THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase 1b/2 study of oral decitabine/cedazuridine (ASTX727) and venetoclax in combination with the targeted mutant IDH1 inhibitor ivosidenib or the targeted mutant IDH2 inhibitor enasidenib

2020-1220

Study Chair: Courtney DiNardo, 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

There are 2 phases to this clinical research study: Phase 1b and Phase 2.

The goal of Phase 1b is to find the recommended dose of oral decitabine/cedazuridine (also called ASTX727) that can be given in combination with venetoclax and either ivosidenib or enasidenib to patients with acute myeloid leukemia (AML).

The goal of Phase 2 is to learn if the combination of oral decitabine/cedazuridine, venetoclax, and ivosidenib or enasidenib can help to control the disease.

The safety and tolerability of the study drugs will also be studied in both phases.

This is an investigational study. Oral decitabine/cedazuridine is FDA approved and commercially available for the treatment of myelodysplastic syndrome and chronic myelomonocytic leukemia. Venetoclax, ivosidenib, and enasidenib are FDA approved and commercially available for the treatment of certain types of AML. It is considered investigational to give the study drugs together to patients with AML.

The study doctor can explain how the study 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. If you take part in this study, travel to the clinic for study visits may be a burden.

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

You will receive the study drug combination for as long as the doctor thinks it is in your best interest.

Oral decitabine/cedazuridine will be provided at no cost to you during this study. You and/or your insurance provider will be responsible for the cost of all other drugs you receive during this study, including venetoclax and ivosidenib or enasidenib.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive the standard treatment for the disease, such as intensive chemotherapy, azacitidine or decitabine alone or in combination with venetoclax, or an IDH inhibitor alone. You may choose to receive other investigational therapy, if available. 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 4 tablespoons) will be drawn for routine tests and biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.
- You will have a bone marrow biopsy and aspirate to check the status of the disease and for biomarker testing, which may include genetic biomarkers. 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 are in Arm A only (described below), you will have an EKG to check your heart function.
- If you can become pregnant, a part of the above blood sample or a urine sample 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 options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a study arm based on what mutation (genetic change) your disease has.

- If you are assigned to **Arm A**, you will receive oral decitabine/cedazuridine and venetoclax in combination with **ivosidenib.**
- If you are assigned to **Arm B**, you will receive oral decitabine/cedazuridine and venetoclax in combination with **enasidenib.**

After you are assigned to either Arm A or Arm B, you will be assigned to either Phase 1b or Phase 2 based on when you join the study. Up to 26 participants (17 in Arm A and 9 in Arm B) will be enrolled in Phase 1b of the study, and up to 90 participants (30 in arm A and 60 in Arm B) will be enrolled in Phase 2.
If you are enrolled in Phase 1b, you will be assigned to a dose level based on when you join this study. In Arm A of Phase 1b, up to 3 dose levels of oral decitabine/cedazuridine and venetoclax will be tested. In Arm B of Phase 1b, up to 2 dose levels of oral decitabine/cedazuridine will be tested.

In both Arm A and Arm B, the first group of participants in each group will receive the lowest dose level of study drugs (oral decitabine/cedazuridine for both arms, venetoclax for Arm A only). Each new group will receive a higher dose of oral study drugs than the group before it, if no intolerable side effects were seen. This will continue until the highest tolerable dose of study drugs is found.

If you are enrolled in Phase 2, you will receive oral decitabine/cedazuridine and venetoclax at the recommended dose that was found in Phase 1b.

All patients in both phases of Arm A will receive the same dose of ivosidenib. All patients in both phases of Arm B will receive the same dose of venetoclax and enasidenib. Arms B1 and B2 will enroll 30 new patients and 30 patients whose disease has come back or has not responded to treatment.

Up to 116 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each cycle is 28 days.

Starting the day before you receive your first dose (Day -1), you will be given standard drugs to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

You will take decitabine/cedazuridine by mouth on Days 1-5 of each cycle. Do not crush, chew, or break the tablets; each dose should be swallowed whole. You must

fast (not eat or drink anything but water, black coffee, or tea) for at least 2 hours before and for 2 hours after taking oral decitabine/cedazuridine. For 4 hours before and 4 hours after your dose, you should not take antacids or any other medicine that can change the amount of acid in your stomach. These medicines may cause the study drug not to be absorbed as well in your body.

You will take venetoclax by mouth with a glass (about 8 ounces) of water on Days 1-14 of each cycle. You should take venetoclax within 30 minutes after a meal, preferably a low or moderate-fat breakfast. During Cycle 1, you will start with a lower dose of venetoclax on Day 1. The dose will be gradually increased until you reach your target dose on Day 3 or 4, depending on which study group you are assigned to. You will continue to receive the target dose of venetoclax for the rest of the study.

