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| ID: UMCC 2017.077 | Abraxane With Anti-PD1/PDL1 in Patients With Advanced Urothelial Cancer | NCT03240016 |

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

## 1. KEY INFORMATION ABOUT THE RESEARCHERS AND THE STUDY

**Study title:** ABLE: Phase 2, Single Arm, Two-Stage Study of Abraxane with Anti-PD1/PDL1 in Patients with Advanced Urothelial Cancer

**Company or agency sponsoring the study:**
The University of Michigan is the sponsor of this trial and Dr. Ajjai Alva is the lead investigator.

The study is also supported by the Celgene Corporation, who is supplying the drug Abraxane.

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

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

### 1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find childcare, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This is a Phase II study, which means the goal is to test the effectiveness and safety of the investigational combination of abraxane and the anti-PD1 immunotherapy drug called pembrolizumab. The purpose of this study is to determine the effectiveness of the combination. Another purpose of the study is to determine if people with urothelial cancer are able to tolerate the combination.

This research is studying a new drug in small numbers of people to learn about its safety and its effect on your body at certain doses as a treatment for Advanced Urothelial Cancer. This study will test the effectiveness and safety of the investigational combination of abraxane and the anti-PD1 immunotherapy drug called pembrolizumab. The purpose of this study is to determine the effectiveness of the combination. Another purpose

of the study is to determine if people with urothelial cancer are able to tolerate the combination. Your health-related information and biospecimens (blood and urine) will be collected for this research study.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include:

- Risks of Pembrolizumab: Itching of the skin, loose or watery stools, cough, joint pain, fever, back pain, immune –related reactions and rash
- Risks of Abraxane: Decreased levels of red blood cells, the cells that carry oxygen (anemia), decreased levels of a type of white blood cell (neutrophils, leukocytes) that helps fight infection, decreased levels of platelets, the cells that help the blood clot, abdominal pain, constipation, diarrhea, nausea and vomiting
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More detailed information will be provided later in this document.

This study may not offer any benefit to you now but may benefit others in the future by creating knowledge about how best to treat your disease in the future. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be 24 months.

You can decide not to be in this study. Alternatives to joining this study include: standard treatment for this condition, taking part in a different study, or having no treatment.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

## 2. PURPOSE OF THIS STUDY

**2.1 Study purpose:**

This study is looking at the commonest type of bladder cancer called urothelial carcinoma. A common treatment option for urothelial carcinoma is chemotherapy combination containing a drug called cisplatin. You are being asked to take part in this study because you have advanced urothelial cancer. Advanced means that the cancer has spread to other parts of the body beyond where it started (metastatic) or has progressed locally and cannot be surgically removed.

Immunotherapy is a type of therapy that boosts the body's natural defenses (immune system) to fight cancer. Pembrolizumab (Keytruda®) is a type of immunotherapy drug. Pembrolizumab is approved by the FDA for the treatment of patients with metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy or whose tumors have progressed after platinum-containing chemotherapy. Abraxane is approved by the U.S. Food and Drug Administration (FDA) for use in certain metastatic breast cancers, locally advanced or metastatic non-small cell lung cancer, and metastatic pancreatic cancer. Abraxane is not yet approved by the FDA by itself for urothelial cancer.

## 3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you do not 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?**
You are being asked to take part in this study because you have a type of cancer called urothelial carcinoma that has spread to other parts of the body (metastatic) or has progressed and cannot be surgically removed.

Every study has strict guidelines for determining which people may participate. These are called eligibility criteria. You will need to meet all of these criteria before you can participate in this study. If you agree to consider participating in this study, you will undergo evaluations to see if you meet the eligibility criteria for this study. Even though you may meet all the criteria for participation, it is possible that you may not be enrolled in this study for other reasons.

**3.2 How many people (subjects) are expected to take part in this study?**
About 36 people are expected to participate in this study, all at the University of Michigan.

## 4. INFORMATION ABOUT STUDY PARTICIPATION

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

**Study Visits:**
The study team will explain the research study and answer any questions you have about the study. If you still want to participate in the study the study team will request you sign the consent form prior to any activities pertaining 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.

Once it is determined you are eligible to enter the study, tests and procedures done at your study visits as part of your regular cancer care will continue, but some may be done more often because you are participating in this research study. Also, some of the tests or procedures may have to be repeated if, for example, they were done too long ago or the results are not normal.

Some tests and procedures may be done that are not part of your regular cancer care and are being done only for this research study. Tests and procedures that are performed more often or are not part of your standard cancer care will be identified below as “for research”.

Refer to the study calendar at the end of this consent form for information about what to expect during each study visit.

**Before you can begin the study (Screening Period):**
You will need to have certain exams, tests, or procedures to find out if you can be in the study. These will be done after you sign the consent but before you can start study treatment (called the screening period). If you have had some of the screening procedures 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 or procedures will be performed at screening:

- You will be asked about your medical history, including any past treatments
- You will be asked about any medications you have taking, including over the counter medicines, vitamins, or herbal treatments
- You will be asked about any side effects you have experienced
- You will be asked about how well you are able to perform daily tasks (performance status)
- Physical exam, including weight, and vital signs

- Blood for routine tests to check your health (blood counts, blood chemistry) and organ function
- Blood to test for hepatitis B, hepatitis C, and HIV
- Pregnancy test will be performed if you are a woman able to have children. This may be a blood test or a urine test.
- Computed tomography (CT) of the chest and CT or magnetic resonance imaging (MRI) of the abdomen and pelvis. A CT or MRI of the brain may be performed if clinically indicated.
    - 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" (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.
    - An MRI scan takes an image of your body using magnets
- Correlative studies for research will be performed on some of your samples.
    - Approximately 4 teaspoons of blood will be collected for correlative studies.
    - A part of your tumor tissue collected during a previous biopsy or surgery (archival) will be used for correlative studies. You will not need to have a new biopsy for this part of the study.
    - Refer to "Research Samples Stored for Future Use" below for more information.
- You will be asked to complete questionnaires asking about your symptoms and health. 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.

**While you are receiving the study intervention (Study Intervention Period):**
The study intervention period consists of blocks of time called "cycles" and each cycle lasts 21 days (three weeks). You may continue to receive the study drugs until your disease gets worse or you choose to withdraw from the study, or your doctor decides it is in your best interest to stop taking the study drugs. You will be asked to come to the clinic on Day 1 and Day 8 of each cycle.

You will receive abraxane intravenously on Day 1 and Day 8 of every cycle. You will also receive pembrolizumab intravenously on Day 1 of every cycle.

The following tests and procedures will be performed at one or more study visits. Refer to the study calendar at the end of this consent form for information about which procedures will be performed at certain study visits.

- You will be asked about your medical history, including any past treatments
- You will be asked about any medications you have taking, including over the counter medicines, vitamins, or herbal treatments
- You will be asked about any side effects you have experienced
- You will be asked about how well you are able to perform daily tasks (performance status)
- Physical exam, including weight, and vital signs
- Blood for routine tests to check your health (blood counts, blood chemistry) and organ function
- Computed tomography (CT) of the chest and CT or magnetic resonance imaging (MRI) of the abdomen and pelvis. A CT or MRI of the brain may be performed if clinically indicated.
    - 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" (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.
    - An MRI scan takes an image of your body using magnets

- You will be asked to complete questionnaires asking about your symptoms and health. 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.

**End of Treatment and Follow-up Visits:**
After your last dose of study drugs, you will be asked to come back to the clinic for and End of Treatment Visit.

If you complete 17 cycles of study drug, decide to withdraw, or your study doctor decides it is in your best interest to stop taking the study drug, you will be asked to come back for an End of Treatment Visit. Afterwards, you will be followed every 12 weeks for 2 years via phone call or clinic visit. Refer to the study calendar at the end of this consent form for information about which procedures will be performed at certain study visits.

**Research Samples Stored for Future Use:**
The study team will keep some of your samples to store and use in future research. The future research may be similar to this study or may be completely different. Some of these tests may include your genes or genetic information. 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. Your samples would be kept at the University of Michigan. Samples will be stored indefinitely or until they are used up.

Blood, tumor tissue, and related medical information (for example, your diagnosis, disease history, prior treatments, blood work results, or CT scans) will be stored so that we may study them in future research. Approximately 4 teaspoons of blood will be collected to store for this purpose. The tumor tissue sample will come from a previous biopsy (archival) and you will not need to have a new biopsy. For information related to loss of confidentiality, genetic risks, and risk of blood draws, please refer to Section 5.1 of this consent form.

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

Samples will be labeled with your subject number and the date the sample was collected. The University of Michigan will retain the link to the subject number. We may share your stored samples and related medical information with other researchers inside and outside of the University of Michigan so that they can use it in their research and evaluations with the aim of helping future patients. Dr. Alva will be responsible for reviewing and approving requests for specimens from potential research collaborators outside of the University of Michigan. No identifiable information that could be directly linked to you will be provided. The use of your samples may be used for research similar to this study or may be completely different. Once we have shared your samples and medical information with other researchers, we will not be able to get it back.

You will not find out the results of future research on your samples. Allowing us to do future research on your samples will not benefit you directly.

The University of Michigan, the investigators, or a collaborating researcher may benefit financially from future research on your samples and related medical information.

You will be asked to affirm in Section 12 of this consent form that you understand your required participation in this sub-study.

**Optional – Tumor biopsy at disease progression:**
You will also be able to take part in an optional tumor biopsy for research. If you decide to participate in the optional tumor biopsy collection, you will have an additional tumor biopsy performed at the time of disease progression. Participation in this optional tumor biopsy is completely voluntary. You can still participate in the main study even if you do not want to participate in the optional tumor biopsy at progression.

You may need to have an ultrasound, x-ray, or CT scan to guide the biopsy collection. For information related to risks of biopsies and imaging, please refer to Section 5.1 of this consent form.

If you agree to allow the collection of an optional tumor biopsy at the time of disease progression, the tumor tissue sample and related medical information (for example, your diagnosis, disease history, prior treatments, blood work results, or CT scans) will be stored for future research. Optional tumor tissue will be stored and used in the same manner as other samples collected as part of the main study as described above in the section "Research Samples Stored for Future Use".

Your decision whether or not to participate in the optional tumor biopsy at time of disease progression will be documented in Section 12 of this consent form.

**Optional - Photographs:**
Photographs may be taken to document and monitor any skin lesions, or cancer visible on your skin. Care will be taken to ensure that these photographs do not reveal your identity. The photograph will only show the lesion and surrounding skin. Every attempt will be made to avoid taking a full face photograph. If this is not possible, the photograph will be 'de-identified' as much as possible so that we minimize the chance that someone could identify you from the picture. There is a risk that a photograph may not protect your identity. You will be asked to document your decision in Section 12 of this consent form. You can take part in this study even if you decide not to let us take photographs.

**4.2 How much of my time will be needed to take part in this study?**
The length of your study visits will vary depending on which procedures need to be done. The screening visit may take approximately 4 hours.

Abraxane will be administered intravenously (through a vein; IV) over 30-40 minutes. Pembrolizumab will be administered intravenously (through a vein; IV) over 60 minutes. If the first infusion of pembrolizumab is administered with no major side effects or complications, subsequent infusions may be delivered over 30 minutes. On days when you receive study drug, these visits may take approximately 2-3 hours. If you need to have CT or MRI scans, these visits will take longer.

**4.3 When will my participation in the study be over?**
The study intervention period consists of blocks of time called "cycles" and each cycle lasts 21 days (three weeks). You may continue to receive the study drugs until your disease gets worse, you choose to withdraw from the study, or your doctor decides it is in your best interest to stop taking the study drugs. We estimate that the average subject will receive the study drugs for approximately 6 cycles. Abraxane can be discontinued after 6 cycles at your doctor's choice, or if you have too many side-effects and pembrolizumab alone could be continued.

Abraxane alone can be continued if pembrolizumab is stopped for pembrolizumab related toxicities, and vice versa.

After your last dose of study drugs, you will be asked to come back for an End of Treatment Visit. Afterwards, you will be followed every 12 weeks for 2 years via phone call or clinic visit.

**4.4 What will happen with my information and/or biospecimens used in this study?**
With appropriate permissions, your samples 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?**
Your study doctor and study staff will monitor you closely for side effects. Even with frequent blood tests and other examinations, taking the study drug involves risks, and some side effects cannot be predicted. Side effects can range from mild to severe and life-threatening. Many side effects will get better when you stop taking the study drug, but some may be long lasting or may never go away. Side effects may even cause death. You should tell your study doctor immediately about any side effects that you have or any change in how you feel while on this study. If you have side effects, your dose may have to be reduced, or you may have to stop taking the drugs and wait until you feel better before you start again. Your study team may give you medicines or lower your dose of drugs to help lessen side effects. If any side effect is intolerable, you may have to permanently stop taking the drugs.

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 investigational study treatment, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the investigational study treatment if the side effects are too serious. If you have signs of infection, you will receive appropriate antibiotics. If you have signs of bleeding you may need to receive transfusions of platelets, plasma, or red cells. If you are at risk of having blood clots, you may receive an anticoagulant (blood thinner). If your hemoglobin level is too low, you may receive a red cell transfusion. If you start feeling sick to your stomach, you may be given medications to help reduce nausea. If you have vomiting, you may be given fluids through an IV.

