THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A phase 1b study of ensartinib in combination with platinum-based chemotherapy and bevacizumab in ALK-positive non-small cell lung cancer (NSCLC)
2020-0838

Subtitle: Combination of ensartinib, chemo, and bevacizumab

Study Chair: Yasir Elamin

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if ensartinib and bevacizumab given in combination with carboplatin and pemetrexed can be used to control the disease in patients with ALK-positive non-small cell lung cancer (NSCLC). The safety, effectiveness, and possible side effects of this combination will also be studied.

This is an investigational study. Ensartinib is not FDA approved or commercially available. It is currently being used for research purposes only. Bevacizumab, carboplatin, and pemetrexed are FDA approved and commercially available for NSCLC and for the treatment of other cancers as well. It is considered investigational to give these drugs in combination to patients with NSCLC.

Please note: If you take part in this study, you may be given either bevacizumab or a biosimilar of that drug (which means it is identical to the study drug). Everything stated in this document about bevacizumab also applies to its biosimilar, including information about FDA approval status, side effects, and cost.

The study doctor can explain how the study drugs are designed to work.

The study drug combination 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 may not want to take part in the study because other standard treatments are available or because you cannot visit MD Anderson for extra visits.

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

You may receive 4 cycles of ensartinib, carboplatin, pemetrexed, and bevacizumab. You may continue receiving ensartinib and bevacizumab for as long as the study doctor thinks it is in your best interest.

Ensartinib will be provided at no cost to you during this study. You and/or your insurance provider will be responsible for the cost of carboplatin, pemetrexed, and bevacizumab.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other FDA-approved drugs such as chemotherapy or FDA approved ALK inhibitors. 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. Talk to your study doctor about your choices, including their potential risks and benefits, before you decide if you will take part in this study.

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.
- You will have an EKG to check your heart function.
- Blood (about 6 teaspoons) will be drawn for routine testing.
- Urine will be collected for routine tests. If the study doctor thinks it is needed, you will collect all of your urine over a 24-hour period. The study staff will provide you with instructions for collecting the sample at home, and bags or bottles if needed.
- You will have a CT or PET-CT scan and an MRI of the brain to check the status of the disease. If it is not safe to do an MRI, you will have a CT scan of the brain instead.
- You will have an eye exam.

- If you can become pregnant, part of the urine or blood sample above will be used for a pregnancy test. To take part in this study, you must not be pregnant. If the urine test is positive, blood will be drawn to confirm the result.

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.

Up to 25 participants will be enrolled in this study. Up to 20 will take part at MD Anderson.

Study Drug Administration
Each cycle is 21 days.

If you are found to be eligible to take part in this study, during Cycles 1-4 (Induction Therapy), you will receive ensartinib, carboplatin, pemetrexed, and bevacizumab.

On Day 1 of each cycle, you will be given the following drugs by vein:
- Carboplatin will be given over about 15-60 minutes
- Pemetrexed will be given over about 10 minutes
- Bevacizumab will be given over about 90 minutes. If the first dose is well-tolerated, the second dose may be given over 60 minutes. If the second infusion is well-tolerated, the third dose may be given over 30 minutes.

You will take ensartinib tablets by mouth 1 time every day at about the same time. Ensartinib can be taken with or without food, but the tablets are better-tolerated with food.

If you miss a dose of ensartinib and less than 12 hours have passed, you should take the missed dose as soon as possible. If more than 12 hours have passed, you should take your next dose at the regularly scheduled time.

If you vomit after taking ensartinib, you should not to retake the dose. Take your next dose at the regularly scheduled time. If you continue vomiting, you should contact the study doctor.

After Cycle 4, you may be able to continue taking ensartinib and bevacizumab followed by phase of Ensartinib. You may continue with bevacizumab and/or pemetrexed for as long as the study doctor thinks it is in your best interest. This is called Maintenance Therapy

You will also be given the following drugs to help decrease the risk of side effects:
- Seven (7) days before your first dose, you will take a folic acid supplement. You will continue taking this supplement until 21 days after the last dose of pemetrexed.

- Seven (7)-14 days before the first dose, you will be given a vitamin B12 injection into the muscle. This will be repeated every 9 weeks until 21 days after the last dose of study drugs. You will not continue these injections during Maintenance Therapy.
- The day before your first dose, the day you receive the first dose, and the day after, you will take dexamethasone tablets by mouth 2 times a day.

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

Study Visits

On **Day 1 of Cycles 1-4:**

- You will have a physical exam.
- Blood (about 4-6 teaspoons) will be drawn for routine tests.
- Urine will be collected for routine tests (except for Cycle 1). If the study doctor thinks it is needed, you will collect all of your urine over a 24-hour period.

