INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

TITLE: A Phase II Study of Cladribine and Low Dose Cytarabine in Combination With Venetoclax, alternating with Azacitidine and Venetoclax, in Patients with Higher-risk Myelodysplastic/Myeloproliferative Neoplasms or Higher-risk Myelodysplastic Syndromes with Excess Blasts

PROTOCOL NO.: 2021-1116

SPONSOR: MDACC (MD Anderson Cancer Center)

INVESTIGATOR: Guillermo Montalban-Bravo, MD
1400 Holcombe Blvd. Unit 0428
Houston, Texas 77030
United States

STUDY-RELATED PHONE NUMBER(S): 713-794-3604
713-792-2121 (24 hours)

_____ _____
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).

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.

STUDY SUMMARY

The goal of this clinical research study is to learn if the combination of cladribine, cytarabine, venetoclax, and azacitidine can help to control myelodysplastic or myeloproliferative neoplasms (types of cancer, such as higher risk chronic myelomonocytic leukemia [CMML]) and/or higher-risk myelodysplastic syndrome (MDS) with excess blasts. The safety and tolerability of this drug combination will also be studied.

This is an investigational study. Cladribine is FDA approved and commercially available for the treatment of hairy cell leukemia. Cytarabine is FDA approved and commercially available for the treatment of acute non-lymphocytic leukemia, acute lymphocytic leukemia (ALL), and chronic myeloid leukemia (CML). Venetoclax is FDA approved and commercially available for Chronic Lymphocytic Leukemia (CLL) and acute myeloid leukemia (AML). Azacitidine is FDA approved and commercially available for the treatment of myelodysplastic syndrome (MDS) and chronic myelomonocytic leukemia (CMML). It is considered investigational to combine these drugs as well as to treat myelodysplastic or myeloproliferative neoplasms and MDS. The study doctor can describe how the drugs are designed to work.

The study drugs 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.

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

You may remain on this study for as long as the study doctor thinks it is in your best interest.

You and/or your insurance provider will be responsible for the costs of all drugs given as part of this study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard of care treatments for myelodysplastic or myeloproliferative neoplasms or MDS outside of this study. Your study doctor will talk to you about other treatments or therapies that are available and their benefits/risks. You may choose to receive other investigational therapy, if available. You may choose not to have treatment at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

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 7 teaspoons) will be drawn for routine testing and biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.
- Urine will be collected for routine testing.
- You will have an EKG and an echocardiogram (ECHO) and/or MUGA scan to check your heart function.
- You will have a bone marrow aspiration and/or biopsy, which will include testing for cytogenetics, mutations, and biomarkers. Cytogenetic testing looks at how mutations (genetic changes to cells) may affect how the disease may react to the study drug. To collect a bone marrow biopsy/aspirate, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and bone is withdrawn through a large needle.
- If you can become pregnant, your urine or blood will be used for a pregnancy test. To take part in this study, you must not be pregnant.

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

Up to 120 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle is 28 days.

Treatment in this study will be given in 2 parts: **Induction** and **Consolidation/Maintenance**.

- During Induction, you will receive up to 2 cycles of cladribine, cytarabine, and venetoclax.
- During Consolidation/Maintenance, you will receive azacitidine and venetoclax for 2 cycles and then cladribine, cytarabine, and venetoclax for 2 cycles. You will repeat this pattern of 2 cycles each for up to a total of 18 Consolidation/Maintenance cycles.

Induction Therapy (All Patients)

- On Days 1-3 of Cycle 1, you will receive cladribine by vein over about 1-2 hours every day.
- On Days 1-5 of Cycle 1, you will receive cytarabine as an injection under the skin 2 times each day. On Days 1-3, you will receive the cytarabine injection about 3-6 hours after the start of the cladribine infusion. Depending on when you start your cytarabine injections, you may receive an injection on Day 6 to complete your planned doses.
- You may learn how give yourself the injection of cytarabine at home.

- On Days 1-7 of Cycle 1, you will take venetoclax 1 time each day by mouth as instructed by your doctor. If you are taking certain drugs (such as antifungal medicines) that may affect how your body processes the study drug, your dose of venetoclax may be lowered. Depending on how your body reacts to venetoclax, your doctor may choose a different dose for you to take for the rest of the study. This will be discussed with you.

You may be hospitalized for the first 28 days of this study and then as needed for side effects. The study doctor will tell you more about this.

