THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Molecular and Germline testing for the MD Anderson Cancer Center Personalized Cancer Therapy Program
PA11-0852

Study Chair: Funda Meric-Bernstam

_____ _____
Participant's Name Medical Record Number

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

If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.

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

STUDY SUMMARY

Cancer develops due to a variety of genetic changes, such as mutations (changes in the normal order of DNA, the genetic material of cells). In order to better understand cancer genetics, researchers often test the tumor as well as normal cells (such as blood cells, saliva or cheek cells, or normal tissue cells).

The main goal of this study is to perform molecular testing on tumor tissue to learn which genes are mutated (have changed) to provide personalized cancer therapy options to patients at MD Anderson. Your doctor may be able to use testing information on your tumor to identify clinical trials that may be most relevant to you.

Another goal of this laboratory research study is to learn how often different genes mutate in patients with different cancers. Researchers will also use the information

learned from this study to develop a database of the different kinds of mutations in cancer-related genes.

Comparing the test results from normal cells with the test results from tumor cells allows researchers to compare 2 different types of genetic mutations within cancer cells:

1. Some changes only happen in the tumor. These changes are called “somatic mutations”.
2. Some changes are found in both tumor cells and normal cells. These changes are called “germline mutations”.

Germline mutations are hereditary (run in the family), but somatic mutations are not hereditary. Certain germline mutations may change the risk of developing new cancers or other diseases developing, the likelihood of benefiting from certain therapies, and the likelihood of having side effects from certain therapies.

Researchers also hope to better understand how mutations in cancer-related genes may affect a patient's response to different therapies. Researchers can use this information to select specific therapies for future patients that are more likely to be effective. Your doctor may be able to use the results of the genetic testing performed in this study to find clinical trials that may be the most beneficial for you. Future patients may benefit from what is learned. There may be no benefits for you in this study.

This study is investigational. Your participation is completely voluntary. You may choose not to participate in the study. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including potential expenses and time commitment. If you take part in this study, you may experience risks associated with genetic testing.

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

Your active participation will be over after you sign this consent form and your tissue and blood samples have been collected. Your medical records may continue to be reviewed for up to 20 years.

There will be no additional cost to you for tests that are being performed for research purposes only. You and/or your insurance provider will be responsible for standard tests or procedures that you would have even if you are not taking part in this study.

You may choose not to take part in this study.

1. STUDY DETAILS

Up to 15,000 patients will take part in this study. All will be enrolled at MD Anderson.

Medical Record Information

If you agree to take part in this study, information about your disease and your previous and future treatments and outcomes will be recorded from your medical records.

Your medical record information will be entered into a password-protected database that can only be accessed by authorized members of the research staff and your treating physician at MD Anderson.

Not all patients on the study will have genetic tests. However, if you have this testing, the results of these tests will be placed in your medical records after the tests are validated.

Sample Collection

If you have tissue leftover from a previous biopsy and if you are planning to have a new surgical procedure or biopsy, tissue from the procedure(s) will be collected to look for mutations in cancer-related genes and biomarker testing.

Blood (about 6 teaspoons) may also be drawn so that researchers have a sample of normal cells to compare to cancer cells. This blood may be drawn for biomarker testing, and/or for validation of results found during biomarker testing. Blood may also be drawn to track circulating free DNA (cfDNA). Biomarker and cfDNA testing looks at the number of tumor cells that are in blood at baseline collection and how it may change during and at the end of a specific treatment. The blood samples may also be used in research to help develop new treatments.

You may be offered RNA testing to identify possible RNA-guided treatments. This will be discussed with you, including the results of the test.

The frequency of these draws and collections will depend on your diagnosis, genetic mutations, and/or treatment schedule outside of this study, depending on what the doctor thinks is needed.

Testing Outside of MD Anderson

Some of your sample material may be sent to institutions outside of MD Anderson for advanced testing.

If your tumor tissue is stored at another institution, a company called eHealth Global that specializes in picking up and delivering this kind of tissue, may be used to collect and deliver your samples to MD Anderson. If eHealth Global is used, they may have access to certain identifiable health information, which will include the accession number of your tissue sample, your demographic information (to know where to pick up the sample), and your Medical Record Number (used to label the sample so that the laboratory knows that it is for your tests). eHealth Global will not keep this information and it will only be used to move your samples from the outside institution to MD Anderson.

Some of your samples may be sent to outside institutions or companies (such as Guardant Health Inc.) for clinical laboratory improvements amendments (CLIA)-verified advanced testing. A CLIA-certified lab has to meet certain standards for all lab testing to ensure accuracy, reliability, and timeliness of patient test results regardless of where the test is performed. Your name and a sample identifier, along with information about your sample and disease that are necessary to complete the testing will be provided along with your sample. The information from the CLIA-certified tests done at outside companies or institutions will become part of your medical record.

If your sample is sent to outside institutions for standard research testing only, no identifying information about you will be included with the sample. Results from standard research tests from outside companies or institutions will not be included in your medical record and you will not receive information about the results of these tests.

Other Information

Your samples and personal health information will be used in research to explore machine leaning, artificial intelligence tools, and digital pathology tools that help identify and predict markers of disease.

If at any time you withdraw your consent for this study, any DNA testing that has already been performed on your samples (such as tissue, blood, or material (DNA) created from your samples) and entered into your permanent medical record will be kept, but no additional DNA samples will be collected and any of your unused DNA samples left in the research laboratory will be destroyed.

Your DNA and clinical information that is linked to your records will be deposited in publicly available databases for researchers worldwide to learn from. The de-identified information from your blood samples will be sent to the National Human Genome Research Institute (NHGRI) through the National Institute of Health (NIH) and will be added to a genetic library. Your de-identified blood samples will be sent to an NHGRI-sponsored laboratory for detailed analysis. The results of your research blood test will be available only to researchers who have received approval from an NIH (US Government) Data Access Committee. This information (always de-identified) will only be made available to researchers who are approved to gain access.

2. POSSIBLE RISKS

The known risks of genetic testing are listed in this form, but they may vary from person to person. You should discuss these with the study doctor.

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

Not all patients on the study will undergo genetic tests, the tests performed may not cover all genes, and new genetic mutations are always being discovered. **Even if you**

state that you prefer to be contacted with medically relevant findings, if you are NOT contacted by researchers, there is still a chance that you may have genetic mutations.

Through your participation in this study, you may learn information about your genetic risk for cancer and/or other non-cancer diseases. The genetic testing done through this research study cannot find all types of hereditary risks, and this testing may not be as accurate as genetic testing performed in CLIA-certified laboratories. The research testing may identify certain conditions that may require additional genetic testing in a clinical laboratory or another CLIA-certified laboratory. **For this reason, participation in this research study is not a replacement for genetic counseling and clinical genetic testing, if your doctor thinks it is needed. Learning about your genetic risks** may be stressful and may have implications for you as well as your family members. If you are concerned about any genetic risks because of your personal and family history, you should discuss this concern with your treating doctor and health care team so that you can be referred for risk assessment, genetic counseling, and/or consideration for clinical genetic testing to address your specific concern.

If you choose to be contacted about your results of any genetic testing, these results may be put in your health records after confirmation with additional tests. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

Any research testing done in the research laboratory will NOT be entered into your permanent medical record and will not be made available to you. However, your treating doctor at MD Anderson will have access to these test results, and if they think these results are important to your care, they can order additional tests in a clinical laboratory to confirm the test results. Your doctors at other institutions will not have access to the results of this research testing, unless your treating doctor at MD Anderson has first confirmed the research results in the clinical laboratory. Some of the research testing on your tumor will be done in the clinical laboratory at MD Anderson. These results will be available to you and will be in your electronic medical record. These results will be available to your physicians at MD Anderson. These results also will be available to physicians at other institutions that are involved in your care. If you have already any of this testing done at MD Anderson, an outside institution, or your oncologist already plans to order clinical testing, then these tests may not be repeated and only research testing in the laboratory may be performed.

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

This study may involve unpredictable risks to the participants.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, and the doctor thinks it is needed, you will have a saliva or cheek cell sample collected instead of the blood draw above.

To collect a saliva sample, you will be given a small plastic container to spit into. To collect a cheek cell sample, a cotton swab will be brushed along the inside of your mouth or cheek to collect the cells.

If during the genetic analysis, genetic mutations that are relevant to the care of yourself or your family members are found, the researchers will try to return this information to you. However, analysis may not be immediately done, and lack of information should not be perceived as lack of genetic findings. Importantly, new scientific findings occur frequently, and your genetic analysis may not be repeated when new disease-related genes are discovered.

Optional Procedure #2 (**Only for adults 18 and older)**: If you agree, additional blood (about 1.5 tablespoons) will be drawn for circulating tumor cell (CTC) testing. This tests for tumor cells in the blood, which will be used for additional biomarker testing.

Optional Procedure #3: If you agree, you will be contacted if you are found to have an unexpected germline mutation that may be medically significant for you or your family. Genetic counseling will be arranged for you and your family members to discuss the findings and associated risks. The genetic counselor will also discuss with your family members their choice to have genetic testing.

Optional Procedure #4: The kind of genetic research done in this study has the potential to identify unsuspected genetic mutations (changes). These may change your risk for:

- Hereditary cancer
- Side effects of specific drugs or procedures
- Serious but treatable conditions (like heart disease)
- Serious, but untreatable conditions (like Alzheimer's disease, polycystic kidney disease)

If you are a carrier of a genetic mutation, your children or other family members may also have a hereditary risk for serious diseases.

In the event of your death, if you agree, you will be asked to allow researchers to contact your power of attorney to share your unexpected genetic results that may have medical significance for you or your family with your family members. If you agree, please provide the contact information of 2 family members for your power of attorney to contact below. When family members are contacted, they will be told there was a genetic finding. The family members will be given the choice about learning what the findings were.

If your family members agree to learn about the findings, genetic counseling will be arranged for your family members to discuss the findings and associated risks. The

genetic counselor will also discuss with your family members their choice to have genetic testing.

If your family members do not agree to learn about the findings, they will not be contacted.

You do not have to agree to take part in the optional procedures in order to be enrolled in this study.

There will be no additional cost to you for taking part in optional procedure #1. For optional procedures #2 and #3, if you and your family elect to have genetic counseling and testing, the costs of genetic counseling and genetic testing will not be covered by the study. You and/or your family members' insurance providers will need to pay for these costs.

Optional Procedure Benefits:
The optional procedure will help researchers compare genetic changes in your tumor to those in your blood. This may help determine which changes are truly in the tumor, and thus may be better targets for therapy. However, there may be no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned.

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

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests will not be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

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

Optional Procedure #1: Do you agree to have a saliva or cheek cell sample collected instead of the blood draw if the study doctor thinks it is needed?

YES NO

Optional Procedure #2 for adults 18 and older (if you are under 18, please select no): Do you agree to have blood drawn for CTC testing?

YES NO

Optional Procedure #3: Do you agree to be contacted if an unexpected germline mutation that may be medically significant for you or your family is found?

YES NO

Optional Procedure #4: Do you agree to allow the study team to contact your power of attorney to share any unexpected genetic results with them?

YES NO

If your answer is Yes, please name 2 family members for researchers to contact. When family members are contacted, they will be told there was a genetic finding. The family members will be given the choice about learning what the findings were.

Name of the Family Member 1:

Relationship:

Telephone No:

Name of the Family Member 2:

Relationship:

Telephone No:

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson, Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, or Taiho Oncology for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

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

provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

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

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

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

Additional Information

4. You may ask the study chair (Dr. Funda Meric-Bernstam, at 713-792-6940) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

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

6. This study or your participation in it may be changed or stopped at any time by the study chair, Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, Taiho Oncology, or the IRB of MD Anderson.

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

8. This study is sponsored and/or supported by: Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, and Taiho Oncology**.**

9. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson, Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, Sanofi, Taiho Oncology, and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover material that is stored at MD Anderson in future research. Leftover material stored by Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, and Taiho Oncology**.** Sanofi may be used in future research.

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

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

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

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

Genetic Research

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

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same

protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

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

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

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Institute for Personalized Cancer Therapy, LOXO Pharmaceuticals, Guardant Health, Inc., CytomX, and Taiho Oncology, who are sponsors or supporters of this study, and/or any future sponsors/supporters of the study
- Study collaborators: eHealth Global, Illumina, Ambry, the University of Utah, Foundation Medicine, Genomic Health, Exosome Diagnostics, Life Technologies, Myriad, Complete Genomics, Molecular Health, Columbia University, CGI Laboratories (Cancer Genetics, Inc.), Beijing Genomics Institute, Genentech, CytomX, Nanostring, Stemcentrix/Abbvie, Novartis, Bayer, University of Texas Southwestern, Nantomics, Boston Gene, Pangea, Sanofi, Tempus, Omniseq, OneCell Diagnostics, University of Texas School of Biomedical Informatics, Rice University, Lunit, Akoya, Hamamatsu, Broad Institute, Gritstone, Daiichi, AstraZeneca, Boehringer Ingelheim, FMSS – Université de Sherbrooke (Marilyne Labrie, PhD), and Georgetown University
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

The purpose of collecting and sharing this information is to help researchers to link their laboratory findings with clinical information and/or outcome data in an effort to learn about genetic mutations in cancer and how to improve therapy for cancer.

Dr. Funda Meric-Bernstam will receive the research samples. Your doctor and the research team may share your study information with the parties named in Section A above.

Study collaborators may receive de-identified data, tissue, and/or blood for research purposes. Blood samples will be shared with OneCell Diagnostics for research in developing new tools for CTC testing. Samples used for research in developing new treatments will be shared with the MD Anderson Shukla Lab and other collaborators.

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

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

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

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

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

CONSENT/AUTHORIZATION
(Adult Participants Only)

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

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

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

PARENT/GUARDIAN PERMISSION

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE

_____
PRINTED NAME OF PARENT/GUARDIAN

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE
Signature of Other Parent (Optional, unless required by the IRB.)

_____
PRINTED NAME OF PARENT/GUARDIAN

____The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____Other parent is deceased, unknown, incompetent, or not reasonably available.

____Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

____The IRB has determined that the signature of both parents is NOT required.

ASSENT OF MINOR

(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other:_____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____
SIGNATURE OF MINOR (Age 13-17) DATE

_____
PRINTED NAME OF MINOR