THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase Ib Study of Immunotherapy with Ex Vivo Pre-Activated and Expanded CB-NK Cells in Combination with Cetuximab, In Colorectal Cancer Patients with Minimal Residual Disease (MRD)

2021-0076

Study Chair: Maria Pia Morelli, MD

_____ _____
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.

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

STUDY SUMMARY

The goal of this clinical research study is to learn about the safety and effects of CB- NK cells in combination with cetuximab when given to patients with high-risk colorectal cancer (CRC) who have completed standard-of-care treatment for the disease but are still positive for minimal residual disease.

This is an investigational study. CB-NK cells are not FDA approved or commercially available. They are currently being used for research purposes only. Cetuximab is FDA approved and commercially available for the treatment of CRC. It is investigational to give CB-NK cells and cetuximab together.

As part of this study, you will also receive lymphodepletion chemotherapy (explained below under "Study Therapy Administration"). The drugs given for lymphodepletion chemotherapy (cyclophosphamide and fludarabine) are FDA approved and commercially available for this use.

The study doctor can explain how the study therapy is designed to work.

The study therapy may or may not help to control the disease. Future patients will benefit from what is learned in this study. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you will need to visit MD Anderson to receive study therapy and have tests (described below under "1. Study Details"). You may not want to take part if you are concerned about the number of study visits.

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

You will receive 3 infusions of lymphodepletion therapy (cyclophosphamide and fludarabine, 1 infusion of cetuximab, and 1 infusion of CB-NK cells. You will receive the CB-NK cells in the hospital where you will be observed or a minimum of 24 hours after the infusion. After the infusions, you will have a follow-up visit at 3 months. You may continue to have follow-up visits every 3 months until the study ends, or you withdraw from the study.

CB-NK cells and cetuximab will be provided to you at no cost during this study. You and/or your insurance provider will be responsible for the cost of cyclophosphamide and fludarabine.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other therapy. This may include other investigational therapy, if available. The study doctor will discuss the options available to you, including their risks and benefits. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer. The study doctor will discuss this with you.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will be performed within 40 days before the start of study treatment (unless otherwise noted), to help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG and an echocardiogram (ECHO) to check your heart function.
- Blood (about 12 tablespoons) will be drawn for routine tests, immune system testing, research testing, and to test for infectious viruses (hepatitis B and C and HIV [the AIDS virus]). Throughout the study, research tests may include:
    - Biomarker testing – Biomarkers are found in the blood/tissue and may be related to your reaction to the study therapy.

  - Circulating tumor DNA (ctDNA) testing – ctDNA testing measures the amount of tumor DNA in the blood. Note that some ctDNA testing will be done as part of your standard of care testing in addition to research testing.
  - Tumor marker testing – Tumor markers may be related to the status of the disease.
  - Cytokine testing – Cytokines are proteins that may affect the immune system.
  - Flow cytometry – Flow cytometry looks at immune system cells to better understand if they are active and ready to fight against cancer cells.
  - Chimerism testing – CB-NK cells are made with NK cells from donors. Chimerism testing measures how many NK cells in your body are from the donor and how many are yours.
  - ADCC assay – ADCC assay tests whether the CB-NK cells are still active after infusion.
- Urine will be collected for routine tests.
- You will have a CT scan to check the status of the disease. If you have already had a CT scan within 30 days before starting study therapy, you may not need to repeat this test.
- Leftover tumor tissue from a previous procedure will be collected to confirm you have CRC.
- If you can become pregnant, part of the above blood draw will be used for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

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

Study Therapy Administration

Negative days are the days before you receive CB-NK cells.

If you are found to be eligible to take part in this study, you will first receive lymphodepletion chemotherapy for 3 days in a row, starting about 5 days before you receive CB-NK cells. On **Days -5, -4, and -3**, you will receive cyclophosphamide and fludarabine by vein over about 30 minutes each. Blood (about 2 teaspoons) will be collected for research circulating tumor DNA (ctDNA) testing on each day. Lymphodepletion chemotherapy is not intended to treat the cancer. It is meant to help prepare your body to receive cetuximab and CB-NK cells.

On **Day -2**, you will not receive any study drugs.

On **Day -1**, you will receive cetuximab by vein over about 2 hours.

On **Day 0**, you will receive CB-NK cells by vein over about 20-30 minutes.

