PRINCIPAL INVESTIGATOR: Mark Roschewski, M.D.

STUDY TITLE: Phase 2 Trial of Pembrolizumab in Relapsed and Refractory Gray-Zone Lymphoma (GZL), Primary Central Nervous System Lymphoma (PCNSL), and other Extranodal Diffuse Large B-cell Lymphomas

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: 03/05/2021

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.

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?

B-cell lymphoma is a cancer of certain white blood cells (called lymphocytes) that are found in lymph nodes and the cancer affects the lymphatic system. The lymphatic system helps to fight infections and disease. Types of B-cell lymphomas such as gray-zone and extra-nodal (including primary central nervous system, breast, testicular, leg-type, intravascular, and others) are rare and often aggressive sub-types of lymphoma that are resistant to current, approved therapies.

In this research study, the goal is to start to collect information if it may be effective to give pembrolizumab to patients with these types of rare, aggressive B-cell lymphomas. We will also collect research blood, tissue, and other samples to study in the laboratory to learn more about these types of lymphoma and how pembrolizumab may be working (or not) to treat it. Based on what we learn, we may continue to study pembrolizumab in future studies.

Pembrolizumab is FDA approved to treat a variety of cancers, including classical Hodgkin lymphoma. Pembrolizumab is not approved to treat the type of cancer you have. Pembrolizumab works in the body with your immune system to fight cancer cells. We hope to learn more about how it may work to treat the types of lymphoma included in this study.

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

You are invited to take part in this research study because you have a form of cancer called B-cell lymphoma, including gray-zone lymphoma or extra-nodal lymphoma (such as primary central nervous system, breast, testicular, leg-type, or intravascular) (DLBCL). You have received at least one previous treatment for the cancer, and the cancer has either remained stable or has worsened during or after your last treatment.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 52 participants are expected to take part in this study. This study is only being conducted at the NCI.

DESCRIPTION OF RESEARCH STUDY

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

The study doctor or staff will explain the requirements to take part in the study. If you agree to take part and have signed the informed consent form, you will undergo screening tests and procedures to see if you qualify for the study. These will be done after you sign consent for another screening study. Not everyone who wants to be in the study will be able to join.

During the study

After it is determined that it is safe for you to continue, you may need to have a few additional standard tests completed if not done recently. You will also have additional samples collected for research tests. You may then begin treatment on the study. You will be seen in the clinic at least every 3 weeks while on the study. This is described in detail below.

<u>Pembrolizumab Treatment</u>

All patients on this study will receive pembrolizumab. Treatment will be given in a series of cycles. Each cycle is 21 days (or 3 weeks). Pembrolizumab is given in the outpatient clinic by intravenous (or IV) infusion over about 30 minutes.

You may continue the treatment if you do not have unacceptable side effects, your cancer does not progress or gets worse, and the study doctors feel as though it is in your best interests. If you do well on treatment for a long time, you may be offered the opportunity to stop treatment so that we can watch and see how you do. In some cases, patients who stop treatment may be able to restart later if their cancer progresses or their doctor feels it is necessary. This may not always be possible and your doctor will talk more about these options with you, based on how you do and your cancer responds to the pembrolizumab during the study.

Study Procedures

Similar to the tests done at the beginning of the study, the following will be repeated during the study to see how you are doing and how the cancer may be responding to treatment:

- Clinical Assessments and Procedures:
  - History and physical exam, including obtaining information about how you function in your daily activities, side effects and symptoms, and a review of your medications
    - Standard blood and urine tests: Tests to measure your liver, kidney, and thyroid function, red and white blood cells, platelets, electrolytes and others will be done. Urine tests will be repeated about every other cycle, unless your doctor wants to repeat them more often.
    - Tests to measure how well your blood clots (also called coagulation studies)
    - Tests routinely done in patients with your type of cancer to confirm the status of your disease
    - As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS prior to starting treatment. Patients with HIV may take part in this study if felt safe to do so. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.
  - A bone marrow aspiration will be done prior to starting treatment if not done within the last 3 months since completing the last treatment received to confirm the stage and course of your disease. These are done by numbing your hipbone using a small needle containing a local anesthesia, and then a needle will be put into the hipbone, and a small amount of bone marrow will be taken out through the needle. This will be repeated on study if needed to confirm response.
  - A lumbar puncture may be done to confirm the stage and course of your disease prior to starting treatment and during treatment if needed to confirm response.
  - An ophthalmologic exam may be done prior to starting or during treatment; these will be required prior to treatment in patients with primary central nervous system lymphoma.

- Imaging to show all sites of disease, including CT and/or MRI scans, and PET scans if needed to confirm response. These will be repeated at the end of cycles 2 and 6, and at about months 9, 12, and every 6 months thereafter during treatment. These may also be repeated between assessments if your doctor thinks that you may have had a complete response to treatment (known as a CR or complete response) or if it is felt that your cancer may be progressing. All imaging will be done similarly as those that you have had as part of other standard treatment prior to this study. The type of imaging will be decided by your doctor.
- Gadolinium enhanced MRI: 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.
- PET Scan: You will have PET (Positron Emission Tomography) scan at baseline and Post-treatment visits . The PET scanner is a doughnut-shaped machine that uses x-rays combined with a dose of a radioactive substance (tracer) to create computer pictures showing the inside of your body.

  Before the scan, you will have a radioactive substance injected into your arm after which, you will need to wait for approximately 30 minutes for the substance to be absorbed. After 30 minutes, you'll lie on a narrow, padded table and be positioned for the scan. The scan itself is painless and won't make much noise. During this time, you will need to lie very still. It will take about another 30 minutes to complete.
- CT Scans: 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.

- Research Sample Collection:
  - Blood Samples: Blood (about 2-3 tablespoons) will be collected for laboratory studies at the beginning of the study and at about the same time as each imaging assessment, and if at any time your doctor thinks you have responded or may have progressed during or after treatment.
  - Cheek Swab or Saliva Samples: A cheek swab and/or saliva sample to collect normal tissue will be done, likely at the beginning of the study only. To obtain a cheek swab, a small brush is rubbed against the inside of the cheek to wipe off some cells. To obtain saliva, a special collection tube will be used and may take a few minutes to get the amount of saliva needed; you may be asked not to eat or drink for about 30 minutes or rinse your mouth just before collection.
  - Cerebrospinal Fluid (or CSF) Samples: If you have a routine procedure to collect CSF (such as a lumbar puncture) we will collect samples at the same time for

research tests. If you have a special type of access device (known as an Ommaya®), we will ask for CSF samples at the same time points as the blood samples during the study.

- Tissue Samples: If tissue from your original diagnosis and/or from a procedure for your disease is available (taken either before or during the study), this will also be collected for the study. If prior tissue is not available or is not enough for the planned research tests, a biopsy will be required prior to starting treatment.
- Biopsies:

The biopsies are an optional part of the study (unless one is required prior to starting if prior tissue is not available or adequate) and you will only be asked to do so if it is felt to be safe. We will ask you to undergo a tumor biopsy at the beginning of the study, after about 2 cycles of treatment, and again if your disease should progress during or after treatment on this study. The tissue is being collected for special research tests.

Your doctor or the study team will discuss the biopsies with you. The biopsies to be performed are exclusively for research purposes and will not benefit you. They might help other people in the future.

You may agree to biopsies now and change your mind later. If at any time you do not want to have a biopsy done, please tell us.

A part of all biopsies done may be sent to the clinical laboratories for a standard of care evaluation to confirm the stage and grade of your disease, portions of the samples will also be used for research tests.

- Tumor Biopsy: Usually tissue can be obtained safely and comfortably with local anesthesia. If you require sedation before undergoing a biopsy, you will be informed of the risks and you will be asked to sign an additional consent prior to undergoing the procedure. Biopsies will NOT be done on this study if they require general anesthesia. We may ask that you have ultrasound to help clearly locate your tumor when doing a biopsy.

The following sections describe studies to be done on your samples for research:

What tests will be done on my samples?

Your tissue (tumor and normal tissue) and samples that are collected will be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) are the molecules inside cells that carry genetic information and pass it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow. To determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for

years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins. When we are examining these pieces of your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings".

These include:

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

However, the analyses that we perform in our 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 tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to have an additional tube of blood drawn to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic healthcare provider to discuss the results.

Who else besides the investigators on this study will know the results of my sample testing?

Once we obtain any of the samples listed above, the investigators take all your personal information off those samples and label them with a study code number. Only the investigators on this study know who the sample came from. The key linking your personal information with the code number is kept in a secure computer data base, with access only to the limited research staff who will be discussing this study with you. Once the sample has been labeled with a code, it is sent to a variety of NIH laboratories for storage and testing. No one testing your samples will be able to link the results to you personally. Specimens obtained during your participation in this study may be sent for testing to investigators outside of NCI or the NIH. All samples will be coded to protect your privacy and no personal information will be included. Other investigators on this study will have access to limited clinical and biologic data such as age, gender and disease status.

How long will your samples be stored?

The samples collected during this study will be stored for as long as the study is open. When this study is closed, we will keep the samples for future research.

When you are finished taking the drugs (treatment)

You will be asked to return to the clinic about 30 days after the last dose of pembrolizumab. At this visit we will repeat most of the tests and procedures above, and see how you are doing. We

may continue to contact you more frequently after this visit if you continue to experience side effects from the medications.

After this visit and if your cancer has not progressed, we will ask you to return to clinic at about the following times after treatment for as long as your disease does not recur (come back) or progress: every 3 months in year 1, every 6 months in year 2-5, and once each year thereafter. We may contact you by phone (or mail, email, etc.) more frequently between visits to see how you are doing.

If or when your cancer progresses, or if you start another cancer treatment, we will contact you by phone (or mail, email, etc.) to see how you are doing for the rest of your life, or until the study is closed (whichever is sooner).

REPRODUCTIVE RISKS AND BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, you will need to practice effective birth control before starting study treatment, during study treatment, and after treatment as noted below.

Men and women of reproductive potential must refrain from sexual activity (abstinence) or use (or have their partner use) effective birth control during treatment and for at least 120 days after the last dose of pembrolizumab.

The following are the acceptable birth control methods:

Highly effective options; **one** method may be used:

- intrauterine device (IUD)
- vasectomy of a female subject's male partner
- contraceptive implant (e.g., rod) into the skin

Additional effective method options; **two** methods must be used:

- diaphragm with spermicide (cannot be used with a cervical cap/spermicide)
- cervical cap with spermicide (only in women who have never been pregnant)
- contraceptive sponge (only in women who have never been pregnant)
- male condom OR female condom (cannot be used together)
- hormonal contraceptive (such as birth control pills, skin patch, vaginal ring, or injection)

Please discuss this with your doctor. If you think that you or your partner is pregnant, you must tell your study doctor or nurse **IMMEDIATELY**.

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. You should tell your study doctor and/or a member of the study team about any side effects you are having. You may be given medicines to help treat the side effects and prevent them from becoming worse. In some cases, side effects can be serious or

long-lasting or may never go away. There is also the risk of death from either the treatment or your disease. In addition to the risks listed below, there could be unknown or unexpected side effects.

Risks and side effects related to the treatment and the procedures on this study are identified below:

Pembrolizumab (KEYTRUDA™)

Pembrolizumab may affect how different parts of your body work, such as your liver, kidneys, heart, and blood. The lists below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Pembrolizumab 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:

Very common side effects:

- Itching
- Diarrhea, loose or watery stools
- Cough

Common side effects:

- Joint pain, there are also some reports of joint inflammation, stiffness and/or swelling
- Rash
- Fever
- Back pain
- Pain in belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach

Uncommon side effects:

- Inflammation of the lungs that you may feel short of breath and cough
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus

- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (including peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection

Rare side effects:

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the muscles so you may feel weak or have pain in your muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs

- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness

In addition to the above, if you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

Patients treated with pembrolizumab BEFORE going on to receive an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), should inform their transplant physicians that they have received pembrolizumab in the past.

In patients with any hematologic malignancy (cancers of the blood like Hodgkin lymphoma, multiple myeloma): there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab BEFORE an allogeneic stem cell transplant. Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver and gastrointestinal symptoms), including death, have been received for patients who received pembrolizumab BEFORE an allogeneic stem cell transplant.

Tell your study doctor right away if you have any of these symptoms as they may need to be treated urgently. You will be followed closely for any undesirable or unexpected side effects during your participation in this study and each time you receive Pembrolizumab.

There may be other side effects of Pembrolizumab 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.

Risks from tests and procedures:

- Blood draws: The possible side effects of drawing blood include pain, bleeding, bruising, dizziness, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein.
- Bone marrow: A numbing agent that can cause a stinging or burning sensation may be injected at the site of your bone marrow biopsy. The biopsy needle will go through the skin into the bone and may produce a brief, sharp pain. As the bone marrow liquid is taken from the bone, there may be a brief, sharp pain. Since the inside of the bone cannot be numbed, this procedure may cause some discomfort, however not all patients experience discomfort. The possible side effects associated with a bone marrow biopsy include pain, bleeding, bruising, and infection, as well as a reaction to the numbing agent.
- CSF collection: If this is done, it will be done by lumbar puncture (also referred to as a spinal tap) or from an Ommaya. During a lumbar puncture, a needle is carefully inserted into the spinal canal low in the back (lumbar area). A numbing agent may be used prior to inserting the needle. The risks of collection are similar to blood and bone marrow testing; rarely patients may have a headache or nerve damage due to the procedure.

- Tumor biopsy: The likely side effects include discomfort or pain, redness, swelling, and/or bruising at the site of the needle insertion. Bleeding from the site of the needle insertion is a less likely risk. Rarely, significant infection or bleeding from this procedure, allergic reaction to the anesthetic, or formation of a scar at the site of needle entry occurs. If you will have sedation with the procedure, these risks will be discussed with you prior to the procedure. You will be asked to sign a separate consent form prior to any biopsy procedure.
- Imaging/scans: CT, PET, and/or MRI scans are used to monitor your disease while you are in this study and involve the following risks.

  You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

  - Contrast Agents – CTs and PET scans: There is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems.

    For IV contrast: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

    For oral contrast: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after drinking the contrast.
  - Radiation – CT and PET Scans: During your participation in this research study, you may be exposed to radiation from up to a maximum of 5 CT Scans and 2 PET Scans in a single year. The amount of radiation exposure from these procedures is equal to approximately 7.9 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." This study will 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 CT and PET scans that you get in this study will expose you to the roughly the same amount of radiation as 26.3 years' worth 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 0.8 out of 100 (0.8%) and of getting a fatal cancer is 0.4 out of 100 (0.4%).
  - 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.

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 related to gadolinium enhanced 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. 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.

- Risks of 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.
- Urine Collection: There is no physical risks involved with urine collection.
- Eye examination: There are no expected long-term risks expected with the eye exams if you need to have one based upon your disease.

Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Privacy Risks Associated with Return of Incidental or Secondary Findings

Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives.

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.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if pembrolizumab may be effective in treating rare and/or aggressive types of lymphoma. We also hope to learn more about how these lymphomas and ways to treat them by studying blood and other tissue samples in the laboratory. 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. 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.
- Not receiving any treatment or care at all.

Please talk to your doctor about these and other options.

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 you become pregnant
- if you are unable to comply with study requirements
- if study therapy is delayed for too long
- if you need a medication that is prohibited on this study
- if your disease comes back during treatment and your doctor does not think you are receiving benefit
- 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
- if the study is stopped by the study doctor and/or supporters

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 the study collaborators, including those providing the study medications, 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 can**not** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide 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.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

Merck, Inc. is providing pembrolizumab 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.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

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 any payment for taking part 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, 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 you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- 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.

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
- Qualified representatives from Merck, Inc, the pharmaceutical company who produces the study drug 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, Mark Roschewski, M.D., Mark.Roschewski@nih.gov, 240-760-6183. 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 to the oral short-form consent process only:

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: _____.