UMCC 2018.050

# Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutations

NCT03570619

# UNIVERSITY OF MICHIGAN
# CONSENT TO BE PART OF A RESEARCH STUDY

## INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

## 1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

**1.1 Study title:** IMPACT: Immunotherapy in Patients with Metastatic Cancers and CDK12 Mutation

**1.2 Company or agency sponsoring the study:** The University of Michigan

Financial support for this study is provided by Bristol Myers Squibb (BMS)

**1.3 Names, degrees, and affiliations of the researchers conducting the study:**

**Principal Investigator:**
Ajjai Alva, MD Department of Internal Medicine, Hematology/Oncology, University of Michigan

## 2. PURPOSE OF THIS STUDY

**2.1 Study purpose:**

Cancer is caused by changes (mutations) to genes that control the way our cells function; especially how they repair mistakes that crop up during regular growth and turnover. Some of these mistakes cause cancer, some cause cancer to grow. The normal proof-reading system in the cells tries to fix the DNA mistakes. CDK12 is part of the proof-reading system that fixes DNA mistakes. Cancer cells that carry a broken form of CDK12 cannot correct the DNA mistakes well. However, cancer cells that grow due to these mistakes could have a weakness. The mistakes in the DNA could mark those cells apart and make them sensitive to a type of treatment called immune therapy that is designed to activate the patient's own immune system to go fight the cancer. Learning more about how genes work and how they affect cancer could also lead to improvements in treating cancer.

The purpose of this study is to test the effectiveness (how well the drug works), safety, and tolerability of the investigational drug nivolumab as well as the combination of nivolumab plus ipilimumab for metastatic prostate cancer and other cancer types that have a broken form (called mutations) of the CDK12 gene.

Nivolumab and ipilimumab are two immunotherapy drugs that have been approved by the Food and Drug Administration (FDA) for the treatment of metastatic melanoma (a type of skin cancer) and kidney cancer. Nivolumab is also approved the treatment of previously treated advanced lung, head & neck, liver and kidney cancers. Nivolumab and the combination of nivolumab and ipilimumab has not yet been approved for the

treatment of prostate cancer or other cancers that have CDK12 mutations. The test used to find out if your cancer has the CDK12 mutation has not been approved or cleared by the FDA.

## 3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

### 3.1 Who can take part in this study?

Adult men or women who have metastatic adenocarcinoma of the prostate or other advanced metastatic carcinomas that have CDK12 mutations.

There are many other inclusion and exclusion criteria (a sort of checklist) which the doctors will use to determine if you can participate in this study. It is important that you discuss your full medical history and all of your medications with your doctor.

### 3.2 How many people (subjects) are expected to take part in this study?

A total of approximately 65 subjects at several institutions will take part in this study, including approximately 15 subjects from the University of Michigan.

## 4. INFORMATION ABOUT STUDY PARTICIPATION

### 4.1 What will happen to me in this study?

The study team will explain the research study and answer any questions you have about the study. If you want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Many of the procedures that will be performed during the study, including routine blood tests, disease evaluations, physical examinations, vital signs (blood pressure, heart rate, breathing rate, and temperature) and measurement of height and weight, would normally be done as part of your standard of care regardless of study participation. However, some of these may be done more frequently as a result of your participation in this study. Tests and procedures that are done more often than your regular medical care because of your study participation and that are solely for research purposes will be identified below. The study staff will inform you of the types of tests and procedures you have to undergo during the study.

**During the study you must:**

- Follow the instructions you are given.
- Come to the study center for your visits with the study doctor.
- Tell the study doctor or study staff about any changes in your health and/or medications you are taking.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

**Before starting the study:** Some exams, tests, and procedures including cancer genomic testing, will be required to find out if you can be in this study. If you have had some of the tests recently, they may not need to be repeated. The screening tests and procedures do not have to be completed in one day and you are allowed to take breaks if you have multiple procedures in one day.

The following tests and procedures will be performed during screening and/or at one or more study visits. Refer to the study calendar below for information about which procedures will be performed at certain study visits.

- **Medical history**: including any past treatments, surgeries, infection and autoimmune diseases.

- **Medications**: It is important that you tell your doctor about all of the medications that you have been taking, including over the counter medicines, vitamins or herbal treatments.

- **Physical exam/Vital Signs**: including measurement of your height (screening only), weight, blood pressure, heart rate, respiratory rate and temperature.

- **Performance status**: Your ability to perform day to day activities and care for yourself

- **Routine blood tests (approximately 2 teaspoons)**: will be drawn for tests to check blood counts, chemistry, thyroid health and blood markers for cancer

- **Pregnancy test**: (urine or blood – approximately 1 teaspoon): if you are a woman able to have children

- **Scans of your cancer**: these could include Computed tomography (CT) of the chest, CT or magnetic resonance imaging (MRI) of the upper and lower belly or bone scan (prostate only).
    - A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
    - A MRI scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie down on a narrow bed which will slide into a tunnel that is 6 feet long by 22 inches across and is open at each end. You will be asked to lie quietly for about one hour, during which time you will hear a loud machine-like noise. A MRI scan takes about an hour and a half to complete.
    - **Bone scan**. A bone scan is a procedure in which a very small amount of radioactive material is injected into a vein in your arm. The radioactive material is then transported by your blood into your bones. This will allow the doctor to monitor the cancer in your bones before, during, and after you receive the study treatment.

- **Toxicity evaluation:** You will be asked about any side effects or illnesses you experience.

- **Tumor tissue:** Your doctor will check to see if you have enough stored tissue sample of your tumor that was collected previously. If you do not have enough stored tissue, you will be asked to undergo a fresh tissue biopsy prior to starting treatment. You may still participate in this study even if you do not have enough stored tissue or undergo a fresh tissue biopsy. An optional tissue biopsy may be collected at end of treatment. You can make your choice in Section 12 for the optional biopsies. *This tumor tissue is for research purposes.*

- **Blood for Research (approximately 3-5 tablespoons):** Will be drawn for testing for biomarkers (testing of substances such as proteins that tell us how the drug is working in your body). *This is for research purposes.*

- **Questionnaire:** You will be asked to complete a quality of life questionnaire asking about your symptoms and how your disease and symptoms make you feel. You may find some of the questions uncomfortable to answer. You do not have to answer any question you do not want to answer. *This is for research purposes*.

**Study Intervention (for Research):**

If you qualify to participate in the study based on the results of the screening tests and procedures, you will return to the study doctor's clinic.

If you have metastatic adenocarcinoma of the prostate, you may qualify for either Cohort A or C. If you have another advanced metastatic carcinoma that have CDK12 mutations, you may qualify for Cohort B.

For this study, a treatment cycle is defined as 21 days if your study treatment regimen is with nivolumab and ipilimumab. If your study treatment is nivolumab only, then a cycle is defined as 28 days.

Cohorts A or B: You will receive the combination of nivolumab and ipilimumab given intravenously (through a vein in your arm or port) every three weeks for a maximum of 4 cycles as long as you are tolerating the intervention. Beginning with Cycle 5 you will receive nivolumab alone every 4 weeks for up to 92 weeks as long as you are tolerating the intervention and your disease hasn't progressed. Total study therapy duration will last up to 104 weeks as long as you are tolerating the intervention and disease hasn't progressed.

Cohort C: You will receive nivolumab-only given intravenously (through a vein in your arm or port) every four weeks for a maximum of 26 cycles as long as you are tolerating the intervention. Total study therapy duration will last up to 104 weeks as long as you are tolerating the intervention and disease hasn't progressed.

**Follow-up:**

If you stop the study intervention for any reason you will be asked to return for end of treatment visit 3-4 weeks after your last dose of study intervention.

After you complete the end of treatment you will have an office visit or be contacted by a member of the study team every 3 months for up to 2 years from when you stopped the study intervention.

See the table for a summary of the study intervention and procedures.

**Study Procedures Table:**

| Procedures | Screening | Cycle 1 Day 1 | Cycle 2 Day 1 | Cycle 3 Day 1 | Cycle 4 Day1 | Day 1 of Cycle 5 and beyond | End of Treatment Visit | Follow Up |
|---|---|---|---|---|---|---|---|---|
| Medical history | X | | | | | | | |
| Medication review | X | X | X | X | X | X | X | |
| Toxicity evaluations | X | X | X | X | X | X | X | X |
| Physical Exam/vital signs | X | X | X | X | X | X | X | |
| Performance Status | X | X | X | X | X | X | X | |
| Pregnancy Test | X | | | | | | | |
| Routine Blood Tests | X | X | X | X | X | X | X | X |
| Scans/Imaging of your cancer | X | | | | | X<br>Every 12 weeks | | |
| Questionnaires | X | | | | | X<br>Every 12 weeks | | |
| Archive Tumor Tissue submission | X | | | | | | | |
| Fresh Biopsy | X *(optional)* | | | | | | X *(optional)* | |
| Research blood | | X | X | X | | X<br>Every 12 weeks | X | |
| Survival Status | | | | | | | | X |

We will collect and store information about your genes. The DNA contained in your genes holds the instructions that your body uses to grow and function. Your genes are responsible for your physical features such as eye color, blood type, and how your body breaks down medications. Genes can also be responsible for some medical conditions.

*Genomic* information relates to the structure and function of all of the genetic material in the body.

We will submit your genomic information to a repository to be used for scientific purposes. A repository contains information from many people. Some repositories are maintained by the University of Michigan, some are maintained by the federal government, and some are maintained by private companies.

Researchers all over the world can take information from the repository and use it in their studies. Their studies may be similar to this one or may be completely different.

Because this research receives funding from the National Institutes of Health (NIH), we will submit your genomic information to a public repository approved by NIH. NIH is a national research agency and is part of the federal government.

We will label your genomic information with a code, instead of your name or other information that people could use to directly identify you. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally. NIH prohibits people from trying to identify individuals whose genomic information is in an NIH-designated repository.

Researchers will have *unrestricted access* to your specific genomic information. Unrestricted access means that researchers may obtain genomic information from the repository without special approval from NIH.

If you allow us to put your genomic information in the repository, you can change your mind later and ask us to remove it. Keep in mind, however, that we cannot take back information that other researchers have already obtained from the repository.

<u>OPTIONAL Research Samples Stored for Future Use:</u>
We will keep some of your research blood and tumor tissue, as well as medical information (such as gender, race, and how your cancer responded to the study intervention, etc.) so that we may study them in future research. The future research may be similar to this study or may be completely different and may include genetic analysis on your tissue. Your samples would be kept at the University of Michigan. Samples will be stored indefinitely or until they are used up.

By taking part in this study, you are giving us your permission to use your blood, tumor tissue and medical information for future research. Even if you give us permission now to keep some of your blood, tissue and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your blood and tissue, we may not be able to take the information out of our research.

We may share your blood, tumor tissue and medical information with other researchers, so that they can use it in their research with the overall aim of helping future patients. No identifiable information that could be directly linked to you will be provided. Their research may be similar to this study or may be completely different. Once we have shared your blood, tissue and medical information with other researchers, we will not be able to get it

back. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your blood and tumor tissue samples. Allowing us to do future research on your blood, tissue and medical information will not benefit you directly.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the future research on your blood, tumor tissue and medical information. You will not have rights to these discoveries or any proceeds from them
You will be asked to affirm in Section 12 of this consent form that you understand your participation in this Optional sub-study (storage of research samples for future use)

**4.2 How much of my time will be needed to take part in this study?**
The initial screening visit will take approximately 2-5 hours. Each study visit is expected to take approximately 4-6 hours.

**4.3 When will my participation in the study be over?**
The maximum time you will be in the study is up to 104 weeks of study treatment and will depend on how your disease responds to the study intervention and how well you tolerate the study intervention. After you stop taking the study intervention you will be asked to come back for an end of treatment visit and then we will follow you either by phone or a clinic visit for up to 24 months. Your participation may end sooner if you decide to no longer participate, your study doctor feels it is in your best interest to stop your study participation, your disease progresses or the study is ended. You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular physician first.

**4.4 What will happen with my information and/or biospecimens used in this study?**
Your biospecimens and collected information may be shared with Bristol Myers Squibb.

With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

## 5. INFORMATION ABOUT RISKS AND BENEFITS

**5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?**
The drugs used in the study may cause certain side effects and discomforts. You may have all, some, or none of the known side effects. There is also a risk that other rare or unknown side effects may occur. Your doctors and nurses will check you closely for side effects, and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study medication is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death. If you have any side effects, it is important that you report them to your study doctor or research staff.

We will minimize the risks by monitoring you carefully. We will provide the usual supportive care that would be

routinely given to someone with your condition. If you have side effects from the study intervention, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the study intervention if the side effects are too serious.

The known or expected risks are:

**Side Effects ASSOCIATED WITH NIVOLUMAB**

Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects that you experience.

Very common side effects of nivolumab are [≥ 1/10 or ≥ 10%]

- Diarrhea
- Feeling tired or lack of energy
- Skin itching
- Skin rash

Common side effects of nivolumab include: [≥ 1/100 to <1/10 or ≥ 1% to < 10%]

- Abdominal pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- Allergic reaction/ hypersensitivity
- ALT increased: lab test result associated with abnormal liver function
- Amylase increased: lab test result associated with pancreas inflammation
- AST increased: lab test result associated with abnormal liver function
- Bilirubin increased (lab test results associated with abnormal liver function)
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased appetite
- Dizziness or vertigo (feeling off balance which can lead to dizziness)
- Dry mouth
- Dry skin
- Fever
- Headache
- Increased blood sugar
- Lipase increased: lab test result associated with pancreas inflammation
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Loss of color (pigment) from areas of skin
- Low levels of sodium in the blood
- Low platelet counts (thrombocytopenia): this may increase your risk for skin bruising, nose bleeds, and bleeding from the gums
- Low red blood cell counts (anemia): this may make you feel weak and tired

- Lung inflammation (pneumonitis): It is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.
- Nausea
- Pain in the muscles, bones, ligaments, tendons, and nerves
- Reaction related to infusion of the medicine. The symptoms may include but not limited to fever, rash, pain, swelling
- Redness of the skin
- Shortness of breath
- Swelling, including face, arms, and legs (edema)
- Thyroid gland function decreased or may be increased; increased thyroid stimulating hormone- a lab test result associated with abnormal thyroid function
- Thyroid stimulating hormone increased: lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Vomiting

Uncommon side effects of nivolumab include: [≥ 1/1,000 to < 1/100 or ≥ 0.1% to <1%]

- Bronchitis: inflammation of the lining of bronchial tubes, which carry air to and from the lungs
- Decreased secretion of hormones produced by adrenal glands
- Decreased thyroid stimulating hormone - a lab test result associated with abnormal thyroid function
- Dehydration
- Diabetes: a disease that results in too much sugar in the blood
- Dry eye
- Erythema multiforme: a skin disorder that is considered to be an allergic reaction to medicine or an infection. Symptoms may include symmetrical, red raised skins areas that can appear all over the body, more noticeable on the fingers and toes. These patches often look like “targets” (dark circles with purple-grey centers)
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Joint pain and stiffness
- Kidney function failure, kidney disease
- Liver inflammation
- Low blood pressure

- Low white blood cell counts (neutropenia): these put you at higher risk for infection
- Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue
- Respiratory failure: a condition in which not enough oxygen passes from your lungs into your blood, or when your lungs cannot properly remove carbon dioxide
- Skin disease with thickened patches of red skin, often silvery scales (Psoriasis)
- Trouble falling and/or staying asleep (Insomnia)
- Underactive function of the pituitary gland situated at the base of the brain
- Upper respiratory tract infection: A common viral / bacterial infection that affects the nose, throat, and airways

- Vision blurred

Rare side effects of nivolumab include: [≥ 1/10,000 to < 1/1,000 or ≥ 0.01% to <.1%]

- Autoimmune hemolytic anemia: a malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were foreign substances to the body
- Cranial nerve disorder
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids and diabetic coma
- Disease caused by the body's immune system attaching healthy organs
- Double vision
- Drug induced liver injury
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains
- Inflammation of blood vessels
- Inflammation of the brain, potentially life-threatening or fatal
- Inflammation of the heart
- Inflammation of the lining of the brain and spinal cord
- Lung infiltrates, associated with infection of inflammation
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Pericarditis: a swelling and irritation of the thin saclike membrane surrounding the heart (pericardium)
- Polymyalgia rheumatica: an inflammatory disease that causes muscle pain and stiffness, especially in the shoulders
- Rhabdomyolsis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Rupture of the intestines/hole in the intestine
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Severe allergic reaction may include but not limited to high grade fever, rash, swelling and pain
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membrane, resulting in blistering and shedding of skin

- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn

The following events have been identified during post-approval use of nivolumab. Because reports are voluntary from a population of unknown size, an estimate of frequency cannot be made.

- Graft-versus-host-disease: a condition that occurs when donor bone marrow or stem cells attack the recipient
- Hemophagocytic lymphohistiocytosis (HLH) syndrome: a disease that may affect your body's defense system, called immune system. Certain white blood cells may attack other blood cells. These abnormal blood cells collect in your spleen and liver, causing these organs to enlarge. The symptoms may include fever, rash, and low blood cell counts
- Solid organ transplant rejection
- Vogt Koyanagi Harada syndrome: a disease that affects the pigmented tissue; this may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss , ringing in the ears and /or the skin leading to loss of skin color

**Additional information on pneumonitis:**
Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest x-rays and/or CT scans. Complications, including fatal events, have occurred in patients who received allogeneic hematopoietic stem cell transplantation (HSCT) after nivolumab.

**Please inform your study doctor or nurse <u>AT ONCE</u> if you experience any of the following:**

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example, any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab treatment, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

**Additional information on transplant risks:**
Complications, including fatal events, have occurred in patients who received allogeneic hematopoietic stem cell transplantation (HSCT) before or after nivolumab.

Complications, including rejection, have also been reported in patients who have received an organ or tissue transplant. Treatment with nivolumab may increase the risk of rejection of the organ or tissue transplant.

## Side Effects ASSOCIATED WITH NIVOLUMAB combined with Ipilimumab

Very common side effects (≥ 1/10 or ≥10%) of nivolumab combined with ipilimumab are:

- ALT increased: lab test result associated with abnormal liver function
- AST increased: lab test result associated with abnormal liver function
- Decreased appetite
- Diarrhea
- Feeling tired or lack of energy
- Fever
- Lipase increased: lab test results associated with pancreas inflammation
- Nausea
- Skin itching
- Skin rash
- Thyroid function decreased

Common side effects (≥ 1/100 to <1/10 or ≥1% to <10%) of nivolumab combined with ipilimumab include:

- Abdominal pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- Allergic reaction/hypersensitivity
- Amylase increased: lab test result associated with pancreas inflammation
- Bilirubin increased: lab test result associated with abnormal liver function
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased secretion of hormones produced by adrenal glands
- Dehydration
- Diabetes: a disease that results in too much sugar in the blood
- Dizziness or vertigo (feeling off balance which can lead to dizziness)
- Dry eye
- Dry mouth
- Dry skin
- Hair loss
- Headache
- Heart rate increased
- Increased blood sugar
- Inflammation of the colon (may also include small intestine)
- Inflammation of the eye

- Inflammation of the mouth
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the thyroid gland
- Kidney function failure, kidney disease
- Joint pain or stiffness
- Liver inflammation
- Loss of color (pigment) from areas of skin
- Low blood pressure
- Low levels of sodium in the blood
- Low platelet counts (thrombocytopenia): this may increase your risk for skin bruising, nose bleeds, and bleeding from the gums
- Low red blood cell counts (anemia): this may make you feel weak and tired
- Lung inflammation (pneumonitis): it is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported in patients treated with nivolumab. While many patients with X-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue
- Pain in the muscles, bones, ligaments, tendons, and nerves
- Reaction related to infusion of the medicine. The symptoms may include but not limited to fever, rash pain, swelling
- Redness of the skin
- Kidney failure or damage to your kidneys
- Shortness of breath
- Sodium levels in blood low
- Swelling, including face, arms, and legs (edema)
- Thyroid gland function may be increased; increased or decreased thyroid stimulating hormone- a lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Trouble falling and/or staying asleep (insomnia)
- Vision blurred
- Vomiting

Uncommon (> 1/1,000 to <1/100 or ≥0.1% to <1%) side effects of nivolumab combined with ipilimumab include:

- Bronchitis: Inflammation of the lining of bronchial tubes, which carry air to and from the lungs
- Cranial nerve disorder
- Diabetes complications resulting in excess blood acids and diabetic coma
- Disease caused by the body's immune system attacking healthy organs
- Double vision
- Drug-induced liver injury
- Erythema multiforme: a skin disorder that's considered to be an allergic reaction to medicine or an infection. Symptoms may include symmetrical, red, raised skin areas that can appear all over the body,

more noticeable on the fingers and toes. These patches often look like “targets” (dark circles with purple-grey centers)
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the brain (potentially life threatening or fatal)
- Inflammation of the heart
- Inflammation of the kidney
- Inflammation of the stomach
- Low white blood cell counts (neutropenia): these put you at higher risk for infection
- Lung infiltrates, associated with infection or inflammation
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue
- Respiratory failure: a condition in which not enough oxygen passes from your lungs into your blood, or when your lungs cannot properly remove carbon dioxide
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Psoriasis: characterized by thickened patches of red skin, often silvery scales
- Underactive function of the pituitary gland situated at the base of the brain
- Upper respiratory infection: a common viral / bacterial infection that affects the nose, throat, and airways

Rare side effects (≥ 1/10,000 to < 1/1,000 or ≥0.01% to <0.1%) side effects of nivolumab combined with ipilimumab include:
- Autoimmune hemolytic anemia: a malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were foreign substances to the body
- Diabetes complications resulting in diabetic coma
- Inflammation of blood vessels
- Inflammation of the lining of the brain and spinal cord
- Pericarditis: a swelling and irritation of the thin saclike membrane surrounding the heart (pericardium)
- Rosacea: acne-like skin condition resulting in redness of face
- Polymyalgia rheumatica: an inflammatory disorder that causes muscle pain and stiffness, especially in the shoulders
- Rupture of the intestine/hole in the intestine
- Severe allergic reaction may include but not limited to hg
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn

The following events have been identified during post-approval use of nivolumab or nivolumab combined with ipilimumab. Because reports are voluntary from a population of unknown size, an estimate of frequency cannot be made.

- Drug hypersensitivity syndrome: a severe, unexpected reaction to a medicine, which affects several organ systems at the same time
- Graft-versus-host-disease: a condition that occurs when donor bone marrow or stem cells attack the recipient
- Hemophagocytic lymphohistiocytosis (HLH) syndrome: a disease that may affect your body's defense system, called immune system. Certain white blood cells may attack other blood cells. These abnormal blood cells collect in your spleen and liver, causing these organs to enlarge. The symptoms may include fever, rash, and low blood cell counts
- Solid organ transplant rejection
- Vogt-Koyanagi-Harada (VKH) disease: a disease that may affect several parts of the body, including the eyes, ears, nervous system, and skin. The symptoms may include eye swelling, pain and/or blurred vision; hearing loss, ringing in the ears; and /or loss of skin color

**Risks of CT Scan**

The contrast substance injected during the CT scan may cause pain, burning feeling, sweating and rarely a serious allergic reaction that can be serious. If you know you're allergic to iodine you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated and if you're older. In addition, your thyroid function may be affected. Please inform your doctor if this is the case.

CT imaging uses ionizing radiation, which increases your risk to develop cancer. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation. The estimated additional lifetime risk of developing a potentially fatal cancer from a standard CT scan is approximately 1 in 2,000.

**Risks of MRI Scan**

Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks of MRI include: feeling fearful of being in a small enclosed space (claustrophobia) when you are lying inside the MRI scanner, feeling uncomfortable because of the loud noises made by the machines, and feeling uncomfortable with the physical sensations you may feel during the process. You are also exposed to some risk because of the injected contrast, gadolinium-DTPA, which may cause headache, nausea, and local burning sensation.

The contrast agent, gadolinium has been linked to development of Nephrogenic Fibrosing Dermopathy (NFD) (also known as Nephrogenic Systemic Fibrosis (NSF) This causes a thickening of the skin, organs and other tissues, and is a rare complication in patients with kidney disease that undergo an MRI with contrast material. To help prevent this, we will check how well your kidneys work before you have any MRIs. Because of the use of contrast, all female subjects who are able to have children will be required to use adequate birth control. If you have implanted metal objects such as a pacemaker, artificial limbs, or metal joints, you will not be able to have an MRI done, and may not be able to take part in this research.

**Bone Scan**

During a bone scan, you will be injected with radioactive material which collects in your bones and then shows up on a special camera. This means that you will be exposed to a low level of radiation. The tracer contains about the same amount of radiation as an x-ray. The injection of radionuclide may cause some discomfort and bruising.

**Blood tests**
Blood samples will be taken from a vein in your arm during the study. The taking of a blood sample may cause some discomfort and bruising, and there is a potential for infection. Other risks, although rare, include dizziness and fainting.

**Tumor Biopsy**
Risks associated with biopsy should be discussed with your study doctor and may include pain, bleeding, spread of cancer and infection. It is also possible to have an allergy to the anesthesia used.

- Genetic material, including DNA and RNA, will be obtained from samples, stored in freezers, and used for profiling and analyzing your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison. The goal is to identify key changes in the genes important to cancer cells that could potentially influence clinical decision making for your cancer. However, success or clinical benefits from the profiling of your cancer DNA is not guaranteed.

- Some cells from your tumor may be grown and used to create cell lines that can be used as an ongoing source of genetic material or used for laboratory research. Additional analysis of the sequencing data will be used for research purposes, for example to discover new, unknown associations between genes and cancer. This type of research may affect the lives of future patients with cancer.

- It is possible that a mutation found in the tumor DNA is also a mutation in your normal tissue (inheritable, or passed down in families). Your study doctor will discuss this result with you. If your test results show that you have gene mutations that are inherited, your doctor should recommend that you meet with a genetic counselor. This referral is considered standard care and is not part of this study.

- As with all medical screening tests, there is a chance of a false positive or a false negative result. A “false positive” refers to the identification of a genetic change that is not present. A “false negative” is the failure to find a genetic change that indeed exists. The tests have been designed to ensure that the possibility of incorrect results is low.

**Questionnaires**
Filling out the questionnaires could lead you to feel uncomfortable or upset. Please tell the study doctor or study staff if you feel uncomfortable or upset while filling out a questionnaire. You have the right to refuse to answer any questions.

**Research samples/Loss of Confidentiality**
Your samples will be coded, however, there is a risk of loss of confidentiality of your information. If your samples are provided to research collaborators the following information may be made available: your diagnosis and treatments, the time the samples were collected in relation to your study regimen, your disease status, and demographic data (for example gender, race, age, etc.). Please ask the Study Doctor or Study Coordinator if you would like to know more about how your information will be protected.

**Pregnancy**

**Women**

If you are a woman of child bearing potential, you must not have sexual intercourse or you must use reliable birth control throughout the study and for 5 months after the last dose of study drugs. The study doctor will discuss methods of birth control with you if needed.

If you are pregnant or become pregnant or are nursing a child during the study, there may be risks to your unborn baby or nursing child. Some drugs cause premature (early) birth or birth defects. Nobody knows what all of these risks are right now.

If you become pregnant or think you may be pregnant during the study, immediately stop using the study drugs and contact the study doctor's office **immediately**. You must not breast-feed an infant during the study. Please also inform the study doctor if you become pregnant up to 5 months after the completion of the study drugs.
If there is ANY chance that you can get pregnant, you must either agree to not have vaginal intercourse or you must use TWO types of birth control (one from each list below) AT THE SAME TIME.

You must use two types of birth control at the same time for medical reasons all during study treatment (including during temporary breaks from treatment), and for at least 5 months after study treatment has stopped. You must talk to the doctor before changing any birth control methods you have already agreed to use.

**Primary forms**
- tubal sterilization (tubes tied)
- partner's vasectomy
- intrauterine device

**Secondary forms**
- male latex condom with or without spermicide
- diaphragm with spermicide
- cervical cap with spermicide
- vaginal sponge (contains spermicide)

Any birth control method can fail. The reports of birth control failing are more frequent for female patients who use only a single form of birth control. Using two forms of birth control at the same time greatly reduces the chances of pregnancy.

**Men**

All men must use an acceptable form of birth control while taking part in the study and for 7 months after treatment has stopped because the effects on sperm are not known. Acceptable forms of birth control are male latex condom (with or without spermicide) or vasectomy. Also, men should not donate sperm or semen while taking part in the study because the effects on sperm are not known.

The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished. If you become pregnant during the study, the study doctor or his/her staff will ask to contact you and your pregnancy physician for information about the pregnancy until the child is born and may share this information with the sponsor.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

As with any research study, there may be additional risks that are unknown or unexpected.

**5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?**
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

**5.3 If I take part in this study, can I also participate in other studies?**
*Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies*. You should not take part in more than one study without approval from the researchers involved in each study.

**5.4 How could I benefit if I take part in this study? How could others benefit?**
You may or may not receive any personal benefits from being in this study. However, others may benefit from the knowledge gained from this study.

**5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?**
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

## 6. OTHER OPTIONS

**6.1 If I decide not to take part in this study, what other options do I have?**
You do not have to be in this study to get treatment for your cancer. Other possible options include:

- Treatment with standard of care drugs such as: enzalutamide, abiraterone + prednisone, or chemotherapy such as docetaxel or cabazitaxel.
- You could participate in other research trials, if one is available.
- You could choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

You should talk to your study doctor and your regular physician about each of your options and their risks and benefits before you decide if you want to take part in this study.

## 7. ENDING THE STUDY

**7.1 If I want to stop participating in the study, what should I do?**
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below).

**7.2 Could there be any harm to me if I decide to leave the study before it is finished?**
If you decide to leave the study early, please notify someone on the study team. They will instruct you on how to stop the study safely and you will be advised whether any additional test may need to be done for your safety.

**7.3 Could the researchers take me out of the study even if I want to continue to participate?**
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

## 8. FINANCIAL INFORMATION

**8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?**
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

Nivolumab and ipilimumab will be provided by BMS free of charge.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices (such as the cost of the infusion)
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services
- Treatment of complications

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Ajjai Alva, at (734) 936-0091 or (734) 936-4000 (24-hour paging). The doctor will either treat you or send you to another doctor for treatment. You or your insurance provider will be billed for all costs of treatment for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

By signing this form, you do not give up your legal rights to seek payment if you are harmed as a result of being in this study.

**8.2 Will I be paid or given anything for taking part in this study?**
You will not be paid to take part in this study.

**8.3 Who could profit or financially benefit from the study results?**
Information obtained from this study may help the supporter BMS and/or the University of Michigan learn more about the causes, risks, treatments, or how to prevent this and other health problems. BMS, the University of Michigan, and/or physicians at the university could profit financially from this information. Dr. Alva and Dr. Vaishampayan serve as paid consultants to BMS.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

## 9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

### 9.1 How will the researchers protect my privacy?

The University of Michigan has rules to protect information about you. Federal and state laws also protect your privacy. Upon enrolling in this study, you will be assigned a unique identification number. All records related to the study will use this identification number instead of your name or other personally identifying information whenever possible. We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the SPONSOR which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of the following for example: reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file.

You have the right to request access to your protected health information that is used or shared during this research and that is related to your study treatment for your disease, but you may access this information only after the study is completed. To request this information, please contact the researchers listed in Section 10 "Contact Information" (below).

**Genetic Risks:**

The federal 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 does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain 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 obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

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.

**9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?**

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease or other communicable disease status
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University of Michigan, Food and Drug Administration (FDA), and/or other government officials, auditors and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- BMS or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular University of Michigan medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

**9.3 What happens to information about me after the study is over or if I cancel my permission?**
As a rule, the researchers will not continue to use or disclose information about you but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help the University of Michigan and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices." This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Section 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

**9.4 When does my permission expire?**
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

## 10. CONTACT INFORMATION

**10.1 Who can I contact about this study?**

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

| | |
|---|---|
| Principal Investigator: | Ajjai Alva, MD |
| Mailing Address: | University of Michigan<br>1500 East Medical Center Drive, 7316CC<br>Ann Arbor, MI 48109-5946 |
| Telephone: | 734-936-0091 |
| Emergency Contact: | 734-936-4000 (Hospital Operator - 24-hour paging) |

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
*When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.*

## 11. RECORD OF INFORMATION PROVIDED

**11.1 What documents will be given to me?**

Your signature in the next section means that you have received signed and dated copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*
- Other (specify):_____

## 12. SIGNATURES

**Consent/Assent to Participate in the Research Study**

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with_____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

**Consent/Assent for Participating in Optional Biopsies**

This study involves optional biopsies. I understand that it is my choice whether or not to take part in these optional biopsies. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

**Screening biopsy**

_____ Yes, I agree to take part in the optional screening biopsy.

_____ No, I do not agree to take part in the optional screening biopsy.

**End of treatment biopsy**

_____ Yes, I agree to take part in the optional end of treatment biopsy.

_____ No, I do not agree to take part in the optional end of treatment biopsy.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

**Consent/Assent to Collect and Store OPTIONAL Research Samples for Unspecified Future Research**
This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to take part in this optional research. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep and store my blood and tissue samples for future research.

_____ No, I do not agree to let the study team keep and store my blood and tissue for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

**Principal Investigator or Designee**

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

UMCC 2018.050

# PERSONAL CENSUS FORM

Name _____ Date _____

The National Cancer Institute requires that The University of Michigan Comprehensive Cancer Center report race and ethnicity information about people who participate in clinical research to ensure that all populations are offered the opportunity to participate.

☐ Check here if you do not wish to provide some or all of the information below.

1. What race do you consider yourself to be? (Please select *one or more*)
   - ☐ American Indian/Alaska Native[a]
   - ☐ Asian[b]
   - ☐ Black or African American[c]
   - ☐ Native Hawaiian or Other Pacific Islander[d]
   - ☐ White[e]
   - ☐ More than one race[f]
2. Do you consider yourself to be Hispanic[g]? ☐ Yes ☐ No

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[a] American Indian or Alaska Native- A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

[b] Asian- A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand and Vietnam.

[c] Black or African American- A person having origins in any of the black racial groups of Africa. (Terms such as “Haitian” or “Negro” are sometimes used in addition to “Black” or “African American.”)

[d] Native Hawaiian or Other Pacific Islander- A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

[e] White- A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

[f] More than one race- (It is preferred that this be selected in addition to the selection of the specific races listed above, but this may also be solely selected.)

[g] Hispanic or Latino- A person of Mexican, Puerto Rican, Cuban, Central or South American, or other Spanish culture or origin, regardless of race. The term “Spanish origin” is sometimes used in addition to “Hispanic” or “Latino.”