**Risks of Abraxane:**

Very Common (occurring in 10% or more of people):

- Decreased levels of red blood cells, the cells that carry oxygen (anemia)
- Decreased levels of a type of white blood cell (neutrophils, leukocytes) that helps fight infection
- Decreased levels of platelets, the cells that help the blood clot
- Abdominal pain
- Constipation
- Diarrhea
- Nausea, vomiting
- Inflammation of the mouth and mouth sores
- Feeling weak and having no energy

- Chills
- Fatigue
- Buildup of fluid in the body or extremities, causing swelling
- Fever
- Increased level of a liver enzyme (alanine aminotransferase) in the blood
- Weight decreased, decreased appetite
- Dehydration
- Low levels of potassium in the blood
- Joint pain, musculoskeletal pain
- Muscle aches
- Dizziness
- Taste changes which may affect the way foods normally taste
- Headache
- Weakness, numbness, and pain from nerve damage, usually in the hands and feet (peripheral neuropathy)
- Depression
- Problems falling or staying asleep (insomnia)
- Cough
- Difficult or labored breathing
- Nosebleed
- Hair loss
- Nail disorder including loosening or separation of the nail from the nail bed and discoloration
- Itching
- Rash, including generalized rash

<u>Common (occurring in 1% or more people but less than 10% of people):</u>

- Fever with low white blood cell count
- Decreased levels of a type of white blood cell (lymphocytes) that helps fight infection
- Decreased levels of all components of the blood (red blood cells, white blood cells, and platelets)
- Condition in which the heart does not pump blood as well as it should (congestive heart failure)
- Fast heart beat or heart beats that are fast, strong, or irregular
- Excessive tears
- Visual impairment
- Inflammation of the colon (colitis)
- Dry mouth
- Heartburn
- Difficulty swallowing
- Blockage of the intestine or bowel which can cause nausea, vomiting, and pain (intestinal blockage)
- Chest pain
- Infusion site reactions
- Inflammation of the mucosal membranes (mucosal inflammation)
- Bile duct infection
- High levels of bilirubin in the blood. Bilirubin is a bile pigment produced by the liver which is normally and continually excreted from the body. This may indicate that too many red blood cells are being destroyed or that the liver or gallbladder is not functioning properly.
- Upper or lower respiratory tract infection including bronchitis

- Candida infection, which is a type of yeast infection
- Infection of follicles, which are the pockets from which hair grows
- Nail infection
- Pneumonia
- A serious condition that occurs in response to an infection that causes widespread inflammation, resulting in poor blood supply to vital organs (sepsis). Symptoms may include a fast hear rate, fever, confusion, and rapid breathing.
- Urinary tract infection
- Increased levels of liver enzymes (aspartate aminotransferase or alkaline phosphatase) in the blood
- Increased levels of creatinine in the blood, a substance normally eliminated by the kidneys into the urine
- Muscular weakness
- Loss of muscle coordination, including awkward, unsteady walking
- Anxiety
- Acute kidney failure which is when both of your kidneys fail and your body holds fluid which can be serious or life-threatening. Your blood pressure rises and harmful wastes build up in your body. You may experience fatigue, nausea, and loss of appetite. You may need treatment to replace the work of your failed kidneys, such as dialysis.
- Blood in the urine
- Vomiting or coughing up blood
- Nasal congestion
- Pain in the middle part of the throat that includes the base of the tongue, the tonsils, the soft palate, and the part of the throat that is behind the mouth and nasal cavity
- Buildup of fluid around the lungs in the chest cavity (pleural effusion), which can cause shortness of breath and may require treatment
- Inflammation of the lungs (pneumonitis)
- Blood clot formed in the veins of the leg which may manifest as a dull ache or heaviness in the limb (deep vein thrombosis). If the clot moves to other organs, it can be serious or life-threatening.
- A blood clot that causes a sudden blockage in a lung blood vessel, usually due to a blood clot that traveled to the lung from the leg (pulmonary embolism). A pulmonary embolism is a serious condition that can cause: permanent damage to part of your lung from lack of blood flow to lung tissue; low oxygen levels in your blood; damage to other organs in your body from not getting enough oxygen. If a clot is large, or if there are many clots, a pulmonary embolism can cause death.
- Dry skin, redness of the skin
- Reddening, swelling, numbness, and peeling of the skin usually on the palms of your hands or the soles of your feet
- Flushing
- High or low blood pressure
- Swelling in the arms or legs caused by a blockage in the lymphatic system

<u>Uncommon (occurring in 0.1% or more people but less than 1% of people):</u>

- Decrease in the production of cells responsible for fighting infection, carrying oxygen, and clotting blood
- Clotting in small blood vessels of the body resulting in a low platelet count
- Heart beats too fast, too slow, or in an abnormal or irregular rhythm
- Sudden, unexpected stopping of the heart (cardiac arrest)
- Decrease in the heart's ability to pump blood. This may be serious or life-threatening.

- Irritation and redness of the thin membrane covering the eye (conjunctivitis)
- Appearance of cyst-like areas of fluid in the macula of the eye, causing swelling to the retina
- Inflammation of the cornea of the eye. Eye pain, tearing, and sensitivity to light are common symptoms.
- Damage to the macula, the part of the eye associated with vision
- Sleepiness
- A vague feeling of bodily discomfort, feeling bad
- Allergic reaction (hypersensitivity) that may include a rash, hives, fever, difficulty breathing, and low blood pressure
- Injection site infection
- Significant inflammatory response to an infection with or without a fever (neutropenic sepsis)
- Fluid retention
- Facial paralysis
- A condition called hemolytic uremic syndrome which is associated with the decrease in red blood cells, platelets, and kidney function. This may cause high blood pressure or swelling of the face, hands, feet, or the entire body. This can progress to acute kidney failure which can be life-threatening.
- Dry throat or nasal dryness
- Allergic skin irritation or rash
- Skin disorder with lesions that look like rings and can sometimes be painful or itchy
- Skin exfoliation
- Hives

Rare (occurring in 0.01% or more people but less than 0.1% of people):

- A type of heart block in which the electrical conduction between the atria and the ventricles is impaired

The following events were identified post-marketing in people taking abraxane. The frequency of these events are not known:

- Inflammatory reaction in areas that were previously treated with radiotherapy
- Weakness or paralysis of a cranial nerve
- Slight or incomplete paralysis of the vocal cord
- Radiation-induced lung disease following treatment with radiotherapy
- Sensitivity or an immune system reaction triggered by light
- A condition called Stevens-Johnson syndrome (SJS), which is a skin condition that causes painful blisters and sores of the skin and mucous membranes, especially in the mouth. May cause difficulty eating and swallowing. This is similar to the skin damage from a severe burn and is serious and life-threatening.
- A condition called toxic epidermal necrolysis (TEN), which is a rare, life-threatening skin condition that is usually caused by a reaction to a drug. The top layer of the skin detaches from the lower layers of skin all over the body. This is similar to the damage from a severe burn and is serious and life-threatening.

**Risks of Pembrolizumab:**

Pembrolizumab is also known as KEYTRUDA® (approved in the USA and several other countries) and is available by prescription to treat malignant melanoma (a type of skin cancer), head and neck squamous cell carcinoma, and non-small cell lung cancer that has spread to other parts of the body. In clinical trials, both men and women with cancer were treated, some for up to approximately 2 years. Safety was studied across several cancers treated

with different doses: 2mg/kg every 3 weeks, 10mg/kg every 2 or 3 weeks, and 200mg fixed dose every 3 weeks. The side effects seen were similar.

Pembrolizumab is being studied by its manufacturer in clinical trials to see if it is effective in treating more than 30 types of cancer, as a single therapy or in combination with other therapies, and to see what side effects are associated with its use.
trials.

Very common (side effects seen in ≥10% or more of people treated with pembrolizumab) include:

- Fatigue
- Rash
- Loss of pigment from areas of skin
- Pain in joints
- Back pain
- Cough
- Difficulty breathing
- Headache
- Itching
- Diarrhea
- Fever
- Asthenia
- Weight loss
- Musculoskeletal pain
- Decreased appetite
- Low levels of sodium in the blood
- Constipation
- Nausea
- Abdominal pain
- Elevated LFTs
- Vomiting
- Swelling of legs or hands
- Urinary tract infection
- Anemia
- Increased blood creatinine
- Blood in Urine

Severe and Fatal Immune-Mediated Adverse Reactions (side effects seen in <1% of people treated with pembrolizumab) include:

- Inflammation of lungs so you may feel short of breath and cough. Rarely this might lead to death.
- Inflammation of the inner lining of the colon
- Mild elevation of liver enzymes
- Inflammation of the pituitary gland (a gland in the head), which may cause headaches, sick to your stomach, changes in behavior, double vision, few to no menstrual cycles, weakness, vomiting, and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) may not make enough hormone, causing tiredness, weight loss, muscle weakness, feeling faint, joint, muscle, and abdominal aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Too much thyroid hormone so you may feel anxious, angry, cannot sleep, weak, tremble, increased sweating, weight loss, hair loss, tired, have loose and watery stools
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard bowel movements.
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to the back, feel sick to your stomach, and vomiting that gets worse when you eat
- Too much sugar in your blood (diabetes) so you may feel thirsty and are likely to need regular insulin shots
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain.
- Inflammation of the skin so you may have peeling of the skin, itching, skin redness

