PRINCIPAL INVESTIGATOR: Milos Miljkovic, M.D.

STUDY TITLE: A Phase I Study of Subcutaneous Recombinant Human IL-15 (s.c. IL-15) and Alemtuzumab for Patients with Refractory or Relapsed Chronic and Acute Adult T-cell Leukemia (ATL)

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: 09/18/2020

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.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

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

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

The general purpose of this study is to develop treatments for T-cell leukemias and lymphomas (TCLL), such as adult T-cell leukemia (ATL), cutaneous T-cell lymphoma (CTCL), peripheral T-cell lymphoma (PTCL), and T-cell prolymphocytic leukemia (T-PLL), that are more effective than existing therapies. The experimental part of this treatment program is to test whether giving

recombinant human interleukin 15 (IL-15) in combination with alemtuzumab (also known as Campath) will improve the outcome of therapy for your disease.

IL-15 is a man-made version of a small protein (cytokine) that is naturally produced in your body by certain white blood cells and increases the activity and strength of the immune system. People with cancer can have a weak immune system. This weakness can be caused by the cancer itself, or by treatments such as radiation, chemotherapy or other drugs that work against the immune system. It is hoped that IL-15 can "boost" or strengthen a person's immune systems as they fight against cancer.

IL-15 has been administered to over 20 participants in three clinical studies. The IL-15 was given into the vein in two of the studies and subcutaneously in the third study. All of the participants in these studies showed an increase in the number of their immune system cells. In some of the participants, the increase was dramatic. Participants had minor side effects and only two serious side effects. One participant had inflammation of the pancreas and another one had inflammation of the stomach.

Alemtuzumab is a monoclonal antibody that works by attaching to a protein on your tumor cells. Recent evidence indicates that the effects of cancer therapy may be improved by combining other cancer therapies with monoclonal antibodies. Monoclonal antibodies are purified proteins that are specially made to attach to pieces of foreign substances (such as cancer cells) with the goal of inactivating them. We say this therapy is experimental because we do not know if it will improve your health.

IL-15 is not approved by the US Food and Drug Administration (FDA). Alemtuzumab is approved by the FDA for the treatment of B-cell chronic lymphocytic leukemia (B-CLL).

The goals of this study are to determine the safe dose of IL-15 when combined with alemtuzumab to be used in humans, identify the side effects of the combination treatment, and the effects on your immune system, and determine if this treatment has activity against your cancer.

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

You are being asked to take part in this study because you have adult T-cell leukemia, cutaneous T-cell lymphoma (CTCL), peripheral T-cell lymphoma (PTCL), or T-cell prolymphocytic leukemia (T-PLL) and other treatments have not helped you.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 30 participants will participate in this study. At the beginning of the study, 3 participants will be treated with a low dose of the IL-15. If this dose does not cause bad side effects, the dose of IL-15 will slowly be made higher as new participants take part in the study.

DESCRIPTION OF RESEARCH STUDY

This trial is designed to test the safety of different doses of IL-15 when given as a subcutaneous injection (SC) for 10 days followed by 4 weeks of alemtuzumab given as an intravenous infusion in participants with TCLL. You will receive daily subcutaneous injection of IL-15 – five doses per week for two weeks (10 total doses) beginning on Monday and ending on Friday. During the third week, you will receive alemtuzumab on Day 1, Day 2, Day 3 and Day 5 (usually Monday,

Tuesday, Wednesday and Friday.) You will start with a small dose of alemtuzumab (3 mg) and you will be given a higher dose each on the next two days [10 mg on Day 2 (Tuesday) and 30 mg on Day 3 (Wednesday) and Day 5 (Friday)]. During the next three weeks, you will receive alemtuzumab 30 mg three times a week on Monday, Wednesday and Friday.

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

Before you begin the study

Before you begin the study, you will come in for one or two visits to find out if you are eligible to participate in the study. You will be asked to sign a separate "Screening" informed consent form before any of the tests are performed. Many of these tests are performed as part of your regular medical care or during the prior treatments for your cancer. These tests need to be performed within 28 days before you enroll in this study. After all of these examinations are performed and we determine you are eligible for the trial, you will be asked if you choose to participate in this research study.

During the study

If the screening process shows that you can be in the study, and you choose to be in it, then we will ask you to come to the clinic about 30 times during the treatment portion and periodically after you finish treatment. Participants with TCLL involving their skin may have pictures of the wounds (lesions) caused by the TCLL taken at regular intervals during treatment and see a dermatologist to document any changes in these lesions that may occur.

The following will be repeated during the study to see how you are doing and how the cancer may be responding to treatment:

- Review of medical history, and a physical exam (check weight and vitals), including obtaining information about how you function in your daily activities, side effects and symptoms, and review of medications
- Routine blood and urine tests
- MRI Scan: Magnetic Resonance Imaging or MRI is a scan that provides your doctor with multiple detailed pictures of the inside of the body. MRI does not use radiation. In order to visualize some structures in the body, including tumors, a special dye or contrast agent may have to be injected into you intravenously. This test takes between 35-120 minutes to complete depending on the area of the body being scanned. You will lie on a stretcher with your head in a head rest to prevent movement during the scan. The stretcher will be placed in a strong magnetic field, but you should not feel anything from the magnet. You must remove anything that is metal before having this test. You will hear a loud, repetitive, thumping noise. Younger patients and patient who have difficulty holding still or tolerating being placed in a scanner, can receive medications to make them sleep through the procedure by a doctor called an anesthesiologist. If you are awake for the procedure, you will be able to communicate with a technician at all times and can request to be removed from the scanner at any time.
- CT Scan: A Computerized Tomography or CT scan provides multiple detailed pictures of the inside of the body, like an MRI scan, but the CT scan uses radiation, similar to an

X-ray. CT scans may be done with or without oral or intravenous contrast. The scan may take between 30-90 minutes to complete depending on the areas of the body being scanned and the type of scanner.

- PET Scan: A Positron Emission Tomography scan or PET scan for short lets doctors see the activity of cells in specific tissues of the body. A sugar, which is attached to a chemical that gives off a signal, is injected into you/your child intravenously before the scan. The scanner records the signals through the body.

During the first 2 weeks of the study, we will ask you to come to the clinic Monday through Friday of each week. At these visits you will:

- Be given the IL-15 under your skin with a needle;
- Take medicine such as ibuprofen (e.g. Advil), acetaminophen (e.g. Tylenol), before the IL-15 injection. These will help to decrease the side effects caused by the IL-15;
- Have a physical exam and have your vital signs (heart rate, blood pressure, respiration, temperature and oxygen level) measured;
- Be asked to give blood samples for routine analysis and for research;
- Be asked questions about your health and any medicines you are taking;
- Be asked to stay in the clinic for 4 to 6 hours so we can address any problems you have from the IL-15.

On Day 1 of the 3rd week of the study, you will be admitted to the NIH Clinical Center inpatient unit for the alemtuzumab infusions. You may be discharged from the inpatient unit and treated in the outpatient clinic when your experience with the treatment indicates that the alemtuzumab can be given safely in an outpatient setting. During your stay on the inpatient unit and/or in the outpatient unit, you will:

- Receive the alemtuzumab infusion in your vein through a small catheter on Days 1, 2, 3 and 5 (usually Monday, Tuesday, Wednesday and Friday);
- Take medicine such as acetaminophen (e.g. Tylenol) and diphenhydramine (Benadryl) before the alemtuzumab infusion. These will help to decrease the side effects caused by the alemtuzumab;
- Take a blood thinner such as rivaroxaban (a tablet) or enoxaparin (a shot under the skin) during alemtuzumab treatment and for two weeks afterwards to decrease your risk of developing a blood clot in the veins or lungs.
- If you are at risk of your disease spreading to (or coming back within) your central nervous system, you may also receive a dose of the drugs cytarabine and methotrexate injected into your spinal fluid.
- Have a physical exam and have your vital signs measured on the treatment days;
- Be asked to give blood samples for routine analysis and for research;
- Be asked questions about your health and any medicines you are taking;
- Be asked to stay in the outpatient clinic for 4 to 6 hours, if necessary, so we can address any problems you have from the alemtuzumab;

- Be scheduled to have a CT scan on Friday, so we can see how your TCLL is responding to the treatment.

During the 4th, 5th and 6th weeks of the study, you will be admitted to the NIH Clinical Center inpatient unit for the alemtuzumab infusions; unless your experience with the treatment during week three indicates that the alemtuzumab can be given safely as an outpatient. If you are able to receive the alemtuzumab in the outpatient clinic, you will come to the clinic on Monday, Wednesday and Friday. At these visits you will:

- Receive the alemtuzumab infusion in your vein through a small catheter on Monday, Wednesday and Friday;
- Take medicine such as acetaminophen (e.g. Tylenol) and diphenhydramine (Benadryl) before the alemtuzumab infusion. These will help to decrease the side effects caused by the alemtuzumab;
- If indicated, you may receive repeated doses of cytarabine and methotrexate injected into your spinal fluid every 6-8 weeks for up to 3 (three) doses in the clinic.
- Have a physical exam and have your vital signs measured on the treatment days;
- Be asked to give blood samples for routine analysis and for research;
- Be asked questions about your health and any medicines you are taking;
- Be asked to stay in the clinic for 4 to 6 hours, if necessary, so we can address any problems you have from the alemtuzumab.

When you are finished taking the treatment

When you finish taking the experimental therapy, you will come to the clinic for follow-up visits and assessments every two months for the first 6 months and then every three months for up to 2 years. These clinic visits will include having blood samples collected for routine analysis and for research and CT scans.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for four months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

If you choose to take part in this study, there is a risk that the study treatment may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

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

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

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

Here are important things to know about side effects:

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

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

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

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

Risks of IL-15

You may have side effects from the IL-15 while on the study. We pay close attention to any side effects you have. However, we don't know all the side effects that may happen. Side effects may be mild or very serious. We may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the IL-15. In some cases, side effects can be serious, long lasting, or may never go away. It is possible that IL-15 could increase the growth of your leukemic cells, that is the IL-15 could make your TCLL worse. There also is a risk of death.

Please talk to us about any symptoms you have while you are in the study.

In studies with humans, <u>common and not very common risks and side effects related to the IL-15 included the following</u>:

POSSIBLE, SOME MAY BE SERIOUS
• Anemia which may require blood transfusion • Abnormal heartbeat • Pain in belly • Diarrhea, nausea, vomiting • Chills, tiredness, fever • Swelling of arms, legs • Swelling and redness at the site of the medication injection • Severe blood infection • Bruising, bleeding • Infection, especially when white blood cell count is low • Muscle weakness • Dizziness, headache • Shortness of breath • Dry skin • Rash • Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles • High blood pressure which may cause blurred vision • Low blood pressure which may cause feeling faint

Other risks seen with IL-15 that are possibly related to the drug include:

- Chest pain
- bronchopulmonary hemorrhage and diffuse alveolar hemorrhage (bleeding in the lungs)
- Confusion, psychosis (i.e., delusions, hallucinations)
- Kidney failure - signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Papilledema (changes in vision due to increased pressure in the brain)
- Uveitis (inflammation of the eye – symptoms may include redness, pain, blurred vision)
- Pneumonitis (inflammation of the lungs) - symptoms may include new or worsening cough, chest pain, shortness of breath.
- Inflammation of the lining of the first part of the small intestine symptoms may include nausea, vomiting, stomach burning, pain, indigestion
- Liver damage which may cause yellowing of eyes and skin, swelling and may result in liver failure
- Decreases in blood levels of albumin, phosphorus (these are standard blood tests)
- Low number of white blood cells, cells that help fight infection (lymphopenia, leukopenia, neutropenia)
- Low platelets, cells that help blood to clot (thrombocytopenia)

- Low blood oxygen – symptoms may include changes in skin color, confusion, cough, fast heartbeat, shortness of breath
- Immune related adverse events: hives, hypothyroidism and production of autoantibodies – symptoms made include joint pain, tiredness fever, rashes, allergy-type symptoms, muscle weakness