If you do not have a response to treatment after Cycle 1, you may repeat the Induction therapy during Cycle 2. If you do not have a response to treatment after Cycle 2, you may proceed with Consolidation/Maintenance in Cycle 3 and continue to receive treatment, if you are receiving benefit and your doctor thinks it is in your best interest.

Consolidation/Maintenance Therapy
If you have a response to induction therapy, you will receive Consolidation/Maintenance therapy:

- On Days 1-7 of Cycles 1 and beyond, you will take your dose of venetoclax by mouth 1 time each day.
- On Days 1-7 of Cycles 1-2, 5-6, 9-10, 13-14, and 17-18, you will receive azacitidine as an injection under the skin or by vein over about 30-60 minutes, 1 time each day.
- On Days 1-3 of Cycles 3-4, 7-8, 11-12, and 15-16, you will receive cladribine by vein over about 1-2 hours every day.
- On Days 1-5 of Cycles 3-4, 7-8, 11-12, and 15-16, you will receive cytarabine as an injection under the skin 2 times each day. On Days 1-3, you will receive the cytarabine injection about 3-6 hours after the start of the cladribine infusion. Depending on when you start your cytarabine injections, you may receive an injection on Day 6 to complete your planned doses.

If the disease is well controlled and your blood cell counts are low after completing 4 consolidation/maintenance therapy cycles, you may continue treatment with azacitidine and venetoclax only. This will be discussed with you.

The number of days and dosing of each of the above study drugs may be reduced if your doctor thinks it is in your best interest.

You may receive other standard of care drugs your doctor thinks are needed as part of your medical care and to prevent or lessen the severity of some possible side effects.

Please notify your doctor if there is a change in your medications or if a new medication is added as it may interfere with your study drug. While on study, do not consume grapefruit, grapefruit hybrids, pomelos, start fruit, or Seville oranges.

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

Study Visits

At the beginning of **each cycle**:

- You will have a physical exam.
- Blood (about 7 teaspoons) will be collected for routine testing.

At least **every week** during the first cycle of induction therapy, then **every 2-4 weeks after that**, blood (about 2 teaspoons) will be drawn for routine tests. If the study doctor thinks it is needed, this will be done more often.

During **Cycle 1 of induction therapy and reinduction if needed**, your blood sample will be used to check for a side effect called tumor lysis syndrome (TLS) several times.

On **Day 28 of Cycle 1 of induction therapy, Cycle 3 of overall study treatment, and then every 3-4 cycles after that:**

- Blood (about 2 teaspoons) will be drawn for biomarker testing.
- You will have a bone marrow aspirate and/or biopsy to check the status of the disease and to test for cytogenetics, mutations, and biomarkers. If the study doctor thinks it is needed, you may have a bone marrow aspirate and/or biopsy **between cycles** to check the status of the disease.

During the first cycle of induction therapy, all tests will be done at MD Anderson. After that, you may be able to have laboratory (blood) work done at a local clinic and the results reported to the research nurse for the study.

Follow-Up

After you stop receiving the study drugs:

- You will have a physical exam.
- Blood (about 7 teaspoons) will be drawn for routine testing.
- You will have a bone marrow aspirate and/or biopsy to check the status of the disease and to test for cytogenetics, mutations, and biomarkers

You may then be called every 6 months to ask about how you are doing. Each call should last about 5-10 minutes. The study staff may collect this information from your medical records.

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 drugs/procedures.

Cladribine, cytarabine, venetoclax, and azacitidine may each cause a low blood cell count (red, 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.

Cladribine Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue/lack of energy	• headache • skin rash • nausea	• low blood cell counts (red, white) • infection

Occasional (occurring in 3-20% of patients)

• swelling • fast heartbeat • dizziness • chills • difficulty sleeping • itching • skin redness • sweating	• loss of appetite • vomiting • diarrhea • constipation • abdominal pain • low platelet counts • weakness	• pain (such as muscle/joint) • cough • difficulty breathing • nosebleed • injection site swelling, pain, and/or heat

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

• blood clots in a vein (possible pain, swelling, and/or redness) • stroke • nervous system damage • damage to many nerves (loss of motor or sensory function) • progressive multifocal leukoencephalopathy (PML – a disease with	• very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • anemia due to destruction of red blood cells • abnormal liver tests (possible liver damage	• lung inflammation (possible difficulty breathing) • allergic reaction • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • breakdown products of the cancer cells entering the blood

brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • loss of alertness	and/or yellowing of the skin and/or eyes) • paralysis (both legs or below the neck) • kidney failure	stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Frequency Unknown

• abnormal blood acid/base balance (possible organ damage)	• inability to produce urine

Cytarabine Side Effects

Frequent:

• fever • skin rash • anal and/or rectal inflammation • anal sores • loss of appetite	• diarrhea • mouth sores and/or blisters • nausea • vomiting • low blood cell counts (red, white, platelet)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • blood clots in a vein (possible pain, swelling, and/or redness)

Less Frequent:

• chest pain • inflammation of the tissue around the heart (possible chest pain) • dizziness • headache • nerve damage (possible dizziness and/or headache) • inflammation of nerves (possible pain and/or loss of motor or sensory function) • hair loss (partial or total) • itching • skin freckling	• skin sores • hives • abdominal pain • death of tissue in the intestines • esophageal sore • throat inflammation • inflammation of the pancreas (possible abdominal pain) • sore throat • inability to urinate • jaundice (yellowing of skin and/or eyes) • painful red eyes • decreased kidney function	• difficulty breathing • injection site swelling • allergic reaction (swelling of face, mouth, and/or tongue) • 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)

Infrequent:

• chest pain due to heart trouble • stoppage of heart and	• mental status change • paralysis • enlarged bowel	• breakdown of muscle tissue (possible kidney failure)

lung function • inflammation of the membranes around the spinal cord and brain (possible headache and/or coma) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)	(possible abdominal pain) • high blood levels of uric acid (possible painful joints and/or kidney failure) • abnormal blood test (possible pancreas inflammation and/or damage) • liver damage due to blood clots	• lung inflammation (possible difficulty breathing) • injection site pain and/or swelling • cytarabine syndrome (bone/chest/muscle pain, painful red eyes, fever, skin rash, and/or fatigue/lack of energy)

Additional side effects seen only in high dose cytarabine:
It is not well known how often the following side effects may occur.

• enlarged heart • decreased brain function affecting movement • coma • nervous system damage (possible seizure and/or coma) • nerve damage (possible numbness, pain, and/or loss of motor function) • personality change • sleepiness • skin peeling	• stomach and/or small intestine ulcer • abdominal wall inflammation • inflammation of the pancreas (possible abdominal pain) • air-filled cysts in the intestines • decreased blood flow to part of the bowel (possibly causing death of tissue)	• pus-filled areas in the liver • liver damage • damage to the surface of the eye • bleeding in the eye • difficulty breathing • fluid in the lung (possible difficulty breathing)

When cytarabine is given directly into the spine, it may also cause the following side effects:

• decreased brain function (possible paralysis and/or coma) • fever • nausea/vomiting	• paralysis (possibly of the nerves in the neck and/or both legs) • difficulty swallowing • blindness	• double vision • cough • hoarseness • voice loss

<u>Venetoclax Side Effects</u>

Common (occurring in more than 20% of patients)

• swelling (arm/leg) • fatigue • high blood sugar (possible diabetes) • abnormal salts,	• diarrhea • nausea • low blood counts (red, platelets, and white) • abnormal liver tests	• muscle and/or bone pain • upper respiratory tract infection • cough

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)	(possible liver damage)	

Occasional (occurring in 3-20% of patients)

• fever • headache • dizziness • skin rash • vomiting • constipation • abdominal pain • mouth blisters/sores (possible difficulty swallowing) • joint pain	• high blood levels of uric acid (possible painful joints and/or kidney failure) • pneumonia • difficulty breathing • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)	• bacteria in the blood • tumor lysis syndrome (TLS)--breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

TLS is a problem that can occur when cancer cells break down rapidly and the body has to get rid of the broken up cell parts. Sometimes your body, especially the kidneys, cannot remove the cell parts quickly enough, so the level of some of these cell products in your blood, such as salts and acids, can rise. This can happen especially in participants with large tumors or a high number of cancerous white cells in the blood. TLS can lead to serious problems, such as effects on your kidneys and heart (including abnormal heart rhythms), seizures, or even death.

If you develop TLS, your urine may look dark, thick, or cloudy. You may have fever, chills, nausea/vomiting, diarrhea, confusion, shortness of breath, irregular heartbeat, fatigue, muscle pain, joint discomfort, and/or seizure. If you notice any of these, tell your doctor or nurse right away. Your study doctor will closely watch and treat you as needed to lower the risk of any serious changes in your blood or other complications of TLS. You may need to have extra blood tests or EKGs to check for signs of TLS.

