THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Pilot Trial of Fecal Microbiota Transplantation and Re-Introduction of Anti-PD-1 Therapy in dMMR Solid Tumor Anti-PD-1 Non-Responders

2020-0186

Subtitle: Fecal Microbiota Transplantation for Anti-PD-1 Non-responders

Study Chair: Michael Overman, 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 FDA-approved treatments pembrolizumab and nivolumab do not work for some patients who have certain types of colorectal cancer.

The goal of this clinical research study is to learn if adding fecal microbiota transplants to treatment with either pembrolizumab or nivolumab can help to improve the success of this treatment for these patients. The safety and tolerability of this treatment combination will also be studied.

This is an investigational study. Pembrolizumab and nivolumab are each FDA approved and commercially available to treat patients with colorectal cancer. Fecal microbiota transplants contain the normal bacteria and viruses found in fecal (stool) material. Fecal microbiota transplants are investigational. Giving pembrolizumab or nivolumab with fecal microbiota transplants to treat patients with colorectal cancer is investigational. The study doctor can describe how the transplant is designed to work.

The study treatment may 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 may be concerned about the number of visits to MD Anderson to receive study treatment.

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

The fecal microbiota transplant will be provided at no cost to you. You and/or your insurance provider will be responsible for the costs of nivolumab/pembrolizumab.

You will receive study treatment for up to 6 months. If additional fecal microbiota supply is available after 6 months and the study doctor determines that you are benefitting, you may continue to receive study treatment after the 6 months study treatment period.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive another therapy. This may include other investigational therapy, if it is available. The study doctor will discuss with you 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. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 3 tablespoons) and urine will be collected for routine and tumor marker testing. Tumor markers may be related to the status of the disease. If the study doctor thinks it is needed, this blood will also be used to check for hepatitis. If you can become pregnant, part of this blood or urine sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.
- You will have CT scans to check the status of the disease.
- You will provide a stool sample to learn about the types of bacteria that are present.
- You will have a core tumor biopsy for biomarker testing, including tests for genetic biomarkers. Biomarkers are found in the blood and tissue and may help researchers see how you react to the study treatment. To perform a core biopsy, the affected area is numbed with anesthetic and a sample of tissue is removed using a hollow core needle that has a cutting edge. If leftover tumor tissue from an earlier test or surgery is available, this tissue can possibly be used instead of performing a new biopsy.
- You will complete a questionnaire about your eating habits. This will be done at home using your computer and a secure study code. Completing the questionnaire should take about 30-60 minutes.

Up to 15 participants will be enrolled in this study. All will take part in the study at either MD Anderson or an MD Anderson Sister Institute (Sheba Medical Center).

Study Treatment

If you are found to be eligible to take part in this study, you will begin to prepare to receive a fecal transplant and then start taking either pembrolizumab or nivolumab.

On Day -6, you will follow a clear liquid diet and drink a laxative solution. The study staff will provide more instructions about this.

Then, on Day -5, you will have a colonoscopy to transplant fecal material from a donor into your intestine. Donors will be patients who previously received successful treatment with either pembrolizumab or nivolumab for colorectal cancer. All donors will be carefully screened to ensure their donated fecal matter meets safety guidelines.

If candidate donors are not identified, you will receive transplant product from healthy donors that are also carefully screened.

You will then start receiving either pembrolizumab or nivolumab on Day 1 of Cycle 1. Both drugs are given by vein over 30 minutes. Your doctor will decide if you will receive pembrolizumab or nivolumab.

If you receive pembrolizumab, each cycle is 21 days (3 weeks) long. On Day 1 of each cycle, you will receive pembrolizumab by vein over 30 minutes.

If you receive nivolumab, each cycle is 14 days (2 weeks) long. On Day 1 of each cycle, you will receive nivolumab by vein over 30 minutes.

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

Your participation on the study will be over after the follow-up visits.

Study Visits – For Patients Receiving Pembrolizumab

On **Day 1 of each cycle**:

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine and research testing. On this study, "research tests" includes tests of the immune system and biomarker testing, which may include genetic biomarkers.
- You will provide a stool sample (Cycles 1, 2, 4, 5, 6 and 8 only).

At **Week 3**, you will have a core tumor biopsy for biomarker testing, including tests for genetic biomarkers.

At **Week 9 and every 9 weeks** after that, you will have CT scans to check the status of the disease.

At **Month 3**, you will repeat the questionnaire about your eating habits.

Study Visits – For Patients Receiving Nivolumab

On **Day 1 of each cycle:**
- You will have a physical exam.
- Blood (about 2-3 tablespoons) will be drawn for routine and research testing, including tests for biomarkers.
- You will provide a stool sample (Cycles 1, 3, 5, 6, 8, 10, 11 only).

At **Week 4**, you will have a core tumor biopsy for biomarker testing, including tests for genetic biomarkers.

At **Week 8 and every 8 weeks** after that, you will have CT scans to check the status of the disease.

At **Month 3**, you will repeat the questionnaire about your eating habits.

End-of-Treatment Visit
After you stop receiving the study treatment:
- Blood (about 4 teaspoons) will be drawn for research testing.
- You will provide a stool sample.
- You will repeat the questionnaire about your eating habits.

Long-term Follow-up
About 30 days after you receive your last treatment, then every 6 months for up to 3 years, the study staff will call you to see how you are doing. This call should last about 5-10 minutes.

It is possible that you may continue receiving nivolumab/pembrolizumab after 6 months. In this case, you will be followed per the standard of care, including imaging scans.

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 effects you may have, even if you do not think they are related to the study procedures.

Among patients who have had **fecal transplantation** by colonoscopy, 1% or fewer have experienced the following side effects:

• fever • nausea/vomiting • abdominal pain • bloating	• hole in the intestines (possibly leaking contents into the abdomen)	• aspiration (stomach contents entering the airway) • bleeding

The procedure may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Receiving fecal microbiome transplants either by mouth or through colonoscopy may cause long-term risks such as obesity and other issues that may increase your risk of heart disease. This may occur in 5% or fewer of participants.

There is a small risk that this procedure and the transplant material may increase your risk of developing an illness or an invasive infection that could be difficult to treat from the standard treatments. This may cause a serious illness or disease especially if you have a suppressed immune system. There is even a risk of being infected with SARS-CoV-2 (COVID-19) from a donor who did not show any symptoms of the virus. To lower the risk of infection, donors are screened for risk factors for exposure to SARS-CoV-2, monkeypox, and other infections, and donated samples are screened for many types of bacteria and viruses.

Pembrolizumab and nivolumab each 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 difficulty breathing.

Pembrolizumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • fever • skin rash and/or itching • 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)	• high blood sugar (possible diabetes) • high blood levels of fat (possible heart disease and/or stroke) • loss of appetite • nausea • constipation • diarrhea • abdominal pain • low blood cell count (white/red/platelets)	• abnormal liver test (possible liver damage) • pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

If you have a stem cell transplant from a donor after you receive pembrolizumab, you may have an increased risk of complications, such as severe graft-versus-host disease (when transplanted donor tissue attacks the recipient's organs such as skin, liver, and/or intestines) and/or clotting of blood within the liver. Deaths have been reported in patients who received a stem cell transplant from a donor after pembrolizumab therapy. If you decide to receive a stem cell transplant from a donor, please tell your transplant doctor that you received pembrolizumab in the past.

Occasional (occurring in 3-20% of patients)

• swelling (face/arm/leg) • inflammation of the tissue around the heart (possible chest pain) • irregular heartbeat • headache • confusion • patches of skin color loss • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • overactive thyroid gland (possible weight loss, diarrhea, mood swings, difficulty sleeping, heart rate changes, and/or sweating)	• low blood sugar • weight loss • fluid in the abdomen • blood in the urine • vomiting • abnormal liver test (possible yellowing of the skin and/or eyes) • weakness	• nerve damage (possible numbness, pain, and/or loss of motor function) • difficulty breathing (possibly due to lung inflammation) • flu-like symptoms • infusion reaction (possible dizziness, low blood pressure, nausea, pain, and/or difficulty breathing

Frequency Unknown

• heart failure • heart attack • build-up of fluid around the heart (possible heart failure)	• abnormal connections or passageways between organs or vessels • bleeding in the rectum and/or uterus	• blockage in the lung (possible pain and/or shortness of breath) • nosebleed • coughing up blood

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

• low blood pressure (possible dizziness/fainting) • heart inflammation • build-up of fluid in the tissue around the heart • blood vessel inflammation (possible bleeding, skin rash, numbness/weakness, fever, weight loss, fatigue, and/or bruising, depending on where the inflammation occurs) • seizure • immune system damage to the nervous system (causing muscle weakness, numbness and/or paralysis) • spinal cord inflammation (possible pain, weakness, loss of feeling or movement, and/or paralysis) • brain inflammation (possible paralysis and/or coma) • shedding, scaling and/or inflammation of the skin (possible fatal loss of bodily fluids) • large skin blisters • very severe blistering skin disease (loss of large portion of skin	• low hormone blood levels (possible weakness, bone changes, and/or cramping) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • pituitary gland inflammation (possible headaches) • inflammation of the thyroid gland (possible tenderness in the neck) • diabetes requiring insulin • severe high blood sugar due to uncontrolled diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the pancreas (possible abdominal pain) • inflammation of the intestines (possibly with a hole in the intestines, which may lead to contents leaking into the abdomen) • anemia due to destruction of red blood cells	• inflammation inside the eye (possible vision problems) • inflammation of an eye nerve (possible vision loss, loss of color vision, pain when moving your eyes, and/or loss of peripheral vision in one or both eyes) • kidney inflammation (possible kidney damage/failure) • kidney failure • build-up of fluid around the lungs • immune response that causes the body to attack itself (possible organ damage) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • immune response (causing muscle weakness) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

and/or with ulcers of the skin and digestive tract)	• liver damage (hepatitis) • inflammation/scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver), which may cause liver damage, stomach pain, yellowing of the skin/eyes, fatigue, and/or itching	• Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling and changes in vision, hearing loss, and/or white patches on the skin)

If you have a solid tumor type and you have an organ transplant, pembrolizumab may increase your risk for the transplant to be rejected by your body.

Pembrolizumab works by boosting the immune system. This may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue. These side effects can affect more than one of your normal organs and tissues at the same time.

Nivolumab Side Effects

Common (occurring in more than 10% of patients)

• fatigue/lack of energy •	• skin rash • itching	• diarrhea

Occasional (occurring in 3-10% of patients)

• fever • underactive thyroid gland (possible increased thyroid stimulating hormone lab test result, weight gain, heart failure, and/or constipation) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating)	• abnormal digestive blood test (possible inflammation of the pancreas) • nausea/vomiting • abdominal pain • loss of appetite • low red blood cell count • headache	• abnormal liver test (possible liver damage and/or yellowing of the eyes and/or skin) • pain (including muscle/bone) • lung inflammation (pneumonitis), and/or bronchitis (possible difficulty breathing) • stuffy nose

If you have a stem cell transplant from a donor before or after you receive nivolumab, you may have an increased risk of complications, such as severe graft-versus-host disease (when transplanted donor tissue attacks the recipient's organs such as skin, liver, and/or intestines) and/or clotting of blood within the liver. Deaths have been reported in patients who received stem cell transplant from a donor before or after nivolumab therapy. If you decide to receive a stem cell transplant from a donor, please tell your transplant doctor that you received nivolumab in the past.

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

• fast heartbeat • abnormal EKG • heart inflammation/ inflammation of the tissue around the heart (possible chest pain) • high blood pressure • low blood pressure (possible dizziness and/or fainting) • swelling of the brain (possible headache and/or mental status changes) • inflammation of the brain and spinal cord (possible altered consciousness) • inflammation of the membrane around the spinal cord and brain (possible headache and/or coma) • swelling (face/arms/legs) • chills • difficulty sleeping • dizziness • dry/red skin • hives • skin blisters • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • hair loss (partial or total) • decreased production of adrenal hormones	• abnormal blood test (possible pancreas damage) • high blood sugar (possible diabetes) • abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • mouth blisters/sores (possible difficulty swallowing) • constipation • dehydration • dry mouth • inflammation of the intestines • hole in the intestines or stomach (possibly leaking contents into the abdomen) • liver inflammation • liver failure/damage • low blood cell count (platelets, white) • viral/bacterial infection that affects nose, throat and airways (upper respiratory tract infection) • destruction of red blood cells due to the body attacking itself (called autoimmune hemolytic anemia) • abnormal kidney test (possible kidney damage) • kidney failure • breakdown of muscle tissue (possible kidney failure)	• lung infiltrates (possible infection or inflammation) • difficulty breathing which can lead to respiratory failure • cough • infusion reaction (possible fever, rash, pain, and/or swelling) • immune response causing the body to attack itself (possibly causing muscle weakness) • neuromuscular disease (possible weakness of eye, face, breathing and swallowing muscles) (myasthenic syndrome, myasthenia gravis) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • abnormally excessive sweating involving the arms, legs, hands and feet, underarms, and face, usually unrelated to body temperature or exercise

(possible weakness and/or low blood pressure) • inflammation of the thyroid gland (possible tenderness in the neck) • pituitary gland failure (possible hormone imbalance) • blood vessel inflammation • low blood levels of sodium (possible headache, confusion, seizures, and/or coma)	• damage to the nervous system (causing numbness and/or paralysis) (Guillain-Barre syndrome) • nerve damage (possible numbness, pain, and/or loss of motor function and/or “pins and needles” sensation) • nerve damage (affecting the head and neck) • muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision	• Flu like symptoms (which may include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, feeling tired) • patches of skin color loss • inflammation of multiple areas of the body (see below) • Hemophagocytic lymphohistiocytosis (HLH) syndrome (see below)

You may need to take drugs to reduce inflammation while taking nivolumab. Long-term use of these drugs may increase your risk of infection. These infections may occur anywhere and may be fatal. Treatment with antibiotic or antifungal drugs may be required to treat these infections.

At this time, it is not known whether taking a COVID-19 vaccine may affect the way that the study drug works in your body or if the study drug may affect the way the vaccine works in your body. No information is known about the interaction between a COVID-19 vaccine and nivolumab.

The study drug works by boosting the immune system. This may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue.

Nivolumab may cause serious side effects that affect your immune system. Some of these side effects start as inflammation in different areas of the body like the skin, hormone glands, pancreas, pituitary gland, eye, kidney, or stomach. Tell the study staff right away if you have diarrhea, nausea, vomiting, blurred vision, dizziness, fainting, or you are feeling cold all the time.

Nivolumab may cause Hemophagocytic lymphohistiocytosis (HLH) syndrome at a rare frequency. HLH is a disease that may affect your body's defense system, (your immune system) and certain white blood cells made by your immune system may attack other blood cells. These abnormal blood cells collect in your spleen and liver, causing these organs to enlarge, possibly causing fever, rash, and low blood cell counts.

Frequency unknown

• graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body)	• Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling, hearing loss, and/or loss of skin color) • risk of organ transplant rejection

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.

Having **biopsies** 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.

Having a **colonoscopy** could cause bleeding if a biopsy is performed. It could also cause infection, side effects to the medication used to induce sleep, or a tear in the intestine.

Collecting a **stool sample** may cause you to feel uncomfortable.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

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.

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 research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

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 acceptable methods of birth control 30 days before starting study treatment, while on this study, and for 6 months after taking your last dose of any of the study drugs. Acceptable methods of birth control include sterilization of you or your partner, hormonal birth control methods that stop ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices. If you use hormonal birth control, you must also use a barrier method (condom or diaphragm).

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, you will have a biopsy at any time that the disease appears to get worse. Tissue collected will be used for research testing (such as tests of the immune system) that may include genetic research 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

Having **biopsies** 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.

The results of any **genetic tests** may 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 biopsy if at any point the disease gets worse?

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 or the NIH 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. Michael Overman 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 who can help you safely stop study treatment. The study doctor will also decide if you need to have any visits or tests to check on your health. 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 without your consent at any time by the study chair, the NIH, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Possible reasons your participation in this study may be stopped include if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, including the results of all of your standard tests performed as part of this research, 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.

9. This study is sponsored and/or supported by: the National Institutes of Health (NIH).

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 the NIH 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. Leftover samples will not be stored by or used in future research by the NIH.

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

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
   - National Institutes of Health (NIH), who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - 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

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

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)