Other Immune-Mediated Adverse Reactions

- Inflammation of the middle layer of your heart wall (myocarditis) that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting. Sometimes this condition can lead to death.
- Inflammation of the thin saclike membrane surrounding the heart (pericardium).
- Inflammation of the blood vessel that causes blood vessel walls to thicken and narrow, cutting off vital blood supply to tissues and organs.
- Inflammation of the brain (encephalitis) and/or spinal cord membrane (meningitis). Inflammation of the spinal cord can cause the myelin and axons to be damaged (demyelination) which can cause paralysis and sensory loss (myelitis)
- Weakness and rapid fatigue of muscles (Myasthenic syndrome/myasthenia gravis (including exacerbation)).
- Immune system can attack the nerves (Guillain-Barré syndrome).
- Inflammation of the nerves that may cause pain, weakness or tingling in the hands and feet, and may spread to the legs, arms, and upper body leading to severe muscle weakness and possible temporary paralysis.
- Nerves that control involuntary body function can be damaged. Blood pressure, temperature control, digestion, bladder function and sexual function can be affected.
- Inflammation of the middle layer of the eye.
- Inflammation of the iris of the eye.

- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to the back, feel sick to your stomach, and vomiting that gets worse when you eat.
- Inflammation of the lining of the stomach.
- Inflammation of the small intestine which may result in abdominal pain, bleeding, and other abdominal symptoms.
- Low levels of parathyroid hormone (hypoparathyroidism)._
- Red blood cells may be destroyed faster than they can be made (hemolytic anemia).
- Not enough new blood cells being made (aplastic anemia.)
- Severe systemic inflammatory syndrome, can be fatal.
- Inflammatory state affecting the whole body (systemic inflammatory response syndrome).
- Inflammation of the lymph nodes (histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis)),
- Growth of tiny collections of inflammatory cells in different parts of the body. The growths most commonly occur in the lungs, lymph nodes, eyes, and skin.
- Low blood platelets.
- Solid organ transplant rejection.
- Severe infusion related reactions.

Some of the symptoms listed in the sections above have been reported to occur simultaneously in patients treated with pembrolizumab. For example, Vogt-Koyanagi-Harada (VKH) syndrome is a grouping of symptoms including headache, loss of vision, eye pain, sensitivity to light, neck stiffness, hearing problems, and dizziness, that is caused by immune system activation against certain cells in the body. (You should report any symptoms to the study team.)

Additional serious side effects seen in less than 1% of people treated with pembrolizumab include dizziness or fainting (low blood pressure), flushing or pain at the site of infusion.

Pembrolizumab can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis (allergic reaction). Signs and symptoms of infusion-related reactions include chills and shivering, wheezing, itchy skin, flushing, rash, low blood pressure, low oxygen in the blood, and fever.

**Risks of Procedures:**

Blood Draw Risks: Collection of blood samples may cause pain, bleeding, bruising or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having your blood drawn at any time during your study participation.

Tumor Biopsy: Potential risks and discomforts that you may experience as a result of the procedure depend upon the location of the tumor. The more common risks/discomforts include pain, bleeding, infection, damage to tissues, and healing complications. Your doctor will further explain any specific risks that may apply based on the procedures, and you will sign a separate consent for the procedure which will provide risk information in more detail. In order to make the procedure more comfortable, you will get a local anesthetic to numb the area. A mild sedative may also be given to you.

CT Scans: CT imaging uses ionizing radiation, which increases your risk of 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 contrast substance injected during the CT scan may cause pain, burning feeling, sweating, and rarely an allergic reaction that can be serious. If you know you are allergic to iodine, you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you are diabetic, dehydrated, and if you're older. In addition, your thyroid function may be affected.

MRI Scans: Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks if 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). NFD is a thickening of the skin, organs, and other tissues and is a rare complication in subjects with kidney disease who 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.

Questionnaires: As part of the study, you will be asked to complete questionnaires. Some of the questions may seem very personal or embarrassing. They may make you uncomfortable. You may refuse to answer any of the questions that you do not wish to answer. If the questions make you uncomfortable, we can help you to find a counselor.

**Privacy and Confidentiality Risks:**

There are also non-physical risks associated with taking part in this study, such as the risks associated with a loss of privacy or confidentiality. For example, if your identity as a participant in this research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The researchers believe that the risks of such improper disclosure are very small because strict privacy and confidentiality procedures for this research have been adopted.

**Reproductive Risks:**

**Women:**

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. These birth control methods must be used for 28 days prior to starting the investigational study treatment, all during investigational study treatment (including during temporary breaks from therapy), and for at least 6 months after the last dose of study drug. The following methods are considered acceptable birth control methods:

Primary Forms

- Tubal sterilization (tubes tied)
- Partner's vasectomy
- Intrauterine device
- Hormonal contraceptives (includes transdermal patch, injectables, implantables)

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 females 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. In addition, women must not breast-feed for at least 6 months after the last dose of study drug.

**Men:**
Men must agree to either abstain from sexual activities that could result in pregnancy or use an acceptable form of birth control all during investigational study treatment (including during temporary breaks from therapy) and for at least 6 months after the last dose of study drug. Acceptable forms of birth control are male latex condom (with or without spermicide). Men must use a male latex condom even if they have previously had a vasectomy. In addition, men should not donate sperm or semen while taking part in the study and for at least 6 months after the last dose of study drug.

**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

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**.**

If you think you have an injury or illness that is related to your participation in this clinical trial, it is important that you tell your study doctor immediately. If you have a clinical trial related injury or accident, the study staff will make sure that you get medical treatment.

You will receive appropriate medical care for any side affects you have while participating in this study. Your study doctor may also lower the drug dose or stop drug if you experience side effects.

You must inform your study doctor immediately if there are any changes in your health/condition, or if you have any concerns regarding the study. If for any reason you are seen by another healthcare provider or admitted to another hospital, you should make known your participation in this research study. These healthcare providers may wish to contact your study doctor to discuss your condition. Your study doctor may need to contact your other doctors if you develop any potentially significant, unexpected diseases or conditions that may have been caused by the study intervention or procedures or are discovered during the study.

**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 direct personal benefits from being in this study. There is a chance that the study intervention may improve your quality of life or increase the length of disease-free survival. The researchers hope that the information learned from this study will help other patients with this type of cancer in the future.

**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 participate in this trial to receive care for your cancer. There may be other ways of treating your cancer. These include:

- You may receive other available standard treatments such as pembrolizumab immunotherapy alone, or atezolizumab, another immunotherapy drug or carboplatin and gemcitabine chemotherapy for your cancer
- You may be eligible for other cancer research studies
- You may receive treatment for pain or other symptoms only
- You may choose to receive no treatment at all

Please talk to your doctor about your choices before you decide if you will 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).

You are free to partially or completely end your participation in the study. An example of partially ending your participation would be to discontinue receiving study intervention, while still allowing continuation of study follow-up procedures.

Please note that any information collected before you withdraw will be kept and used to complete the research.

Please note that even if you withdraw consent for further follow-up or contacts, if the study doctor becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

You may participate in an optional tumor biopsy performed at the time of disease progression (see "Optional – Tumor biopsy at disease progression" in Section 4.1, above). Please note that if you decide to withdraw from the main study and had agreed to participate in the optional tumor biopsy, you will not be automatically withdrawn from the optional tumor biopsy. If you wish to also withdraw your samples from the optional tumor biopsy, you will need to tell your study doctor.

**7.2 Could there be any harm to me if I decide to leave the study before it is finished?**
Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks can be evaluated by your doctor. They will also tell you how to stop safely and discuss what follow-up care and testing could be most helpful for you. 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 your study doctor or one of the researchers listed in Section 10 "Contact Information" (below).

**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 required or 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.

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
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services
- The drug pembrolizumab

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 Celgene Corporation is supplying the drug Abraxane at no charge to you.

What if I am injured while taking part in this study?

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. Alva immediately, 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 will get free medical care at the UMHS for any hospitalization or ER visits directly caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.

The UMHS will pay for your treatment only if the need for treatment has been caused by the study drug, device, or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

By signing this form, you do not give up your right 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?**

No, you will not be paid for taking part in this study.

**8.3 Who could profit or financially benefit from the study results?**

The company whose product is being studied: Celgene Corporation (supplier of Abraxane)

The University of Michigan and the researchers conducting the study have no financial interest in the outcome of the study.

The University of Michigan, the investigators, or a collaborating researcher may benefit financially from future research on your samples and related medical information as described in Section 4.1 above under "Research Samples Stored for Future Use".

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?**
Your participation will occur at the University of Michigan medical center. The University of Michigan study team will use your medical records during the course of participation to conduct the study. Study data will include your medical history, physical examinations, laboratory and pathology evaluation results, imaging studies, study intervention, side effects reported, other medications you are taking, and other medically relevant information needed for the trial.

The University of Michigan has rules to protect information about you. Federal and state laws also protect your privacy. We will take measures to protect the privacy and security of your personal information, but we cannot guarantee complete confidentiality of study data. Once your health information is shared with someone outside of the study team, it may no longer be protected.

HIV and hepatitis are reportable diseases. If you test positive for HIV or hepatitis, the law mandates that your study doctor disclose your identity to the appropriate people (such as health care workers who are involved in your care) and appropriate authorities.

Your data will be kept confidential, to the extent permitted by applicable laws, in the following manner:

- Your name will not be used in any reports about the study
- You will be identified only by a study code: a subject ID number, and initials
- Your identifying information will be kept secure

You will be assigned a subject code number to help ensure that your medical and personal information is kept confidential. The key to this code will remain at the University of Michigan. All data, forms, records, and samples related to the study will use this subject code number.

The study team will use the study data for research purposes to support the scientific objectives of the study. Study data (that does not directly identify you) may be published in medical journals or shared with others as part of scientific discussions.

Samples banked for future research will also be coded and the key to this code will remain at the University of Michigan. No identifiable information that could be directly linked to you will be provided.

**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 and/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 identifiers

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, 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.
- Study sponsors or funders, 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 UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- 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.

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.

**9.3 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 University 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 Question 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 will not expire unless you cancel it. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

## 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 E. Medical Center Dr., 7316 Cancer Center<br>Ann Arbor, MI 48109 |
| 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 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):_____

# Study Calendar

| Assessment | Screening | Cycle 1 | | Cycle 2 | | Cycle 3 | | Subsequent Cycles | | EOT | Follow-up (every 12 weeks for 24 months) [4] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Day 8 | Day 1 | Day 8 | Day 1 | Day 8 | Day 1 | Day 8 | | |
| Informed Consent | X | | | | | | | | | | |
| Tumor tissue specimen identified from a previous biopsy | X | | | | | | | | | | |
| Medical history, physical exam, medication history, weight, and vital signs | X | X | | X | | X | | X | | X | |
| Performance Status | X | X | | X | | X | | X | | X | |
| Quality of Life questionnaire | X | | | X | | X | | X | | X | |
| Toxicity Evaluation | X | X | | X | | X | | X | | X | |
| Pregnancy test (blood or urine test) | X | | | | | | | | | | |
| Blood for HIV and hepatitis tests | X | | | | | | | | | | |
| Blood to check your blood counts and blood chemistry [1] | X | X | X | X | X | X | X | X | X | X | |
| Blood collected to check your organ function | X | | | | | X | | X [2] | | X | |
| Blood collected to bank for future research | X | | | | | | | | | | |
| Tumor response assessment [3] | X | | | | | X | | X [3] | | | X |
| Optional – Tumor Biopsy | | | | | | | | | | X | |
| Pembrolizumab Administration | | X | | X | | X | | X | | | |
| Abraxane Administration | | X | X | X | X | X | X | X | X | | |

Cycles are 21 days long. EOT = end of investigational study treatment

[1] Blood tests may be performed on Day 15 of any cycle at the discretion of the study doctor.
[2] Performed every 42 calendar days.
[3] Tumor assessments will be performed every 2 cycles (i.e., every 6 weeks) for the first 4 assessments after baseline, and then every 3 cycles (i.e., every 9 weeks). Assessments include: CT scans of the chest; CT or MRI of the abdomen/pelvis; and CT or MRI of the brain if indicated.
[4] Follow-up via phone call or clinic visit.

## 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.

Legal Name: _____

Signature: _____

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

**Consent/Assent for an Optional Tumor Biopsy at Disease Progression:**

This project involves an optional tumor biopsy at the time of disease progression. I understand that it is my choice whether or not to have the optional tumor biopsy. 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 allow the collection of a tumor biopsy at disease progression.

_____ No, I do not agree to allow the collection of a tumor biopsy at disease progression.

Legal Name: _____

Signature: _____

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

**Consent/Assent for Optional Photographs**

I understand that the study team may want to take photographs to document and monitor any skin lesions, or cancer visible on my skin. Every attempt will be made to avoid taking a full face photograph. There is a risk that a photograph may not protect my identity. You can take part in this study even if you decide not to let us take photographs.

_____ Yes, I agree to allow photographs to document and monitor any skin lesions.

_____ No, I do not agree to allow photographs to document and monitor any skin lesions.

Legal Name: _____

Signature: _____

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

**Consent/Assent for Samples to be Stored for Future Research**

I understand that by participating in this study, some of my blood and tissue samples, and medical information will be stored for future research. I understand that my samples and information will be stored at the University of Michigan indefinitely or until they are used up. I understand that I can withdraw my consent at any time and ask that the specimens be destroyed. However, any specimens and information that have already been analyzed cannot be removed from the research.

Legal Name: _____

Title: _____

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.

Legal Name: _____

Title: _____

Signature: _____

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

UMCC 2017.077

# 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

---

[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."