THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A pilot study to assess changes in tumor biology following second-line treatment with pembrolizumab plus lenvatinib in patients with advanced pancreatic ductal adenocarcinoma
2021-0274

Subtitle: MK3475-C13-03

Study Chair: Brandon G. Smaglo

_____ _____
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 the combination of pembrolizumab and lenvatinib can help to control pancreatic ductal adenocarcinoma. The safety of this combination will also be studied.

This is an investigational study. Pembrolizumab and lenvatinib are FDA approved and commercially available for the treatment of other types of cancer. Lenvatinib has also been FDA approved both by itself and in combination with other drugs to treat several types of cancer. However, their use in treating pancreatic ductal adenocarcinoma is considered investigational. At this time, this combination is being used in research only. 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.

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

You will receive up to 17 cycles of study treatment, and your participation may last up to about 2 years.

Pembrolizumab and lenvatinib will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other chemotherapy that may be appropriate. The study doctor will discuss the possible risks and benefits of these treatments. You may choose to receive other investigational therapy, if available. The study doctor will discuss the possible risks and benefits of these treatments. 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.
- You will have 3 EKGs in a row (triplicate EKGs) and either a MUGA scan or echocardiogram (ECHO) to check your heart function.
- Urine will be collected for routine tests.
- Blood (about 3 tablespoons) will be drawn for routine tests, biomarker testing, genetic testing, and testing for viruses (such as hepatitis B and C and HIV [the AIDS virus]). Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.
- You will have a tumor biopsy for biomarker testing. The study doctor can explain what kind of biopsy will be performed to collect this sample. If you have banked (archival) tumor tissue available, and the sponsor agrees, that sample may be used instead of a fresh tumor biopsy. The study doctor can discuss this with you further.
- You will have a CT scan to check the status of the disease.
- If you can become pregnant, part of the above blood sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.

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

Up to 15 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration
Each study cycle is 42 days (6 weeks).

If you are found to be eligible to take part in this study, you will take 2 **lenvatinib** capsules at the same time by mouth every day while on study. You can take each dose with or without food. If needed, due to side effects or your inability to swallow pills, you may receive a lower dose (1 capsule) or a liquid formulation. The study doctor will discuss this with you further if needed.

Caregivers should not open the capsule, in order to avoid repeated exposure to the contents of the capsule. If you miss a dose and do not take it within 12 hours of your scheduled dosing time, you should skip that dose and take the next dose at the usual scheduled time. If you vomit after taking your dose, do not retake that dose. Just take the next dose at the scheduled time. Please return any empty packaging and unused product at your next study visit. Do not throw away any medicines in the trash or down the drain.

You will receive **pembrolizumab** by vein over about 30 minutes on Day 1 of each cycle.

If you develop any side effects your study doctor may need to pause and/or change the dose of your study drug, or to stop the study drug completely. This will be discussed with you, if needed.

You will be taken off study and stop receiving the study drugs if the disease gets worse, intolerable side effects occur, your doctor thinks it is in your best interest to stop participating, you need a treatment that is not allowed on this study, or you are unable to follow study directions.

Study Visits

On **Day 1 of Cycle 1:**
- You will have a physical exam.
- You will have triplicate EKGs about 2 hours after your dose to check your heart function.
- You will have imaging scans (CT or PET/CT scans).
- Blood (about 2 ½ tablespoons) will be drawn for routine tests and tumor marker tests. Tumor markers may be related to the status of the disease.
- If you can become pregnant, part of the above blood sample will be used for a pregnancy test.

On **Day 8 of Cycle 1:**
- The study team will call you to check on how you are doing, including any side effects you are having. The phone call should take about 15 minutes. You may be asked to have additional blood pressure monitoring done at home or a local pharmacy, if the doctor thinks it is needed.

On **Days 15 and 22 of Cycle 1:**
- You will have a physical exam.
- Blood (about 2 tablespoons) and urine will be collected for routine tests. On Day 22, blood (about ½ tablespoon) will also be drawn to test the amount of protein in your blood.

On **Day 36 of Cycle 1:**
- You will have a physical exam.
- You will have an EKG.
- Blood (about 2 tablespoons) and urine will be collected for routine tests.

On **Day 1 of Cycle 2:**
- You will have a physical exam.
- You will have triplicate EKGs about 2 hours after your dose.
- Blood (about 3 ½ tablespoons) will be drawn for routine tests, biomarker testing, genetic testing, and tests to measure the amount of protein in your blood.
- Urine will be collected for routine tests.
- You will have a tumor biopsy for biomarker testing.
- You will have imaging scans (CT or PET/CT scans).
- If you can become pregnant, part of the above blood sample will be used for a pregnancy test.

