

PRINCIPAL INVESTIGATOR: Byram H. Ozer, MD, PhD

STUDY TITLE: Phase II Trial of the Immune Checkpoint Inhibitor Nivolumab in Patients with Select Rare CNS Cancers

STUDY SITE: NIH Clinical Center

Cohort: Affected patient

Consent Version: 02/13/2025

WHO DO YOU CONTACT ABOUT THIS STUDY?

PI: Dr. Byram H. Ozer phone: 240-760-6316 email: byram.ozero@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term “you” refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether the experimental drug, nivolumab, can shrink tumors in patients with rare Central Nervous System (brain or spine) tumors or increase the time it takes for these tumors to grow or spread throughout the body. Nivolumab has been approved by the FDA for patients with other types of cancers like melanoma, non-small cell lung cancer, and renal cell carcinoma. Safe doses and timeframes have been determined. However, this drug has not been tested or approved by the FDA in patients with your type of cancer.

Therefore, nivolumab is considered experimental in this study.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to be part of this study because you have been diagnosed with a recurrence (the return) of your rare central nervous system tumor.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

We plan to have up to 158 people start Nivolumab on this study. About 89 will take part at the NIH and up to 69 people at other participating sites.

DESCRIPTION OF RESEARCH STUDY**WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?****Before you begin the study**

- Before you begin the study, we will take an MRI (imaging) or a Body CT scan (if systemic disease present) of your cancer. You will also need blood tests to check your liver and kidney function before you begin this study. We may also need to collect your urine for 24 hours depending on the result of the blood tests. If your liver or kidneys are not working well enough or if any of your test results do not meet eligibility criteria, you will not be able to participate in this study.

You will also complete the following:

- An electrocardiogram (ECG)
- Hepatitis B and C tests
- Full physical and neurological examination
- We will analyze a small piece of cancer tissue from a previous biopsy and the pathology report. This tissue and pathology report are required in order to confirm what type of tumor you have. No additional procedure will be required if there is cancer tissue available from a previous operation.

- If you are able to become pregnant, we will check to see that you are not pregnant (blood or urine sample).
- While on this study, you will be strongly recommended to follow requirements to limit transmission of COVID-19, such as wearing masks, social distancing and maintaining good hand hygiene even after vaccination.

DURING THE STUDY

During the study, the following tests will occur:

Before you start treatment:

- You will complete a questionnaire about the severity of your symptoms and the interference these symptoms have in your daily life over the last 24 hours. You will complete this questionnaire before you start study therapy and whenever you have a Body CT scan (if systemic disease present), or MRI as outlined in the protocol.
- A blood test to analyze the number of immune cells will be done.
- A blood test to analyze how well your immune cells work will be done.
- Blood tests to monitor your endocrine function (your body's ability to produce hormones needed to make many of your body's organs work) will be done.
-

Study Drug:

You will be given nivolumab intravenously (through your vein) every 2 weeks for 4 treatments. Then you will be given nivolumab every 4 weeks for 14 treatments.

While you are on nivolumab (once a month):

- Routine blood tests
- Blood tests to monitor your endocrine function (your body's ability to produce hormones needed to make many of your body's organs work)
- A blood test to analyze the number of immune cells.
- You will be asked to report any symptoms you experience.
- If you are able to become pregnant, we will check to see that you are not pregnant.

While you are on nivolumab (every other month):

- You will have an MRI or a Body CT scan, if disease is present, to see if nivolumab is working.

- You will also complete a questionnaire about your quality of life.
- Neurologic function test.
- A blood test to analyze how well your immune cells work.

Tissue and Blood Analysis

If there remains enough tumor tissue, then other research studies will be performed such as studying molecular pathways, biological and genetic characteristics, or tumor markers to help us to better understand your disease. We will perform gene sequencing on your blood and/or tissue samples. Your blood and tissue samples contain genes, which are made up of DNA (deoxyribonucleic acid) which serves as the "instruction book" for the cells that make up our bodies. Sequencing will determine the exact order of the base pairs (chemical letters) in [the tumor being studied, or blood]. Your sample(s), and medical information will help us study how genes are linked to your cancer.

The analyses that are performed at the NCI laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the results of testing on your specimens that is performed in our research lab. There may be exceptions to what we share with you, and this is described later in this consent form in the section for "**Return of research results.**"

When you are finished taking the nivolumab

After 1 month after the last dose of nivolumab (then at your doctor's discretion for up to 5 years):

- Blood tests to monitor your body, like endocrine function (your body's ability to produce hormones needed to make many of your body's organs work)

After you stop taking nivolumab (monthly):

- You will be asked to report any symptoms you experience.

