Protocol Title: PD-1 inhibition to determine CNS reservoir of HIV-infection
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PRINCIPAL INVESTIGATOR: Lauren Reoma, MD

STUDY TITLE: PD-1 inhibition to determine CNS reservoir of HIV-infection

STUDY SITE: National Institutes of Health Clinical Center

Cohort: *Patient*

Consent Version: *1/9/2022*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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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 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.

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?

Purpose of This Study

The purpose of this study is to learn if a drug normally used to treat patients with certain types of cancer, called pembrolizumab, can be safely taken by HIV positive patients.

Background

HIV infection affects more than 36 million people in the world. There are more than 1 million deaths and 2 million new infections each year. Even patients with well controlled disease continue to be at risk for serious infections and cognitive problems. There is some evidence that HIV can "hide" in in the brain, even in people with well controlled HIV without cancer. This may allow the virus to "wake up" and continue the disease progress.

Pembrolizumab (KEYTRUDA ®, made by Merck) is part of a group of drugs called monoclonal antibodies. These drugs enlist the body's natural immune system to fight off cells, such as cancer

cells.

Pembrolizumab is FDA approved to treat some types of cancers. We know of only two patients living with HIV-1 who have been treated with pembrolizumab for other viral infections of the brain. However, there have been studies in patients who have had cancer and were living with HIV-1 who received pembrolizumab. In these patients, pembrolizumab was associated with no change in safety events. In one study using pembrolizumab, in one patient with cancer living with HIV-1, the virus that causes Kaposi's sarcoma worsened, but that virus was already a problem for that patient. Pembrolizumab is not FDA approved to treat HIV. We are doing this study to see if it is safe to use in the HIV positive patients without cancer. This study is not for the treatment of HIV and only one dose of the drug will be used. We will also look at the effects it has on the body's response against the HIV virus in your blood and cerebral spinal fluid (CSF).

Study Population

This study is recruiting up to 20 patients who are HIV-1 positive. The study will be done at NIH in Bethesda Maryland.

Procedures

For this study, you will need to have 5-9 visits to the NIH Clinical Center in Bethesda, MD. Some of the visits may be spread out over several days. These visits will happen over 52-64 weeks and will be outpatient. Inpatient visits can be done instead for your medical or scheduling needs. The visits and tests that will be done are described below. All study procedures are done for research and safety purposes.

Study Table	√ Screening Visit Week -52 to 0	√ Week -12 to 0	√ Week 0	√ Week 3	√ Week 6	√ Week 12	√ Week 18	√ Week 24	√ Week 52
History	√	√	√	√	√	√	√	√	√
Physical exam		√	√	√	√#	##	##	√#	√#
Neurologic exam		√	√	√	√#	##	##	√#	√#
Pregnancy testing	√	√	√	√	√	√	√	√	√
Clinical and/or Research Blood Draw	√	√	√ *	√	√#	√	√	√#	√#
Lumbar Puncture (LP; Spinal Tap)		√		√				##	#
Leukapheresis		##		##				##	
Brain MRI		√		√				√#	#
FDG-PET/CT		√		√					
Pembrolizumab Dose			√						

*No clinical blood draw at Week 0 visit

In the event of an epidemic or pandemic, the timing of these study procedures are optional and can be performed when you can safely travel to the Clinical Center, at least once before you complete the study. For the MRI and lumbar puncture, if they are missed at the week 24 timepoint due to an epidemic/pandemic, they can be moved to the week 52 visit. If this is unable to be completed at week 52, a make-up final study visit will be allowed as soon as you can safely travel to the NIH Clinical Center.

Optional

History and Physical examination

You will have a physical and neurological examination. This physical examination is for research purposes only. It does not replace any exam you may receive from your own doctors.

We may ask you questions about your medical history over the phone or through a telehealth visit.

Intravenous Lines

We will place an intravenous (IV) catheter which is a small plastic tube inserted into a vein in your arm using a needle. The needle will be removed, leaving only the catheter in the vein. The catheter will be taped to the skin to hold it in place. The IV will be used to give the study drug and during the MRI procedure to give IV contrast.

Blood Drawing

You will have a blood draw from a vein. This may require a needle stick in your arm or hand, or if you already have an IV catheter in place, we may be able to draw through that. We will collect samples for clinical and research testing. We will draw no more than 30 teaspoons of blood at any one time. We will draw no more than 277 teaspoons of blood during the entire study. During this study it is possible you may have blood drawn at a laboratory closer to home, such as Quest and/or Labcorp, if you are not able to come to the NIH Clinical Center. We will make an appointment for you at your convenience within a 1-week pre-determined period of time, and you will need to go to the laboratory close to home for a standard blood draw.

Lumbar Puncture

You will undergo a lumbar puncture (sometimes called a "spinal tap") to obtain cerebral spinal fluid (CSF) samples at your week -12 to 0, week 3 and week 52 visit. This procedure involves inserting a small needle into your lower back. The study staff will help position you either on your side or sitting up. The lower part of your back will first be cleaned with antiseptic, and then the study doctor will inject a small amount of local anesthetic to numb the area. Once numb, a very thin needle will be inserted into the spinal canal in your lower back [well below where the spinal cord ends]. About 6 teaspoons of spinal fluid will be removed for analysis and storage. Your body usually replaces this fluid within 1-2 hours.

After the lumbar puncture is complete, you will be monitored for about 30 minutes. To prevent side effects, it is important that you not do any strenuous physical activity for 24 hours following the procedure. This includes lifting, bending, doing housework and gardening, or exercising.

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the body. We will obtain pictures of your brain for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. You will be in the scanner about 60-120 minutes. You may be asked to lie still for up to eight minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time.

During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (IV) catheter (small tube). It will be done for research 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.

Positron Emission Tomography (PET)

PET/CT scan

You will have PET (Position Emission Tomography) /CT (Computed Tomography) scan at your week -12 to 0 and week 3 visit. The PET/CT PET/CT is a doughnut-shaped machine that uses x-rays and a small amount of radioactive chemical to obtain images. It gives information on brain chemistry and function.

About 1 hour before the scan we will test your blood sugar either by doing a finger stick, or by removing a small amount of blood from your IV. Then you will have an IV placed (described above). The IV will be used to inject a small amount of radioactive sugar which can be detected by the PET scanner. You will be asked to rest quietly for about 60 minutes in a dimly-lit room while the FDG is absorbed by your body.

Following the 1-hour rest period, you will be asked to urinate, and then you will be placed in the PET/CT scanner.

The PET/CT machine is big enough for you to slide into by lying on a table in the middle of the 'donut hole' area. We may fit you with a plastic mask to hold your head in place during the scan.

The entire PET/CT scan will take about 15-45 minutes. During this time, you will need to lie very still. The scan itself is painless. You will hear buzzing and clicking sounds. You will be able to communicate with the PET technician at all times during the scan. You may ask to be moved out of the machine at any time.

After the scan, you will be asked to urinate. You should also urinate as often as possible for the rest of the day to help eliminate the radioactive FDG from your body.

Leukapheresis

The procedure for obtaining blood cells through leukapheresis is a very common procedure that is done routinely here in the Clinical Center with very few risks. White blood cells (lymphocytes) are removed from you using a serum cell separator machine. This requires putting

a needle into your arm to obtain blood to go into the machine. The machine divides whole blood into red cells, plasma (the liquid part) and lymphocytes (white cells). The lymphocytes will be taken out, and the plasma and red cells returned to you through a second needle in your other arm. The procedure takes between 3-4 hours to complete.

Contraception

You must agree to use 2 effective methods of contraception (birth control) from the time you enroll in the study until *4 months* after your last exposure to Pembrolizumab (when pregnancy is possible).

Effective methods of contraception for this study include:

1. hormonal contraception (birth control pills, birth control patches, injected hormones, hormonal implants or vaginal ring),

2. intrauterine device,

3. barrier methods (condom or diaphragm) combined with spermicide, and

4. surgical sterilization (hysterectomy, tubal ligation, or vasectomy).

It is important for you to know that no method of birth control is totally effective in preventing pregnancy except for surgical sterilization (hysterectomy, tubal ligation or vasectomy) or total abstinence from sexual intercourse.

If you have had a hysterectomy, tubal ligation, or vasectomy (or have a partner with a hysterectomy, tubal ligation or vasectomy), you do not have to use 2 methods of birth control.

Pregnancy Testing

If you are pregnant, you cannot be in this research study because the drug used in this study can harm a developing fetus. Women who are able to become pregnant will have a pregnancy test at the screening visit, on the day of pembrolizumab administration and at each follow up visit. If you become pregnant or father a child while you are in this study, please inform us.

If you or your partner becomes pregnant after you receive study drug, we will refer you to the NIH OB/GYN service for evaluation and counseling. You will still come for study visits and may have other study procedures. We may ask to evaluate and follow you or your partner throughout the pregnancy.

Study Drug Premedication

A half-hour before the study medication is given, you will be given pre-medications with acetaminophen (Tylenol) and diphenhydramine (Benadryl) to prevent infusion reactions. Acetaminophen is a common, over-the-counter pain and fever reducer, and diphenhydramine is an over-the-counter allergy medication.

Study Drug

The drug used in this study is called Pembrolizumab (KEYTRUDA ®, made by Merck) is part of a group of drugs called monoclonal antibodies. These drugs enlist the body's natural immune system to fight off cells, such as cancer cells. This medication will be given through your IV over a period of 30 minutes.

Storage and Sharing of Samples and Data

Your blood samples, spinal fluid, laboratory and MRI data will be stored securely on the NIH campus.

Your name and identifying information will not be on the samples and data. The samples and data will either have a code that links to your identifying information or will be stored without a code linking them to you. If they are coded, the key to the code will be kept at NIH in a separate, secure area and will not be shared.

Your research samples and data may be shared with others, including those not at NIH. Your samples and data may be sent to a repository for storage and may be released for research purposes. Some repositories restrict access to the samples and data they contain to researchers and projects they approve. Some repositories permit unrestricted access. The samples and data may be used for other research projects, including those not related to HIV. If you do not want your samples and data used for other projects, you should not participate in this study.

If you are enrolled in 13-N-0149, your data and samples may be shared with investigators of those studies. The data and samples may be shared with your name and identifying information. Sharing these data and samples will help minimize your need to repeat procedures if data or samples are already collected.

Research using samples and data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your samples and data.

If you withdraw from this research study before it is complete, you may ask that your remaining samples be destroyed. Results obtained before you withdraw will be kept. Your privacy will be protected as much as possible. We will not be able to remove samples or data that have already been sent to a repository or distributed to others.

Risks, Inconveniences and Discomforts

Study Drug: Pembrolizumab

There is a risk of serious side effects with the study drug. This drug is FDA approved for the treatment of certain cancers, but not for HIV infection.

Common side effects seen in cancer patients taking this drug included: upset stomach and constipation, coughing and trouble breathing, rashes and itchiness, tiredness, nausea, diarrhea, and joint pain or swelling. These common side effects, as well as blood testing, such as sugar and cholesterol tests, were abnormal in more than 20% of patients receiving this drug.

In people who have received this drug for the treatment of their cancers there is a risk of autoimmunity in approximately 20% of people. This means that the body is mistaking itself for something foreign and attacks one or more of its own organs. These are the major severe side effects that can be seen with this drug. They include: trouble with the thyroid gland, lung inflammation, bowel inflammation, liver inflammation, brain inflammation, heart issues, kidney problems, type 1 diabetes, arthritis, and other very rare immune problems. These problems can be seen more than 1 year after receiving the study drug. Some people with thyroid disease from

pembrolizumab required life-long thyroid replacement medications. Some people have even died from these auto-immune diseases after receiving pembrolizumab. We will monitor you for these types of diseases throughout the study and give you medical care if needed.

During the study you are advised to report to the investigators any new or worsening cough, chest pain, shortness of breath, diarrhea, severe abdominal pain, yellowing of the skin, nausea, vomiting, easy bruising or bleeding, persistent or unusual headache, extreme weakness or fatigue, dizziness, fainting, vision changes, blood in the urine or pain on urination, hair loss, heat or cold intolerance, unusual sweating, or unusual weight loss or gain.

The drug used in this study can harm a developing fetus and is an FDA pregnancy category D, meaning that there is known evidence of human fetal risk from study data.

This drug theoretically could cause "IRIS," which is also known as immune reconstitution inflammatory syndrome, in people with HIV infection. IRIS is a syndrome where your immune system increases and over-reacts to an infection such as a virus and causes inflammation around the areas that are infected. With one-time dosing, the drug is expected to remain in the body for more than one month. Most people tolerate the drug infusion with little difficulty – there is only a 0.1% chance of a reaction to the infusion reported in prior clinical trials.

History and Physical examination

There is minimal medical risk or discomfort from the physical exam.

Blood Drawing

Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

Intravenous Lines

The risks of IV insertion include temporary pain and bleeding or bruising at the site where the IV enters the skin. In placing the IV, there is a small chance of fluid leaking into the tissue surrounding the IV and infection, which may cause some swelling and discomfort. Rarely, the IV site may become infected, which might require treatment with antibiotics.

Contraception

It is important for you to know that no method of birth control is totally effective in preventing pregnancy except for surgical sterilization (hysterectomy or tubal ligation for women and vasectomy for men) and total abstinence from heterosexual sexual relations.

MRI

People are at risk for injury from the MRI magnet if you 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 us. 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.

Receiving contrast with an MRI

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 may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and 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.

Lumbar Puncture

The lumbar puncture may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. After the lumbar puncture you may get a headache. About a third of adults report a headache after an LP. To minimize the risk of a headache, the doctor will use a small needle and may prescribe bed rest for one or more hours after the procedure. If a headache occurs, it is usually mild and can be controlled by bed rest, drinking lots of fluids and a pain pill, such as acetaminophen. Rarely, the headache is severe

and may require additional treatment with a "blood patch". In this procedure, a small amount of your own blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache. A rare but serious complication of a LP, if it is done when the pressure inside the head is higher than normal (such as when a brain tumor is present), is known as medullary herniation which can result in death. Increased intracranial pressure is very unlikely to be present. The LP will not be done if there are any clinical indications that you have increased intracranial pressure, a skin infection in the lower back area, or bone malformation of the lower back (including severe scoliosis) which would make a LP difficult.

To minimize these risks, the lumbar puncture procedure will be performed by a medical professional specifically trained to do this procedure.

Sedation with MRI and/or Lumbar Puncture

Benzodiazepines are a class of drugs that act as tranquilizers and are commonly used in the treatment of anxiety. Benzodiazepines can cause sedation. Other possible side effects include confusion, dizziness and agitation. If you get a benzodiazepine, you will need to stay in the clinic after the scan until we determine it is safe for you to leave NIH. You will not be allowed to drive yourself home. You will need to arrange for someone to drive you or we will provide a taxi to take you home.

PET/CT

Some patients feel anxious from being in a small space. You may also be uncomfortable lying on the table. We will do our best to make sure you are comfortable during the scan. If you are pregnant or breastfeeding, you will not be able to take part in this study.

Leukapheresis

The risks of leukapheresis include pain, bruising, lightheadedness or dizziness, nausea, vomiting and chills. Bruising may last up to 72 hours.

Tingling around the mouth, fingers, or toes and mild muscle cramps may develop from slight lowering of the blood calcium by the blood thinner used during the procedure. These symptoms can be treated by either temporarily stopping the procedure or by giving a calcium pill. Leukapheresis uses a completely closed sterile system. The risk of infection is minimized by cleaning the skin before the needle stick. No infections from leukapheresis have been noted in thousands of such procedures performed over the last 10 years at the NIH.

Rarely, there can be a malfunction of the apheresis machinery that might prevent the return of your blood being processed in the machine. The amount of blood lost would be very small and not harmful. It is also rare for people to faint, have seizures, or have air trapped in the bloodstream.

Temporary or permanent nerve damage may occur at the needle placement sites. This is very rare. At the NIH, to this point, there have been no cases of permanent nerve damage with leukapheresis.

During the leukapheresis procedure, your platelet count may decrease because platelets are collected with the white blood cells. Platelets are cells that help your blood to clot. Taking aspirin in combination with a lowered platelet count may increase your chance of developing bleeding.

Therefore, you should not take aspirin or aspirin-containing drugs for 2 weeks after the procedure without physician approval.

Radiation Safety

What if you are nursing? If you are nursing, you cannot be in this research study because the radiation may harm your baby. If you are nursing a baby, please tell your doctor.

During your participation in this research study, you will be exposed to radiation from up to three lumbar punctures under fluoroscopy and up to two FDG-PET/CT scans per year. The amount of radiation exposure you will receive from these procedures is equal to approximately 1.47 rem. A 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." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The fluoroscopy and FDG-PET/CT that you get in this study will expose you to roughly the same amount of radiation as 4.9 years worth of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation

Study Drug Premedication

Acetaminophen is a common, over-the-counter pain and fever reducer. Overdoses of acetaminophen can cause irreversible liver failure, and acetaminophen in combination with high levels of alcohol, and certain seizure or anti-tuberculosis drugs are more at risk for liver failure. Diphenhydramine is an over-the-counter allergy medication which can cause sleepiness, short-term memory problems, dry mouth, trouble urinating and constipation.

Risks of Storing/sharing of samples and data

Even though we will remove information that could identify you from the samples and data that are sent to repositories or shared, there is a very small chance that the samples and data could be identified as yours.

Anticipated Benefits

There is no direct benefit to you from participating in this research study, however, we hope to learn more about the safety of pembrolizumab in patients with HIV infection.

Right of Withdrawal and Conditions for Early Withdrawal

You may withdraw from the study at any time and for any reason without loss of benefits or privileges to which you are otherwise entitled. We can remove you from the study at any time if we believe that continuation is not in your best medical interest or if you are unable to comply with the requirements of the study.

Results From this Study

We will share with you any new information that may relate to your willingness to continue to participate in this study. We will discuss the results of research tests with you that are important for your clinical care.

Study Termination

The study will be terminated if the study drug becomes unavailable or if the study drug is found to be harmful to individuals with HIV infection. In the event of study termination, if you have received study medication, we will continue to follow you clinically until the end of the study if needed.

Alternatives to Participation

This study does not provide treatment and does not replace any therapy that your own doctor is giving you. You may choose not to participate.

PAYMENT

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

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be compensated for research-related discomfort and inconveniences in accord with NIH guidelines. You will receive up to $2945.00.

	Total Occurrences	Pay	Pay for Study Completion
FDG-PET/CT	2	$190.00	$380.00
MRI	3	$130.00	$390.00
Lumbar puncture	3	$150.00	$450.00
Leukapheresis	3	$175.00	$525.00
Antecubital venous catheter	5	$30.00	$150.00
Gadolinium administration	3	$20.00	$60.00
Blood Draw	9	$50.00	$450.00
Clinic Visit	9	$60.00	$540.00
Total			$2945.00

If you are unable to finish the study, you will receive compensation for the parts you completed. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A “Form 1099-Other Income” will be sent to you if your total payments for research participation are $600 or more in a calendar year.

REIMBURSEMENT

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

NIH will provide travel to and from the Clinical Center in Bethesda, Maryland within the United States. Accommodations may also be provided if an overnight stay is necessary.

If your travel to the NIH Clinical Center (e.g. flight, hotel) is arranged and paid for by the NIH, the agency making the reservations and their representatives will have access to your identifiable 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.

CONFLICT OF INTEREST (COI)

The 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 Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

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, National Institute of Neurological Disorders and Stroke, or their agent(s)
- Qualified representatives from Merck, the pharmaceutical company who produces Pembrolizumab.

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.

POLICY REGARDING 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, Lauren Reoma, MD, lauren.reoma@nih.gov, 301-435-7531 Other researchers you may call are: Amanda Wiebold, RN, at 301-594-5194. 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

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

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: _____.