On **Day 22 of Cycle 2:**
- You will have a physical exam.
- Blood (about 2 ½ tablespoons) will be drawn for routine tests and to test the amount of protein in your blood.
- Urine will be collected for routine tests.

On **Day 1 of Cycle 3 and beyond (every 6 weeks):**
- You will have a physical exam.
- You will have triplicate EKGs on Day 1 of Cycle 6 and every 4 cycles after that (Cycles 10, 14, 18, and so on).
- Blood (about 2 ½ tablespoons) will be drawn for routine tests and tests to measure the amount of protein in your blood. If the disease appears to respond to the treatment, blood (about ½ tablespoons) will be drawn for biomarker testing.
- Urine will be collected for routine tests.
- You will have imaging scans (CT or PET/CT scans) on Day 1 of every cycle until Cycle 9, and then every 2 cycles after that (Cycles 11, 13, 15, and so on).
- If you can become pregnant, part of this sample will be used for a pregnancy test.

On **Day 22 of Cycle 3 and every song after that:**
- You will have a physical exam.
- Blood (about 2 ½ tablespoons) will be drawn for routine tests and tests to measure the amount of protein in your blood.
- Urine will be collected for routine tests.

End-of-Treatment Visit

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

- You will have a physical exam.
- You will have triplicate EKGs.
- Blood (about 3 tablespoons) will be drawn for routine, biomarker, and genetic testing.
- You will have a CT scan to check the status of the disease.

Follow-Up

About 30 days after your last dose of study drug, you may have a clinic visit or a phone call with the study staff. This call may last 20-30 minutes. You will be asked how you are doing and if you have started any new anti-cancer medications. If you have a clinic visit, you will also have the following procedures:

- You will have triplicate EKGs.
- Blood (about 2 tablespoons) and urine will be collected for routine tests.

Long-Term Follow-Up

If you stopped taking the study drugs because the disease got worse or you started a new anti-cancer therapy, you will be called by the study staff about every 12 weeks until you withdraw from the study or the study ends. These calls usually last about 20-30 minutes. During these calls, you will be asked about your health status.

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. Throughout the study, the study doctor will monitor your symptoms with appropriate tests and procedures. 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, as you may need urgent treatment if they are serious or potentially life-threatening. If you develop any side effects, the study doctor may need to temporarily stop and/or change the dose of study drug, or stop the study drug completely.

Pembrolizumab and lenvatinib may each cause low blood cell counts (red, white, 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 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.
- 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.

Pembrolizumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • fever • skin rash and/or itching • 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) • high blood levels of fat (possible heart disease and/or stroke) • loss of appetite • nausea • constipation • diarrhea • abdominal pain	• low blood cell counts (red, white, platelets) • abnormal liver test (possible liver damage) • pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

Occasional (occurring in 3-20% of patients)

• swelling (face/arm/leg) • inflammation of the tissue around the heart (possible chest pain) • irregular heartbeat • headache • confusion • patches of skin color • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• overactive thyroid gland (possible weight loss, diarrhea, mood swings, difficulty sleeping, heart rate changes, and/or sweating) • low blood sugar • weight loss • fluid in the abdomen • blood in the urine • vomiting • abnormal liver test (possible yellowing of the skin and/or eyes)	• weakness • nerve damage (possible numbness, pain, and/or loss of motor function) • difficulty breathing (possibly due to lung inflammation) • flu-like symptoms • infusion reaction (possible dizziness, low blood pressure, nausea, pain, and/or difficulty breathing)

Frequency Unknown

• heart failure • heart attack • build-up of fluid around the heart (possible heart failure)	• abnormal connections or passageways between organs or vessels • bleeding in the rectum and/or uterus	• blockage in the lung (possible pain and/or shortness of breath) • nosebleed • coughing up blood

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

• low blood pressure (possible dizziness/fainting) • heart inflammation • build-up of fluid in the tissue around the heart • blood vessel inflammation (possible bleeding, skin rash, numbness/weakness, fever, weight loss, fatigue, and/or bruising, depending on where the inflammation occurs) • seizure • immune system damage to the nervous system (causing muscle weakness, numbness and/or paralysis) • spinal cord inflammation (possible pain, weakness, loss of feeling or movement, and/or paralysis) • brain inflammation (possible paralysis and/or coma) • shedding, scaling and/or inflammation of the skin (possible fatal loss of bodily fluids) • large skin blisters • very severe blistering skin disease (loss of large portion of skin	• low hormone blood levels (possible weakness, bone changes, and/or cramping) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • pituitary gland inflammation (possible headaches) • inflammation of the thyroid gland (possible tenderness in the neck) • diabetes requiring insulin • severe high blood sugar due to uncontrolled diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • low pancreatic enzyme level (possible bloating, gas, abdominal discomfort, diarrhea, oily stool, and/or weight loss) • inflammation of the pancreas (possible abdominal pain) • inflammation of the stomach (possible belly pain, fullness, nausea,	• inflammation inside the eye (possible vision problems) • kidney inflammation (possible kidney damage/failure) • kidney failure • inflammation or swelling of the nerve fibers of the eye which send visual information from your eye to your brain (possible sudden onset of vision loss, loss of color vision, pain when moving your eyes, and/or loss of peripheral vision) • build-up of fluid around the lungs • immune response that causes the body to attack itself (possible organ damage) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • immune response (causing muscle weakness) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • severe life-threatening infection (possible low

and/or with ulcers of the skin and digestive tract)	vomiting, and/or loss of appetite) • inflammation of the intestines (possibly with a hole in the intestines, which may lead to contents leaking into the abdomen) • anemia due to destruction of red blood cells • liver damage (hepatitis) • inflammation/scarring of the bile ducts (tubes that carry digestive fluid that is made in the fluid), which may cause liver damage, stomach pain, yellowing of the skin/eyes, fatigue, and/or itching	blood pressure, kidney failure, and/or heart failure) • Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling and changes in vision, hearing loss, and/or white patches on the skin) • Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, or have a fast heartbeat. You may also experience difficulty with physical exercise, pale or yellow skin, dark urine, or fever.

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

Pembrolizumab 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. These side effects can affect more than one of your normal organs and tissues at the same time.

If you have a stem cell transplant from a donor after you receive pembrolizumab, you may have an increased risk of complications, such as severe graft-versus-host disease (when transplanted donor tissue attacks the recipient's organs such as skin, liver, and/or intestines) and/or clotting of blood within the liver. Deaths have been reported in patients who received a stem cell transplant from a donor after pembrolizumab therapy. If you decide to receive a stem cell transplant from a donor, please tell your transplant doctor that you received pembrolizumab in the past.

Lenvatinib Side Effects

Common (occurring in more than 10% and up to 80% of patients)

• high or low blood	• underactive thyroid	• joint pains

pressure • swelling of the legs • fatigue (feeling very tired or weak) • headache • hoarse voice • hand-foot syndrome (redness, soreness, and swelling of the skin on the hands and feet) • rash • low level of platelets in the blood which may lead to bruising • feeling dizzy • odd taste sensation • trouble sleeping • hair loss	gland and change in blood test result for thyroid stimulating hormone (high) – may result in fatigue, weakness, dry skin, hair loss, intolerance to cold • loss of appetite or weight loss • dry, sore, or inflamed mouth or throat • changes in blood test results for potassium levels (low) and calcium levels (low) – may increase the chance of having an abnormal heart rhythm • nausea (feeling sick) and vomiting (being sick), constipation, diarrhea, abdominal pain, indigestion	• low level of platelets in the blood which may lead to bruising • high levels of protein in the urine • bleeding (most commonly nose bleeds but may include bleeding from other sites such as blood in the urine, bruising, bleeding from the gums, coughing up blood) • musculoskeletal, muscle, limb, or back pain • cough • urinary infections (increased frequency in urination and pain in passing urine)

Occasional (occurring in 1-10% of patients)

• heart problems, heart palpitations or heart attack- may cause chest pain or pressure, pain in the arms, back, neck, or jaw, shortness of breath, rapid or irregular heart rate, coughing, bluish color to lips or fingers, feeling very tired • fistula formation or bowel perforation- abnormal connections between different organs in the body or between an organ and another part of the body such as the skin or windpipe, or formation	• blood clot in the legs or lungs (pulmonary embolism) – which may cause swelling of the calf associated with warmth or tenderness, sudden onset of shortness of breath, rapid breathing, tightening of chest or chest pain, cough or coughing up blood, rapid heart rate and a blue tinge to the lips • changes in blood test results for magnesium (low) – may increase the chance of having an abnormal heart rhythm • changes in blood test	• changes in white blood cells (low) which may increase risk of infections • changes in blood test results for liver • liver damage or failure- may cause yellowing of the skin or eyes (jaundice), tiredness or sickness, loss of appetite, abdominal pain or high temperature • changes in blood test results for kidney function • blockage in the lung (possible pain and/or shortness of breath)

of a hole in the wall of the gut which can cause severe abdominal pain • damage such as stroke and/or heart attack) • stroke, mini-stroke, or bleeding in the brain- may result in numbness or weakness on one side of the body	results for cholesterol (high) • dry skin, thickening and itching of the skin • loss of body fluids (dehydration) • feeling bloated or having as in the bowel • malaise (feeling unwell) • inflammation of the gallbladder • Hepatic encephalopathy- may result in confusion, drowsiness, poor concentration or loss of consciousness	• Bleeding inside the body particularly from the gut – may cause black, tarry, or bloody stools • Dehydration and kidney failure – may result from diarrhea, vomiting (being sick) which are very common side effects • Heart failure – a decreased pumping ability of the heart which may cause severe shortness of breath

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

Rare but serious (occurring in fewer than 1% of patients)

• Painful infection or irritation near the anus • Splenic infarction (severe pain in the upper left part of the belly (abdomen) which may be associated with fever, chills, nausea and vomiting) • Aortic dissection- tearing in the wall of the aorta (a large artery) which may cause severe pain in the back, chest, or abdomen and internal bleeding • Posterior reversible encephalopathy syndrome (PRES)- a fatal condition that may have the following symptoms: headache, confusion, convulsions,	• inflammation of the pancreas which may cause severe pain in the abdomen or back • osteonecrosis (bone damage) of the jaw- may cause pain in the mouth, teeth, and or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw	• Pneumothorax- a leak of air from the lung into the chest so the lung cannot inflate. This may cause sudden chest pain or sudden shortness of breath. There may be a higher chance of this occurring if cancer has spread to the lungs or if treatment is for solid tumor cancers or in patients under the age of 25. • impaired healing- wounds (may take longer to heal)

and vision disturbance		

Lenvatinib may also increase the risk of bleeding from tumor sites in patients with anaplastic thyroid cancer. This bleeding may be serious and could result in death.

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 and **ECHOs** may cause discomfort while lying on the exam table. The tape on the EKG pads may cause skin irritation.

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. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. 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 or father a child, you must use a highly effective method of birth control during the study and for at least 30 days after your last dose of lenvatinib (all participants) or 120 days after your last dose of pembrolizumab (females only), whichever is later.

Male participants with female partners must use a condom during vaginal intercourse, and their female partners must also use an additional birth control method from the list below.

Acceptable methods of birth control for female participants (or female sexual partners of male participants) include:

- Combined (estrogen- and progestogen-containing) hormonal birth control (including pills, patches, or injections)
- Progestogen-only hormonal birth control (pills, injections, or implants)
- Intrauterine hormone-releasing system (IUS) or device (IUD)
- Surgical sterilization of yourself or your partner (bilateral tubal occlusion [“tubes tied”] for females or vasectomy for males)

Males: Do not donate sperm while on this study. 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

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 #1: If the CT scans show that the disease may be getting worse and you agree, you will have a tumor biopsy performed for biomarker research testing and the expression of certain genes in the cells. These samples will be compared to the other tumor samples collected during the study.

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: Do you agree to have a tumor biopsy 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 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. Brandon G. Smaglo, at 713-792-2828) 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 the study, you will be removed from study drug and will be asked to come to the clinic for safety tests. If you withdraw from this study, you can still choose to be treated at MD Anderson.

If you stop being in the research, data already collected 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, Merck (the study drug manufacturer), the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

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

   The results of any genetic tests may be put in your health records. The study team will discuss this with you if it applies.

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 Merck, and/or shared with other researchers and/or institutions for use in future research.

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

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

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review

Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

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

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

Genetic Research
Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

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

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

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

Conflict of Interest

Dr. Michael Overman (Study Co-Chair) has received compensation from Merck as a Consultant. The financial interests are within the limits of the conflict of interest policy.

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

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Any future sponsors/supporters of the study
   - Merck (the manufacturer of the study drug)
   - 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.

   To protect your identity, the data and samples collected from you will be labeled with 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 data and samples. 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.

   Biological samples that are collected for biomarker study testing will be shared with a laboratory owned or contracted by Merck (the study supporter and manufacturer of the study drug). When samples are sent to the Merck laboratory, any identifying information will be removed and replaced with a unique study identification number.

   If results from this study are published, such as in medical journals or online, your name and other identifying information will not be used.

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

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.)