After you stop taking nivolumab (every 2 months for a year, then every 3 months for a year, then every 4 months for a year, and then every 6 months)

- Blood test to analyze the number of immune cells
- MRI or a Body CT scan, if systemic disease is present
- Neurological function test

BIRTH CONTROL

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

Women of child-bearing potential on the study should use two methods of birth control. The use of an intrauterine device (IUD), hormonal (birth control pills, injections, or implants), tubal ligation, or a partner's vasectomy, and abstinence are considered 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.

Women of child-bearing potential will be required to use birth control during the trial, and for 5 months after stopping nivolumab.

Men that can father children will not be required to use contraception such as latex condoms while in this study.

If you become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately.

Risks to Reproduction, Unborn Babies and Nursing Infants

Nivolumab has been studied in laboratory, and animal experiments to see if it causes problems with pregnancy or birth defects. However, even when the results are all normal it is still not possible to say that nothing bad will happen when a woman gets pregnant while taking nivolumab.

Information about birth defects:

No information is available at the present time.

Information about harm to developing babies:

No information is available at the present time.

Information about harm that may result from nursing:

Because many medicinal products, including antibodies, can be secreted in human milk, a risk to newborns/infants cannot be excluded.

Human Pregnancy Outcomes with nivolumab: The use of nivolumab in pregnant individuals has not been formally studied in clinical studies. One case has been identified of a nivolumab treated male patient with a partner who became pregnant. The pregnancy was uneventful and at birth, the infant was slightly underweight.

RISKS OR DISCOMFORTS OF PARTICIPATIONPossible Risks of Nivolumab**Special precautions**

Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of the common and less common side effects can be serious. **Call or see your healthcare provider right away if you develop any problems listed below or if the symptoms get worse.**

Common side effects:

• Fatigue	• Fever	• Constipation
• Hypothyroidism (low or not enough thyroid hormone in bloodstream)	Upper respiratory infections	Joint pain or stiffness
• Nausea	• Vomiting	• Difficulty breathing
• Diarrhea	• Decreased appetite	• Hair loss
• Anemia (low red blood cells), may require blood transfusion	• Dry mouth	• Abdominal pain
• Headache	• Sweating	• Dizziness, fainting
• Blurry vision, dry eyes	• Thrombocytopenia (low blood platelet count)	• Trouble falling asleep
• Neutropenia (low white blood count)	• Can't sleep	• Weight gain or loss
• Mouth ulcers and sores	• Feeling cold	• Cough
• High blood sugar (hyperglycemia)	• Inflammation of the colon (colitis) – Can be fatal	• Muscle pain, weakness, stiffness, spasms, or paralysis
• Inflammation of the lung (pneumonitis) – Can be fatal	• Tingling, burning, or numbness in arms and legs	• Feeling uncharacteristic anxiety or anger
• Rash (including inside of your mouth), itching, hives, redness, dry skin, skin color changes		

- **Allergic reactions during/after infusion:** Fever, chills, flushing, change in blood pressure, swelling of the face/lips/throat, difficulty breathing which may be serious.

Less common side effects:

• High or low blood pressure	• Salt craving	• Serious lung infection, bronchitis
------------------------------	----------------	--------------------------------------

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (1)

Version Date: 02/13/2025

Page 6 of 20



IRB NUMBER: 17C0102

IRB EFFECTIVE DATE: 3/13/2025

• Few to no menstrual cycles	• Dehydration	• Darkening of skin like a suntan
• Increased blood acid levels	• Loss of appetite	• Yellowing of skin or eyes
• Chest pain	• Fluid around lungs	• Heartburn
• Changes in rhythm or rate of heartbeat	• Inflammation of the liver (hepatitis) – Can be fatal	• Increased sensitivity of skin to sunlight
• Low platelets, decreased or increased white blood cells	• Inflammation of the kidney, kidney failure requiring dialysis	• Erythema multiforme, psoriasis, rosacea
• Pain or swelling in your arms, legs, joints, ankles, or body	• Abnormal blood chemistry, incl abnormal liver, kidney function tests	• Pain in right upper stomach that moves to your back
• Changes in mood or behavior: decreased sex drive, irritability, forgetfulness (memory loss)	• Changes in vision (including decreased or blurry vision, possible blindness), eye pain, redness, or bleeding and eye movement problems	