You will be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

You will no longer be able to receive the study therapy if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Study Visits

You will have study visits **on Days -8, -5, -4, -3, -2, and -1. You will be admitted for your CB-NK cell infusion and observation on Day 0. You will return to the clinic for follow-up study visits on Days 1, 3, 8, 14, 21, 28, and 90; and then at Weeks 24, 36 and 52**. At each visit, you will have some or all the following tests:

- You will have a physical exam.
- You will have an EKG and/or an ECHO to check your heart function.
- Blood (up to 9 tablespoons) will be drawn for routine and/or research tests.
- Urine will be collected for routine tests.
- If you can become pregnant, part of the above blood draw will be used for a pregnancy test.

In addition to the above tests, **every 12 weeks and at any time the study doctor thinks it is needed**:

- Blood (about 6 tablespoons) will be drawn for research tests.
- You will have a CT or PET/CT scan to check the status of the disease.

Long-term Follow-up (Years 2-5)

Every 3 months, the study staff will also check on how you are doing and if you have started a new anti-cancer therapy. To collect this information, they may review your medical records, ask you in-person at a clinic visit, and/or call you. If you are called, each call should take about 5-10 minutes.

Long-term follow-up will continue for up to 5 years or until you withdraw from the study or the study ends.

Based on the results of the research tests during the study, you may not have long-term follow-up. This will be discussed with you.

Disease Relapse

If the disease relapses (comes back), you will be asked to take part in another research study in which you will have a tumor biopsy. You will be given another consent form, and the study doctor or study staff will discuss it with you in detail before you choose whether to take part. You do not have to agree to take part in the biopsy study in order to take part in this research study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are

rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side affects you may have, even if you do not think they are related to the study procedures.

Cetuximab, cyclophosphamide, and fludarabine may cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.

CB-NK Cell Side Effects

This is an early study of CB-NK cells, so the side effects are not well known. At this time, there are no known side effects of CB-NK cells. The following may be observed at differing degrees of severity.

- Cytokine release syndrome - this involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills), and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, confusion, difficulty speaking, and/or decreased brain function (possible paralysis and/or coma).
- Neurological toxicities (ICANS), with a possible onset from a few days to up to 8 weeks after infusion, that can significantly impair one's ability to drive and/or operate heavy machinery. Such neurological toxicities can be severe or life-threatening and includes the following symptoms: changes in thinking and alertness or confusion, coma, headache, anxiety, tremor, unsteady balance, dizziness, weakness of arms or legs, abnormal speech and difficulty speaking, nervous system damage, brain swelling, seizures, permanent disability(ies), and/or death.
- Infusion reaction (possible chills and/or hives)

Cetuximab Side Effects

Common (occurring in more than 20% of patients)

• heart attack • fatigue/lack of energy • headache • difficulty sleeping • fever • skin rash (possibly acne-like), peeling, and/or itching • dry skin • nail changes • low blood levels of magnesium (possible weakness and/or seizures) • weight loss	• dehydration • abdominal pain • constipation • diarrhea • mouth blisters/sores (possible difficulty swallowing) • vomiting • nausea • loss of appetite • low white blood cell count • abnormal liver tests (possible liver damage) • weakness	• pain • nerve damage (loss of sensory function) • difficulty breathing • cough • sore throat • infection • severe rash at the site of previous radiation • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Occasional (occurring in 3-20% of patients)

• confusion • depression • anxiety • chills/shivering • skin sores • hair loss (partial or total) • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)	• low blood levels of calcium and/or potassium (possible weakness and/or cramping) • dry mouth • abnormal taste • upset stomach • joint pain • painful red eyes	• blockage in the lung (possible pain and/or shortness of breath) • immune reaction • infusion reaction (possible chills and/or hives) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Frequency unknown but occurring in 1-10% of patients

• hair growth • changes in body salts such as sodium and/or potassium (possible fatigue and/or weakness)

Rare but serious (occurring in fewer than 3% of patients)

• heart attack • stoppage of heart and lung function • decreased blood supply to the heart	• large skin blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• eye ulcer • kidney failure • lung inflammation (possible difficulty breathing)

• irregular heartbeat • inflammation of the membranes around the spinal cord and brain (possible headache and/or coma)	• very severe blistering skin disease (loss of large portion of skin)	

Cyclophosphamide Side Effects

Common (occurring in more than 20% of patients):

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • inability to regulate water/salt balance which can cause frequent urination and dehydration	• headache • abdominal pain • loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle • low blood counts (red, platelet, white)	• fever with dangerously low white blood cell count (febrile neutropenia) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, acute leukemia [a type of blood cancer], lymphoma [a type of lymph node cancer], thyroid cancer, and/or sarcoma [a type of cancer that can start in the soft tissue, bone, or other tissue].

Rare but serious (occurring in fewer than 3% of patients)

• irregular heartbeat • build-up of fluid around the heart (possible heart failure) • build-up of blood in the sac around the heart (possible impaired heart function) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding)	• wound healing problems • low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing)

• heart damage/failure, death of heart tissue, or other severe heart problems • heart attack, which can be serious and life-threatening • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall) • very severe blistering skin disease (loss of large portion of skin)	pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding) • inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function • blood in the urine • blurry vision	• problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multiorgan failure • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Fludarabine Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue • pain • loss of appetite	• nausea • vomiting • low blood cell count (red, white, platelets)	• weakness • difficulty breathing • cough • infection

Occasional (occurring in 3-20% of patients)

• chest pain (possibly due to heart trouble) • heart failure • heart attack • fast and/or irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • vein inflammation • swelling • chills • stroke • headache • difficulty sleeping	• skin rash and/or itching • sweating • hair loss (partial or total) • high blood sugar (possible diabetes) • mouth blisters/sores (possible difficulty swallowing) • diarrhea/constipation • digestive system bleeding • gallstones • blood in the urine • difficult and/or painful urination	• inability to urinate • abnormal liver tests (possible liver damage) • abnormal sensation (such as pins and needles) • vision problems • hearing loss • sore/swollen throat • lung damage/inflammation (possible difficulty breathing) • coughing up blood

Rare but serious (occurring in fewer than 3% of patients)

• build-up of fluid in the tissue around the heart • weakness in wall of artery (possible serious bleeding complications) • multiple blood clots (possible organ dysfunction and/or failure) • bleeding in the brain • abnormal brain function (affecting balance and coordination) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • mental status change • coma	• painful blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • dehydration • abnormal pancreas tests • bladder inflammation with bleeding (possible pain and/or urge to urinate) • bone marrow failure due to abnormal tissue growth • destruction of red blood cells and platelets due to abnormal antibodies • anemia due to destruction of red blood cells	• nerve damage affecting the eye and/or causing wrist weakness • paralysis • blindness • inflammation of an eye nerve • kidney failure • high blood levels of uric acid (possible painful joints and/or kidney failure) • bleeding in the lungs and/or airways • failure to breathe • low oxygen level in the blood (possible lightheadedness) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • breakdown products of the cancer cells

• seizure • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• condition causing increased bleeding and/or bruising • liver failure • nerve damage (possible numbness, pain, and/or loss of motor function)	entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Fludarabine may rarely cause you to develop another type of cancer (such as skin cancer and/or acute myeloid leukemia [a type of blood cancer].

Frequency Unknown

• testes/sperm damage	• graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body)

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other 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.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped.
Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel “closed in” while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

EKGs/ECHOs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

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.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study and for 6 months after your last dose of study drugs if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, talk to the study doctor about the best birth control method for you to use during this study.
Acceptable birth control methods include:

- Hormonal birth control methods that stop ovulation
- Barrier methods
- Hormone-releasing or copper intrauterine devices (IUD)
- Surgical sterilization (such as vasectomy [for males] or bilateral tubal ligation [“tubes tied” for women])

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, leftover tissue from a previous biopsy, if available, will be collected for research testing which may include genetic testing.

You do not have to agree to the optional procedure in order to take part in this study. There are no benefits to you for taking part in the optional procedure. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure.

Optional Procedure Risks

There are no expected risks in allowing **leftover tissue** to be collected for research testing.

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 allow leftover tissue from a previous biopsy, if available, to be collected for research testing?

YES **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 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. Maria Pia Morelli, at 713-792-2828) 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 decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. 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 continue to 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 without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

   Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

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

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson 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 samples that are stored at MD Anderson 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
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.

A federal law, called 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:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

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

A. During the course of this study, MD Anderson will be collecting and using your 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
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   To protect your identity, the samples collected from you will be labeled a unique number instead of your name or other identifying information. Only the study doctor or study staff will have access to the code that can link you to your samples.

   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 or receive study-related treatment 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 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.

E. 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.

CONSENT/AUTHORIZATION

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