If you are in Arm A, you will take ivosidenib by mouth with or without food on Days 8-28 of Cycle 1 and then Days 1-28 of each cycle after that. If you take ivosidenib with food, you should avoid eating a high-fat meal with your dose.

If you are in Arm B, you will take enasidenib by mouth with or without food on Days 8-28 of Cycle 1 and then Days 1-28 of each cycle after that.

If you miss a dose of one of the study drugs, you should take the dose as soon as possible if it is within 6 hours (or 12 hours, for oral decitabine/cedazuridine) after the missed dose. If it has been more than 6 hours (or 12 hours, for oral decitabine/cedazuridine), or if you vomit any of the study drugs, do not make up the dose. Wait and take the next dose as scheduled.

You will be given a drug diary during this study. You should write down when you take each dose of study drug, along with any missed or vomited doses, in this drug diary. You should bring the drug diary with you to each clinic visit.

After you have received the study drug for 12 cycles, or if you are unable to come to the clinic for your study visits (during the COVID-19 pandemic, for example), the study drugs may be shipped to you directly.

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

Study Visits

Please note that if you are unable to come to the clinic for the below study visits (during the COVID-19 pandemic, for example), your visit may be performed remotely by video call and certain procedures may be performed at a laboratory closer to your home. The study doctor will discuss this with you, if needed.

On **Day 1 of Cycle 1:**

- You will have a physical exam.
- Blood (about 3 tablespoons) will be drawn for routine tests. Blood will be drawn before your dose and 6-8 hours after your dose.

On **Day 2-4 of Cycle 1,** blood (about 3 teaspoons) will be drawn for routine tests.

On **Day 5 of Cycle 1,** blood (about ½ teaspoon each time) will be drawn before and 9 times over about 8 hours after your dose for pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points.

If you are in Arm A of Phase 1b only, **on Days 7 of Cycle 1 and 2**, blood (about ½ teaspoon each time) will be drawn before and 3 times over the 8 hours after the dose for PK testing.

On **Days 8 and 22 of Cycles 1 and 2:**

- Blood (about 2 teaspoons) will be drawn for routine tests.
- If you are in Arm A of Phase 1b only, on Days 8 and 15, blood (about ½ teaspoon) will be drawn before the dose for PK testing

One (1) time between Days 21-28 of Cycle 1:

- You will have a bone marrow biopsy and aspirate
- Blood (about 2 teaspoons) will be drawn for biomarker testing.

On **Day 1 of Cycle 2:**

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- If you are in Arm A only, you will have an EKG to check your heart function.

During **Cycles 3 and beyond:**

- On Day 1 of each cycle, you will have a physical exam.
- On Day 1 of each cycle, blood (about 2 teaspoons) will be drawn for routine tests. At the end of Cycles 3 and 5, an additional sample (about 3 teaspoons) will be drawn for biomarker testing.
- If the doctor thinks it is needed, you will have a bone marrow biopsy and aspirate every 3 cycles for biomarker testing.

If the disease gets worse, you will have a bone marrow biopsy and aspirate and blood (about 3 teaspoons) will be drawn for biomarker testing.

After you have received the study drugs for 12 cycles, you will return to the clinic every 3 months. At these visits, you will have a physical exam and blood (about 2 teaspoons) will be drawn for routine tests. The study doctor may continue to have monthly virtual visits with you through video calls in between the 3-month visits. If called, each call should take about 10 minutes.

End-of-Study Visit

After your last dose of the study drug, you will have an End-of-Study Visit. The following tests and procedures will be performed:

- You will have a physical exam.

- Blood (about 3 tablespoons) will be drawn for routine tests and biomarker testing.
- You will have a bone marrow biopsy and aspirate to check the status of the disease and for biomarker testing.

Follow-Up Visits

After you have received the study drugs for 12 cycles, you will return to the clinic every 3 months for follow-up visits.

If you stop taking the study drugs, the study team will call you or speak to you during a clinic visit to check on how you are doing every month for up to 3 years after the last participant has enrolled in the study. If called, each phone call should take about 5minutes.

Other Information

Talk to the study team about any drugs you take during this study, including over-the-counter and prescription medications and herbal remedies.

While taking venetoclax, avoid having any grapefruit, Seville (sour) oranges, star fruit, pomegranate, and products containing juices of these fruits.

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.

Oral decitabine/cedazuridine, venetoclax, ivosidenib, and enasidenib may cause low blood cell counts (red blood cells, white blood cells, and/or platelets):

- 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.

Oral Decitabine/Cedazuridine (ASTX727) Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • low blood level of albumin (possible swelling, weakness, and/or fatigue)	• nausea • low blood cell counts (red, white, platelets)	• abnormal liver tests (possible liver damage)

Occasional (occurring in 3-20% of patients)

• irregular heartbeat • swelling • low blood pressure (possible dizziness and/or fainting) • falls • fever • difficulty sleeping • nerve damage (loss of motor or sensory function) • dizziness • skin rash • low blood sugar • high blood sugar (possible diabetes)	• low blood levels of calcium (possible weakness and/or cramping) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • constipation • diarrhea • weight loss • abdominal pain • loss of appetite • vomiting	• mouth blisters/sores (possible difficulty swallowing) • joint/muscle pain • abnormal kidney test (possible kidney damage) • decreased kidney function • difficulty breathing • cough • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

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

• skin condition with fever and skin lesions • lung inflammation (possible difficulty breathing)	• differentiation syndrome (fever, difficulty breathing, swelling, altered mental status and/or kidney 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)

Additionally, oral decitabine/cedazuridine (ASTX727) side effects are expected to be similar to decitabine.

Decitabine Side Effects

Common (occurring in more than 20% of patients)

• swelling (including arm/leg) • pale skin • fever • fatigue • headache • difficulty sleeping • dizziness • high blood sugar (possible diabetes)	• 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	• constipation • diarrhea • vomiting • loss of appetite • low blood cell counts (red, white, platelets) • shivering • cough • difficulty breathing • infection

Occasional (occurring in 5-20% of patients)

• swelling (face) • abnormal heart sound • low blood pressure (possible dizziness/fainting) • high blood pressure • fast heartbeat • chest pain • heart failure • pain • chills • confusion • anxiety/depression • numbness • skin rash/redness • itching • night sweats • hair loss (partial or total) • dry skin • hives • lymph node swelling • toothache	• mouth blisters/sores (possible difficulty swallowing) • weight loss • abdominal pain • abdominal swelling • heartburn • tongue/mouth pain • lip blisters/sores • difficulty swallowing • upset stomach • fluid in the abdomen • dehydration • hemorrhoids • difficult, painful, and/or frequent urination • bacteria in the blood • high blood platelet count (possible increased clotting) • abnormal liver tests (possible liver damage or yellowing of the skin and/or eyes)	• weakness/tenderness • muscle spasms • joint pain • walking/balance problems (possible falling) • blurry vision • abnormal kidney test (possible kidney damage) • high blood levels of uric acid (possible painful joints and/or kidney failure) • sore throat • low oxygen level in the blood (possible lightheadedness) • fluid in or around the lungs (possible difficulty breathing) • runny or stuffy nose • nosebleed • injection site swelling

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

• irregular heartbeat • enlarged heart • heart attack • heart and lung failure • bleeding around the brain • mental status change • skin condition with fever and skin lesions • blood in the urine	• kidney failure • lung inflammation • blood clots in the lung (possible failure to breathe) • stopped breathing • coughing up blood • enlarged spleen • gallbladder inflammation (possible abdominal pain)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Venetoclax Side Effects

Common (occurring in more than 20% of patients)

• fatigue • diarrhea	• nausea • low blood counts (red, platelets, white)	• upper respiratory tract infection

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • fever • headache • 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)	• vomiting • constipation • back pain • high blood levels of uric acid (possible painful joints and/or kidney failure)	• pneumonia • cough • 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.

Based on studies in animals, venetoclax may cause the following side effects:

• swelling and itching of the head, ears, arms and/or legs	• hair color change • gallbladder damage	• decrease in sperm

Based on studies in animals, venetoclax may cause of loss of weight or the premature loss (miscarriage) of a developing baby. This has not been seen in humans at this time.

