SUMMARY OF CHANGES

A Phase I Study of Ipilimumab and Nivolumab in Advanced HIV-Associated Solid Tumors, with Expansion Cohorts in HIV-Associated Solid Tumors and a Cohort of HIV-Associated Classical Hodgkin Lymphoma

Version 15.0

NCI Protocol #: AMC-095
Local Protocol #: AMC-095

NCI Version Date: 24AUG2023
Protocol Date: 24AUG2023

I. Changes Required by Request for Rapid Amendment for Nivolumab from Dr. Howard Streicher (streicherh@ctep.nci.nih.gov), dated 03AUG2023:

#	Section	Description of Change

1.	6.1	The nivolumab CAEPR was updated to version 2.5 dated June 10, 2023. Changes include:
		• Added New Risk:
		  • Rare but Serious: Blood and lymphatic system disorders – Other (lymphatic dysfunction)
		  • Rare but Serious: Immune system disorders – Other (Sarcoid-granuloma)
		• Added a footnote for eye disorder – other (Vogt-Koyanagi-Harada)
		• Replaced immune-mediated hepatitis with immune-related hepatitis
		• Deleted footnote for Metabolism and nutrition disorders - Other (diabetes mellitus with ketoacidosis)
		• Replaced immune-mediated nephritis with immune-related nephritis
		• Added an abbreviation for bronchiolitis obliterans with organizing pneumonia (BOOP)
		• Replaced skin and subcutaneous disorder with skin and subcutaneous tissue disorders
		• Removed references to BMS-936558, MDX-1106 to align with version 2.5 of the CAEPR.

2.	ICF - Risks of Nivolumab	The condensed risk profile has been modified as follows: • Added New Risk:

#	Section	Description of Change
		• Rare: Swelling of arms and legs which may cause a feeling of heaviness and tightness • Occasional Risk: • Urination was replaced with urine Additionally, references to BMS-936558 and MDX-1106 were removed to align with the language provided in the Nivolumab risk profile.

II. Administrative and Editorial Changes:

#	Section	Description of Change
3.	Global	The version/version date were updated to version 15.0 dated 24AUG2023.

MODEL INFORMED CONSENT FORM

Study Title for Study Participants

Testing Ipilimumab and Nivolumab in Advanced HIV-Associated Tumors

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

A Phase I Study of Ipilimumab and Nivolumab in Advanced HIV associated Solid Tumors with Expansion Cohorts in HIV Associated Solid Tumors and a Cohort of HIV-Associated Classical Hodgkin Lymphoma

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WHAT IS THE USUAL APPROACH TO MY HIV-ASSOCIATED CANCER?

You are being asked to take part in this study because you are an HIV-positive patient with an incurable cancer for which no standard therapy is available or you were diagnosed with Hodgkin lymphoma and it came back after standard therapy. You may have already been treated with chemotherapy, radiation therapy or other treatments, and your disease is now growing. People who are not in a study may try other types of chemotherapy.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test the safety while giving both ipilimumab and nivolumab or just nivolumab alone while treating HIV-positive people with incurable cancers or relapsed Hodgkin lymphoma**.** We would also like to find out what effects, good and bad, this combination of drugs may have on your cancer. The FDA approved nivolumab to treat melanoma, non-small cell lung cancer, and Hodgkin lymphoma and approved ipilimumab to treat advanced melanoma. The combination of nivolumab and ipilimumab is considered to be investigational and not approved for use with your type of cancer. The drugs are being used as nivolumab alone and nivolumab in combination with ipilimumab.

Your immune system defends your body against harm. It defends you from bacteria, viruses, and other agents that cause disease. Your immune system finds these harmful agents by using antibodies. An antibody is a type of blood protein that tags infected cells and other harmful agents. Your immune system finds the antibodies and destroys what they tagged. Antibodies for tumor cells can be made in a lab to treat diseases. There are several approved antibodies for treating cancer and other diseases. Both study drugs, ipilimumab and nivolumab, are types of antibodies used to treat cancer.

Researchers think that one way cancers grow is by escaping the immune system. Ipilimumab works against a protein called CTLA-4 to stop it from shutting down the immune system for a time. Nivolumab works against a protein called PD-1 in the same way. It is believed that these antibodies

may help your body destroy cancer cells by helping your immune system to keep fighting cancer. In laboratory studies and in some patients with advanced melanoma, it has been possible to get rid of some cancers by using a combination of nivolumab and ipilimumab in this way.

Up to 84 people will take part in this study at different centers across the U.S. and one center in Australia.

WHAT ARE THE STUDY GROUPS?

In this study, we will test different doses of nivolumab in combination with ipilimumab. Different doses of the study drugs ipilimumab and nivolumab will be given to several study participants. The first group of study participants will receive the lowest dose. If the drug does not cause serious side effects, it will be given to the next group study participants at a higher dose. The doses will continue to increase for every group of study participants until side effects occur that require the dose to be lowered.

You will be placed in one of two groups (also called "Strata") based on your CD4 count. Subjects in Stratum 1 will have a CD4 count over 200. Subjects in Stratum 2 will have a CD4 count between 100-200.

Depending on the dose level we are testing when you start the study, you will get nivolumab or nivolumab and ipilimumab. Both drugs will be given through a needle in your vein (intravenously or IV).

For Stratum 1, if you are receiving nivolumab only, you will receive the treatment every 2 weeks. Nivolumab is infused over a 60 minute time period. If you are assigned to receive nivolumab and ipilimumab, you will receive nivolumab treatment every 2 weeks, with ipilimumab given with the first treatment, and with every third or sixth nivolumab treatment after that, depending on the dose assigned. Ipilimumab is infused over a 90 minute time period. The study doctor will tell you what dose you are taking.

If your cancer shrinks or does not grow during the first 8 weeks of treatment, you will continue treatment. Patients in all of the above groups will receive nivolumab every two weeks for up to a total of 46 cycles (up to 92 weeks). If you are assigned to receive nivolumab and ipilimumab, you will receive either 16 ipilimumab treatments every 6 weeks, or 8 ipilimumab treatments every 12 weeks, depending on the dose at which you are enrolled.

The dose for stratum 2 participants will be determined based on any bad side effects seen in Stratum 1. This is being done because the highest tolerable dose of the combination of nivolumab and ipilimumab may be different for people with different CD4 counts. The dose and schedule of this treatment will be determined by the dose and schedule established in Stratum 1.

Expansion Group:

Once we have found the highest dose that is safe and does not cause bad side effects, a total of 24 patients will be treated at this dose level as part of the study expansion group for some solid tumors If this dose is not safe in Stratum 2 patients, they will not be included in this group. For participants with a CD4 count above 200 this has been determined to be nivolumab every 2 weeks, with ipilimumab every 6 weeks, for 24 weeks. Then it will be a higher dose of nivolumab administered every 4 weeks without ipilimumab. Another twenty four (24) patients will be treated with nivolumab alone. The dose that will be used is the FDA approved dose for nivolumab alone among various solid tumors.

Twelve (12) more patients with Hodgkin lymphoma will be treated with nivolumab alone. The dose that will be used has been shown to be safe and is FDA approved for Hodgkin lymphoma.

HOW LONG WILL I BE IN THIS STUDY?

You will receive treatment for up to 92 weeks. After you finish nivolumab or nivolumab plus ipilimumab, your doctor will continue to watch you for side effects and follow your condition for 16 weeks or 112 days.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study.

Before you begin the study

You will need to have the following extra procedures to find out if you can be in the study:

- Blood tests for immune safety and hormonal levels will be done (about 2 tablespoons of blood) (These tests include antinuclear antibodies (ANA), adrenocorticotropic hormone, thyroid stimulating hormone, free T4 level)
- Part of your biopsy sample (tissue) that was taken to diagnose your cancer will be shipped to a BMS laboratory. This sample will be tested for the proteins that the study drugs target. BMS will not receive any information that links your identity to your samples. This test is being done for research. You will not be told the results of this test.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the blood, skin biopsy (for participants with Kaposi sarcoma [KS]), or anal swab samples that will be used for this study. These procedures will be paid for by the AIDS Malignancy Consortium (AMC).

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra procedures. They are not part of the usual approach for your type of cancer.

- Blood tests for research purposes
- If you have anal cancer, an anal swab will be performed – this is an optional test being done for research purposes only. The swab will be sent to a central laboratory that will determine whether there is a virus called human papilloma virus (HPV), and whether there are abnormal cells in the anal canal. You will not be billed for this test. The results will not be sent to you or your doctor, or placed in your medical records.
- If you have Kaposi sarcoma: You will have two skin biopsies for research studies before treatment, two skin biopsies before starting cycle 5, and two skin biopsies at the end of the study. Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site, which can be treated with regular pain medications. Rarely, an infection can occur. You will be asked to sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from [*institution name*].