Risks of Alemtuzumab

Likely: These side effects occur in greater than 50% of people

- Mild flu-like symptoms such as chills, fever (usually occur only with the first dose and decreased or absent with each following dose). Stopping or increasing the time it takes to give you alemtuzumab may make these side effects go away.
- Decreased white blood cells (including normal T-cells), which may increase the risk of infection (bacterial, viral, fungal, parasitic); you will be given medicines to prevent infections.
- Decreased red blood cells (anemia), which may make you feel more easily tired, or even out of breath when performing simple daily tasks. It may also cause you to feel lightheaded or have a rapid heartbeat. If you become symptomatic, red blood cell transfusion may be needed.
- Decreased platelet counts, which may increase the risk of bleeding or bruising. If bleeding becomes serious such bleeding from the gastro-intestinal tract, platelet transfusion will be warranted.
- Asymptomatic virus infection, in particular a virus called cytomegalovirus (CMV). CMV is a common virus that infects most people worldwide. It is a member of the herpesvirus family. Other members of the herpesvirus family cause chickenpox, infectious mononucleosis, fever blisters, and genital herpes. These viruses all share the ability to remain alive, but dormant, in the body for life. The virus lives in the body silently without causing obvious damage or illness but may reactivate when the immune system weakens. Even upon reactivation, there are usually no symptoms produced and is detected only on a blood test. You will be monitored closely with a blood test each time you return to clinic for signs of this infection.

Less likely: These side effects occur in 10-50% of people:

These usually occur only with the first dose and are decreased or absent with each following dose.

- skin rash
- itching
- nausea
- vomiting
- diarrhea
- general sick feeling
- decreased appetite

- headache
- fatigue
- low or high blood pressure
- shortness of breath
- cough
- rapid heart beat
- sweating
- muscle pain
- sepsis - increased risk of bacterial and fungal infections

Occasional: These side effects occur in <10% of people:

- dizziness
- dysesthesia or paresthesia (abnormal touch sensation)
- tremors
- insomnia
- sweating
- abnormal taste
- vasodilatation (increased blood flow)
- confusion
- anxiety
- constipation
- leg edema

Unlikely: These side effects occur in <1% of people**.**

- joint pain
- conjunctivitis
- deep vein thrombosis

Unlikely, but serious: These side effects are severe, life threatening, or cause death.

- **Abnormal clotting of the blood resulting in serious complications such as clotting of blood vessels in the lungs:** two participants on this study have developed blood clots in the lungs. The clots were found during a planned CT scan, and neither participant had symptoms or further complications. However, this is a serious side effect that may lead to death. To decrease the risk of blood clots, you will be required to take a low dose of a blood thinner during alemtuzumab treatment and for two weeks after the treatment ends (six weeks total).
- Allergic reactions with any of the following symptoms:
- Marked lowering of the blood pressure, throat tightness, shortness of breath, severe skin rash

- Development of other cancers or recurrence of a past cancer.
- Heart rhythm, kidney, and lung problems caused by chemicals released into your blood from dead cancer cells; you will receive extra fluids before you start your treatment with alemtuzumab to flush any extra chemicals out of your body, and you will also be given medicine to help control the chemical balance of your blood.
- Serious viral infection
- Changes in liver enzymes
- Cardiac arrhythmias
- Seizure
- Leukoencephalopathy – Progressive loss of neurological function, the most prominent symptoms are clumsiness, progressive weakness, visual, speech and sometimes personality changes

Since alemtuzumab can cause a prolonged lowering of lymphocytes (white blood cells), you may develop an increased risk for serious infections, the development of other tumors, or the recurrence of a previous cancer. Also, it is important to know that participants may develop other unexpected side effects, and these could lead to serious organ damage or even death.

Risks of Additional Study Treatment

If you are at risk of your disease spreading to (or coming back within) your central nervous system, you may receive up to three (3) doses of cytarabine and methotrexate injected into your spinal fluid. Methotrexate and cytarabine can cause inflammation of spinal membranes, manifesting as headaches, vomiting, and fever. In very rare cases, the inflammation associated with methotrexate may cause transient paralysis or a seizure. A third drug (hydrocortisone) is given to prevent this from happening but does not completely remove the risk.

In order to give the treatment into your spinal fluid (also referred to as "intrathecal" administration), you may experience transient back and neck stiffness or pain shortly after administration of the medications. Your doctors can explain this in more details and answer any questions that you may have if they feel the benefits of this additional treatment outweigh the risks.

Risks of Study Procedures

- Blood Sampling: The blood samples collected as part of this study are not expected to produce any important decrease in the total amount of blood in your body. Side effects may include pain and discomfort, bruising, and rarely inflammation of the vein, bleeding or infection. Additionally, some subjects can experience light-headedness or fainting.

  Risks of body scans: CT scans, PET and/or MRI scans are used to monitor your disease while you are in this study. CT and PET scans expose you to radiation and the amount depends on the number of body areas scanned. In addition, CT, PET and MRI scans may involve use of contrast (oral and/or IV) so that the cancer may be seen better on the images. In the small group of people who have a reaction, the most common symptoms are nausea, pain in the vein where the contrast was given, headache, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely, these symptoms

may require treatment. In very rare cases, people have had more severe allergic reactions that result in skin rashes, shortness of breath, wheezing, or lowering of the blood pressure. If you have had a reaction in the past, be sure to tell your doctor or nurse about it. Please ask the study doctor if you have questions about the risks of these scans. If done, MRI scans do not involve radiation risk. The scans that you will receive during this study are considered standard for your type of disease.

- Risks of ibuprofen (e.g. Advil), acetaminophen (e.g. Tylenol): Taking these medicines can cause stomach ache, constipation, diarrhea, dizziness, headache, and nausea.
- Risks of anticoagulation prophylaxis: Taking these medications carries a risk of bleeding and other safety issues, such as spontaneous bleeding.
- Risks of bone marrow biopsy: Side effects may include pain and discomfort, bleeding or bruising, and rarely inflammation at the biopsy site or infection.
- Risks of having pictures taken of the skin wounds (lesions) caused by the TCLL: There are no risks involved in having pictures taken of your skin lesions caused by the TCLL.

Radiation Exposure from Imaging

During your participation in this research study, you will be exposed to radiation from CT of the neck, chest, abdomen, and pelvis, and from FDG PET/CT of the torso and the extremities. The amount of radiation exposure you will receive from these procedures is equal to approximately 15 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 FDG PET/CT that you get in this study will expose you to the roughly the same amount of radiation as 51 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 1.5 out of 100 (1.5%) and of getting a fatal cancer is 0.8 out of 100 (0.8%).

Radiation Exposure in People Capable of Becoming Pregnant

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.

MRI Risks

Your doctor may want you to get a magnetic resonance imaging (MRI) scan. 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. We will place soft padding or a coil around your head. You will be in the scanner about 45 minutes. You may be asked to lie still for up to 15 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.

It is very important for the experiment that you do not move your head or body inside the scanner. We will use padding around your head to help keep it in place.

We may place a bar in your mouth to help keep your head still.

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

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

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

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

Risks for gadolinium enhanced MRI scans:

Procedure

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

Risks

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

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms 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" which 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 not normal or if you received gadolinium within the previous month.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA recently 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 than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain.

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.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The major aim of this study is to see if treating subjects with IL-15 in combination with alemtuzumab is safe, and then to see if the treatment may cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

What other choices do I have if I do not take part in this study?

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

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

Please talk to your doctor about these and other options.

Stopping Therapy

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

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe

- if new information shows that another treatment would be better for you

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

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

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the study team 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.

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, 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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the 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 not receive compensation for participation in this study.

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

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. 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.

Will taking part in this research study cost you anything?

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

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

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

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, Center for Cancer Research, or their agent(s)
- Qualified representatives from The Biopharmaceutical Development Program (BDP) at NCI, the pharmaceutical company who produces IL-15.

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, Milos Miljkovic, M.D., Phone: 301-250-5216, Email: milos.miljkovic@nih.gov. 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:

Witness:

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: _____.