THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase I Study of Nivolumab in Combination with Ipilimumab for the Treatment of Patients with High Risk or Refractory/Relapsed Acute Myeloid Leukemia and Myelodysplastic Syndrome Following Allogeneic Stem Cell Transplantation
2017-0349

Study Chair: Gheath Alatrash

_____ _____
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

There are 2 parts to this study: Phase 1 (dose escalation) and Phase 2 (dose expansion).

The goal of Phase 1 of this clinical research study is to find the highest tolerable dose of nivolumab or ipilimumab alone that can be given to patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) after receiving an allogeneic stem cell transplant as part of standard care.

The goal of Phase 2 of this study is to learn if the dose of nivolumab and ipilimumab alone found in Part A can be given in combination that may help to control AML and MDS.

The safety of this drug combination will also be studied in both parts. Researchers want to learn if nivolumab and ipilimumab may help to prevent the return of leukemia. Researchers also want to learn if these 2 drugs may cause graft-versus-host disease

(GVHD) to flare up after the transplant. GVHD happens when transplanted donor tissue attacks the tissues of the recipient's body.

This is an investigational study. Ipilimumab is FDA approved and commercially available for the treatment of melanoma. Nivolumab is FDA approved and commercially available for the treatment of certain types of melanoma and lung cancers. The use of ipilimumab in combination with nivolumab after a stem cell transplant for AML and MDS is considered investigational and is being used for research purposes only.

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

The study drugs may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal. You may choose not to take part in this study because of potential costs and/or a prolonged stay out of town.

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 as long as the doctor thinks it is in your best interest.

Nivolumab and ipilimumab will be provided at no cost to you while you are on the study. You and/or your insurance provider will be responsible for the cost of the stem cell transplant and all standard of care tests and medications.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive treatment with other chemotherapy. 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 to help the doctor decide if you are eligible:

- You will have a physical exam.

- Blood (about 3-5 tablespoons) will be drawn for routine tests. This routine blood draw will include a pregnancy test, if you can become pregnant. This pregnancy test may also be a urine test. To take part in this study, you cannot be pregnant.
- You will have a bone marrow aspirate for cytogenetic testing. If you have AML, this sample will also be used for minimal residual disease (MRD) testing. To collect a bone marrow aspirate, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow is withdrawn through a large needle. Cytogenetic testing looks at how genetic changes to cells may affect how the disease may react to the study drug. MRD testing looks for small amounts of remaining AML in the bone marrow. The test to look for MRD is performed routinely in a certified laboratory at MD Anderson and will be used to make decisions about your treatment. The test is investigational and not FDA approved for doctors to decide whether and what type of treatment a patient should receive after a stem cell transplant.
- For patients with extramedullary AML (myeloid sarcoma), you will have a PET/CT scan within 60 days of being enrolled in this study to check the status of the disease.

If you had these tests/procedures recently, they may not need to be repeated. The study doctor will discuss this with you.

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 assigned to 1 of 3 study groups based on when you join this study. Up to 5 participants will be enrolled in Part A and up to 5 participants will be enrolled in Part B (10 participants total). In Phase 2, up to 7 groups of 3 participants will be enrolled in Part C (21 participants total).

Phase 1

Phase 1 is made up of 2 parts: Part A and Part B.

If you are enrolled in **Part A** of the study, the dose of nivolumab you receive will depend on when you joined this study. The first group of participants in Part A will receive the starting dose level of nivolumab. Depending on the side effects seen, the next group may receive a lower or higher dose level of nivolumab.

If you are enrolled in **Part B** of the study, the dose of ipilimumab you receive will depend on when you joined this study. The first group of participants in Part B will receive the starting dose level of ipilimumab. Depending on the side effects seen, the next group may receive a lower or higher dose level of ipilimumab.

Phase 2 (Part C)

If you are enrolled in Phase 2, you will receive a combination of nivolumab and ipilimumab. The dose of nivolumab and ipilimumab you receive will depend on when you join the study and the results seen in Parts A and B of the study.

Up to 31 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Part A:
You will receive nivolumab by vein over about 30 minutes on Days 1 and 15 of Cycles 1-6. Each cycle of will be 4 weeks. However, cycles may be longer or shorter depending on how the disease responds to the treatment and what the doctor thinks is in your best interest.

Part B:
You will receive ipilimumab by vein over about 90 minutes on Day 1 of Cycles 1-6. Each cycle will be about 3 weeks. However, cycles may be longer or shorter depending on how the disease responds to the treatment and what the doctor thinks is in your best interest.

Part C
During combination therapy, you will receive nivolumab by vein over about 30 minutes on Days 1, 15 and 29 of each cycle for 6 cycles. Each cycle will be about 6 weeks. However, cycles may be longer or shorter depending on how the disease responds to the treatment and what the doctor thinks is in your best interest.

You will also receive ipilimumab by vein over about 90 minutes on Day 1 of each cycle for 6 cycles. On Day 1, you will receive nivolumab first and then about 30 minutes later, you will receive ipilimumab.

All Arms:
Tacrolimus will be administered per standard of care. Your tacrolimus dose (which you started taking before or after your stem cell transplant) may be gradually lowered if you do not have GVHD. Your doctor will discuss this with you.

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

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

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

Study Visits

At the start of each cycle, you will have a physical exam.

Once every 2 weeks, blood (about 1 tablespoon) will be drawn for routine tests. If the doctor thinks it is needed, you may have this blood draw more often. If the doctor thinks it is acceptable, you may have these blood draws at a local lab or clinic. The results will be sent to the study doctor at MD Anderson. This option will be discussed with you.

On Days 30, 60, 90, and 120 (+/- 7 days) after the stem cell transplant, if your doctor thinks it is needed, you will have a bone marrow aspiration to check the status of the disease and for chimerism testing. Chimerism testing looks to see how much the blood cells and tissue are mixed between the donor and recipient. This test shows how well the transplant has "taken." If the bone marrow aspiration is not performed, blood (about 1 tablespoon) will be drawn for the chimerism testing.

Any time that the doctor thinks it is needed while you are on study:

- Blood (about 1-2 tablespoons) may be drawn for routine tests.
- You may have a bone marrow aspiration to check the status of the disease. If you have AML, this sample may also be used for MRD testing.
- For patients with extramedullary AML (myeloid sarcoma), you will have a PET/CT scan.

End-of-Study Visit

Within 30 days after your last dose of study drugs:

- You will have a physical exam.
- Blood (about 2-3 tablespoons) will be drawn for routine tests.
- If the doctor thinks it is needed, you will have a bone marrow aspirate/biopsy to check the status of the disease.
- For patients with extramedullary AML (myeloid sarcoma), you will have a PET/CT scan

Long-Term Follow-Up

If the disease appears to be getting better after you complete study treatment, you will be followed as part of your regular care. If the disease did not respond or get better during the study, additional treatment options will be discussed with you.

Other Testing

The study staff may ask you to take part in another MD Anderson lab research study (LAB99-062) for the collection of additional tumor tissue, blood, and/or bone marrow testing, stool samples and nail clippings. The samples will be sent to Dr. Al-Atrash's lab at MD Anderson for testing. The laboratory methods used for these tests are not FDA approved. The results of these tests will not be used to decide whether or what type of therapy you should receive after allogeneic stem cell transplant. The study doctor will discuss this with you and, if you decide to take part, you will sign a separate consent document.

You do not need to take part in this additional research study in order to take part in this study.

2. POSSIBLE RISKS

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

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

Nivolumab, ipilimumab, and tacrolimus 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.