During the study

You will need these tests and procedures that are part of regular cancer care. They are being done more often because you are in this study.

- CT (computed tomography) whole body scan
- PET/CT scan if you have Hodgkin lymphoma.
- Bone marrow biopsy if you have Hodgkin lymphoma
- Pregnancy test. If you are a woman of childbearing potential, you will also be required to have a blood or urine pregnancy test prior to each treatment before the first five treatments and every 12 weeks after that until treatment is completed. The blood or urine pregnancy test must be negative within 72 hours before every treatment.
- During the first cycle of treatment, you will be evaluated for side effects on a weekly basis
- For participants with Kaposi sarcoma: the study doctor will examine your KS lesions, will take measurements of some of the lesions and will count them, and may take photographs of the lesions to document their appearance. Additional photographs will be taken during the course of the study to document any changes in appearance. At no time will your entire face appear, and any distinguishing features will be removed from the photo so that you cannot be identified. Only your initials and subject number will be used to identify the photo.

However, there are some extra blood tests that you will need to have during the study if you decide to take part in this study.

- Blood tests for immune safety and hormonal levels will be done (about 2 tablespoons of blood). (ANA, Adrenocorticotropic hormone, Thyroid Stimulating Hormone, Free T4 level). These will be performed before starting cycle 4 and every 12 weeks thereafter until you finish the study.
- Blood tests for research purposes (up to 55 ml, or about 4 tablespoons). We will collect blood 1 day before treatment, after treatment, and one week after treatment every 6 weeks or every 12 weeks, depending on the dose you get.

A study calendar that shows how often these tests will be done is attached.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, there is a risk that the ipilimumab (MDX-010) and nivolumab (BMS-936558, MDX-1106) may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

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 ipilimumab (MDX-010) and nivolumab 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 will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

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 go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- 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. He or she 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.

The tables below show the most common and the 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.

Risks of Ipilimumab

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.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- 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.
- 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

Risks of Nivolumab

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 urine; dizziness or fainting.

RARE, AND SERIOUS
In 100 people receiving Nivolumab, 3 or fewer may have:

- Swelling of arms and legs which may cause a feeling of heaviness and tightness
- 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 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.

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

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study.

Nivolumab and ipilimumab can cause birth defects or death to an unborn baby.

- Women are required to use **TWO** barrier methods of birth control at the same time or abstain from heterosexual intercourse. Women will be required to use birth control at least 28 days before starting the study, during the trial, and for 6 months after stopping nivolumab and ipilimumab
- Men are required to use **TWO** barrier methods of birth control at the same time or abstain from heterosexual intercourse. Men will be required to use birth control at least 28 days before starting the study, during the trial, and for 31 weeks after stopping nivolumab and ipilimumab.

You must continue these TWO methods of birth control or abstinence even if your therapy is interrupted. The use of an Intrauterine device (IUD), tubal ligation, and a partner's vasectomy are considered to be highly effective methods. Additional effective methods include latex condom, diaphragm, and a cervical cap. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, or you are a man and your partner becomes pregnant while you are participating in this study please inform your treating physician immediately.

While taking study drug and for 30 days after stopping treatment, you should not get any other vaccines for infectious diseases. You may get any routine vaccinations, including seasonal influenza, at least 2 weeks prior to study treatment.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

It is not possible to know at this time if the study drugs, nivolumab with or without ipilimumab will be effective. This study may or may not help you. This study will help researchers learn things that will help people in the future.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The 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.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal

rights.

For questions about your rights while in this study, call the _____ *(insert name of 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.)*

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The ipilimumab and nivolumab will be supplied by the National Cancer Institute at no charge while you take part in this study. It is possible that the ipilimumab and nivolumab may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

There will be no charge for non-standard blood tests determining.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- The pharmaceutical company that is providing ipilimumab and nivolumab for the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.

- The Food and Drug Administration and the National Cancer Institute in the U.S.

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.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

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 center*] at [*Insert telephone number*].

ADDITIONAL RESEARCH STUDIES SECTION

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor (specify: will/will not) know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the 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 LABORATORY STUDIES AND DONATION OF LEFTOVER TISSUE SAMPLES TO THE AIDS AND CANCER SPECIMEN RESOURCE (ACSR)

Researchers are trying to learn more about cancer, HIV/AIDS, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in this study, the study doctor for the main study would like to collect these specimen types, depending on your type of cancer:

- **If you have anal cancer**, the researchers would like to collect anal swab samples to study ways to prevent, detect, or treat human papillomavirus (HPV) and HIV-related diseases and cancer.
- **If you have Kaposi sarcoma**, the researchers would like to collect additional biopsies, called punch biopsies, to learn about, prevent, detect, or treat HIV-related diseases and cancer.
- **If you have a low level of HIV in your blood** (low HIV viral load or an undetectable HIV viral load), the researchers would like to collect extra blood samples. The samples will be used

to see if ipilimumab and nivolumab changes the amount of less active HIV (latent reservoirs) found in your immune cells.

- **Donation of left over study specimens to the ACSR for all study participants:** If you choose to take part in this clinical trial, the researchers would like to collect unused blood and biopsy tissue left over after the study is done. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking." The Biobank is being run by the **AIDS and Cancer Specimen Resource** and is supported by the National Cancer Institute.

WHAT IS INVOLVED?

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

1) **If you have anal cancer**, the researchers will collect additional anal swab samples collected before treatment, before cycle 5, and after stopping treatment. A doctor or nurse will insert a swab (similar to a Q-tip™) into your anus. The end of the swab will be rubbed against the skin inside the anus.

   a) **If you have Kaposi sarcoma**, the researchers will collect punch biopsies before treatment, before cycle 5, and after stopping treatment. A punch biopsy involves removal of a small piece of one of your KS tumors (about the size of a sesame seed).

   b) **If you have a low level of HIV in your blood** (low HIV viral load or an undetectable HIV viral load), the researchers will collect 100 mL (about 7 tablespoons) of blood before you start chemotherapy, during Cycle 16, after you stop study treatment, and when you finish the study. If your viral load becomes very low or undetectable during the study, we will only ask to collect a blood sample after you finish chemotherapy.

   c) **For anal swabs, punch biopsies, and blood for HIV viral load,** your sample and some related health information will be sent to a researcher for use in the study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.

   d) **Donation of left over study specimens to the ACSR for all study participants:** Your sample and some related health information will be stored in the ACSR Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record may be updated after the study is over.

2) Qualified researchers can submit a request to use the materials stored in the ACSR. A science committee at the ACSR will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.

3) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.

4) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise. Side effects may include bleeding; infection; discomfort, pain, bruising and/or tenderness at the site where the blood is taken; and fainting or feeling faint.
2) Insertion of anal swabs will likely cause some discomfort. Minor bleeding (less than a quarter of a teaspoon) occurs in more than half of men and women due to the insertion of the swabs. The bleeding stops almost right away.
3) Risks of the punch biopsy include: discomfort, pain, bleeding and/or infection at the biopsy site.
4) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
5) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
6) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

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

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. The ACSR and AMC staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom the ACSR and the AMC send your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

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?

There are no additional costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products,

you will not share in any profits.

WHAT IF I CHANGE MY MIND?

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 in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

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)*.

SAMPLES FOR FUTURE RESEARCH STUDIES:

Please circle your answer to show whether or not you would like to take part in each option:

My samples and related information may be donated to ACSR Biobank for use in future health research.

YES NO

If I am enrolled in the AMC-095 study, I agree to have my samples undergo genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

YES NO

If I am enrolled in the AMC-095 study, I agree to have anal swab (cytology) samples collected for research to learn about, prevent, diagnose, or treat HPV and HIV-related diseases and cancer.

YES NO Not applicable

If I am enrolled in the AMC-095 study, I agree to have punch biopsy samples of my KS lesions collected for research to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

YES NO Not applicable

If I am enrolled in the AMC-095 study and have a low or undetectable HIV viral load, I agree to provide additional blood samples for HIV latent reservoir testing.

YES NO

This is the end of the section about optional studies.

MY SIGNATURE AGREEING TO TAKE PART IN THE MAIN 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 copy of this form. I agree to take part in the main study *and 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_____

In the opinion of the Investigator, is the participant capable of complying with this protocol (*circle one)*?

YES NO

Investigator's Name (print)	Investigator's Signature and Date

ATTACHMENT 1: AMC CERTIFICATE OF CONFIDENTIALITY

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.

ATTACHMENT 2: STUDY CALENDAR

You will receive nivolumab every 2 weeks (or 4 in the combination therapy expansion cohort). This 2 week period of time is called a cycle. The cycle will be repeated up to 46 (or 23) times. If you are assigned to receive nivolumab plus ipilimumab, the ipilimumab will be given after the first nivolumab dose, and then with every third or sixth nivolumab dose, depending on the dose assigned. If the cancer does not grow, patients in all of the above groups will receive nivolumab every two weeks (every two and then four weeks in the combination therapy expansion cohort) for up to a total of 46 (or 23) doses (up to 92 weeks). If you have Hodgkin lymphoma, you will only receive nivolumab every 2 weeks.

Each cycle is numbered in order. The chart below shows what will happen to you during Cycle 1 and future treatment cycles as explained previously. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Cycle 1 (This cycle lasts for 2 weeks)

Day	What you do
Before starting the study	• PPD testing, if previously negative • Get routine blood tests • Complete pre-treatment testing • Samples for research studies: blood, biopsy tissue (if you have Kaposi sarcoma), and anal swabs (if you have anal cancer) • Radiologic evaluation (PET/CT scan if you have lymphoma, chest x-ray if you have Kaposi sarcoma) • Bone marrow biopsy if you have lymphoma
Day 1	• Receive nivolumab or the combination of nivolumab and ipilimumab • Get routine and research blood tests • Get physical exam
Day 8	• Get routine blood tests • Blood for research studies • Get a physical exam, and talk to your doctor about how you are feeling.
Last day of cycle	• Blood for research studies

Cycles 2-4 (These cycles last for 2 weeks)

Day	What you do
Day 1	• Keep getting nivolumab or the combination of nivolumab and ipilimumab if you have no bad side effects. Call the doctor at

Day	What you do
	_____ [insert phone number] if you do not know what to do. • Get routine blood tests and exams every cycle (more if your doctor tells you to). • Pregnancy test (for females of childbearing potential) before each dose of ipilimumab • If receiving certain doses of nivolumab and/or ipilimumab on Day 1 of Cycle 4 you will have blood tests pre-dose day 1, post-dose day 1, and day 8

Cycles 5-46 (23 in the combination therapy expansion cohort) (These cycles last for 2 weeks or 4 in the combination therapy expansion cohort)

Day	What you do
Before Day 1 of cycle 5	• If you have Kaposi sarcoma and agreed to give extra samples, the researchers will collect 2 punch biopsies of KS lesions • If you have anal cancer and agreed to give extra samples, the researchers will collect an additional anal swab sample
Day 1 (odd numbered cycles)	• Keep getting nivolumab if you have no bad side effects and your cancer is not getting worse. Call the doctor at _____ [insert phone number] if you do not know what to do. • Get routine blood tests and exams every cycle (more if your doctor tells you to). • Get routine CT scans, or PET/CT scans every 12 weeks (every 6 cycles). Scans may be done more often if needed to monitor your cancer. If you have lymphoma, you will have scans at weeks 17, 25, and/or 49.
Day 1 (all cycles)	• Keep getting nivolumab or the combination of nivolumab and ipilimumab if you have no bad side effects and your cancer is not getting worse. Call the doctor at _____ [insert phone number] if you do not know what to do. • Get routine blood tests every cycle (more if your doctor tells you to). • If you are assigned to receive nivolumab and ipilimumab every 3rd cycle, you will get ipilimumab after getting nivolumab for cycles

Day	What you do
	7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, and 46 (in the combination therapy expansion you will receive ipilumumab every 6 weeks for a total of four doses) • If you are assigned to receive nivolumab and ipilimumab every 6th cycle, you will get ipilimumab after getting nivolumab for cycles 7, 13, 19, 25, 31, 37, and 43. • Research blood tests will be performed at: o Cycle 5 pre-dose day 1 o If receiving treatment you will either have blood draws at Cycles 7, 10, 13, 19, 22, 25, 28, 31, 34, 37, 40, 43, and 46 OR Cycles 7, 13, 19, 25, 31, 37, and 43.You will have blood tests pre-dose day 1, post-dose day 1, and day 8 of each cycle depending on the dose you are taking, (in the combination therapy expansion blood draws will occur every 6 weeks for 24 weeks). o Cycle 16 day 1 (cycle 15 day 1 in the combination therapy expansion cohort)

End of Study

Day	What you do
End of study assessment	• This will be done 6 weeks (±1 week) after the last dose of study treatment and again at 16 weeks (±1 week) after last dose of study treatment and will include: o medical history and physical examination, o routine blood tests, o assessment for toxicities. • Samples for research studies: blood, biopsy tissue (if you have Kaposi sarcoma), and anal swabs (if you have anal cancer) will be collected at 6 weeks after the last dose of study treatment. • If you have lymphoma, bone marrow biopsy.