant/LAR name (Print)		
LAR relationship to participant		

Witness signature (if required)

- ❑ Witness for non-English speaking participant: I declare that I am fluent in both English and in the participant's (or LAR's) language, and I confirm that the consent discussion was appropriately interpreted for the participant (or LAR).
- ❑ Other: I confirm that the consent discussion occurred, and that the participant agreed to participate in this study by signing this form, making his/her mark, or verbally agreeing.

Name of witness: _____

Signature of witness: _____ **Date:** _____
(The name of the witness must be documented in the EMR.)

Interpreter (if required)
Name of interpreter (if present): _____
ID number (if phone interpreter): _____
(The interpreter's name or ID number must be documented in the EMR.)

The participant/Legally Authorized Representative must be provided with a **signed copy** of this form.