I. SUMMARY OF CHANGES – Consent Form

#	Section	Comments
1.	Header	Updated version date.
2.	Possible Side Effects of Nivolumab	Added new risks to Rare, and Serious as requested in the RRA: • A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss • Swelling of the bowels Provided Further Clarification: • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting is now reported as Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urination; dizziness or fainting. • A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss is now reported as A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause blurred vision, ringing in the ears, changes in hair or hair loss • Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) is now reported as Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)

Research Study Informed Consent Document

Study Title for Participants: Testing immunotherapy with nivolumab and ipilimumab for kidney transplant recipients with advanced cancer that cannot be removed by surgery or treated with standard drugs

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10214, Immune Checkpoint Blockade for Kidney Transplant Recipients with Selected Unresectable or Metastatic Cancers (NCT03816332)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have received a kidney transplant and have advanced or metastatic cancer that cannot be surgically removed or treated with standard non-immune-based drugs.

Taking part in this study is your choice.

You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:
Can we safely and effectively use nivolumab alone or with ipilimumab to treat cancer in patients who have received a kidney transplant?

Nivolumab and ipilimumab are a type of cancer therapy known as immunotherapy, which stimulates the immune system to help the body fight cancer. Nivolumab and ipilimumab bind to proteins found on T cells (a type of white blood cell). This helps the immune system find and attack cancer cells. Nivolumab and ipilimumab are approved by the Food and Drug Administration (FDA) to treat many types of cancer, but in this trial, they are considered experimental.

We are doing this study because we want to find out if this immunotherapy approach is safe for kidney transplant recipients and whether it is better or worse than the usual approach for your cancer. The usual approach is defined as the care given to most people with your cancer.

What is the usual approach to my cancer?

The usual approach for patients who are not kidney transplant recipients is treatment with immunotherapy. Immunotherapy, including with nivolumab and ipilimumab, has either been approved for your type of cancer or has shown evidence of efficacy against your type of cancer. However, in patients with a kidney transplant, immunotherapy may cause the body to reject the transplanted kidney, thus immunotherapy is not usually an option for these patients. The usual approach for patients who are kidney transplant recipients includes chemotherapy, surgery, radiation therapy, or targeted therapies. Patients who have already tried these standard treatments usually receive comfort care to help relieve symptoms.

What are my choices if I decide not to take part in this study?

- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will continue taking drugs that suppress your immune system, but at lower doses, so that the study therapy may be able to do its job more effectively. Your study doctor will spend up to 4 weeks adjusting the doses of your immunosuppressive drugs. Then you will get study drugs (starting with nivolumab alone) for up to 2 years. A change to nivolumab combined with ipilimumab can be considered if your cancer progresses during the study.

After you finish your treatment, your doctor and study team will watch you for side effects. For the first 3 months after you finish treatment, they will check on you once a month via phone call. For the rest of the first year after you finish treatment, they will check on you every 2 months. Then they will check on you every 3 months during the second year, every 4 months during the third year, and then every 6 months during the fourth year. This means you will keep seeing your doctor for 4 years after treatment.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study treatment may cause side effects. These side effects may be worse and may be different than you would get with the usual, non-immune-based treatment for your cancer.

Some of the most common side effects that the study doctors know about are:

- Your body may reject your kidney transplant. If this happens, you will need to have a biopsy of your transplanted kidney. You may need to increase the doses of your immunosuppression drugs which may increase the risk of infection. Rejection may also result in kidney failure. You would then require lifelong dialysis and your transplanted kidney may need to be removed.
- Your immune system may attack normal parts of your body, which may result in severe and possibly fatal side effects.

There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence, in people with your type of cancer, that treatment with nivolumab alone or in combination with ipilimumab can shrink or stabilize tumors. In some patients, the drugs being used in this study have helped the body keep control of cancer for several years. However, we do not know if this will happen in people with kidney transplants, and we do not know if the study drugs will cause the transplanted kidney to be rejected. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop the study treatment, let your study doctor know as soon as possible. It's important that you stop safely. If you decide to stop receiving study treatment, it will be important to continue to let the study doctor know how you are doing, but whether or not to do so is your decision.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes, and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), FDA, or study sponsor (National Cancer Institute [NCI]). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety of the study drugs nivolumab and ipilimumab, along with the immunosuppressive drugs prednisone and tacrolimus, in patients who have received a kidney transplant. Nivolumab and ipilimumab could shrink your cancer, but they could also cause side effects, including rejection of your transplanted kidney, which are described in the risks section below. The study doctors hope to learn if the study drugs will help shrink your cancer while allowing your transplanted kidney to continue functioning.

Nivolumab and ipilimumab are approved by the FDA to treat several cancers, including melanoma, lung cancer, kidney cancer, and certain types of colon cancer. However, these drugs have not been tested in patients who have received a kidney transplant.

There will be about 16 people taking part in this study.

What are the study groups?

In this study, you will receive the immunosuppressant drugs prednisone and tacrolimus. These will be taken by mouth every day. You will keep a medication diary for these drugs. This helps you keep track of when you take prednisone and tacrolimus. The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the medication diary, any remaining prednisone or tacrolimus pills, and the pill bottles.

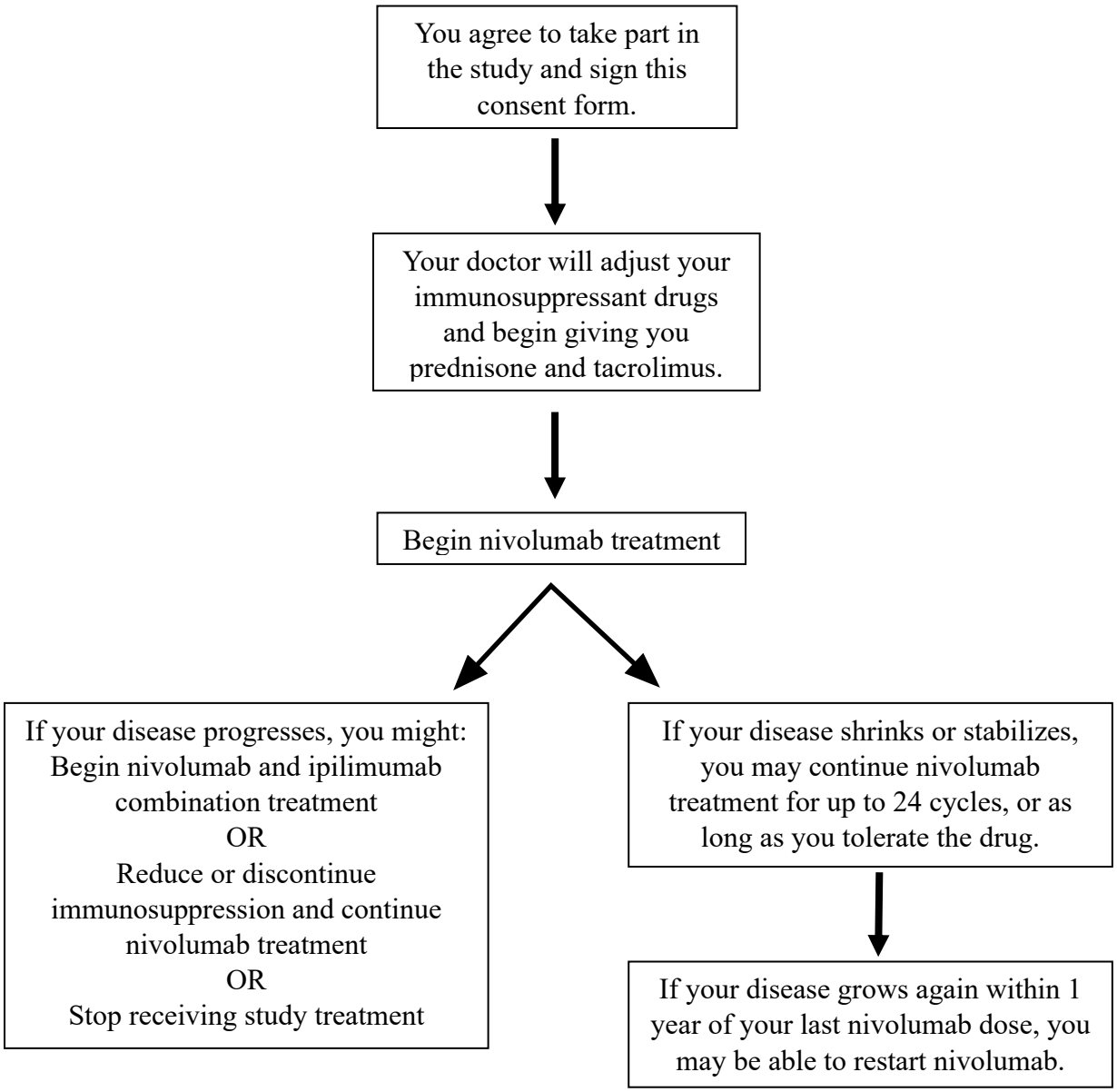
You will also get the study drug, nivolumab. You will get nivolumab through a vein in your arm on the first day of each cycle. Each cycle lasts 28 days (4 weeks). This study has 24 cycles. If your cancer begins to progress during the study, you may also get the study drug ipilimumab. Ipilimumab will also be given through a vein in your arm.

You may be able to receive additional doses of nivolumab if your disease progresses within 1 year of completing nivolumab treatment and your tumor showed a response to the study drug.

If your cancer progresses, you may choose to receive nivolumab in combination with ipilimumab or you may choose to reduce or discontinue the immunosuppressive drugs. You may also choose to stop receiving study treatment.

If your cancer shrinks or stabilizes, you may continue study treatment for up to 24 cycles, or as long as you are tolerating the study drugs. You may restart nivolumab if your cancer begins to grow again within 1 year of your last dose of nivolumab.

Another way to find out what will happen to you during this study is to read the chart below. Start reading from the top and read to the bottom, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study.

If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

- An electrocardiogram (EKG) and echocardiogram will be done to evaluate the activity of your heart.
- A blood test will be done before you begin study treatment, every 2 weeks during the first 12 weeks of nivolumab treatment, then every four weeks after that. If you are receiving nivolumab plus ipilimumab combination treatment, blood tests will be done every three weeks for the first 12 weeks of combination treatment, then every four weeks after that. Additional samples may be collected if your disease gets worse or if you have side effects due to the study drug(s). Each time, about 1.5 tablespoons of blood will be taken from a vein in your arm. This test will look for small pieces of DNA from your transplanted kidney, that might be able to indicate if your kidney is prone to injury, or if your body is rejecting your kidney. However, whether this is true in patients also receiving nivolumab alone or in combination with ipilimumab, is unknown.
- A urine test to measure kidney health will be done before you begin study treatment, every 2 weeks during the first 12 weeks of nivolumab treatment, then every four weeks after that. If you are receiving nivolumab plus ipilimumab combination treatment, tests will be done every three weeks for the first 12 weeks of combination treatment, then every four weeks after that.

This study may use genetic tests that may identify changes in the genes in your tumor DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If there are changes found that could cause health problems, then your study doctor will discuss your options with you.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in the usual care for your cancer. Described below are procedures that will be done for research purposes only.

- You will also have a blood test before you begin study treatment, after you have been receiving treatment for 4 weeks, and when you stop receiving study treatment. If you begin taking nivolumab and ipilimumab combination treatment, you will have a blood test when you begin receiving nivolumab and ipilimumab, after you have been receiving combination treatment for 3 weeks, after you have been receiving combination treatment for 12 weeks, and when you stop receiving study treatment. Each time, about 8 tablespoons of blood will be collected and used to measure your immune response to the

study drug(s). Additional samples may be collected if your disease gets worse or if you have side effects due to the study drug(s).

- If you have had a tumor biopsy or cancer surgery in the past, your study doctor will request the original tumor samples from the medical facility where that procedure was done.
- If your body begins to reject your transplanted kidney, a biopsy of your transplanted kidney will be collected at that time as part of the usual care for managing transplant rejection. For the biopsy procedure, the study doctor will use a needle to take small pieces of your kidney. This process may be repeated several times in the same appointment in order to get enough tissue. The study doctor will then use a microscope to closely examine these pieces in order to decide how to best treat and manage the rejection. During this procedure, some extra kidney tissue will be collected to measure how the study drug(s) are affecting your immune system's response to your transplanted kidney.

You also have the option of having a biopsy of your cancer collected before you begin study treatment, after you have been receiving treatment for 4 weeks (or 3 weeks if you are receiving nivolumab and ipilimumab combination treatment), and if your body begins to reject your transplanted kidney. This will be used to measure how the study drugs are affecting your tumor and your immune cells. See the section "Optional studies that you can choose to take part in" for more information.

Patient study calendars are attached at the end of this document. They show how often these biopsies and blood sample collections will be done.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that nivolumab alone or in combination with ipilimumab may cause your body to reject your transplanted kidney.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 31 weeks (about 8 months) after your last dose of nivolumab or ipilimumab.

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

The drugs used in this study could cause your body to begin rejecting your transplanted kidney.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may make it hard for you to have children.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. They can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

PLEASE NOTE THE FOLLOWING IN REVIEWING THESE RISKS:

Nivolumab and ipilimumab are agents involved in the inhibition of "immune checkpoints," and may result in severe and possibly fatal side effects, probably due to activation and growth of immune cells (T-cells) and your immune system attacking normal body parts. Such side effects have been reported in patients receiving nivolumab. In clinical trials, most of these side effects were reversible and managed by stopping treatment temporarily and administering corticosteroids and supportive care. The following side effect charts were written for people who do not have a transplanted kidney.

Possible Side Effects of Nivolumab:
(Table Version Date: December 2, 2020)

Special precautions Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**
COMMON, SOME MAY BE SERIOUS In 100 people receiving Nivolumab, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Nivolumab, from 4 to 20 may have:
• Anemia which may require blood transfusion • Swelling and redness of the eye • Pain • Diarrhea, nausea • Dry mouth • Fever • Swelling and redness at the site of the medication injection • Bruising, bleeding • Pain or swelling of the joints • Loss of appetite • Reaction during or following a drug infusion which may cause fever, chills, rash Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath. • Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness. • Skin: itching; rash, blisters including inside the mouth; loss of skin pigment • Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urination; dizziness or fainting.

RARE, AND SERIOUS

In 100 people receivingNivolumab, 3 or fewer may have:

- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Swelling of the bowels

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea, and vomiting, and can result in coma
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures, or injury to the brain which may cause headache, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs, and facial muscle movement
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin, and gut damage), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received Nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

Possible Side Effects of Ipilimumab:
(Table Version Date: March 29, 2019)

Special precautions Side effects of ipilimumab (MDX-010) may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when ipilimumab (MDX-010) is used in combination with BMS-936558 (nivolumab). **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**
COMMON, SOME MAY BE SERIOUS In 100 people receiving ipilimumab (MDX-010), more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Skin: itching; rash, blisters including inside the mouth (can be severe); hives

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ipilimumab (MDX-010), from 4 to 20 may have:
• Abnormal heartbeat • Hearing loss • Swelling and redness of the eye • Pain • Difficulty swallowing, eating • Constipation, vomiting • Weight loss, loss of appetite • Fever • Dehydration • Pain or swelling of the joints • Reaction during or following a drug infusion which may cause fever, chills, rash • Low blood pressure which may cause feeling faint Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Lung problems (pneumonitis). Symptoms may include: new or worsening cough, chest pain, shortness of breath. • Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.

- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Muscle problems, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- Nerve problems that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs, and facial muscle movement.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.

RARE, AND SERIOUS

In 100 people receiving ipilimumab (MDX-010), 3 or fewer may have:

- Bleeding
- Blockage of the bowels which may cause constipation
- Fluid around heart
- Severe illness with multiorgan failure
- Confusion

Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea, and vomiting, and can result in coma
- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin, and gut), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received ipilimumab therapy, since the risk and severity of transplant-associated complications may be increased.
- Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck

Possible Side effects of Prednisone
(Table Version Date: September 22, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Prednisone, more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness, blurred vision • Pain in belly • Loss of bone tissue • Mood swings • In children and adolescents: decreased height • Swelling of the body, tiredness, bruising • Increased appetite and weight gain in the belly, face, back and shoulders • Difficulty sleeping • Skin changes, acne

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Prednisone, from 4 to 20 may have:
• Blood clot which may cause swelling, pain, shortness of breath • Infection • Kidney stones • Diabetes • Glaucoma • Cloudiness of the eye, visual disturbances, blurred vision • A tear or a hole in the bowels which may cause belly pain or that may require surgery • Heartburn • Damage to the bone which may cause joint pain and loss of motion • Numbness and tingling of the arms, legs and upper body • Muscle weakness • Non-healing wound

RARE, AND SERIOUS In 100 people receiving Prednisone, 3 or fewer may have:
• Bleeding from sores in the stomach • Broken bones

Possible Side Effects of Tacrolimus
(Table Version Date: March 16, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Tacrolimus, more than 20 and up to 100 may have:
• Anemia which may cause tiredness, or may require blood transfusions • Constipation, diarrhea, nausea, vomiting • Bruising, bleeding • Diabetes

COMMON, SOME MAY BE SERIOUS In 100 people receiving Tacrolimus, more than 20 and up to 100 may have:
• Abnormal body movement • Feeling of "pins and needles" in arms and legs • Headache • Dizziness • Difficulty sleeping • Kidney damage which may cause swelling, may require dialysis • Hair loss • Itching, rash • High blood pressure which may cause dizziness, blurred vision • Swelling of the body • Fever • Infection, especially when white blood cell count is low

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Tacrolimus, from 4 to 20 may have:
• Damage to organs (heart, lungs, brain, others) which may cause changes in thinking, confusion, memory loss or shortness of breath • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Change in the heart rhythm, abnormal heartbeat, or heart stops beating • Heart attack or failure which may cause chest pain, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause belly pain or that may require surgery • A new cancer resulting from treatment of earlier cancer • Brain damage, which may cause headache, seizure, blindness

RARE, AND SERIOUS In 100 people receiving Tacrolimus, 3 or fewer may have:
• None

Additional Drug Risks

It is possible that patients taking the study drug will have a delayed response within the first 16 weeks of taking the study drugs. This means that your cancer might get better after it gets worse. If you are continuing to show clinical benefit after your disease progresses (as shown by CT or MRI images), your study doctor may ask you if you would like to continue treatment with the study drug. If you have disease progression later in your treatment, you may be offered to receive the study drug nivolumab and add another study drug, ipilimumab. If your disease progresses, you might also take reduced doses of the immunosuppressant drugs prednisone and tacrolimus, or stop taking them altogether. This could lead to rejection of your transplanted kidney.

The risks of continuing treatment after your cancer gets worse include all of the risks above and the risk that there may be no benefit to receiving the study drug(s).

It is not known if the study drug(s) will provide any benefit after your cancer gets worse. Even if you and your doctor decide to continue treatment with the study drug(s) after your disease gets worse, you may need to stop treatment later due to side effects. These side effects may include results of laboratory tests if the test results show that your cancer has continued to get worse while taking the study drug(s).

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments.
- Write down in your medication diary when you take prednisone and tacrolimus at home.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- **For women:** Do not get pregnant or breastfeed while taking part in this study.
- **For men:** Do not father a baby while taking part in this study.
- **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 31 weeks (about 8 months) after your last dose of study drugs.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer and kidney transplant. This includes:

- the costs of tests, exams, procedures, and drugs, including tacrolimus and prednisone, that you get during the study to monitor your safety and prevent and treat side effects;
- the costs of getting nivolumab and/or ipilimumab ready and giving them to you.
- the blood tests done to study dd-cfDNA from your transplanted kidney; and
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The blood tests done to study how the study treatment is affecting your immune system.

You or your insurance provider will not have to pay for the costs of nivolumab or ipilimumab while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study treatment now or in the future.
- The IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You may not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor may not be told when or what type of research will be done.
- You may not get reports or other information about any research that is done using your information.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*)."

^Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here. ^

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer and a kidney transplant in the future. The results will not be added to your medical records.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to these studies. There is no penalty for saying "no." You and your insurance company will not be billed for theses optional studies. If you sign up for but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies:

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect samples of your tumor tissue for research on how the study treatment is affecting your tumor and your immune cells. You will have two to four biopsy procedures done for this study. One biopsy will be done before you begin taking any study drugs and a second will be done after you have been receiving study treatment for 4 weeks. If you begin receiving nivolumab and ipilimumab combination treatment, a biopsy will be done after you have been receiving combination treatment for 3 weeks. Finally, a biopsy may be done if your body begins to reject your transplanted kidney. The study biopsy will take small pieces of cancer tissue from your body and will be like the biopsy you had that helped diagnose your cancer.

Unknown future studies

If you choose to take part in this optional study, any leftover blood and biopsy tissue obtained during your participation in this trial will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by Dr. Evan Lipson and his team at

Johns Hopkins University. Also, any health-related information, such as your response to cancer treatment, the results of study tests, and medicines you took, will be stored for future use.

We don't know what research may be done in the future using your blood and/or tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in these optional studies?

If you agree to take part, here is what will happen next:

1. Samples of tissue will be collected from optional extra biopsies. Two to four optional biopsy procedures will be performed. For the biopsy procedures, the study doctor will use a needle to take pieces of your tumor. This process may be repeated several times in the same appointment in order to get enough tissue. If a biopsy is not possible or cannot be done safely before you begin the study drug, then your study doctor, with your consent, will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer or had surgery to remove your tumor.
2. Researchers can only get samples from the biopsies after their research has been approved by experts. Researchers will not be given your name or contact information.
3. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your type of cancer in the future. There is a small risk that when this tissue sample is submitted for testing, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.

- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/.

How will information about me be kept private?

Your privacy is very important to the study researchers. They will make every effort to protect it. Here are just a few of the steps they will take:

- They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The laboratories doing research with your samples will receive the following information only: your sample code number; your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
- Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
- Your personal information will not be given to anyone unless it is required by law.
- If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in these optional sample collections?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to these optional sample collections?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about these optional sample collections?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the researchers know. Then, any sample that remains will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I need my tissue samples to be returned?

Tumor tissue can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be retuned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue samples and genetic material (DNA and RNA) that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

What if I have questions about these optional sample collections?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree to the optional extra biopsies, and I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from these studies.

YES NO

Samples for unknown future studies:

1. I agree that my blood samples and related health information may be kept in a biobank for use in future health research.

   YES NO

2. I agree that my tumor tissue and related health information may be kept in a biobank for use in future health research.

   YES NO

3. I agree that tissue from my rejected kidney and related health information may be kept in a biobank for use in future health research.

   YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

My signature agreeing to take part in the study

I have read this consent form, or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "YES."

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Attachment A: Nivolumab Study Calendar for Protocol 10214 Consent Form

Nivolumab only	Screenings	Adjustment of immunosuppressive drugs[A]	Treatment (cycle length = 28 days)												Follow-up	Immune system adverse reaction assessment	If your disease gets worse
			Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5		Cycles 6+				
	Within 28 days of registration	Day -28 to Day 0	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15			
Medication Administration																	
Nivolumab[B]			X		X		X		X		X		X				
Tacrolimus[C]		X	Continue twice daily oral dosing													X	X
Prednisone[D]		X	Continue daily oral dosing													X	X
Medication diary review		X	X		X		X		X		X		X		X		
Administrative Assessments																	
Pre-study procedures including informed consent, pathology review, demographics, and medical history	X																
Concurrent medications	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Clinical Assessments																	
Physical examination and vital signs	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
General well-being assessment	X		X		X		X		X		X		X		X	X	
Review of adverse events			X	X	X	X	X	X	X	X	X	X	X	X	X	X	
ECG and echocardiogram	X																
Efficacy Assessments																	
CT scans: chest / abdomen / pelvis plus additional areas, as appropriate	X						X				Day 1 every other cycle (Cycles 7, 9, 11, *etc.*)				X		
Clinical color photographs with scale ruler of tumors, as appropriate[E]	X		X	X	X	X	X	X	X	X	X	X	X	X	X		
Brain imaging[F]	X																

Nivolumab only	Screenings	Adjustment of immunosuppressive drugs[A]	Treatment (cycle length = 28 days)												Follow-up	Immune system adverse reaction assessment	If your disease gets worse
			Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5		Cycles 6+				
	Within 28 days of registration	Day -28 to Day 0	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15	Day 1	Day 15			
Standard-of-Care Laboratory Assessments																	
Blood draw for general health status	X		X	X	X	X	X	X	X	X	X	X	X	X	X		
Urine test to measure kidney health	X	X	X	X	X	X	X	X	X		X		X				
Pregnancy test[G]	X																
Blood draw to study one's ability to form blood clots	X																
Blood draw to study thyroid function	X		X		X		X		X		X		X		X		
Blood draw to look for small pieces of DNA from your transplanted kidney	X		X	X	X	X	X	X	X		X		X			X	X
Correlative Studies																	
Blood draw to study how the study drugs are affecting your immune system			X		X											X	X
Tumor biopsy[H] **(optional)**	X				X											X	
Kidney transplant biopsy[I]																X	

A: Immunosuppression adjustment will last no more than 28 days.
B: Nivolumab will be given at 480 mg intravenously (IV) on Day 1 and Day 29 of each cycle.
C: Tacrolimus will be dosed by mouth to achieve a goal trough level of 2-5 ng/mL twice a day throughout the study.
D: Prednisone will be doses at 5 mg by mouth every day throughout the study. Patients may remain on a higher-dose prednisone if already taking it before study entry.
E: A biopsy may be performed if clinically indicated.
F: Magnetic Resonance (MR) or Computed Tomography (CT) will be used for brain imaging.
G: For women of childbearing potential.
H: Patients may refuse biopsy and still remain on the study.
I: Patients who experience kidney transplant rejection will stop nivolumab treatment, and a biopsy of the kidney transplant will be obtained.

Attachment B: Nivolumab + Ipilimumab Study Calendar for Protocol 10214 Consent Form

Nivolumab + Ipilimumab	Treatment (cycle length = 21 days)												3-week gap			Treatment (cycle length = 28 days)				Follow-up	Immune system adverse reaction assessment	If your disease gets worse
	Cycle 1			Cycle 2			Cycle 3			Cycle 4						Cycle 5		Cycles 6+				
	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 15	Day 1	Day 15			
Medication Administration																						
Nivolumab[A]	X			X			X			X						X		X				
Ipilimumab[B]	X			X			X			X												
Tacrolimus[C]	Continue twice daily oral dosing																				X	X
Prednisone[D]	Continue daily oral dosing																				X	X
Medication diary review	X			X			X			X			X			X		X				
Administrative Assessments																						
Concurrent medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	
Clinical Assessments																						
Physical examination and vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X	X			
General well-being	X																					
Review of adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	
Standard-of-Care Laboratory Assessments																						
Blood draw for general health status	X			X			X			X			X			X	X	X	X			
Urine test to measure kidney health	X			X			X			X			X			X		X				
Pregnancy test[E]	X																					
Blood draw to study thyroid function	X			X			X			X			X			X		X				
Blood draws to look for small pieces of DNA from your transplanted kidney	X			0			X			X			X			X		X			X	X

Nivolumab + Ipilimumab	Treatment (cycle length = 21 days)												3-week gap			Treatment (cycle length = 28 days)				Follow-up	Immune system adverse reaction assessment	If your disease gets worse
	Cycle 1			Cycle 2			Cycle 3			Cycle 4						Cycle 5		Cycles 6+				
	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 8	Day 15	Day 1	Day 15	Day 1	Day 15			
Efficacy Assessments																						
CT scans: chest / abdomen / pelvis plus additional areas as appropriate							X									Day 1 every other cycle (Cycles 5, 7, 9, *etc.*)				X		
Clinical color photographs with scale ruler of tumors, as appropriate[F]	X			X			X			X			X			X	X	X	X	X		
Correlative Studies																						
Blood draws to study how the study drugs are affecting your immune system	X			X									X							X	X	X
Tumor biopsy[G] **(optional)**				X																	X	
Kidney transplant biopsy[H]																					X	

A: Nivolumab will be given at 3 mg/kg intravenously (IV) for the first 4 cycles. Then it will be given at 480 mg intravenously (IV) on Day 1of each subsequent cycle. There will be a three-week gap between the end of Cycle 4 and the beginning of Cycle 5 (for a total of six weeks between doses).

B: Ipilimumab will be given at 1 mg/kg IV on Day 1 of the first 4 cycles.

C: Tacrolimus will be dosed by mouth to achieve a goal trough level of 2-5 ng/mL twice a day throughout the study.

D: Prednisone will be doses at 5 mg by mouth every day throughout the study. Patients may remain on a higher-dose prednisone if already taking it before study entry.

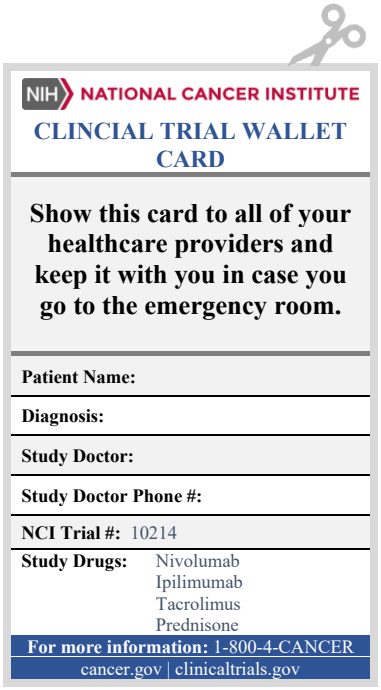
E: For women of childbearing potential.

F: A biopsy may be performed if clinically indicated.

G: Patients may refuse biopsy and still remain on the study.

H: Patients who experience kidney transplant rejection will stop treatment, and a biopsy of the kidney transplant will be obtained.

Attachment C: Patient Clinical Trial Wallet Card



NIH NATIONAL CANCER INSTITUTE

CLINCIAL TRIAL WALLET CARD

Show this card to all of your healthcare providers and keep it with you in case you go to the emergency room.

Patient Name:

Diagnosis:

Study Doctor:

Study Doctor Phone #:

NCI Trial #: 10214

Study Drugs: Nivolumab
Ipilimumab
Tacrolimus
Prednisone

For more information: 1-800-4-CANCER
cancer.gov | clinicaltrials.gov