THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent/Authorization for Participation in Research

Title of Research Study: Improving Response to Immunotherapy in Patients with Advanced Hepatocellular Carcinoma and Chronic Hepatitis C Virus Infection with Direct-Acting Antiviral Therapy

Study Number: 2022-0844

Principal Investigator: Harrys Torres

_____ _____
Participant's Name Medical Record Number

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have advanced hepatocellular carcinoma (HCC) and chronic hepatitis C infection that might benefit from receiving direct-acting antiviral therapy (DAAs).

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

HCC is resistant to most traditional cancer treatments. However, researchers think that patients who have HCC and are treated with DAAs to treat hepatitis C may respond

better to a type of treatment called immune checkpoint therapy (a type of therapy that helps your immune system better target and fight cancer cells).

The goal of this clinical research study is to learn if giving immune checkpoint therapy (such as atezolizumab and bevacizumab) to patients who have HCC and are receiving DAAs may help to control HCC and hepatitis C.

This is an investigational study. Bevacizumab and atezolizumab are FDA approved and commercially available to treat HCC. The DAA therapy you might receive is part of your standard of care and is FDA-approved to treat hepatitis C. It is considered investigational to give bevacizumab and atezolizumab at the same time with DAA therapy to treat both HCC and hepatitis C. The study doctor can explain how the study drugs are designed to work.

How long will the research last and what will I need to do?

It is expected that this study will be open for about 2 years, but you may continue taking the study drugs for as long as the study doctor thinks it is in your best interest.

You will be asked to receive the study drugs and have blood draws, tumor biopsies, and pregnancy tests (if you can become pregnant).

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

While taking the study drugs, your HCC may get worse or the hepatitis C infection may not respond to the DAAs.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

The study drugs may help to control the HCC and hepatitis C. Future patients may benefit from what is learned. However, it cannot be promised that there will be any benefits to you or others from your taking part in this research.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or discontinue participation at any time without penalty or loss of your regular benefits.

Instead of being in this research study, your choices may include receiving DAAs alone. You may choose to receive other treatment for HCC, if available. You may choose to receive other investigational therapy, if available. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their risks and benefits with you. You may choose not to receive treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

Your alternative to participating in this research study is to not participate.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 713-792-6830.

This research has been reviewed and approved by an Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at (713) 792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

It is expected about 15 people at MD Anderson will be enrolled in this research study.

What happens if I agree to be in this research?

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 3-4 tablespoons) will be drawn for routine tests (including a check of your liver function) and for hepatitis B and C testing to learn more about the status of your hepatitis infection.
- You will have a liver core biopsy for immune system testing, including biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs. To perform a liver core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge.
- You will have an MRI and CT scan (with or without contrast) to check the status of the disease.
- If you can become pregnant, blood (about ½ teaspoon) or 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 Drug Administration

If you are found to be eligible to take part in this study, you will receive bevacizumab and atezolizumab about every 3 weeks as part of the standard of care HCC treatment that is managed by your cancer doctor. Your doctor will discuss with you when and how bevacizumab and atezolizumab will be given.

In addition, you will continue receiving your standard of care DAAs (either sofosbuvir + velpatasvir or sofosbuvir + velpatasvir + voxilaprevir) by mouth either 1-2 times a day, depending on what your doctor prescribes you. You may also receive another type of antiviral drug, ribavirin, along with your DAAs. Ribavirin is also given by mouth. The study doctor will discuss with you how and when to take these medications.

Study Visits

At **baseline (your first visit) and then during Weeks 2 and 4 of each cycle that you receive the study drugs,** you will have the following tests/procedures. Each cycle is about 3 weeks, but may change depending on how often you receive your standard of care treatments**:**

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests (including tests to check your liver function) and for tests to check the status of your hepatitis infection. At some visits, blood will also be drawn for immune system testing.
- At baseline, you will have an MRI and CT scan of the liver to check the status of the disease.

End-of-Treatment Visit

As soon as possible after your last dose of study drugs:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests (including tests to check your liver function) and for tests to check the status of your hepatitis infection.
- You will have an MRI and CT scan to check the status of the disease.

Follow-Up

About 4, 12, and 24 weeks after your last dose of study drugs:

- You will have a physical exam (4- and 24-week follow-up visit only).
- Blood (about 4 tablespoons) will be drawn for routine tests (including tests to check your liver function) and for tests to check the status of your hepatitis infection.
- In addition to the above, at the 12-week follow-up visit only:
    - You will have a liver core biopsy for immune system testing.
    - Blood will be drawn for immune system testing.
    - You will have an MRI and CT scan to check the status of the disease.

Early Stopping Visit
If you stop taking the study drugs early, you will come back to the clinic 4 and 12 weeks after you stop taking the drugs. At each visit, blood (about 4 tablespoons) will be drawn for routine tests and for tests to check the status of your hepatitis infection.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:

- Tell the study doctor/study staff about all medications that you are taking or plan to take, including prescription and over-the-counter medications, supplements, vitamins, and herbal remedies.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you.

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 then decide if you need to have any visits or tests to check on your health. If you withdraw from this study, you will be removed from the study drugs and may need to come to the clinic for safety tests. If you withdraw from MD Anderson, 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.

Is there any way being in this study could be bad for me? (Detailed 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 drugs/procedures.

Atezolizumab, bevacizumab, and DAAs may each cause low blood cell counts (red blood cells, platelets, and 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.

Atezolizumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • 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)	• nausea • loss of appetite • diarrhea • low blood cell count (red, white) • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)	• weakness • muscle and/or bone pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing • immune reaction that may cause loss of drug function

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • fever • skin rash/itching • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• high blood sugar (possible diabetes) • vomiting • abdominal pain • constipation	• joint, back, and/or neck pain • lung inflammation (possible difficulty breathing) • infection

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

• heart/heart muscle inflammation • inflammation of the tissue around the	• inflammation of the thyroid gland (possible tenderness in the neck)	• anemia due to destruction of red blood cells • decreased bone marrow function and

heart (possible chest pain) • blood vessel inflammation (possible bleeding and/or bruising) • brain inflammation (possible paralysis and/or coma) • inflammation of the membrane around the spinal cord and brain (possible headache and/or coma) • nerve damage (loss of motor or sensory function, causing numbness and/or paralysis) • paralysis • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • low hormone blood levels (possible weakness, bone changes, and/or cramping)	• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • pituitary gland inflammation (possible headaches) • diabetes requiring insulin • severe high blood sugar due to uncontrolled diabetes • low platelet cell count • abnormal blood test (possible pancreas damage) • abnormal digestive blood test (possible inflammation of the pancreas) • inflammation of the pancreas (possible abdominal pain) • gallbladder inflammation (possible abdominal pain) • inflammation of the intestines	inability to make red blood cells • liver damage • muscle inflammation and weakness • breakdown of muscle tissue (possible kidney failure) • inflammation inside the eye (possible vision problems) • kidney injury • body-wide inflammation • 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) • immune system disease (possible dry mouth/eyes, fatigue, joint pain, and/or organ failure)

Atezolizumab may rarely cause low blood cell counts (platelets). 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.

Atezolizumab may rarely cause severe skin or mucosal reactions. Symptoms may include itching, skin blistering, peeling, or skin sores, and/or sores in the mouth or in the lining of the nose, throat, or genital area.

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

Exact frequency unknown:

• blood clots in a vein (possible pain, swelling, and/or redness) • intestinal blockage • kidney failure	• build-up of fluid around the lungs • blockage in the lung (possible pain and/or shortness of breath)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction

Based on the risks of similar drugs, atezolizumab may cause pigmented tissue (possible eye pain/swelling, hearing loss, and/or loss of skin color).

Atezolizumab may cause birth defects. It is not known how often this may occur.

In rare situations, when atezolizumab is combined with other drugs, an excessive immune response can occur. This side effect, called systemic immune activation, can result in inflammation, infection, and/or organ failure. Symptoms of systemic immune activation may include low blood pressure, high-grade fever, cough, difficulty breathing, severe dizziness, confusion, weakness, kidney failure, liver failure, very low blood cell counts, and/or bleeding within the organs.

If you experience any of these symptoms, you should notify your doctor right away as you may need drugs or other treatment and possible hospitalization.

Atezolizumab works by boosting the immune system. This may result in side effects that have not been seen yet, such as inflammation and inflammation-related side effects in any organ or tissue.

If you need a vaccination, you must receive it at least 4 weeks before receiving atezolizumab. If you know that you will need a vaccination during the study or within 5 months after the last dose of atezolizumab, please tell your doctor.

It is important to tell your doctor the last time you took any drug that stimulates the immune system. It is also important that you do not take any other drugs that may change your immune system (such as interferons or interleukin-2) for 10 weeks after your last dose of atezolizumab.

Bevacizumab Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • headache • dizziness • fatigue • difficulty sleeping • abnormal salts,	• high blood sugar (possible diabetes) • weight loss • loss of appetite • diarrhea • mouth blisters/sores	• pain • bleeding (including nosebleed) • low blood cell counts (white, platelets) • bleeding in the lungs

minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizures)	(possible difficulty swallowing) • nausea • failure of the ovaries to produce hormones, which may be permanent (possible stopped menstrual cycle)	and/or airways • difficulty breathing • cough • infection

Frequency Unknown but occurring in more than 10% of patients

• shedding and scaling of the skin (possible fatal loss of bodily fluids)	• dry skin • abnormal taste	• teary eyes

Occasional (occurring in 3-20% of patients)

• severe heart problems • swelling (arm/leg) • 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) • fainting • anxiety • difficulty forming or speaking words	• voice disorder • wound healing problems after surgery • abdominal pain • dehydration • constipation • vein blockage in the abdomen • hole in the intestines (possibly leaking contents into the abdomen) • hemorrhoids • pelvic pain	• abnormal kidney test (possible kidney damage) • weakness (including muscle weakness) • runny/stuffy nose • infusion reaction (possible chills and/or hives) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Bevacizumab may occasionally cause an abnormal opening that develops between one area of the body and another (for example, an abnormal connection and opening in one or more places between the trachea [breathing tube] and esophagus, which may interfere with swallowing, digestion, and/or choking. Another example is abnormal connections or passageways between different parts of the digestive system and/or the vagina or rectum). These passageways or openings may also happen in the kidney or lungs. This may result in death.

Frequency Unknown

• heart attack • chest pain due to heart trouble • stroke	• temporary stroke symptoms • bleeding around the brain • digestive system bleeding	• vomiting up blood • vaginal bleeding • coughing up blood • allergic reaction

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

• severe increase in blood pressure (possible stroke) • weakness in wall of artery (possible serious bleeding complications) • abnormal changes in the blood vessel that carries blood from the heart • tear in a major blood vessel leading into the heart • tearing of the walls around the heart • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • decreased brain function due to high blood pressure	• decay of body tissue • stomach and/or small intestine ulcer • decreased blood flow to part of the bowel (possibly causing death of tissue) • hole in the gall bladder (possible abdominal pain, gall stones, nausea, and/or infection) • low red blood cell count • bone destruction (including destruction of the jaw bone) • inflammation inside the eye • blurry vision • deafness • kidney failure	• abnormal blood clotting in small blood vessels of the kidney (possible kidney damage) • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • abnormal hole inside the nose • immune system response (possible loss of drug function)

Bevacizumab may rarely cause a low red blood cell count. A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.

Rarely (in about 1-2% of patients), bevacizumab may cause bleeding in the brain in patients who have received bevacizumab for the treatment of primary brain tumors. You will be monitored for this complication and removed from the study if this were to occur.

If you are taking Coumadin (warfarin) or other blood-thinning drugs, you may be at higher risk of blood clots and/or bleeding.

DAA Side Effects

DAAs **commonly (occurring in more than 10% of patients)** may cause the following:

• fatigue • headache • difficulty sleeping	• diarrhea • nausea • low red blood cell count	• liver damage/scarring (cirrhosis)

Ribavirin Side Effects

Common (occurring in more than 20% of patients)

• fatigue/lack of energy • headache • fever • difficulty sleeping • depression • irritability • mood swings • chills • nervousness • dizziness	• difficulty concentrating • hair loss (partial or total) • itching • skin rash • dry skin • nausea/vomiting • loss of appetite • weight loss • diarrhea • abdominal pain	• low blood cell count (white, red) • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • pain • shivering • difficulty breathing • cough

Occasional (occurring in 3-20% of patients)

• chest pain • flushing • agitation • memory loss • eczema (skin inflammation) • sweating • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• abnormal taste • constipation • upset stomach • dry mouth • changes to the menstrual cycle • low platelet cell count • anemia due to destruction of red blood cells • enlarged liver	• weakness • blurry vision • painful red eyes • sore throat • flu-like symptoms • runny nose • infection

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

• tissue swelling • suicidal thoughts • murderous thoughts • aggressive behavior • stroke	• dehydration • blindness • blood clots inside the eye (possible blindness)	• lung inflammation (possible difficulty breathing) • difficulty breathing due to narrowing of the airways

• suicide • drug abuse relapse/overdose • shedding and scaling of the skin (possible fatal loss of bodily fluids) • very severe blistering skin disease (with ulcers of the skin and digestive tract and/or loss of large portion of skin) • severe blisters • diabetes • inflammation of the pancreas (possible abdominal pain)	• detached retina (possible partial blindness) • damage to the retina/swelling of the eye nerve/swelling under the central part of the retina (possible vision loss) • inflammation of an eye nerve • hearing loss • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure)	• multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • worsening of existing sarcoidosis • immune response that causes the body to attack itself • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

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 Side Effects

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.

Liver biopsies may cause internal bleeding. Bleeding may cause signs and symptoms such as pain that is severe or that lasts more than a few hours after the biopsy, low blood pressure, and a fast heartbeat. You may need treatment at a hospital, blood transfusions, and sometimes surgery or another procedure to stop the bleeding. Pain is the most common complication after a liver biopsy. Pain often occurs in the upper right abdomen or right shoulder. In most cases, the pain is mild and goes away within a few hours after the biopsy. If pain is severe or lasts longer, it could be a sign of internal bleeding. Other uncommon complications that may occur after a liver biopsy include infection, which may lead to sepsis, a collapsed lung, called a pneumothorax, a buildup of blood in the space between the lung and the chest wall, called hemothorax, and injury to other organs.

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 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.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

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.

Birth Control Requirements: If you can become pregnant or father a child and you are sexually active, you must use birth control during the study and for 5 months after your last dose of atezolizumab, 6 months after your last dose of bevacizumab or DAAs, or 9 months after your last dose of ribavirin (whichever is latest).

Acceptable methods of birth control include:

- Intrauterine device (IUD)
- Vasectomy of you or your male partner

- Birth control rod implanted into your skin
- Use of 2 of the following:
    - Hormonal birth control (such as pills, patches, rings, and/or injections)
    - Diaphragm with spermicide
    - Cervical cap with spermicide
    - Birth control sponge with spermicide
    - Condom (either male or female) plus spermicide
        - A male and female condom cannot be used together

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.

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

Will it cost anything to be in this study? Will I be paid to be in this study?

You and/or your insurance provider will be responsible for the cost of all drugs given in this study, including DAAs, ribavirin, atezolizumab, and bevacizumab.

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.

You will not receive any compensation for taking part in this study.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

A participant study number will be assigned to you once you have been enrolled in the study. This participant study number will be used to identify your data in the study report and when reporting any data from the study.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. 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.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson, NIH-NCI, or shared with other researchers and/or institutions for use in future research.

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

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card)
- call the study doctor (Dr. Harrys Torres, at 713-792-6830) with any questions you may have

You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. Costs of treatment received because you were hurt or sick will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson 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.

What else do I need to know?

This research is being funded by NIH-NCI and the University of Texas MD Anderson Cancer Center.

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

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

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 not contact you to let you know what they have found. If the researchers return genetic test results to you, it may be because they think you could have a health risk and want to recommend that the test should be re-done by a certified clinical laboratory to check the results. If this happens, then you may want to get a second test from a certified clinical laboratory, consult your own doctor, or get professional genetic counseling. You may have to pay for those additional services yourself.

This research study involves genetic testing, including whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA).

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

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

A. During the course of this study, MD Anderson will be collecting and using 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
   - NIH-NCI, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study, and/or licensees of the study technology
   - 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.

No PHI will be stored on personal computers as per MD Anderson policy. The data will be analyzed using the study number and not your identifying information. Your identifying information and the key linking your information to your study number will be stored according to MD Anderson Policy. Data will be banked and not shared nor used in the future without prior IRB approval. Future use of the data will be consistent with MD Anderson standards.

Patient identifiers, including name and medical record number, will be removed from the data to be used for analysis, and you will be given a study number. The master list containing your name and medical record number will be kept in the study chair's departmental password-protected network drive in a password-protected file. This file will be accessible only to the study chair, approved collaborators, and authorized research staff.

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