Nivolumab combined with ipilimumab

Common (occurring in more than 10%)

• fatigue/lack of energy • fever • itching • skin rash • 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) • diarrhea	• loss of appetite • nausea/vomiting • abnormal liver test (possible liver 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 heart (possible chest pain) • high blood pressure • low blood pressure (possible dizziness and/or fainting) • swelling of the brain (possible headache	• pituitary gland failure (possible hormone imbalance) • blood vessel inflammation • abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • diabetes complications	• muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision • immune response causing the body to attack itself (possibly causing muscle weakness) • neuromuscular disease (possible weakness of eye,

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)	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)	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

<u>Tacrolimus Side Effects</u>

Common (occurring in more than 20% of patients)

• high blood pressure • swelling • headache • difficulty sleeping • fever • itching and/or skin rash • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure,	• high blood levels of fat (possible heart disease and/or stroke) • diabetes • diarrhea • abdominal pain • nausea/vomiting/upset stomach • constipation • loss of appetite • fluid in the abdomen	• tremors • weakness • abnormal sensation (such as pins and needles) • pain • abnormal kidney test (possible kidney damage) • difficulty breathing (possibly due to lung damage)

heart problems, changes in mental status, and/or seizure) • high blood sugar (possible diabetes) • low blood sugar	• low blood cell counts (red, white, platelets) • abnormal liver tests (possible liver damage, and possibly due to scarring and/or blood clots)	• build-up of fluid around the lungs • infection

Occasional (occurring in 3-20% of patients)

• chest pain (possibly due to heart trouble) • build-up of fluid in the tissue around the heart	• fatigue • dizziness • inflammation of the stomach and/or intestines	• decreased urine output • cough • lung inflammation

Exact frequency unknown but occurring in fewer than 15% of patients

• low blood pressure (possible dizziness/ fainting) • abnormal EKG • irregular/fast/slow heartbeat • heart and/or lung failure • heart attack • enlarged heart • decreased blood supply to the heart • decreased blood supply to the brain caused by stroke • blood vessel disorder (possible tissue death) • increased amount of blood • vein inflammation • blood clots in a vein (possible pain, swelling, and/or redness) • abnormal blood clotting • stroke • flushing • fainting • abnormal dreams	• sweating • skin sores • wound healing problems • abnormal blood acid/base balance (possible organ damage) • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • low blood levels of iron (possible low blood red cell counts and/or weak fingernails) • high blood levels of uric acid (possible painful joints and/or kidney failure) • dehydration • throat inflammation (possible esophageal sore) • mouth blisters/sores • increased appetite • cramps • difficulty swallowing	• high red blood cell count (possible headache, dizziness, and/or stoke) • anemia due to destruction of red blood cells • blockage of the bile tract (possible body yellowing and/or abdominal pain) • liver damage • jaundice (yellowing of skin and/or eyes) • leg cramps • muscle pain, twitching, tightness, and/or spasms • painful joint inflammation • joint disease (possible pain) • loss of bone strength (possible broken bones) • immune response that causes the body to attack itself (causing muscle weakness) • nerve damage (loss of motor or sensory

• difficulty thinking • inability to speak • memory loss • difficulty writing • loss of coordination due to brain dysfunction • difficulty walking • chills • confusion • mood swings or changes (such as agitation, anxiety, depression, and/or nervousness) • nightmares • hallucinations (seeing or hearing things that are not there) • psychosis (loss of contact with reality) • seizure • acne • hair loss (partial or total) • shedding and scaling of the skin (possible fatal loss of bodily fluids) • hair growth • skin sensitivity to sunlight or sunlamps • change of skin color	• gas • abdominal wall inflammation • hole in the intestines (possibly leaking contents into the abdomen) • slow emptying of food from the stomach into the intestines • stomach ulcer • intestinal blockage • fluid-filled sac in the pancreas • inflammation and bleeding of the pancreas (possible abdominal pain and/or tissue death) • weight gain/loss • bladder inflammation (possible pain, bleeding, and/or urge to urinate) • difficult, frequent, and/or painful urination • inability to produce urine • blood in the urine • vaginal inflammation • rectal disease • increased risk of bleeding	function) that is possibly due to pressure on the nerves • paralysis • walking/balance problems (possible falling) • vision problems (such as blurry vision and/or lazy eye) • painful red eyes • hearing loss • ear pain • ringing in the ears • kidney failure • infection-related kidney damage (possible kidney failure) • back-up of urine into the kidney • death of kidney tissue (possible kidney failure) • voice changes • sore throat • hiccups • collapsed lung and/or fluid in the lung (possibly difficulty breathing) • runny nose • flu-like symptoms • allergic reaction • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Tacrolimus may cause you to develop another type of cancer (such as bladder, thyroid, or skin cancer).

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

• sudden stopping of the heart	• brain injury that may be reversible (possible headache, confusion,	• destruction of red blood cells (possible kidney damage and/or failure)

• multiple blood clots (possible organ dysfunction and/or failure) • DIC (breakdown of the blood clotting system) (possible severe bleeding, organ dysfunction, and/or organ failure) • abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage) • tissue swelling • coma • difficulty forming or speaking words • anxiety disorder causing inability to speak • decreased brain function (possible paralysis and/or coma)	seizures, and/or vision loss) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • delirium (loss of contact with reality) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • inflammation and bleeding of the pancreas (possible abdominal pain) • decreased bone marrow function and inability to make red blood cells	• increase in white blood cells • breakdown of muscle tissue (possible kidney failure) • liver failure • blindness • damage to an eye nerve (possible vision changes) • deafness • failure to breathe • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • multiorgan failure • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body)

Tacrolimus may rarely cause you to develop another type of cancer (such as lymphoma [a type of lymph node cancer] or leukemia [a type of blood cancer]).

Tacrolimus also may cause heart damage. It is not known how often this may occur.

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

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.

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.

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.

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 or breastfeed a baby while on this study. You must use birth control during the study and for at least 5 months after the last treatment if you are sexually active and can become pregnant.

Birth Control Specifications:

Females: If you are able to become pregnant, you must use one of the following approved birth control methods during the study and for at least 5 months after the last dose of study drug:

- Female sterilization (have had surgical bilateral removal of the ovaries) or tubal ligation at least 6weeks before starting study treatment
- Progestogen only hormonal birth control. Hormonal methods of birth control including oral birth control pills (combination of estrogen and progesterone), vaginal ring, injectables, implants, transdermal and intrauterine hormone-releasing system (IUS); Intrauterine devices (IUD)

If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away. Getting pregnant may result in your removal from this study.

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. Gheath Alatrash, at 713-792-8750) 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. It may be dangerous to suddenly stop study treatment, and the study doctor can discuss ways to safely withdraw. 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. You may be asked whether the study doctor can continue to collect data from your routine medical care. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, 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 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). 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.

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 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

Samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this

research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

Conflict of Interest

Dr. Naval Daver (Study Co-Chair) has received compensation from Bristol-Myers Squibb as a Consultant. The financial interests are within the limits of the conflict of interest policy.

Dr. Betul Oran (Collaborator) has received compensation from Celgene (a partner of Bristol-Myers Squibb) as a Consultant. The financial interests are within the limits of the conflict of interest policy.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

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 supporter of this study, and/or any future sponsors/supporters of the study
   - Center for International Blood and Marrow Transplantation Research (CIBMTR) and National Marrow Donor Program (NMDP)
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study 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.

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

Leftover tissue, blood, bone marrow samples, stool samples and nail clippings collected as part of this study may be sent to Dr. Gheath Al-Atrash's laboratory at MD Anderson for testing. Some samples also may be sent for exploratory biomarker studies to laboratories at Mount Sinai Hospital in New York City, New York, Stanford University in Palo Alto, California, and the Dana-Farber Cancer Institute in Boston, Massachusetts, as part of the National Institutes of Health Cancer Immune Monitoring and Analysis Centers (CIMACs) program.

All research samples will be stored by the MD Anderson tissue bank. Data collected from samples processed by the NCI CIMAC-CIDC Network with the support of PACT Funds will be required to be stored for future use in a controlled-access, federally compliant database. Access to data collected from testing of your samples or from your deidentified, limited data clinical record will be restricted to people allowed by the PACT partnership, which will eventually include appropriate public access by the research community. Under no circumstances will they know your identity, and all information will be treated as confidential.

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 2017-0349.

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

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

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

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

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

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