THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase I/II Trial of anti-CTLA4-NF mAb (BMS-986218) in Combination with Nivolumab and Hypofractionated Stereotactic Radiation Therapy in Patients with Advanced Solid Malignancies
2020-0479

Subtitle: Main research study consent

Study Chair: James Welsh, MD

_____ _____
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 about the safety and effectiveness of giving stereotactic body radiation therapy (SBRT) with BMS-986218 alone and in combination with nivolumab to patients with advanced solid tumors.

This is an investigational study. BMS-986218 is not FDA approved or commercially available. It is currently being used for research purposes only. SBRT is delivered using FDA-approved and commercially available methods. Nivolumab is FDA approved and commercially available for the treatment of many different types of cancer. It is considered investigational to give SBRT with BMS-986218 alone or in combination with nivolumab to treat advanced solid tumors.

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

Treatment on this study 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.

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

All arms may receive up to 4 cycles of BMS-986218 with SBRT. If you are in Arm 2 (Group 2), you may receive nivolumab for up to 26 cycles.

BMS-986218 and nivolumab will be provided at no cost to you while you are on study. You and/or your insurance provider are responsible for the cost of SBRT 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 standard photon radiation therapy outside of this study. You may be choosing to not receive approved therapy(ies) with known clinical benefit in order to enroll on this study. 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 be performed within 14-28 days before your first cycle of treatment to help the doctor decide if you are eligible.

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests and to test for hepatitis C, B, and HIV (the AIDS virus). This routine blood draw will also include a pregnancy test if you can become pregnant. To take part in this study, you must not be pregnant.
- Urine will be collected for routine tests.
- You will have an EKG to check your heart function.
- You will have an MRI, CT, or PET-CT scan to check the status of the disease.

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

Pretreatment Procedures

If you are among the first 20 participants enrolled in each study arm and the study doctor thinks it is safe to do so, blood (about 4 tablespoons) will be drawn and you

will have a core tissue biopsy for biomarker testing (including genetic biomarkers). To perform a core biopsy, the affected area is numbed with anesthetic and a sample of tissue is removed using a hollow core needle that has a cutting edge. Mandatory biopsies will be done under imaging (MRI, CT, or PET-CT scan) and you may be sedated (put to sleep). If you are sedated, you and/or your insurance provider will be responsible for the costs. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs.

Study Groups

If you are found to be eligible to take part in this study and are among the first 6 patients enrolled, you will be assigned to Group 1. If you are among the 7-12th patient enrolled, you will be assigned to Group 2. After that, if you are eligible to take part in the study, you will be randomly assigned (as in the flip of a coin) to 1 of 2 study groups. You have an equal (50/50) chance of being assigned to either group. This is done because no one knows if one study group is better, the same, or worse than the other group.

Group 1 (Arm 1): BMS-986218 and SBRT

In **Group 1**, you will receive BMS-986218 and SBRT. All participants will receive the same dose level of BMS-986218. Up to 40 participants will be enrolled in Group 1 of the study.

Group 2 (Arm 2): BMS-986218, nivolumab, and SBRT

In **Group 2**, you will receive BMS-986218, nivolumab, and SBRT. All participants will receive the same dose level of BMS-986218 and nivolumab. Up to 40 participants will be enrolled in Group 2.

Up to 80 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle for Group 1 and 2 is 28 days.

All participants

You will receive BMS-986218 by vein over about 30 minutes on Day 1 of Cycles 1-4. Then, on Days 36-39 (Days 8-11 of Cycle 2), you will receive SBRT to one or multiple tumor sites. The study staff will explain how the radiation therapy is given.

You will no longer be able to receive treatment and will be removed from the study if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions. If the disease gets worse, you will be able to review and, if you agree, sign a separate consent form to receive 2-4 additional cycles of BMS-986218 alone (Group 1) or in combination with nivolumab (Group 2) with a high plus low dose radiation therapy called RadScopal™. RadScopal™ is a technique in which high dose radiation is used to turn one (1) tumor into a “vaccine” while at the same time using low dose radiation to help pull in immune cells into the other tumors. This is done in order to help improve the response to immunotherapy

Group 2
If you are assigned to Group 2, on Day 1 of Cycles 2-4, before receiving BMS-986218, you will also receive nivolumab by vein over about 30 minutes.

Starting on Cycle 5, you will receive only nivolumab on Day 1 of each cycle for up to 26 total cycles.

All participants will be given standard drugs to help decrease the risk of side effects and to help support your immune system. You may ask the study staff for information about how the drugs are given and their risks.

Study Visits

During **Week 1 of all cycles and Week 2 of Cycle 2**, you will have a physical exam.

Each week until Week 8 (end of Cycle 2, ± 1 week) and during Week 1 of Cycles 3 and 4 after that, blood (about 4-5 tablespoon) will be drawn for routine and biomarker testing. **Starting on Cycle 2**, if you can become pregnant, part of this sample will be used for a pregnancy test.

On **Week 3 of Cycle 1 (before starting SBRT),** you will have a 4-dimension CT (4DCT) scan of your chest to check the status of the disease and to help the doctors decide what dose of SBRT you will receive. A 4DCT is a type of CT scan that looks at how the tumor may move when you are breathing. You may be asked to hold your breath for short periods of time during this test at both time points.

If you are among the first 20 participants enrolled in each study arm and the study doctor thinks it is safe to do so, on **Week 8 (end of Cycle 2, ± 1 week)** and at any time the disease gets worse, you will have a core tissue biopsy and blood (about 1 tablespoon) will be drawn for biomarker testing.

Every 4 months for up to 2 years after starting Cycle 1, you will have an MRI, CT, or PET-CT scan.

Follow-Up
About 30 days, 60 days, 6 Months, and 12 Months after your last dose of study drug, you will come to the clinic for follow-up visits. At these visits:

- You will have a physical exam.
- Blood (about 4-5 tablespoons) be drawn for routine and biomarker tests.
- You will have an MRI, CT scan, and/or PET/CT scan to check the status of the disease.

In addition to the follow-up above, you will have standard of care follow-up visits with the radiation study doctor. It is recommended to follow up at 3 and 6 months after

the completion of the last cycle of BMS-986218 followed by appointments as per standard of care. They will discuss the follow-up visit schedule with you.

Other Information
You should not have any vaccinations while you are taking BMS-986218.

2. POSSIBLE RISKS

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

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

BMS-986218, SBRT, and nivolumab may each 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.

BMS-986218 side effects
This is an early study of BMS-986218, so the side effects are not well known.
Based on early human studies, BMS-986218 may cause:

• fatigue • 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)	• skin itching/rash • constipation • nausea/vomiting • abdominal pain • diarrhea • loss of appetite • low red blood cells	• pain (including back pain) • lung inflammation (possible difficulty breathing) • cough

BMS-986218 may cause dehydration that may be severe enough to require hospitalization.

BMS-986218 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.

BMS-986218 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.

Radiation Therapy Side Effects

It is not known how often the side effects of radiation therapy may occur.
Radiation to the chest and abdomen may cause:

• heart inflammation • heart sac inflammation • chest pain due to heart trouble • heart damage • heart failure • damage to the large artery in the heart, which may lead to heart failure • irregular/fast heartbeat • fatigue • skin redness/irritation/ scaling/sores • scarring of skin in treatment area • hair loss (partial or total) • change of skin color • skin thickening • change in skin texture • loss of appetite • nausea/vomiting • weight loss	• narrowing of esophagus causing swallowing problems • stomach and/or intestinal inflammation (possible indigestion, heartburn, ulcers, cramping, and diarrhea) • stomach damage (possible indigestion, pain, and bleeding) • abnormal connections or passageways between organs or vessels due to tumor destruction • rib fractures • inflammation of esophagus (possible pain on swallowing, heartburn or sense of blockage) • bleeding due to tumor destruction • low blood cell counts (red, white, platelet)	• liver damage (possible liver failure) • weakness • occasional electric shock-like feelings in the lower spine or legs when bending the neck • nerve damage causing pain, loss of strength or feeling in arms • spinal cord damage causing loss of strength or feeling in arms and legs and/or loss of control of bladder and rectum • kidney damage (possible kidney failure and/or high blood pressure) • lung inflammation (possible difficulty breathing, pain, fever, cough) • scarring or shrinking of the lungs

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

are likely to be made worse by chemotherapy before, during, or after radiation therapy.

Nivolumab Side Effects

Common (occurring in more than 10%)

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

Occasional (occurring in 3-10%)

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

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

Rare (occurring in fewer than 3% of patients)

• fast heartbeat • abnormal EKG • heart inflammation/ inflammation of the tissue around the heart (possible chest pain) • high blood pressure • low blood pressure (possible dizziness and/or fainting)	• low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • abnormal blood test (possible pancreas damage) • high blood sugar (possible diabetes)	• nerve damage (affecting the head and neck) • muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision • lung infiltrates (possible infection or inflammation)

• swelling of the brain (possible headache and/or mental status changes) • inflammation of the brain and spinal cord (possible altered consciousness) • inflammation of the membrane around the spinal cord and brain (possible headache and/or coma) • swelling (face/arms/legs) • chills • difficulty sleeping • dizziness • dry/red skin • hives • skin blisters • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • hair loss (partial or total) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the thyroid gland (possible tenderness in the neck) • pituitary gland failure (possible hormone imbalance)	• abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • mouth blisters/sores (possible difficulty swallowing) • constipation • dehydration • dry mouth • inflammation of the intestines • hole in the intestines or stomach (possibly leaking contents into the abdomen) • liver inflammation • liver failure/damage • low blood cell count (platelets, white) • 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) • abnormal kidney test (possible kidney damage) • kidney failure • breakdown of muscle tissue (possible kidney failure) • Guillain-Barre syndrome--damage to the nervous system (causing numbness and/or paralysis)	• difficulty breathing (which can lead to respiratory failure) • cough • infusion reaction (possible fever, rash, pain, and/or swelling) • immune response causing the body to attack itself (possibly causing muscle weakness) • neuromuscular disease (possible weakness of eye, face, breathing and swallowing muscles) (myasthenic syndrome, myasthenia gravis) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • flu-like symptoms • patches of skin color loss • inflammation of multiple areas of the body (see below) • Hemophagocytic lymphohistiocytosis

• blood vessel inflammation	• nerve damage (possible numbness, pain, and/or loss of motor function and/or "pins and needles" sensation)	(HLH) syndrome (see below)

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

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

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

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

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

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

Nivolumab may rarely cause Hemophagocytic lymphohistiocytosis (HLH) syndrome. HLH is a disease that may affect your body's defense system, (your immune system) and certain white blood cells made by your immune system may attack other blood cells. These abnormal blood cells collect in your spleen 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

Using the study drugs together with SBRT 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.

Rarely (in fewer than 3% of patients), major bleeding may occur for lung, mediastinum, liver, and kidney biopsies. Occasionally (in 8-12% of patients) for lung and mediastinum biopsies, you may have a collapsed lung and need to have a chest tube surgically placed. In 15-20% of patients, a collapsed lung that does not require placement of a chest tube may occur.
Biopsies of other organs may have other risks. You should speak with your doctor about the biopsy locations and their risks.

The type of genetic testing being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

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

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

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

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

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

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

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets for up to 5 years and will continue to be stored securely after the study. Only the trial clinical research team will have access to study data.

This study may involve unpredictable risks to the participants.

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

Birth control specifications: If you can become pregnant, you must use at least 1 acceptable form of birth control while you are on study and for:
Group 1: 105 days after the last dose of BMS-986218
Group 2: 155 days (5 months) after the last dose of BMS-986218 and nivolumab or 5 months after the last dose of nivolumab (whichever is later).

Acceptable forms of birth control include:

- Hormonal birth control pills, patch, injections, or implants
- Intrauterine hormone-releasing system (IUS)
- Intrauterine device (IUD)
- Vasectomized partner
- Bilateral tubal occlusion ("tubes tied")

If you can father a child, you must not donate sperm and must use a condom during the study and for:

- **Group 1:** 165 days after the last dose of BMS-986218
- **Group 2:** 215 days after the last dose of BMS-986218 and nivolumab or 7 months after the last dose of nivolumab (whichever is later).

Your female partner should also use an acceptable method of birth control during this same period.

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

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

Getting pregnant **will** result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, the study doctor thinks it is safe to do so, and you were **not** among the first 20 patients enrolled in a study arm, blood (about 3 tablespoons) will be drawn for biomarker testing during screening, 11 days after having SBRT, and if the disease gets worse.

Optional Procedure #2: If you agree, the study doctor thinks it is safe to do so, and you were **not** among the first 20 patients enrolled in a study arm, you will have a core tumor biopsy for biomarker testing during screening, 11 days after having SBRT, and if the disease gets worse.

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. You and/or your insurance provider may be responsible for the cost of radiation therapy while you are on study

Optional Procedure Risks

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

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

Rarely (in fewer than 3% of patients), major bleeding may occur for lung, mediastinum, liver, and kidney are biopsies. Occasionally (in 8-12% of patients) for lung and mediastinum biopsies, you may have a collapsed lung and need to have a chest tube surgically placed. In 15-20% of patients, a collapsed lung that does not require placement of a chest tube may occur.

Biopsies of other organs may have other risks. You should speak with your doctor about the biopsy locations and their risks.

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 blood drawn for biomarker testing?

YES **NO**

Optional Procedure #2: Do you agree to have a tumor biopsy performed for biomarker testing?

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 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. James Welsh, at 1-713-563-2337) 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.

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, 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 supported by: Bristol-Myers Squibb.

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

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Bristol-Myers Squibb 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 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

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a

disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. 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. Ying Yuan (Collaborator) has received compensation as a consultant from Bristol-Myers Squibb and from Juno Therapeutics (a partner of Bristol-Myers Squibb). The financial interests are within the limits of the conflict of interest policy.

Dr. Sumit Subudhi (Collaborator) has received compensation from Bristol-Myers Squibb 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
   - Bristol-Myers Squibb, who is a supporter of this study, and/or any future supporters 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.

Bristol-Myers Squibb is the supporter of this study and is providing the funding and drug support for this study. The samples will be stored in Dr. Welsh's laboratory at MD Anderson. The following individuals will have access to this location: Maria Angelica Cortez, Hampartsoum Barsoumian, and Fatemeh Masrorpour.

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

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

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

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

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

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2020-0479**.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for vulnerable adult participants.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

_____

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION