THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase II Study to Assess the Safety and Efficacy of Tocilizumab in combination with Ipilimumab and Nivolumab in Patients with Advanced Melanoma, Non-small Cell Lung Cancer, or Urothelial Carcinoma 2020-1166

Study Chair: Rodabe Amaria, M.D.

_____ _____
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

You are being asked to take part in this study because you have cancer that is metastatic (has spread) but you would like to participate in a study offering therapy that is different from the current standard of care.

The goal of this clinical research study is to study the effectiveness of a triplet combination therapy (nivolumab, tocilizumab, and ipilimumab) in treating advanced melanoma, non-small-cell lung cancer, or urothelial carcinoma. The safety of this treatment combination will also be studied.

This is an investigational study. Nivolumab, tocilizumab, and ipilimumab are all FDA approved and commercially available. Giving the drugs together is considered investigational. At this time, the treatment combination is being used in research only. The study doctor can explain how the study drugs are designed to work.

Receiving the study drug(s) may help to control the disease. Future patients may benefit from what is learned in this study. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side

effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

You may receive the study drugs for up to 2 years.

Tocilizumab will be provided to you at no cost during the study. You and/or your insurance provider will be responsible for the cost of ipilimumab and nivolumab. If the study drug combination is commercially available when the study ends, you and/or your insurance provider will be responsible for the cost of any further treatment.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard therapy for the disease (which may include surgery, chemotherapy, vaccine therapy, radiation therapy, and/or a combination of chemotherapy and immune system therapy). Your treating doctor will discuss all applicable alternatives with you, as well as their possible risks and benefits. 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 Visit

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 electrocardiogram (EKG) to check your heart function.
- Leftover samples from an earlier tissue collection will be used for genetic and other biomarker testing. Your blood and tissue samples contain genes (which are made up of DNA or deoxyribonucleic acid), RNA (ribonucleic acid), and other biomarkers such as proteins. DNA chains are the building blocks for the cells in your body. RNA (ribonucleic acid) is involved in the building process. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.
- Blood (about 4½ tablespoons) will be drawn for routine tests and genetic and immune markers testing.
- Urine will be collected for routine tests.
- You will have imaging scans performed to check the status of the disease. These may include CT scans of the chest, abdomen, pelvis, and/or specific disease areas (if applicable). If you have tumors in your brain, you will have a magnetic resonance imaging (MRI) or CT scan of the brain to check the status of the disease.
- You will have a biopsy of tumor site(s) to check the status of the disease. This may be either a punch biopsy or an image-guided biopsy. To collect a biopsy,

the area of skin is numbed with anesthetic and a small cut is made to remove all or part of the affected tissue. To collect a punch biopsy, the area of skin is numbed with anesthetic and a small cut is made to remove all or part of the affected tissue. To perform an image-guided biopsy, a needle is inserted into the affected area using imaging such as CT or ultrasound to collect cells or tissue from an organ, lymph node, or suspected tumor mass. Image-guided biopsies may include more than 1 “pass” with a needle in the tumor area. The doctor will use the imaging to guide the needle into the area.

- If you can become pregnant, blood (about ½ teaspoon) or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

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

Up to 55 total participants will be enrolled in this study. All will be enrolled at MD Anderson.

Study Groups and Study Drug Administration

If you are found to be eligible to take part in this study, you will be assigned to a treatment cohort based on your disease type:

- **Cohort 1:** Melanoma (Sub-group 1 or 2)
- **Cohort 2:** Genitourinary cancer
- **Cohort 3:** Lung cancer

Participants in Cohorts 1 (Sub-group 1), 2, and 3 will receive **tocilizumab** every 2 weeks for 12 weeks, for a total of 6 doses. Participants in Cohort 1 (Sub-group 2) will receive **tocilizumab** every week for 6 weeks and then every 2 weeks for an additional 6 weeks, for a total of 9 doses. Tocilizumab is given as a subcutaneous injection (under your skin).

- If you are in Cohorts 1 (Sub-group 1) or 2, your doses on Weeks 0 and 6 will be given to you in the clinic by the study staff. You will be shown how to give yourself the injection, and will then give yourself your doses at home at Weeks 2, 4, 8, and 11. The study staff will contact you by phone to check in with you and answerany questions you have during these “non-clinic-visit” weeks.
- If you are in Cohort 1 (Sub-group 2), your doses on Weeks 0, 3, and 9 will be given to you in the clinic by the study staff. You will be shown how to give yourself the injection, and will then give yourself your doses at home at Weeks 1, 2, 4, 5, 7, and 11. The study staff will contact you by phone to check in with you and answerany questions you have during these “non-clinic-visit” weeks.
- If you are in Cohort 3, all doses of tocilizumab will be given in the clinic by the study staff.

Nivolumab is given by vein over about 30 minutes.

- Cohorts 1 and 2 will receive nivolumab every 3 weeks for the first 12 weeks (4

doses), then every 4 weeks for a total of 2 years.
- Cohort 3 will receive nivolumab every 2 weeks for 2 years.

Ipilimumab is given by vein over about 90 minutes.
- Cohorts 1 and 2 will receive ipilimumab every 3 weeks for 12 weeks for a total of 4 doses.
- Cohort 3 will receive ipilimumab every 6 weeks for up to 2 years.

You will be taken off study if the disease gets worse, intolerable side effects occur, if the study doctor thinks it is in your best interest, or you are not able to follow study staff directions.

Study Visits – Cohorts 1 and 2

On **Day 1:**
- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests.
- Blood (about 2½ tablespoons) will be used for genetic and immune marker testing.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test. To continue on study, you must not be pregnant.

At **Weeks 3, 6, and 9:**
- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests.
- Blood (about 2½ tablespoons) will be drawn for genetic and immune marker testing.
- At **Week 6 only**, you will have a tumor biopsy (similar to the biopsy performed at screening) to check the status of the disease. The study doctor will explain which type of biopsy will be performed.

If you have brain tumor(s), you will have a brain MRI scan performed at **Week 6**.

At **Week 12** (+/- 1 week), you will have imaging scans performed to check the status of the disease, including CT and/or MRI scans of the chest, abdomen, pelvis, and/or specific disease areas like the brain (if applicable).

At **Week 12** and **every 4 weeks** after that:
- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests.

At **Weeks 12 and 24**, blood (about 2½ tablespoons) will be used for genetic and immune marker testing.

You may have other tests performed, or certain tests repeated more often, if your doctor thinks they are needed for your safety. Your doctor will discuss this with you, if needed.

Study Visits – Cohort 3

On **Day 1:**

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests.
- Blood (about 2½ tablespoons) will be used for genetic and immune marker testing.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test. To continue on study, you must not be pregnant.

Every 2 weeks after that (Weeks 3, 5, 7, and so on)**:**

- You will have a physical exam until Week 13, and then every 6 weeks after that.
- Blood (about 2 tablespoons) will be drawn for routine tests.
- Blood (about 2½ tablespoons) will be drawn for genetic and immune marker testing. **(Weeks 2, 6, 8, 12, and 24 only)**
- At **Week 6 only**, you will have a tumor biopsy (similar to the biopsy performed at screening) to check the status of the disease. The study doctor will explain which type of biopsy will be performed.

End-of-Treatment Visit

If you stop receiving the study drug(s) for any reason, you will have an end-of-treatment visit. The following tests and procedures will be performed:

- You will have a physical exam.
- Blood (about 4½ tablespoons) will be drawn for routine tests and genetic and immune markers testing.
- Urine will be collected for routine tests.
- You will have an EKG to check your heart function.
- If you can become pregnant, blood (about ½ teaspoon) or urine will be collected for a pregnancy test.

Safety Follow-Up

If you stop treatment for any reason, the study staff will call you every 90 days after the last dose of study drugs until 2 years have passed after the time you entered the study, you withdraw from the study, or the study ends, whichever happens first.

If you complete 2 years of treatment, the study staff will call you every 90 days after the last dose of study drugs until 1 year has passed after your last dose, you withdraw from the study, or the study ends, whichever happens first.

During the safety follow-up calls, the study staff will ask you how you are doing. Each call will last no more than about 15 minutes.

Other Information

You may not take certain drugs while on study, including prescription drugs, over-the-counter medication, herbal supplements, and/or natural remedies. Please talk to

the study staff about any medications/supplements you are taking now or want to start taking. They will let you know which medications/supplements you cannot take while on study. You will also be given a list of the types of drugs that should be avoided while you are on study.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. 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.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs and procedures.

Nivolumab, tocilizumab, ipilimumab each may rarely 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 (thrombocytopenia) 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 (neutropenia) 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.

Nivolumab Side Effects

Common (occurring in more than 10%)

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

Occasional (occurring in 3-10%)

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

MD Anderson IRB Approved 07/31/2025

decreased thyroid stimulating hormone lab test result, weight loss, heart rate changes, and/or sweating)	• headache	

Rare (occurring in fewer than 3% of patients)

• fast heartbeat • abnormal EKG • heart inflammation/ inflammation of the tissue around the heart (possible chest pain) • high blood pressure • low blood pressure (possible dizziness and/or fainting) • swelling of the brain (possible headache and/or mental status changes) • inflammation of the brain and spinal cord (possible altered consciousness) • inflammation of the membrane around the spinal cord and brain (possible headache and/or coma) • swelling (face/arms/legs) • chills • difficulty sleeping • dizziness • dry/red skin • hives • skin blisters • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the	• low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • abnormal blood test (possible pancreas damage) • high blood sugar (possible diabetes) • abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • mouth blisters/sores (possible difficulty swallowing) • constipation • dehydration • dry mouth • inflammation of the intestines • hole in the intestines or stomach (possibly leaking contents into the abdomen) • liver inflammation • liver failure/damage • low blood cell count (platelets, white) • destruction of red blood cells due to the body attacking itself (called autoimmune hemolytic anemia)	• difficulty breathing which can lead to respiratory failure • cough • infusion reaction (possible fever, rash, pain, and/or swelling) • immune response causing the body to attack itself (possibly causing muscle weakness) • neuromuscular disease (possible weakness of eye, face, breathing and swallowing muscles) (myasthenic syndrome, myasthenia gravis) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • allergic reaction, possibly life-threatening (such as difficulty breathing, low

MD Anderson IRB Approved 07/31/2025

skin and digestive tract) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • hair loss (partial or total) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the thyroid gland (possible tenderness in the neck) • pituitary gland failure (possible hormone imbalance) • blood vessel inflammation	• abnormal kidney test (possible kidney damage) • kidney failure • breakdown of muscle tissue (possible kidney failure) • damage to the nervous system (causing numbness and/or paralysis) (Guillain-Barre syndrome) • nerve damage (possible numbness, pain, and/or loss of motor function and/or “pins and needles” sensation) • nerve damage (affecting the head and neck) • muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision	blood pressure, and/or organ failure) • abnormally excessive sweating involving the arms, legs, hands and feet, underarms, and face, usually unrelated to body temperature or exercise • flu like symptoms (which may include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, feeling tired) • patches of skin color loss • lung infiltrates (possible infection or inflammation) • inflammation of multiple areas of the body (see below) • Hemophagocytic lymphohistiocytosis (HLH) syndrome (see below)

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

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

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

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

fainting, or you are feeling cold all the time.

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

Frequency Unknown

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

<u>Tocilizumab Side Effects</u>

Common (occurring in more than 20% of patients)

• abnormal liver tests (possible liver damage)

Occasional (occurring in 3-20% of patients)

• high blood pressure • headache • dizziness • high blood levels of fat (possible heart disease and/or stroke)	• low white blood cell count • lung inflammation • infusion reaction (possible chills and/or hives)	• injection site swelling, pain, and/or heat • infection

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

• tissue swelling (such as arms/legs) • skin rash	• underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • stomach ulcer • low platelet count	• abnormal liver tests (possible yellowing of skin and/or eyes) • difficulty breathing • immune reaction

Exact frequency unknown

• low blood pressure (possible dizziness/fainting) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • nausea • inflammation of the stomach and/or intestines • hole in the intestines (possible leaking contents into the abdomen)	• inflammation of the pancreas (possible abdominal pain) • liver damage/failure • jaundice (yellowing of the skin and/or eyes) • damage to many nerves (loss of motor or sensory function) • multiple sclerosis (disorder of the central nervous system, causing motor difficulties)	• reactivated or new tuberculosis • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction which may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Tocilizumab may cause you to develop another type of cancer.

Ipilimumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • itching and/or skin rash • weight loss • nausea / vomiting	• diarrhea • loss of appetite • abnormal digestive blood test (possible inflammation of the pancreas)	• constipation • low red blood cell counts • abnormal liver tests (possible liver damage)

Occasional (occurring in 3-20% of patients)

• fever • difficulty sleeping • pituitary gland failure (possible endocrine gland abnormality) • abdominal pain • inflammation of the intestines and colon	• abnormal blood test(possible pancreas damage) • abnormal liver tests (possible liver damage and/or yellowing of the skinand/or eyes)	• liver damage • abnormal kidney test(possible kidney damage) • cough • difficulty breathing

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

• blood vessel disease • blood vessel inflammation (possible bleeding and/or bruising) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • heart inflammation • inflammation of the tissue around the heart (possible chest pain) • brain inflammation (possible paralysis and/or coma) • chills • immune system damage to the nervous system (causing numbness and/or paralysis) • immune response (causing muscle weakness) • nerve damage (loss of motor or sensory function) • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • patches of skin color loss • red, dry, scaly patches of thickened skin (psoriasis) • skin rash (possible	• allergic skin reaction • inflammation of the thyroid gland (possible tenderness in the neck) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • hole in the intestines (possibly leaking contents into the abdomen) • inflammation of the pancreas (possible abdominal pain) • stomach and/or small intestine ulcer • blood in urine • anemia due to destruction of red blood cells • liver failure • muscle inflammation and weakness • joint pain • inflammation inside the eye (possible vision problems) • hearing loss • kidney	• lung inflammation (possible difficulty breathing) • multi-organ disease causing lesions, most often in the lungs • immune reaction (possible organ damage) • immune response that causes an overactive thyroid gland (possible fast heartbeat, sweating, weight loss, nervousness, and/or eye bulging) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • nerve damage (possible numbness, pain, and/or loss of motor function) • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body) • infusion related reaction (possible skin rash, fever, shortness of breath, and/or swelling) • Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye

fever/lymph node swelling/inflammation of internal organs/abnormal blood cell counts)	inflammation/failure • bronchiolitis obliterans (damage of the small airways with difficulty breathing)	pain/swelling, hearing loss, and/or loss of skin color)

Ipilimumab may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere (such as the brain/spinal cord, lungs, and/or blood). It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Frequency unknown

- blistering skin rash
- skin sores
- tissue death
- very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract)

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. In addition, the combination of these drugs may cause the following side effects:

• blood clots in a vein (possible pain, swelling, and/or redness) • bleeding in or around the brain	• liver bleeding • worsening of existing diabetes • blockage in the lung (possible pain and/or shortness of breath)	• reaction related to low white blood cell counts (possible dehydration, chills, kidney failure, and/or fainting)

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 **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.

By taking part in this study, you are **delaying surgery** in order to receive the study drugs. This delay in surgery may result in the disease growing to a point where it is not able to be removed fully by surgery. If that is the case, your doctor will discuss treatment options available to you.

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

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

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

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant, you must use a highly effective method of birth control while on study and for 5 months after your last dose of study drug. Highly effective methods include:

- Progestogen-only hormonal birth control that stops ovulation
- Hormonal methods including birth control pills, vaginal ring, injections, implants, patches, and intrauterine hormone-releasing system (IUS)
- Surgical sterilization of yourself or your partner
- Intrauterine device (IUD)

If you can father a child, you must use a condom (female partner must also use an

acceptable form of birth control) while on study and for 7 months after your last dose of study drug. You must let your sexual partners know that you are on in this research study and that birth control is required. You must not donate sperm.

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

Females: You should not breastfeed while taking the study drug or for up to 24 weeks after the last dose of study drug. 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 may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, at the End of Treatment visit, you may have another tumor biopsy to check the status of the disease. This will only be done if the doctor thinks it can be done safely and you are not already having a non-optional biopsy at this time point.

You do not have to agree to the optional procedure in order to take part in this study. There are no benefits to you for taking part in the optional procedure. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure**.**

Optional Procedure Risks:

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

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: If you are asked, do you agree to have a biopsy at the end of the study/treatment to check the status of the disease?

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 for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about

MD Anderson IRB Approved 07/31/2025

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. Rodabe Amaria, at 713-792-2921) any questions you have about this study. You may also contact the Chair of MD Anderson's InstitutionalReview Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor who can help you safely stop study treatment. It may be dangerous to suddenly stop study treatment. The study doctor will also decide if you need to have any visits or tests to check on your health. If you withdraw from this study, you can still choose to be treated at MDAnderson.

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

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Possible reasons your participation in this study may be stopped include if the disease gets worse, if intolerable side effects occur, or if you are

MD Anderson IRB Approved 07/31/2025

unable to follow study directions.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, 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.

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.

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 researchsamples 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).

MD Anderson IRB Approved 07/31/2025

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).

Conflict of Interest

Outside relationships are disclosed to and approved by the Conflict of Interest Committee, which reviews these relationships for compliance with institutional policy. This review helps the IRB to assure that financial relationships do not have an impact on the conduct of this study. The following members of the study staff have disclosed compensation from the funding source(s) of this study:

- Mehmet Altan (Co-PI)

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
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

To protect your identity, the samples collected from you will be labeled a unique number instead of your name or other identifying information. Only the study doctor or study staff will have access to the code that can link you to your samples.

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

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

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

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

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

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

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

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

MD Anderson IRB Approved 07/31/2025