In addition to the above, you will have some tests only on Day 1 of certain cycles:

- On Cycle 2 only, you will have an EKG.
- On Cycles 2 and 4 only, you will have a CT or PET-CT scan to check the status of the disease**.**
- On Cycle 3 only, you will have an MRI of the brain. If it is not safe to do an MRI, you will have a CT scan of the brain instead.

If you continue on Maintenance Therapy, you will have the following study visits:

On **Day 1 of Cycles 5 and beyond:**

- You will have a physical exam.
- Blood (about 4-6 teaspoons) will be drawn for routine testing.
- Urine will be collected for routine tests. If the study doctor thinks it is needed, you will collect all of your urine over a 24-hour period.
- On Cycle 5 and then every 3 cycles after that (Cycle 8, 11, 14, and so on), you will have an EKG.
- On Cycles 6, 8, and then every 4 cycles after Cycle 9 (Cycles 13, 17, 21, and so on), you will have a CT or PET-CT scan.
- On Cycle 6 and then every 4 cycles after Cycle 9 (Cycles 13, 17, 21, and so on), you will have an MRI of the brain. If it is not safe to do an MRI, you will have a CT scan of the brain instead.

Follow-Up

Thirty (30) days after you last dose of study drugs:

- You will have a physical exam.
- Blood (about 4-6 teaspoons) will be drawn for routine testing.
- You need to have an MRI of the brain. If it is not safe to do an MRI, you will have a CT scan of the brain instead.

After this, the study staff will review your medical records every 6 months for up to 2 years to check on you. You may be called for this. Each call would take about 5-10 minutes.

Other Information

- While on this study, you should not receive other anticancer treatments, other investigational drugs outside of this study, or certain types of medication, including over-the-counter drugs or herbal supplements. These may interact with the study drugs and increase the risk of side effects or reduce the effectiveness of the study drugs. The study doctor will discuss this with you.
- You should not take St. John's Wort and avoid drinking grapefruit or grapefruit juice during this study.

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.

Carboplatin, bevacizumab, pemetrexed, and ensartinib may cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Ensartinib Side Effects

Common (occurring in more than 20% of patients)

• skin rash • itching	• nausea	• abnormal liver tests (possible liver damage)

Occasional (occurring in 3-20% of patients)

• slow heartbeat • fatigue • fever • headache • swelling • dry skin • hair loss (partial or total) • low blood levels of albumin (possible swelling, weakness, and/or fatigue)	• abnormal blood test (possible pancreas damage) • vomiting • constipation • loss of appetite • diarrhea • abnormal taste • mouth blisters/sores • blood in the stool • low red blood cell counts • abnormal blood test	• abnormal liver tests (possible yellowing of the skin and/or eyes) • muscle damage and/or muscle breakdown • weakness • blurry vision • abnormal kidney test (possible kidney damage) • high blood levels of uric acid (possible painful joints and/or kidney failure)

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

• abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage) • extra heartbeats • irregular heartbeat • abnormal sensation (such as pins and needles) • dizziness • change of skin color • flushing	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) • high blood sugar (possible diabetes) • dehydration • low blood cell counts (white/platelets) • weight changes • abdominal pain • dry mouth	• upset stomach • increase in certain pituitary hormones related to sexual development (possible changes in fertility) • increase in estradiol levels in females (a hormone related to ovarian function) • liver damage/failure • arm/leg pain • muscle spasms • lung inflammation (possible difficulty breathing) • difficulty breathing • cough • allergic reaction (possible swelling and/or joint pain)

There is also a risk of allergic reaction related to the yellow dye used in the 100 mg capsule of ensartinib. Although the chance of this reaction is generally low, the frequency is higher in patients who also have allergic reactions to aspirin.

Bevacizumab Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • dizziness • fatigue • headache • difficulty sleeping • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• high blood sugar (possible diabetes) • diarrhea • nausea • mouth blisters/sores (possible difficulty swallowing) • weight loss • loss of appetite	• failure of the ovaries to produce hormones (possible stopped menstrual cycle) • low blood cell count (white blood cells, platelets) • bleeding in the lungs and/or airways • difficulty breathing • nosebleed • cough

Occasional (occurring in 3-20% of patients)

• severe heart problems • swelling (arm/leg) • blood clots in a vein or artery (possible pain, swelling, organ damage, stroke, redness, and/or heart attack)	• voice disorder • anxiety • difficulty forming or speaking words • dehydration • abdominal pain • pelvic pain • constipation • hemorrhoids	• abnormal hole between the rectum and another organ • abnormal kidney test (possible kidney damage) • weakness • pain • wound healing complications after surgery • stuffy/runny nose

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

• fainting • brain injury (possible headache, confusion,	• hole in the intestines (possibly leaking contents into the abdomen)	• death of muscle tissue and/or breakdown of the jaw bone

seizures, and/or vision loss) • decreased blood flow to part of the bowel (possibly causing tissue death) • abnormal connections or passageways between organs or vessels (such as the digestive system, trachea and esophagus, bladder, vagina, kidney, and/or bile duct)	• decreased blood supply to the abdomen • ulcers • low red blood cell count • blockage in the lung (possible pain and/or shortness of breath)	• blurry vision • deafness • infusion reaction, possibly severe (possibly a severe increase in blood pressure causing a stroke) • immune response (possible loss of drug function)

Frequency Unknown

• heart attack • chest pain due to heart trouble • stroke and/or temporary stroke symptoms • bleeding in the brain	• shedding and scaling of the skin (possible fatal loss of bodily fluids) • dry skin • abnormal taste	• vomiting/coughing of blood • disease of the lacrimal apparatus • allergic reaction

<u>Pemetrexed Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue	• nausea	• loss of appetite

<u>Occasional (occurring in 3-20% of patients)</u>

• fast/irregular heartbeat • heart failure • swelling • fever • blood vessel damage (possible blockage of blood flow) • bleeding in the brain • reduced blood supply to the arms and legs • nerve damage (possibly affecting movement and/or causing loss of sensory function) • skin rash and/or peeling • itching • hair loss (partial or total) • darkening of the skin	• allergic skin reaction • vomiting • mouth blisters/sores (possible difficulty swallowing) • diarrhea • constipation • abdominal pain • hole in the intestines (possibly leaking contents into the abdomen) • low blood cell counts (red, white, platelets) • abnormal liver tests (possible liver damage)	• painful red, dry, and/or teary eyes (possible eyelid swelling) • abnormal kidney test (possible kidney damage) • decreased kidney function (possible kidney failure) • sore throat • blockage in the lung (possible pain and/or shortness of breath) • lung damage (possible difficulty breathing) • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • infection

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

• fainting • severe sunburn-like rash at site of previous radiation (called radiation recall) • blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• very severe blistering skin disease (loss of large portion of skin) • intestinal blockage • anemia due to destruction of red blood cells • inflammation of the pancreas (possible abdominal pain) • kidney failure	• lung inflammation (possible difficulty breathing) • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Carboplatin Side Effects

Common (occurring in more than 20% of patients)

• 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 • low blood counts (red/white/platelets) • pain	• abnormal liver tests (possible liver damage) • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• nerve damage (possible numbness, pain, and/or loss of motor function) • hair loss (partial or total)	• abdominal pain • nausea • constipation • diarrhea • weakness	• abnormal liver tests (possible yellowing of the skin and/or eyes) • allergic reaction • infection

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

• high blood pressure • low blood pressure (possible dizziness/fainting) • heart failure • stroke • dehydration • blood vessel blockage	• destruction of red blood cells (possible anemia, kidney damage, and/or failure) • reduced blood supply to the arms and legs • blindness • hearing loss	• difficulty breathing due to narrowing of the airways • tissue death at the injection site caused by drug leakage • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

It is not known how often the following side effects may occur:

• decreased bone marrow function

Folic Acid Side Effects

It is not well known how often the side effects of folic acid may occur:

• fatigue/lack of energy • skin redness	• skin rash • itching • flushing	• difficulty breathing due to narrowing of the airways • allergic reaction

Vitamin B12 Side Effects

It is not well known how often the side effects of vitamin B12 may occur:

• heart failure • decreased blood circulation • blood clots in a vein (possible pain, swelling, and/or redness) • anxiety • headache • numbness • dizziness • nervousness • itching • hives • skin rash	• diarrhea • upset stomach • swollen tongue • nausea • sore throat • vomiting • high platelets, red, and/or white blood cell count (possible headache, blood clot, dizziness, and/or stoke) • difficulty walking • joint inflammation and swelling	• pain (such as back, muscle) • abnormal sensation (such as pins and needles) • weakness • difficulty breathing • fluid in the lung (possible difficulty breathing) • runny nose • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Vitamin B12 may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Dexamethasone Side Effects

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

• high blood pressure • irregular, fast, and/or slow heartbeat • enlarged heart • heart failure • tearing of the walls of the heart (post-heart attack) • blood vessel inflammation (possible bleeding and/or bruising) • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in the arteries • swelling (such as tissue and/or abdominal swelling) • dizziness • shock • fainting • headache • increased pressure in the skull or between the skull and brain (possible headache, vision changes, and/or mental status changes) • seizure • depression • fatigue and anxiety • mood swings • personality changes • mental disorders • euphoria (unusual feelings of happiness or well-being) • difficulty sleeping • fatigue/lack of energy • darkening and/or lightening of the skin • tiny dots on the skin • impaired wound healing	• hives • acne-like rash • hair loss (partial or total) • hair growth • sweating • tissue death • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • decreased ability to process carbohydrates • high blood sugar (possible diabetes) • diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • abnormal blood acid/base balance (possible organ damage) • low blood levels of potassium (possible weakness and/or muscle cramps) • high blood levels of sodium (possible weakness and/or swelling) • sugar in the urine • body-wide loss of proteins (possible weakness and/or swelling) • build-up of fat in abnormal areas • weight gain • increased appetite • digestive system bleeding	• changes to the menstrual cycle • problems with production of sperm • bruising • muscle weakness • inflammation of nerves (possible pain and/or loss of motor or sensory function) • joint disease (possible pain) • pain or loss of function of the hips or shoulders due to bone death • broken bones • loss of muscle • muscle damage causing weakness • nerve damage (loss of motor or sensory function) • loss of bone strength (possible broken bones) • abnormal sensation (such as pins and needles) • tendon tear • collapse of bones in the spine • enlarged liver • abnormal liver tests (possible liver damage) • bulging eye • increased pressure in the eye (possible vision loss, pain, and/or blurry vision) • cataracts (clouding of the lens of the eye) • hiccups • fluid in the lung (possible difficulty breathing)

• skin rash, redness, and/or dryness • fragile and/or thinning skin • skin test reaction impaired (due to a lowered immune system) • stretch marks	• small red or purple spots in the mouth • esophageal sore • hole in the intestines (possibly leaking contents into the abdomen) • nausea • itching near the anus • inflammation of the pancreas (possible abdominal pain) • stomach ulcer	• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • infection • allergic reaction (such as skin reaction) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

Dexamethasone may cause you to develop another type of cancer.

Dexamethasone may cause a false-positive or false-negative skin test (such as a test for tuberculosis [TB]). If you need to have a skin test performed, tell the doctor that you are taking dexamethasone.

Stopping dexamethasone suddenly may cause withdrawal symptoms (such as fever, muscle/joint pain, and fatigue). This is because dexamethasone affects your adrenal glands and may cause your body's hormone levels to change. The study doctor will help you stop dexamethasone safely, if you want to stop taking the study drug. Do not just stop taking dexamethasone.

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

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

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

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

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

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel “closed in” while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**.

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 and for at least 90 days after your last dose of study drugs if you are sexually active.

If you can become pregnant or father a child and are sexually active, you and your partner must use 2 forms of acceptable birth control, including one barrier method (for example, a latex condom, diaphragm or cervical/vault cap when used with spermicidal foam/gel/film/cream/suppository). Acceptable birth control methods include:

- Using a condom along with a diaphragm and spermicidal agent [foam/gel/cream/film/suppository].
- An intrauterine device/system (IUD/IUS), except IUD progesterone T, combined with a barrier method with spermicide.
- Surgical sterilization of yourself (tubal ligation) and/or of your only male partner (vasectomy)
- Oral, injected, or implanted hormonal birth control PLUS a barrier method with spermicide

Please discuss your chosen birth control method(s) with your doctor to make sure they are considered acceptable. Even if you use birth control during the study, there is still a chance you or your heterosexual partner can become pregnant.

Males: You must use a condom with spermicide as one of your chosen birth control methods. You should avoid exposing your partner to your semen in any way (not just intercourse), especially pregnant women, due to the possible study drug exposure. You should tell your female sexual partner about the risks related to pregnancy while you are on this study. Do not donate sperm during this study and for 90 days after your last dose of study drugs. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, during screening, you will have a tumor needle biopsy (core biopsy) for biomarker testing. To perform a core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.

Optional Procedure #2: If the disease gets worse and you agree, you will have a tumor needle biopsy (core biopsy) for biomarker testing.

Optional Procedure #3: If you agree, at screening and on Day 1 of Cycle 2, you will have blood (4-6 teaspoons) drawn for biomarker testing.

Optional Procedure #4: If the disease gets worse and you agree, you will have blood (4-6 teaspoons) drawn for biomarker testing.

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. If you take part in Optional Procedure 1 or 2, you and/or your insurance provider will be responsible for the costs. There will be no cost to you for taking part in the optional procedures 3 or 4.

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.

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

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 an additional tumor biopsy for biomarker testing during screening?

YES **NO**

Optional Procedure #2: Do you agree to have an additional tumor biopsy for biomarker testing if the disease gets worse?

YES **NO**

Optional Procedure #3: Do you agree to have blood drawn for biomarker testing screening and on Day 1 of Cycle 2?

YES **NO**

Optional Procedure #4: Do you agree to have blood drawn for biomarker testing if the disease gets worse?

YES **NO**

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Xcovery Holding Company 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. Yasir Y. Elamin, at 713-792-6363) 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. The study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Xcovery Holding Company, 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: Xcovery Holding Company.

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 Xcovery Holding Company 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. Xcovery Holding Company will not store leftover samples.

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.

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.

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

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

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

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Xcovery Holding Company, 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
- Other sites participating in the study (such as Moffit Cancer Center)

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2020-0838**.

_____ _____
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 DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION