Informed Consent/Authorization for Participation in Research

Title of Research Study: A Randomized Phase 2 Trial of Nivolumab, Relatlimab plus Ipilimumab vs. Nivolumab plus Ipilimumab in first-line advanced renal cell carcinoma (RCC)

Study Number: 2024-1337

Principal Investigator: Eric Jonasch, MD

_____ _____
Participant's Name Medical Record Number

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have advanced renal cell carcinoma (RCC) that has not been treated.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The goal of this clinical research study is to learn about the safety and effects of giving nivolumab, ipilimumab, and relatlimab together to patients with untreated advanced RCC.

This is an investigational study. Nivolumab and ipilimumab together is FDA approved and commercially available for the treatment of untreated advanced RCC. Relatlimab is FDA approved and commercially available for the treatment of melanoma when given in combination with nivolumab, but it is not FDA approved for the treatment of RCC. It is considered investigational to give relatlimab with nivolumab and ipilimumab to patients with untreated advanced RCC.

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

How long will the research last and what will I need to do?

You will be randomly assigned to receive either nivolumab and ipilimumab with relatlimab (the investigational arm) or nivolumab and ipilimumab only (the control arm). You may continue receiving the study drugs for as long as the doctor thinks it is in your best interest.

You will be asked to visit the study clinic at least 1 time either every 4 weeks (if you are in the investigational arm) or every 3 weeks (if you are in the control arm) while you are receiving the study drugs. At each visit, you will have tests and procedures, such as physical exams, blood draws, and imaging scans.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

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 from the study drugs, some of which may be severe or life threatening.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

The study drugs may help to control the disease. Future patients may benefit from what is learned. However, it cannot be promised that there will be any benefits to you or others from your taking part in this research.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or stop participation at any time without penalty or loss of your regular benefits.

Instead of taking part in this study, you may choose to receive nivolumab and ipilimumab outside of this study. You may choose to receive other standard-of-care treatment, such as cabozantinib and nivolumab or lenvatinib and pembrolizumab. You may choose to receive other investigational therapy, if available. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their possible risks and benefits, with you.

You may choose not to have treatment for cancer at all. If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends, and your doctor.

In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, call the study doctor (Dr. Eric Jonasch, at 713-792-2830) or 713-792-2121 (24 hours).

This research has been reviewed and approved by the MD Anderson Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at 713-792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

It is expected about 60 people will be enrolled in the entire study at all locations.

What happens if I agree to be in this research?

Screening Tests
Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (up to 3 tablespoons) will be drawn for routine tests, immune system testing, and circulating free DNA (cfDNA) testing. cfDNA testing measures the amount of DNA traveling in your blood outside of a cell.
- You will have a CT or MRI scan and a bone scan to check the status of the disease. You will also have a scan of your brain (such as an MRI).
- Tumor tissue left over from a previous procedure will be collected for genetic testing to study the characteristics of the disease and to help researchers understand the disease response to the study drugs. If leftover tissue is not available or does not meet study requirements, you may have a biopsy to collect new tissue. The study doctor will tell you what type of biopsy you may have and its risks. Please see the Optional Procedures for the Study section.
- If you can become pregnant, blood (about 1 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.

Study Groups
If you are found to be eligible to take part in this study, you will be randomly assigned (as in a roll of dice) to 1 of 2 study groups. This is done because no one knows if one study group is better, the same, or worse than the other group. You will have a 2 in 3 chance (66%) of being assigned to the investigational arm and a 1 in 3 chance (33%) of being assigned to the control arm.

- If you are assigned to the **investigational arm**, you will receive nivolumab and ipilimumab with relatlimab.
- If you are assigned to the **control arm**, you will receive only nivolumab and ipilimumab.

The study doctor will tell you the arm you are assigned to.

Study Drug Administration

Investigational Arm
Each study cycle is 28 days (4 weeks).

You will receive nivolumab and relatlimab together by vein over about 60 minutes on Day 1 of each cycle (Cycles 1 and beyond).

You will receive ipilimumab by vein over about 30 minutes on Day 1 of every odd-numbered cycle (Cycles 1, 3, 5, 7, and so on).

Control Arm
Each study cycle is 21 days (3 weeks).

You will receive nivolumab by vein over about 60 minutes on Day 1 of each cycle (Cycles 1 and beyond).

You will receive ipilimumab by vein over about 30 minutes on Day 1 of Cycles 1-4 only (up to 4 doses total).

Study Visits

Investigational Arm
On Day 1 of each cycle:

- You will have a physical exam.
- Blood (about 1-2 tablespoons) will be drawn for routine tests. At Cycle 4 only, blood will also be used for immune system and cfDNA testing.
- At Cycle 4 and then every 3 cycles after that (Cycles 7, 10, 13, 16, and so on), you will have an MRI or CT scan to check the status of the disease.
- At Cycle 4 and then only when the study doctor thinks it is needed, you will have a bone scan to check the status of the disease.

Control Arm
On Day 1 of each cycle:

- You will have a physical exam.
- Blood (about 1-2 tablespoons) will be drawn for routine tests. At Cycle 5 only, blood will also be used for immune system and cfDNA testing.
- At Cycle 5 and then every 4 cycles after that (Cycles 9, 13, 17, 21, and so on), you will have an MRI or CT scan to check the status of the disease.
- At Cycle 5 and then only when the study doctor thinks it is needed, you will have a bone scan to check the status of the disease.

End-of-Dosing Visit
As soon as possible after your last dose of study drugs:

- You will have a physical exam.

- Blood (about 1-2 tablespoons) will be drawn for routine, immune system, and cfDNA testing.
- You will have an MRI or CT scan to check the status of the disease. If the study doctor thinks it is needed, you will also have a bone scan.

Follow-Up Visit
At 28 days after your last dose of study drugs:
- You will have a physical exam.
- Blood (about 1 tablespoon) will be drawn for routine tests.

Long-Term Follow-Up
At either 135 days after your last dose of study drugs (if you are in the investigational arm) or 100 days after your last dose of study drugs (if you are in the control arm), and then every 100 days for up to 2 years or until the study closes (whichever happens first), the study staff will call you to check on how you are doing. Each call will take about 15 minutes.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:
- Tell the study team about any symptoms or side effects you have, follow study directions, and come to all study appointments (or contact the study team to reschedule).
- Tell the study doctor/study staff about all medications that you are taking or plan to take, including prescription and over-the-counter medications, supplements, vitamins, and herbal remedies.
- Do not take the following medications while participating in this study. Talk to the study doctor before starting any new medications and if you have any questions about what medications you are not allowed to take. Do not take:
    - medications that reduce the body's immune response
    - corticosteroids
    - other systemic anti-neoplastic therapy (such as chemotherapy, hormonal therapy, immunotherapy, extensive non-palliative radiation therapy, or standard or investigational agents for treatment of metastatic RCC)
    - herbal medications
    - immunizations with any attenuated live vaccines (the inactivated seasonal flu vaccine is allowed)

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you. You may withdraw from participation in this study without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

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 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.

Is there any way being in this study could be bad for me? (Detailed 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.

Nivolumab, ipilimumab, and relatlimab each 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 (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.

Side Effects of Nivolumab combined with Ipilimumab

Common (occurring in more than 10%)

• fatigue/lack of energy • fever • itching • skin rash	• overactive thyroid gland (possible decreased thyroid stimulating hormone	• loss of appetite • nausea/vomiting • abnormal liver test (possible liver

• underactive thyroid gland (possible increased thyroid stimulating hormone lab test result, weight gain, heart failure, and/or constipation)	lab test result, weight loss, heart rate changes, and/or sweating) • abnormal digestive blood test (possible inflammation of the pancreas) • diarrhea	damage and/or yellowing of the eyes and/or skin)

Occasional (occurring in 3-10% of patients)

• chills • headache • dizziness • dry/red skin • patches of skin color loss • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the pituitary gland (possibly headaches)	• abnormal blood test (possible pancreas damage) • high blood sugar (possible diabetes) • constipation • abdominal pain • dry mouth • inflammation of the intestines • mouth blisters/sores (possible difficulty swallowing) • low red blood cell count • liver inflammation • abnormal kidney test (possible kidney damage)	• nerve damage (possible numbness, pain, and/or loss of motor function and/or “pins and needles” sensation) • pain (including muscle/bone) • lung inflammation (pneumonitis), and/or bronchitis (possible difficulty breathing) • difficulty breathing • cough • infusion reaction (possible fever, rash, pain, and/or swelling) • allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Rare (occurring in fewer than 3% of patients)

• fast heartbeat • abnormal EKG • heart inflammation/ inflammation of the tissue around the	• pituitary gland failure (possible hormone imbalance) • blood vessel inflammation	• muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision

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) • swelling (face/arms/legs) • difficulty sleeping • hives • skin blisters • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • hair loss (partial or total) • inflammation of multiple areas of the body (see below) • inflammation of the thyroid gland (possible tenderness in the neck)	• abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • diabetes complications resulting in diabetic coma • dehydration • hole in the intestines or stomach (possibly leaking contents into the abdomen) • liver failure/damage • low blood cell count (platelets, white) • viral/bacterial infection that affects nose, throat and airways (upper respiratory tract infection) • destruction of red blood cells due to the body attacking itself (called autoimmune hemolytic anemia) • kidney failure • breakdown of muscle tissue (possible kidney failure) • Guillain-Barre syndrome--damage to the nervous system (causing numbness and/or paralysis) • nerve damage (affecting the head and neck)	• 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) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • 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) • lung infiltrates (possible infection or inflammation) • Hemophagocytic lymphohistiocytosis (HLH) syndrome (see below)

You may need to take drugs to reduce inflammation while taking nivolumab and ipilimumab. 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.

The study drug(s) work 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 and ipilimumab may cause serious side effects that affect your immune system. Some of these side effects can be rare or occasional and 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 if you have diarrhea, nausea, vomiting, blurred vision, dizziness, fainting, or you are feeling cold all the time.

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

Nivolumab and ipilimumab may cause Hemophagocytic lymphohistiocytosis (HLH) syndrome at a rare frequency. 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 and liver, 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

Relatlimab Side Effects

Very common (occurring in more than 10% of patients)

• fatigue • dizziness • fever • headache • skin rash • loss of appetite	• nausea/vomiting • constipation • diarrhea • abdominal pain • weight loss • low red blood cell count	• cough • muscle pain/weakness • arm/leg/back pain • difficulty breathing • urinary tract infection

More common (occurring in between 5% and 10% of patients)

• chest pain • swelling (arms/legs) • chills • itchy skin • anxiety • heartburn	• 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) • abnormal thyroid test • difficulty swallowing • mouth and/or throat pain	• abnormal liver test (possible liver damage) • lymph node and joint pain • blurred vision • worsening kidney function • cough/productive cough • allergic reaction • night sweats • common cold

The drug 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.

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

• inflammation of the membranes around the spinal cord and brain (possible headache, nausea, vomiting, sensitivity to the light, and/or coma)	• red, dry, scaly patches of thickened skin (psoriasis) • inflammation of the pancreas (possible abdominal pain)	• lung inflammation (possible difficulty breathing)

Study Drug Combination Side Effects

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 collection. An allergic reaction to the anesthetic may occur. A scar may form at the collection site.

A standard **bone scan** exposes you only to the radiation that comes from injecting the standard radioactive imaging solution for bone imaging.

During an **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 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.

If an MRI contrast material is used, your study doctor will tell you about possible side effects or allergic reaction. Contrast agents can cause allergic reactions and kidney damage. Allergic reactions can include mild itching associated with hives but can also result in a serious life-threatening emergency from difficulty breathing. If this occurs, it is treatable. 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.

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.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

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.

Birth Control Requirements: If you can become pregnant or father a child and you are sexually active, you must use at least 2 acceptable methods of birth control during the study and for 23 weeks (for females) or 31 weeks (for males). after your last dose of study drugs. The study doctor will discuss with you the acceptable birth control methods you may use.

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.

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

Will it cost anything to be in this study? Will I be paid to be in this study?

If you are in the investigational arm, nivolumab will be provided at no cost to you during this study. Relatlimab and ipilimumab will also be provided at no cost to you during this study.

If you are in the control arm, you and/or your insurance provider will be responsible for the cost of nivolumab and ipilimumab.

You and/or your insurance provider will not have to pay for certain research exams and procedures done that are covered by the study. These may include archival tissue sample collection, fresh tumor biopsy, and blood or urine pregnancy test (if applicable).

You and/or your insurance provider will be responsible for the costs of routine clinical services (such as diagnostic/therapeutic procedures, drugs, devices, laboratory assays, and other services that would ordinarily be ordered for medical care, regardless of whether or not you are participating in a study). Some examples may include brain scan, IV drug administration, and imaging assessments. There may be extra costs that are not covered by your medical plan that you will have to pay yourself.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will not receive any compensation for taking part in this study.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

A participant study number will be assigned to you once you have been enrolled in the study. This participant study number will be used to identify your data in the study report and when reporting any data from the study.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

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

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

Your information or samples that are collected as part of this research will not be used or shared with another researcher for future research studies without your additional consent. Please see the Optional Procedures for the Study section.

Some of your specimens and genetic and/or health information might also be placed into one or more external publicly accessible scientific databases. Your name and other information that could directly identify you (such as your address or social security number) will never be placed into these external databases. A researcher who wants to study information from these databases must have an approved study and work with the group overseeing the database to obtain the information.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include if the disease gets worse, if intolerable side effects occur, if you are unable to follow study directions, or if the study is stopped.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form)
- call the study doctor (Dr. Eric Jonasch, at 713-792-2830) or 713-792-2121 (24 hours)

A research-related injury is an illness directly caused by your participation in the study. A research-related injury does not include:

- injuries directly caused by the natural worsening (progression) of an underlying disease or medical condition, or
- injuries caused by you not following the instructions in this consent form.

You will not be reimbursed for expenses or receive any money from MD Anderson for this injury. Costs of treatment received because you become injured or ill will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson 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.

What else do I need to know?

This research is being funded by Bristol Myers Squibb (BMS).

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

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

This research study involves genetic testing, 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 Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Optional Procedures for the Study

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures. The optional procedure biopsies will be covered by the study if you agree and if they are needed.

Optional Procedure #1: If tumor tissue leftover from a previous procedure is unavailable or does not meet the study requirements and if you agree, you will have a tumor biopsy at Screening.

Optional Procedure #2: If you are in the investigational arm and if you agree, you will have a tumor biopsy on Day 1 of Cycle 4 or at the time you stop treatment if the disease gets worse, whichever comes first. The study doctor will tell you what type of biopsy you will have and its risks.

Optional Procedure #3: If you are in the control arm and if you agree, you will have a tumor biopsy on Day 1 of Cycle 5 or at the time you stop treatment if the disease gets worse, whichever comes first. The study doctor will tell you what type of biopsy you will have and its risks.

Optional Procedure #4: If you agree, your samples and information that are collected during this research could be used for future research studies or shared with another researcher for future research studies.

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

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.

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 at screening if no leftover tissue from a previous procedure is available or doesn't meet the study requirements?

YES NO

Optional Procedure #2: If you are in the investigational arm, do you agree to have a tumor biopsy on Day 1 of Cycle 4 or at the time you stop treatment if the disease gets worse, whichever comes first?

YES NO

Optional Procedure #3: If you are in the control arm, do you agree to have a tumor biopsy on Day 1 of Cycle 5 or at the time you stop treatment if the disease gets worse, whichever comes first?

YES NO

Optional Procedure #4: Do you agree that your samples and information that are collected during this research could be used for future research studies or shared with another researcher for future research studies?

YES NO

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

   The results of this research may be published in scientific journals or presented at medical meetings. However, your identity will not be disclosed. Your name and other identifying information will be kept confidential.

   Samples may be shipped to:
   Haake Lab
   Vanderbilt University Medical Center
   2220 Pierce Ave, 606 Preston Research Building, Nashville, TN 37232

   K4/517 Clinical Science Center
   University of Wisconsin Carbone Cancer Center
   600 Highland Ave, Madison, WI 53792

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

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

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed

from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

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

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT