THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

EX-VIVO EXPANDED ALLOGENEIC NK CELLS FOR THE TREATMENT OF SOLID TUMORS OF PEDIATRIC ORIGIN IN CHILDREN AND YOUNG ADULTS
2017-0085

Study Chair: Demetrios Petropoulos

_____ _____
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

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.

NK cells are specialized immune cells in the body that have been shown to kill tumor cells (including solid tumor cells) in the laboratory. Previous studies of NK cells in some cancer patients have suggested that they can be given without severe side effects and may help in controlling tumors.

The goal of this clinical research study is to learn the recommended dose of donated natural killer cells that can be given to pediatric cancer patients with solid tumors after receiving chemotherapy (cyclophosphamide and etoposide). The safety of the NK cells given after chemotherapy will also be studied.

In this study, the NK cells being used have already been donated/collected from cord blood (blood collected at birth from the afterbirth of healthy babies). They are then

"expanded," or grown, so that more NK cells can be made from a small sample and given to a patient.

Cyclophosphamide and etoposide are standard chemotherapy drugs that are used in the treatment of pediatric solid tumors. In this study, the drugs are being given both to fight the cancer cells and also to help prevent your body from rejecting the NK cells.

This is an investigational study. NK cell transplants are not FDA approved or commercially available. Cyclophosphamide and etoposide are FDA approved and commercially available for the treatment being used on this study. The use of NK cell transplants in combination with this chemotherapy is investigational.

The study doctor can describe how the study drugs and NK cells are designed to work.

The study drugs and NK cells may help to control the disease. Future patients may benefit from what is learned. 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 may experience side effects that may be severe or fatal.

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

You will receive the NK cells 1 time. You will then have study visits until 30 days after you receive the NK cells. You will be taken off study if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

The NK cells will be grown and given to you at no cost to you. You and/or your insurance provider will be responsible for the costs of cyclophosphamide and etoposide.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other anti-tumor therapy. You may choose to receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. 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.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. Screening tests will help the doctor decide if you are eligible. For this study, screening will have 2 stages.

Stage 1: Blood (about 2 teaspoons) will be drawn to learn your human leukocyte antigen (HLA) type. HLA is a type of protein or marker found on most cells in the body and used to match with a donor. This is being done to make sure that there is available cord donor blood. If there is available donor blood, you will proceed to Stage 2. If no donor blood is available, you will not be eligible to take part in this study. It may take time to get your HLA results. Talk to the study doctor about what kind of delay there may be between Stage 1 and Stage 2.

Stage 2:

- You will have a physical exam.
- Blood (about 4-5 tablespoons) will be drawn for routine testing.
- Urine will be collected for routine tests.
- You will have MRI and/or CT scans to check the status of the disease.
- Depending on the type of disease that you have, you may need to have a tumor biopsy to check the status of the disease. The type of biopsy you have will depend on the location of the disease. The study doctor will describe this procedure in more detail, including its risks.
- Depending on the type of disease that you have, blood (about 1 teaspoon) may be drawn for tumor marker testing. Tumor markers may be related to the status of the disease.
- If the doctor thinks it is needed, you will have an EKG and an echocardiogram (ECHO) to check your heart function.
- If you can become pregnant, urine will be collected 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 treatment options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a dose level of NK cells based on when you join this study. Up to 2 dose levels of NK cells will be tested. Up to 6 participants will be enrolled at each dose level. The first group of participants will receive the lowest dose level. A second group will receive a higher dose, if no intolerable side effects were seen.

After the recommended dose is found, an additional 14 participants may be enrolled in an "Expansion Phase" and receive that dose of NK cells.

All participants will receive the same dose level of standard chemotherapy.

Up to 32 participants will be enrolled on this study. All will take part at MD Anderson.

Study Drug Administration

You will receive cyclophosphamide by vein over about 30 minutes on Days 1-5. You will also receive etoposide by vein over about 60 minutes on Days 1-5. You will then rest (not receive anything) on Days 6 and 7. You will then receive the NK cells by vein.

The nurse and study doctor will determine the length of the infusion based on volume that they get from the lab. It should take no more than 1 hour.

You will be admitted to the hospital within 24 hours before you begin receiving chemotherapy to receive it as an inpatient. You will stay in the hospital for all the chemotherapy and not be discharged until after you have received the NK cell infusion and the doctor thinks that it is safe for you to go home.

You will also receive mesna to help prevent side effects to the bladder. Mesna is given by vein over a short amount of time at 3 different time points. When and how long you receive it will depend on what the study doctor thinks is in your best interest. This will be discussed with you.

You will be given standard drugs and fluids 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.

Within 72 hours before you begin receiving chemotherapy:

- You will have a physical exam.
- Blood (about 3-4 tablespoons) will be drawn for routine tests, to check for the presence of donor cells in your blood, and research tests to check the effects of the NK cells. Some of these tests are being done before you receive the donor cells to compare to samples that are taken after you receive them.
- Urine will be collected for routine tests.

Urine will be collected for routine tests every time you urinate **while you are in the hospital** receiving chemotherapy.

Blood (about 2-3 teaspoons) will be drawn for routine tests **2 times each week from the time you started chemotherapy** until your blood cell counts recover from chemotherapy. This may continue to be done after you leave the hospital.

Within 24 hours before you receive the NK cells, 3-4 days after you receive the NK cells, and then every week until 30 days after you receive the NK cells and then at Months 3, 6, and 12:

- You will have a physical exam.
- Blood (about 2-4 tablespoons) will be drawn for routine tests, to check for the presence of donor cells in your blood, and research tests to check the effects of the NK cells. The research blood draws will continue only until Day 38.
- Depending on the type of disease that you have, blood (about 1 teaspoon) may be drawn for tumor marker testing.

At the last of these visits, you will have MRI and/or CT scans to check the status of the disease around 4 weeks after infusion. If the doctor thinks it is needed, this will be repeated at 8 weeks after your NK cell infusion to check for psuedoprogression. Pseudoprogression is when the tumor may appear to be getting worse soon after cell infusion because the body is mounting an immune response to the tumor. But really either the tumor is stable (has not changed) or is getting better. Depending on the type

of disease that you have, you may need to have additional studies that include MIBG, FDG-PET, bone marrow aspiration and biopsy, tumor marker, and tissue biopsy at these visits to check the status of the disease.

After the last visit, you will continue to be followed by your regular cancer doctor per the standard of care. Information about how you are doing and the disease will be shared with the study doctor for 1 year after the infusion of NK cells. Follow-up may continue after that if you have any ongoing complications or side effects related to the infusion.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. 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.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Expanded NK cells, cyclophosphamide, etoposide, and mesna may each 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.

Expanded NK Cell Side Effects

It is not well known how often the side effects of expanded NK cells may occur.

• high blood pressure • low blood pressure (possible dizziness and/or fainting) • fever • headache • chills	• difficulty breathing/shortness of breath • infusion reaction (possible chills and/or hives) • allergic reaction • graft-versus-host disease (when	• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

• low blood cell count (red/white/platelets) • low oxygen in the blood (possible lightheadedness)	transplanted donor tissue attacks the tissues of the recipient's body)	

The NK cells may be contaminated by bacteria or other germs when they are being made which may cause an infection. The cells will be tested in the lab to make sure the cells are not contaminated.

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	• wound healing problems • low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma)	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing)

the heart (possible chest pain and/or bleeding) • 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)	• hormonal deficiency that affects the body's ability to control blood 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)

Etoposide Side Effects

Common (occurring in more than 20% of patients)

• hair loss (partial or total)	• nausea	• vomiting • low blood cell counts (red, white, platelets)

Occasional (occurring in 3-20% of patients)

• loss of appetite • diarrhea	• mouth blisters/sores (possible difficulty swallowing)	• liver damage

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

• low blood pressure (possible dizziness/fainting) • heart attack • decreased blood supply to the heart • blood vessel spasm (possible blockage of blood flow) • blood vessel inflammation (possible bleeding and/or bruising) • fever • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • seizure	• severe sunburn-like rash at site of previous radiation (called radiation recall) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • enlarged bowel (possible abdominal pain) • failure of the ovaries to produce hormones (possible stopped menstrual cycle) • abnormal blood acid/base balance (possible organ damage)	• nerve damage (possible numbness, pain, and/or loss of motor function) • blindness • inflammation of an eye nerve • lung inflammation and/or damage (possible difficulty breathing) • blue skin • drug leakage from the injection site (possible hardened tissue and/or tissue death) • closing of the throat • allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

High-dose etoposide also may cause the following side effects. It is not known how often these side effects may occur.

- symptoms of drunkenness (possible flushing and/or dizziness)

High-dose etoposide may cause you to develop another type of cancer (such as leukemia, a type of blood cancer).

Mesna Side Effects

It is not known how often the following side effects of mesna may occur.

• flushing • dizziness • fever • increased sensitivity of the senses • headache • sleepiness • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• skin rash, blisters, and/or sores • very severe blistering skin disease (loss of large portion of skin) • loss of appetite • constipation • diarrhea • gas • nausea/vomiting • abnormal taste/change in taste	• blood in the urine • pain • shivering • painful red eyes • cough • sore throat • runny nose • flu-like symptoms • injection site swelling, pain, and/or heat

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

• high blood pressure • low blood pressure (possible dizziness/fainting)	• fast heartbeat • low platelet count	• allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

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.

Having **biopsies and bone marrow aspirates** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

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

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of

your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans / MIBG 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** (including the FDG-PET scans) 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.

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 if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, you must use birth control while you are on study and for at least 28 days after your last dose of study drugs. Males must use a condom and females must use at least 2 of the below methods of birth control.

Acceptable methods of birth control include:

- birth control pills, injections, or implants
- tubal ligation ("tubes tied") or vasectomy
- intrauterine device (IUD)
- barrier method (such as a condom, diaphragm, or sponge) in combination with spermicide

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: Some participants will likely have standard biopsies performed as part of their standard of care while they are enrolled in this study. If this happens to you, and you agree, the study doctor would like to collect samples that are left over from this biopsy and are not needed to perform the standard testing. These samples will be used to look for donor cells and cells that may cause inflammation.

These samples will then be stored in a research bank at MD Anderson for use in future research related to cancer.

Before your samples can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your samples will be given a code number. Only individuals with IRB permission and designated bank staff will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Additionally, if needed for certain types of research in the future and if the IRB approves, the bank staff and approved research staff will be able to link your samples back to you.

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 #2: Some participants may have excess sample in the research laboratory after the research assays are completed.

These samples will then be stored in a research bank at MD Anderson for use in future research related to cancer.

Before your samples can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee

of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your samples will be given a code number. Only individuals with IRB permission and designated bank staff will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Additionally, if needed for certain types of research in the future and if the IRB approves, the bank staff and approved research staff will be able to link your samples back to you.

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:
MD Anderson and others can learn about cancer and other diseases from your banked samples. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your samples may be used for genetic research about diseases that are passed on in families. The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

If you withdraw your consent to the storage of leftover samples in the tissue bank, then they will no longer be collected for storage. Any of your samples that remain in the tissue bank will no longer be used for research and will be destroyed.

However, if any of your de-identified samples were already released for research purposes before you withdrew consent, MD Anderson will not be able to destroy them.

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 tissue left over from standard biopsies to be collected and used for research tests and then stored in a research bank at MD Anderson for use in future research?

YES **NO**

Optional Procedure #2: Do you agree to allow left over blood samples that were collected for research tests to be stored in a research bank at MD Anderson for use in future research?

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. Demetrios Petropoulos, at 713-792-3746) 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. It may be dangerous to suddenly stop study treatment, and the study doctor can discuss ways to safely withdraw. If you withdraw from this study, you can still choose to be treated at MD Anderson.

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.

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

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.

Genetic Research
Research samples collected from you as part of this study may 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.

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

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 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
(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 Protocol 2017-0085.

_____ _____
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.

_**X**__ 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