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.**

<u>Ivosidenib Side Effects</u>

Common (occurring in more than 20% of patients)

• swelling • irregular heartbeat • fever • fatigue • skin rash • 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 levels of uric acid (possible painful joints and/or kidney failure) • diarrhea • nausea • mouth blisters/sores (possible difficulty swallowing) • increase in infection-fighting cells	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • joint pain • abnormal kidney test (possible kidney damage) • difficulty breathing • cough

Occasional (occurring in 3-20% of patients)

• chest pain	• differentiation syndrome (fever,	• tumor lysis syndrome (TLS)--breakdown

• low blood pressure (possible dizziness/fainting) • headache • nerve damage (loss of motor or sensory function) • constipation • loss of appetite • vomiting • abdominal pain	cough, difficulty breathing, swelling in arms/legs, decreased urine output, weight gain, dizziness, altered mental status and/or multi-organ dysfunction) • muscle pain • build-up of fluid around the lungs	products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, irregular heartbeat, and/or other organ damage)

Please note, differentiation syndrome has only been reported in patients with blood cancers and may happen within 5 days or up to 3 months after your first dose of ivosidenib. You will be watched for signs of this condition and you may receive standard medications to help prevent or treat it. Differentiation syndrome can be fatal if left untreated. The study staff will discuss this with you.

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

• sudden stopping of the heart • low blood cell count (red, white, platelets)	• damage to the nervous system (causing numbness and/or paralysis)

If you have advanced blood cancer, you may be at risk for developing posterior reversible encephalopathy syndrome (PRES) or Guillain-Barre syndrome. PRES is a brain condition that may cause headache, confusion, seizures, and/or vision loss. Guillain-Barre syndrome is damage to the nervous system (causing numbness, weakness, and/or paralysis) caused by the body's immune system. You will be watched for signs of these conditions and you may receive standard medications to help prevent or treat them. The study staff will discuss this with you.

Progressive multifocal leukoencephalopathy (PML) was seen in 1 patient who received ivosidenib. PML is brain damage that is likely to result in paralysis and/or coma, which may be permanent. PML can also lead to death.

Other drugs in combination with Ivosidenib may increase your risk of an abnormal EKG. Tell the study doctor about all drugs you are currently taking or are planning to take.

In pregnant women, Ivosidenib may cause miscarriages and birth defects (such as changes in the development of the bones and spleens).

Enasidenib Side Effects

Common (occurring in more than 20% of patients)

• low blood pressure (possible dizziness and/or fainting) • swelling (arms/legs) • headache • fatigue • dizziness • fever with or without low white blood cells • increase in infection fighting cells (without infection)	• 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/vomiting • diarrhea • loss of appetite • abdominal pain	• constipation • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • low blood cell count (red, platelets) • lung infection (pneumonia) • shortness of breath • cough

Occasional (occurring in 3-20% of patients)

• abnormal taste • weakness/numbness (arms/legs) • difficulty breathing • fluid in the lung (possible difficulty breathing)	• differentiation syndrome (possible fever, cough, difficulty breathing, swelling, build-up of fluid in the lung or around the heart, blood clotting problems, weight gain, liver and/or kidney dysfunction)	• tumor lysis syndrome--breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

There are currently no known side effects occurring in **fewer than 3% of patients**.

Based on studies in animals, enasidenib may cause infertility.

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

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

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

biopsy site.

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: You must use highly effective birth control methods while on this study and for at least 90 days after the last dose of study drugs. Highly effective methods include:

- Hormonal birth control (pills or injections)
- Intrauterine device ("IUD")
- Double barrier methods (such as a condom in combination with spermicide)

If you can father a child, you must use a condom while on this study and for at least 90 days after your last dose of study drugs.

Males: You must not donate sperm during the study and for at least 90 days after the last dose of study drugs. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. If your partner/spouse becomes pregnant while you are on this study, the sponsor would like to collect information about the pregnancy. The study sponsor's contact information will be made available so that, if you and your partner wish to, you can share information about the outcome of the pregnancy with the sponsor. If you and/or your partner choose not to share this information, it will not result in any penalty or loss of benefits to which you are otherwise entitled.

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. The sponsor will ask for information about the pregnancy.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree and are enrolled in Arm B of Phase 1b, blood (about ½ teaspoon each time) will be drawn at the following time points for PK testing.

- Days 7 of Cycle 1 and 2, before and 3 times over the 8 hours after the dose.
- Days 8 and 15 of Cycle 1 and 2, before the dose.

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. 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

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.

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 additional blood draws for PK testing if you are in Arm B of Phase 1b?

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 ASTEX Pharmaceuticals 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. Courtney DiNardo, at 713-794-1141) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, ASTEX Pharmaceuticals, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

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

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

9. This study is sponsored and/or supported by: ASTEX Pharmaceuticals.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

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 ASTEX Pharmaceuticals 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 stored by ASTEX Pharmaceuticals will not be used in future research.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples or data 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.

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.

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.

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). The study doctor can discuss with you the tests and procedures that can be completed by your home doctor in more detail.

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
   - ASTEX Pharmaceuticals, 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.

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 Protocol **2020-1220**.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
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 below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) DATE

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION