THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase 2 Study (with Safety Lead in) of the Safety, Tolerability and Efficacy of Anti-CTLA4 (Ipilimumab) and Anti-PD-1 (Nivolumab) in Combination with Radiation Therapy to 50 - 66 Gy in Low-Intermediate Volume, Local-Regionally Advanced HPV-Positive Oropharyngeal Squamous Cell Carcinoma (OPSCC)
2018-0381

Subtitle: IND Trial

Study Chair: Renata Ferrarotto

_____ _____
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 giving ipilimumab and nivolumab in combination with radiation therapy (RT) can help control advanced HPV-positive oropharyngeal squamous cell carcinoma (OPSCC).

This is an investigational study. Nivolumab combined with ipilimumab is FDA approved and commercially available for the treatment of melanoma. Radiation therapy is delivered using FDA-approved and commercially available methods. Combining RT with nivolumab and ipilimumab in patients with OPSCC is investigational.

The study doctor can describe how the study drugs and RT are designed to work.

The study drugs and radiation therapy may or may not help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may have to stay out of town for a long period of time.

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

You will receive nivolumab and ipilimumab for up to 2 cycles and radiation therapy for 5 or 6 weeks.

Nivolumab and ipilimumab will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the costs of RT.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other FDA approved drugs such as chemotherapy or immunotherapy. If you take part in this study, you will not be able to receive standard of care chemotherapy (cisplatin plus radiation), which has been beneficial for some patients. 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. Talk to your study doctor about your choices before you decide if you will take part in this study.

1. STUDY DETAILS

Screening Tests

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

- You will have a physical exam.
- You will have an EKG to check your heart function.
- Blood (about 4-6 teaspoons) will be drawn for routine tests, to check for hepatitis and HIV (the AIDS virus), to learn about some side effects that you may experience, and to learn how and why you respond to treatment.
- You will have FDG-PET scans, MRIs, or CT scans to check the status of the disease.
- You will have fiber-optic exam with laryngopharyngoscopy to find out if there are signs of cancer. For this procedure a small telescope will go up your nose and down into the throat.
- Your swallowing function will be tested with a special type of x-ray called a modified barium swallow. During the test, you will eat and drink foods and liquids

mixed with a "contrast" chemical called barium that will make your throat more visible in the x-rays. A special x-ray tube will be connected to a television screen to allow the doctor to watch the foods and liquids pass from your mouth and down your throat.

- An oral rinse sample will be collected to check for signs of HPV and genetic testing that may be related to the status of the disease. You will be asked to swish with a small amount of mouthwash for 15 seconds, gargle for another 15 seconds, and then spit the mouthwash into a cup.
- You will complete symptom questionnaires. It should take about 10-15 minutes to complete.
- Leftover tumor tissue from a previous procedure will be collected for biomarker testing, including genetic biomarkers. Part of this sample will also be used to check for genetic mutations (changes). If you do not have enough tumor tissue available, you will have a biopsy. The study doctor will tell you what type of biopsy you will have. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.
- If you can become pregnant, blood (about less than ½ teaspoon) 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 180 participants will be enrolled in this study. All participants will take part at MD Anderson.

Study Drug Administration
Each cycle is 6 weeks.

You will receive nivolumab by vein over about 30 minutes on Days 1, 15, and 29 of Cycles 1 and 2. You will receive ipilimumab by vein over about 30 minutes on Day 1 of Cycles 1 and 2.

Beginning on Day 1 of Cycle 2, you will also receive 30 RT treatments. RT will be given 5 days in a row for 6 weeks. If your tumor shrinks considerably after Cycle 1 of nivolumab and ipilimumab, you will receive 25 RT treatments instead of 30. This means you will receive 5 weeks instead of 6 weeks of RT. The doctor will provide more information on how the radiation therapy will be given. You will sign a separate consent explaining how radiation will be given.

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

If the disease gets worse or if intolerable side effects occur such that you are no longer able to take the study drugs/radiation therapy, data (as well as blood, oral rinse, and/or leftover tissue during a tissue biopsy) will still be collected as part of your follow up visits.

Your participation on the study will be over after the long term follow-up visits.

Study Visits

Before every cycle, blood (about less than ½ teaspoon) will be drawn to check your thyroid function.

On Days 1, 15, 29 of Cycles 1 and 2:
- You will have a physical exam.
- Blood (about 3-4 teaspoons) will be drawn for routine tests and to learn how and why you respond to treatment.
- An oral rinse sample will be collected to check for signs of HPV and genetic testing that may be related to the status of the disease.

Between **Days 15-22 of Cycle 1 or** between **Days 36-42 of Cycle 1**, you will have a tissue biopsy for biomarker and immune system testing. To collect a tissue biopsy, the affected area is numbed with anesthetic and a small amount of tissue is removed.

About 7 days after the last day of RT, you will complete questionnaires about your symptoms.

About 7 days before the first dose of RT:
- You will have neck MRI or CT scans.
- You will have a fiber-optic exam with laryngopharyngoscopy to find out if there are signs of cancer.

Every 4 weeks, if you can become pregnant, blood (about ½ teaspoon) will be drawn for a pregnancy test.

Follow-Up
When you stop or complete study treatments, you will begin the follow-up period. During this period, your study doctor will continue to check your health.

Four (4) weeks after the last dose of nivolumab and about 3 months from the end of treatment:
- You will have a physical exam.
- Blood (about 4 teaspoons) will be drawn for routine tests and to learn how and why you respond to treatment.
- An oral rinse sample will be collected to check for signs of HPV and genetic testing that may be related to the status of the disease.
- If you can become pregnant, blood (about less than ½ teaspoon) will be drawn for a pregnancy test.

About 8-10 weeks after RT and then about 3 months after the end of treatment, you will have a neck MRI or CT scan. At 3 months only, you will have FDG-PET/CT.

Long-Term Follow-Up

Every 3 months from the end of treatment during first 2 years, every 6 months for 3 years, and then 1 time every year after that:

- You will have a physical exam.
- Within 3-6 months, you will have a modified barium swallow (3-6 months only).
- Within 18-24 months, you will complete questionnaires about your symptoms. They should take about 10-15 minutes to complete.
- An oral rinse sample will be collected to check for signs of HPV and genetic testing that may be related to the status of the disease.

At 6, 9, 12, and 24 months after RT and then every 6 months for 1 year, you will have a neck MRI or CT scan. At 6 months and then if the doctor thinks it is needed, you will have an FDG-PET/CT scan.

If your doctor thinks the tumor has come back, you will have a tissue biopsy during the follow-up period to check the status of the disease.

Other Information:

- By enrolling in this study, you may be delaying receiving potentially beneficial treatment outside of this study.
- By enrolling in this study, you may receive a lower dose of radiation than is normally given as standard of care.
- By enrolling in this study, you may have side effects that delay radiation therapy.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Nivolumab and ipilimumab may cause low blood cell counts (red blood cells, platelets, and/or white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.

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

Nivolumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue/lack of energy • headache • fever • skin rash • 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 levels of fat (possible heart disease and/or stroke)	• high blood sugar (possible diabetes) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • abdominal pain • diarrhea • loss of appetite • nausea • constipation • abnormal digestive blood test (possible inflammation of the pancreas)	• low blood cell counts (red, white, platelets) • abnormal liver test (possible liver damage and/or yellowing of the skin and/or eyes) • pain • abnormal kidney test (possible kidney damage) • weakness • difficulty breathing • cough • infection

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • dizziness • skin redness • patches of skin color loss • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • inflammation of the thyroid gland (possible tenderness in the neck) • vomiting	• mouth blisters/sores (possible difficulty swallowing) • abnormal blood test (possible pancreas damage) • nerve damage (possible numbness, pain, and/or loss of motor/sensory function) • inflammation of nerves (possible pain and/or	• joint disease • build-up of fluid around the lungs • lung inflammation (possible difficulty breathing) • stuffy nose • immune reaction (possible organ damage) • immune system disease (possible dry mouth/eyes, fatigue,

• inflammation of the intestines • hole in the intestines (possibly leaking contents into the abdomen)	loss of motor or sensory function) • peripheral nerve palsy (weakness, numbness, tingling) • muscle damage causing weakness	joint pain, and/or organ failure) • infusion reaction (possible chills and/or hives)

If you have a stem cell transplant from a donor before or after you receive nivolumab, 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 stem cell transplant from a donor before or after nivolumab therapy. If you decide to receive a stem cell transplant from a donor, please tell your transplant doctor that you received nivolumab in the past.

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

• blood vessel inflammation (possible bleeding and/or bruising) • heart inflammation • brain inflammation (possible paralysis and/or coma) • damage to the nervous system (causing numbness and/or paralysis) • paralysis of nerves controlling the head and neck • skin blisters • diabetes requiring insulin • severe high blood sugar due to uncontrolled diabetes	• hormonal deficiency that affects the body's ability to control blood pressure and react to stress • inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • paralysis (face) • uncontrolled movements • inflammation inside the eye (possible vision problems) • kidney failure • breakdown of muscle tissue (possible kidney failure)	• blockage in the lung (possible pain and/or shortness of breath) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling, hearing loss, and/or loss of skin color)

Frequency unknown

• migraine • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract)	• hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)	• weight loss

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.

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, or appendix. Tell the study staff right away if you have diarrhea, nausea, vomiting, blurred vision, dizziness, fainting, or you are feeling cold all the time.

If you had an organ transplant, nivolumab may increase your risk for the transplant to be rejected by your body.

Ipilimumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • itching and/or skin rash • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • weight loss • nausea • diarrhea	• loss of appetite • vomiting • abnormal digestive blood test (possible inflammation of the pancreas)	• constipation • low red blood cell counts • abnormal liver tests (possible liver damage) • muscle/bone pain

Occasional (occurring in 3-20% of patients)

• fast heartbeat • fever • dizziness	• skin rash with blisters or bleeding	• abnormal liver tests (possible yellowing of the skin and/or eyes)

• difficulty sleeping • death of skin tissue and skin sores • very severe blistering skin disease (with loss of large portion of skin) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• pituitary gland failure (possible endocrine gland abnormality) • Type 1 diabetes, which may require insulin • abdominal pain • inflammation of the intestines • abnormal blood test (possible pancreas damage)	• 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) • 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)	• skin rash (possible fever/lymph node swelling/inflammation of internal organs/abnormal blood cell counts) • large skin blisters • 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)	• anemia due to destruction of red blood cells • bone marrow failure due to abnormal tissue growth • liver failure • liver damage due to inflammation • muscle inflammation and weakness • inflammation inside the eye (possible vision problems) • partial hearing loss • kidney failure • bronchiolitis obliterans (damage of the small airways with difficulty breathing) • lung inflammation (possible difficulty breathing) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

• red, dry, scaly patches of thickened skin (psoriasis)	• stomach and/or small intestine ulcer	• immune response • infection

Ipilimumab may cause dehydration that may be severe enough to require hospitalization.

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

• swelling, pain, and/or heat at the injection site

Radiation Therapy Side Effects

It is not known how often the side effects of radiation therapy may occur.

• swelling • swelling of the arms or torso • skin changes (possible dryness, itching, peeling, and/or blistering)	• hair loss at the treatment site • mouth problems • trouble swallowing • nausea • vomiting • diarrhea	• joint problems • secondary cancers

Radiation therapy may cause you to develop another type of cancer. Side effects may not occur for up to 6 months after RT is over. Side effects will vary depending on what part of the body is receiving RT.

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. The biopsy procedure may injure surrounding tissues or organs. A scar may occur at the biopsy site.

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

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

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

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

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

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you

compensation from such developments. The results of any genetic tests may be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

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 medically acceptable forms of birth control during the study and until at least 23 weeks (for women) or 31 weeks (for men) after the last dose of study drugs/radiation therapy.

Acceptable methods of birth control include the following:

- Hormonal methods of birth control, including birth control pills (combination of estrogen and progesterone)
- Progestogen-only hormonal birth control
- Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS)
- Tubal ligation (tubes tied)
- Vasectomized partner
- Male condoms (female partner must also use an acceptable form of birth control)

Males: You should not donate sperm during study treatment and for 7 months after treatment. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. If your partner/spouse becomes pregnant while you are on this study, the sponsor would like to collect information about the pregnancy. The study sponsor's contact information will be made available so that, if you and your partner wish to, you can share information about the outcome of the pregnancy with the sponsor. If you and/or your partner choose not to share this information, it will not result in any penalty or loss of benefits to which you are otherwise entitled.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. The sponsor will ask for information about the pregnancy.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, leftover biological samples will be stored in a research samples bank at MD Anderson and used in future testing (such as tests of immune system response) related to cancer.

Before your samples can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your samples will be given a code number. Only individuals with IRB permission and designated bank staff will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Additionally, if needed for certain types of research in the future and if the IRB approves, the bank staff and approved research staff will be able to link your samples back to you.

Optional Procedure Risks:
MD Anderson and others can learn about cancer and other diseases from your **banked samples**. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your samples may be used for genetic research about diseases that are passed on in families. **Genetic research** may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests may be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

If you withdraw your consent to the storage of leftover samples in the tissue bank, then they will no longer be collected for storage. Any of your samples that remain in the tissue bank will no longer be used for research and will be destroyed.

However, if any of your de-identified samples were already released for research purposes before you withdrew consent, MD Anderson will not be able to destroy them.

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 allow leftover samples to be stored in a research samples bank at MD Anderson for use in future research related to cancer?

YES NO

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Bristol-Myers Squibb (BMS) 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. Renata Ferrarotto, at 713-792-6363) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from

participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

If you stop being in the research, already collected data may not be removed from the study database. The study staff may ask if they can continue collecting the results of routine care from your medical record. 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, Bristol-Myers Squibb (BMS), the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

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

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

9. This study is sponsored and/or supported by: Bristol-Myers Squibb (BMS).

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

Future Research

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.

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.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or 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 samples are used for future research. If this 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 samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

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

Genetic Research
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.

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 Statement
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:

- Maura Gillison (Co-Investigator)
- Xiuning Le (Co-Investigator)

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
- Bristol-Myers Squibb (BMS), who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Any future sponsors and/or licensees of the study technology
- 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.

Optional research samples will be stored in Dr. Ferrarotto's laboratory at MD Anderson for use in future research.

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO 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