You should wear ear plugs or other hearing protection when involved in a loud activity.

If you notice any rash, hives, itching, or other signs of an allergic reaction such as swelling, wheezing, or you are having a hard time breathing, tell your doctor right away.

At this time, there are no known serious side effects that **occur in fewer than 3% of patients**.

Richter's Transformation (RT) is a change of chronic lymphocytic leukemia (CLL) into a more aggressive lymphoma. Richter's Transformation has happened to a small number of people that received venetoclax. It is not clear at this time if venetoclax treatment caused it to happen, or if it is a complication from the cancer.

Azacitidine Side Effects

The following side effects have been reported when azacitidine is given either by vein or as an injection under the skin:

Common (occurring in more than 20% of patients)

• fever • fatigue/lack of energy • headache • nausea • vomiting	• diarrhea • constipation • loss of appetite • low blood cell counts (red, white, platelets) • weakness	• pain • shivering • cough • difficulty breathing • injection site redness and/or pain

Occasional (occurring in 5-20% of patients)

• chest pain • pale skin • swelling (arm/leg) • abnormal heart sound • fast heartbeat • low blood pressure (possible dizziness/ fainting) • high blood pressure • fainting • dizziness • anxiety • depression • difficulty sleeping • numbness • hives and/or skin redness • skin bump/sores/rash • dry skin and/or itching • sweating	• low blood levels of potassium (possible weakness /or muscle cramps) • weight loss • abdominal pain, tenderness, and/or swelling • bleeding gums • tongue sores • bleeding in the mouth • mouth blisters and/or sores (possible difficulty swallowing) • upset stomach • hemorrhoids • difficulty swallowing • difficult and/or painful urination • blood in the urine • sore throat	• muscle cramps • nosebleed • stuffy and/or runny nose • abnormal breath sounds • wheezing • build-up of fluid around the lungs • lymph node swelling • infection • hardened tissue/inflammation/skin discoloration at the injection site • injection site swelling, itching, and/or rash • increased risk of bleeding after a procedure/surgery • reaction to a blood transfusion

Rare but serious (occurring in fewer than 5% of patients)

• irregular heartbeat • heart failure • bleeding in and/or around the brain	• tarry stool • enlarged spleen • bone marrow failure • liver failure	• allergic reaction, which may be life-threatening (such as difficulty breathing,

• seizures • skin condition with fever and skin lesions • decay of body tissue • lesions due to skin infection • abnormal blood acid/base balance (possible organ damage) • dehydration • gallbladder inflammation (possible abdominal pain) • digestive system bleeding	• kidney failure • build-up of bodily waste products in the blood (possible kidney problems) • coughing up blood • lung inflammation (possible difficulty breathing) • tissue death at the injection site caused by drug leakage • bleeding in the eye • catheter site bleeding • infection at the injection site	low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart 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)

Azacitidine may cause you to develop another type of cancer (such as leukemia, a type of blood cancer).

Using the study drugs together may cause side effects that are unknown and have not been 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 **aspirations/biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the aspiration. An allergic reaction to the anesthetic may occur. A scar may form at the aspiration site.

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

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

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 or for 8 weeks after receiving study drugs. 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 while you are on study and for at least 8 weeks after your last dose of study drugs. Male participants must use condoms. Female participants must use birth control patches, pills, or injections, intrauterine device [IUD], double-barrier method [spermicidal jelly or foam with condoms or diaphragm], or surgical sterilization.

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.

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 routinely 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 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

If you suffer a study-related injury, you may contact Dr. Guillermo Montalban Bravo, at 713-794-3604 or 713-792-2121 (24-hours) with any questions you may have. 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.

Additional Information

4. You may ask the study chair (Dr. Guillermo Montalban Bravo, at 713-794-3604) 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 to which you are otherwise entitled. 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.

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

6. This study or your participation in it may be changed or stopped at any time by the study chair, 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, 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.

   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.

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

Future Research

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

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

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

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

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

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

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

that covers your individual data does not apply to summary results (when data from the whole study is combined).

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.

Outside Care
Part of your care may be provided outside of MD Anderson by your home doctor(s).

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
   - Any future sponsors 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

   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 do its best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by federal law.

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.)