Rare (Serious) side effects:

• Autoimmune disorders	• Fluid in lungs	• Confusion, seizures, stiff neck
• Increase in inflammatory proteins (e.g., lipase)	• Inflammation of the mouth and lining of digestive tract	• Diabetes mellitus (high blood sugar, can result in coma)
• Inflammation of the brain (encephalitis) – Can be fatal. May also include neurological/psychiatric symptoms	• Infections (incl sepsis, lung, and skin infections)	• Blockage of bile ducts
• Inflammation or loss of brain stem and spinal cord function	• Low blood oxygen level	• Immune reaction causing low levels of the blood cells that prevent bleeding (platelets)
	• Hearing loss	

- **Kikuchi lymphadenitis:** Inflammation or enlargement of a lymph node
- **Guillain-Barre Syndrome:** Is associated with progressive muscle weakness or paralysis.

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (1)

Version Date: 02/13/2025

Page 7 of 20


 IRB NUMBER: 17C0102
 IRB EFFECTIVE DATE: 3/13/2025

- **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS):** Drug reaction with rash, blood cell abnormalities, enlarged lymph nodes, and internal organ involvement (including liver, kidney, and lung)
- **Myasthenia gravis:** A nerve disease that may cause weakness of the eye, face, breathing, and swallowing muscles. One death in a patient who received nivolumab combined with ipilimumab was considered due to myasthenia gravis and severe infection (sepsis).
- **Toxic epidermal necrolysis:** A potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn, has occurred in patients who received nivolumab treatment.
- **Rhabdomyolysis** (muscle fiber released into the blood stream which could damage your kidney) and **polymyositis** (chronic muscle inflammation with muscle weakness) have been reported in one patient.
- **Inflammation of the heart (myocarditis):** May cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, difficulty breathing, swelling in your legs. You may also experience a fast or irregular heartbeat that can cause dizziness or fainting. Sometimes this condition can lead to death.
- **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 nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

These symptoms might or might not be caused by problems with your lungs, colon, liver, thyroid, pituitary or adrenal glands, pancreas, kidneys, heart, brain, nervous system, or skin affected by nivolumab.

A new drug may show an increase in side effects or unexpected effects as more studies are conducted. For your safety, you will be followed closely by your Study Doctor and the study staff for any undesirable or unexpected side effects during your participation in this study and each time you receive nivolumab.

There may be other side effects of nivolumab that are unknown. You will be told about any new findings that develop during the course of this study that may affect your decision to stay in the study.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. The primary use of the information you provide is to assess the severity of your symptoms. Submission of this information is voluntary. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the Principal Investigator.

MRIs- People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

RISKS FOR GADOLINIUM ENHANCED MRI SCANS:

Procedure:

During part of the MRI, you will receive gadolinium, a contrast agent, through an intravenous (iv) catheter. It will be done for medical purposes.

It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

Risks:

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms that may occur include coldness in the arm at injection, a metallic taste, headache, and nausea. In an extremely small number of patients, fewer than one in 300,000 people, more severe symptoms have been reported including: shortness of breath,

wheezing, lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called “nephrogenic systemic fibrosis (NSF)”. This condition always involves the skin and can also involve the muscles, joints, and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body, whenever possible. We will also give you additional information called a “Medication Guide.” Upon request, we will give you individual information about retained gadolinium we see on your studies.

Body CT SCAN:

Procedure: If there is systemic disease present, you may have a Body CT (Computed Tomography) scan rather than an MRI before you start the study and then every 8 weeks after you start nivolumab treatment. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes.

RADIATION:

During your participation in this research study, you may be exposed to radiation from Body CT scans each year. The amount of radiation exposure from these procedures is equal to approximately 10.4 rem. The rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called “background radiation.” This study may expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The Body CT scan that you may get in this study will expose you to roughly the same amount of

radiation as 34.7 years of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1 out of 100 (1.0%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

ELECTROCARDIOGRAM

Procedure: An electrocardiogram (ECG) is a test that is performed while you lie still for about 5 minutes. It involves placing electrodes (small stickers that are attached to wires that go to the machine) on the chest and arms/legs and recording the electrical activity of your heart. If you have a lot of hair on your chest, it may hurt a little bit when they remove these stickers.

Risks: Other than possibly experiencing some minor skin irritation from the electrodes, there are no anticipated risks related to complete the electrocardiogram and/or the echocardiogram

This study may involve unpredictable risks to the participants including death.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if this experimental drug, nivolumab, will cause your tumors to shrink or increase the time it takes for your tumors to grow or spread. We do not know if you will receive personal medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

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

Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

In this study, we will use a test that looks at all or most of your genes or DNA. This test may find gene changes that are not related to what is being studied in this research. These are called “secondary findings”. Most of the time when we look for these, we do not find anything. If we were to look for them in 100 people, we would expect them in only about 2 to 4 of those people.

If we discover a secondary finding that might be important to you or your family’s health, we plan to tell you about this. However, before we can tell you, we may need to do the test again in another laboratory to be sure that the result is correct. To do so, we may need to ask you to submit another sample for testing. Once these results are available, we will invite you to schedule a visit, in person (at our expense) or remote so that we can give you more information about this result and to help you seek follow-up care outside of the NIH if it is needed. The NIH will not generally provide any further follow-up testing or care for this condition for you or your family.

We will not be testing the samples we have collected from you for several years. Because of this, just because you haven’t heard from us, you should not assume that you do not have any gene changes that might be important for your health.

We also do not know all the gene changes that can cause health problems. We could learn later that some gene changes that now we don’t think cause health problems are of concern. We will look for gene changes only once and will look for those that are known to cause problems at the time we are looking. We do not plan to look again at a later time for new secondary findings.

It is up to you if you want us to tell you about any secondary findings. At any point you can tell us that you don’t want us to contact you or tell you about any secondary findings.

We can only provide these results to you. If you want us to tell anyone else, then you must provide us with a signed written release of medical information request.

It is very important for you to keep us updated on how to contact you. If we don’t have up to date information, we will not be able to get in touch with you to collect an additional sample or tell you about a secondary finding. If your contact information changes, providing us with the

new information is your responsibility. To tell us of your new contact information, by calling the Neuro-oncology Branch main office at (240) 760-6030.

If you have questions or concerns about learning this kind of genetic information, please speak with someone from the study team.

Risks of returning secondary genetic findings

- The evaluation for unexpected gene changes is limited and may not be as complete as clinical genetic testing that might be available to you outside of the research study.
- If an unexpected gene change result is confirmed, then that test result will go into your NIH medical record. These documents are confidential, but other NIH investigators can see them.
- Learning about the changes in your genes could mean something about your family members and might cause you or your family distress. Before joining the study, it may be helpful to talk with your family members about whether they want you to share your results with them.
- If a gene change is found, it may reveal whether a particular parent passed on the change to a biological child.
- You may receive a result for an unexpected gene change that turns out not to cause that health condition. This may cause you unnecessary distress or lead to unnecessary medical testing risks and costs.

Benefits of returning secondary genetic findings

An unexpected gene change result may be useful because you may be able to do something about it to protect your health or to help you plan for your future.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Bristol Myers Squibb or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

Conflict of Interest (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines, but they do not need to report their personal finances to the NIH.

Bristol Myers Squibb is providing nivolumab for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some non-NIH collaborators on this study who may receive payments or benefits, limited by the rules of their workplace.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address, or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive payment for participation in this study.

REIMBURSEMENT

Will you receive reimbursement or direct payment by NIH as part of your participation?

On this study, the NCI will reimburse the cost for some of your expenses such as those for hotel, travel, and meals. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

COSTS

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.
- Upon this trial's completion, Bristol-Myers Squibb Company will not continue to supply study drug to you. Your doctor is responsible to ensure that you receive appropriate standard of care or other appropriate treatment to treat your condition.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA) which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, Center for Cancer Research, or their agent
- Qualified representatives from Bristol Myers Squibb, the pharmaceutical company, who produces nivolumab.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance

that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research

purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Byram H. Ozer, M.D. PhD., Email: byram.ozero@nih.gov, Telephone: 240-760-6316. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713 if you have a research-related complaint or concern.

Consent Document

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant

Print Name of Research Participant

Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR

Print Name of LAR

Date

Investigator:

Signature of Investigator

Print Name of Investigator

Date

Witness should sign below if:

1. A short form consent process has been used to enroll a non-English speaking subject or
2. An oral presentation of the full consent has been used to enroll a blind or illiterate subject.

Signature of Witness*

Print Name of Witness

Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

_____An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

_____An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: