PRINCIPAL INVESTIGATOR: Robert Kreitman

STUDY TITLE: A Phase I study of Moxetumomab Pasudotox-tdfk (Lumoxiti™) and either Rituximab (Rituxan®) or Ruxience for Relapsed Hairy Cell Leukemia

STUDY SITE: NIH Clinical Center

Cohort: *Standard*

Consent Version: 4/16/2025

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Robert Kreitman, MD
Phone: 301-648-7375
Email: kreitmar@mail.nih.gov

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

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information 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 to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

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?

This study is being carried out to determine the safety of Moxetumomab pasudotox-tdfk in combination with Rituximab or Ruxience in patients with hairy cell leukemia (HCL) or HCL variant. Moxetumomab pasudotox-tdfk is made up of two parts: 1) a modified mouse antibody that attaches to a protein from the immune system, called "CD22", which can be found on the surface of cancer cells, and 2) a toxin. An antibody is a type of protein that your immune system makes

when it sees a foreign substance in your body. The modified mouse antibody used in Moxetumomab pasudotox-tdfk has been changed in the laboratory to contain only the part that attaches to CD22. The second part of Moxetumomab pasudotox-tdfk is a toxin that is made by bacteria. Moxetumomab pasudotox-tdfk is made by combining the portion of the antibody that attaches to CD22 with the toxin. Moxetumomab pasudotox-tdfk (also called Lumoxiti™) was recently approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or resistant HCL who have received at least two prior systemic therapies, including treatment with a purine nucleoside analog. The dose chosen for this study is based on earlier safety and efficacy studies of this agent in adults with cancer.

Rituximab (also called Rituxan®) and Ruxience are antibodies which bind to CD20 protein in cancerous white blood cells. These cancerous cells are then destroyed and their levels in the circulation are decreased helping the body to fight cancer. In the US and Europe rituximab and Ruxience have been approved to use in patients with chronic lymphocytic leukemia and non-Hodgkin's lymphoma. In combination with other drugs, they are also prescribed for rheumatoid arthritis. The two drugs are considered to be similar by the FDA.

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

You are being asked to take part because you have a form of hairy cell leukemia (HCL) or HCL variant that has not responded to standard therapy, including chemotherapy, surgery or radiation therapy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 30 subjects will take part in this study.

DESCRIPTION OF RESEARCH STUDY

Before you begin the study

Before beginning the study, you will need to undergo tests and/or procedures to help your doctor verify whether you can participate. This is called screening. Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study. If you have already undergone some of these examinations very recently, your doctor may decide not to repeat them. You could be hospitalized for any of the required tests. Briefly, these tests, which will be performed, include:

- Medical history and physical examination
- Routine blood and urine tests
- Pregnancy test in women who can have children. Pregnant women will not be allowed on study.
- Hepatitis B (HBcAB and HBsAg) test. Patients positive with Hepatitis B will not be included in the study unless taking appropriate medications and have the levels of Hepatitis B viral DNA within limit. If you are infected with Hepatitis B, we will tell you what the results mean, how to find care, how to avoid infecting others, how we report hepatitis

infection and the importance of informing your partners at possible risk because of your Hepatitis B infection.

- HIV testing: As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will still be able to participate in this study, if you are taking appropriate anti-HIV medications and your CD4 counts are more than 200. 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.

- EKG- a test for your heart
- Test to measure blood oxygen levels
- Bone marrow examination for the confirmation of the diagnosis

Bone marrow biopsy is not needed if participants can provide test slides to be read at the Clinical Center along with reports. In case slides and reports are not available, biopsy will be done. In the procedure of bone marrow biopsy and aspiration using a needle, the small sample of the liquid and solid portion of your bone marrow is collected.

During the study

If the results show that you can be in the study, and you choose to take part, we will conduct the following tests at baseline (before you receive any study drug):

- Scans
    - CT scans from the neck through the pelvis or MRI
    - MRI of the spine
- Ultrasound of the abdomen
- Echocardiogram – an ultrasound of your heart
- Bone marrow tests (Sample will be taken to conduct this test)
- Pulmonary function tests – breathing tests to see how well your lungs are working
- Stress test (Exercise test to see how your heart is working)
- Blood tests for research
- 24 hour collection of urine

You will then receive Moxetumomab pasudotox-tdfk through an IV catheter (a plastic tube usually inserted in a vein on your arm). Each infusion of Moxetumomab pasudotox-tdfk will last for about 30 minutes. You will be given Moxetumomab pasudotox-tdfk every other day for a total of 3 doses per "cycle" On cycle 1 only, Moxetumomab pasudotox-tdfk will begin on the 3rd day after rituximab or Ruxience. On subsequent cycles, spaced 25–28 days apart, rituximab or Ruxience will begin on day 1 and Moxetumomab pasudotox-tdfk on days 1, 3 and 5. Each infusion of rituximab or Ruxience will last for about 1-2 hours except the first infusion which will take approx. 7.5 hours. You will receive combination of these drugs for up to 4 cycles after your disease has

cleared, but for no more than 8 cycles in total if your disease does not get worse and you do not have severe side effects.

The first 13 participants that enroll to this trial will be treated with a combination of Moxetumomab pasudotox-tdfk and rituximab. All the other participants will receive Moxetumomab pasudotox-tdfk and Ruxience.In order to prevent damage to your kidneys, starting from the day before you receive the Moxetumomab pasudotox-tdfk and rituximab or Ruxience through the 8th day of the cycle, we would like you to drink at least 6 liters of water per day. You will be asked to keep a hydration diary. This helps you to keep track of the amount of fluid that you will drink. The study doctor or study nurse will explain you how to use this diary. Each time you visit the clinic, you must bring the diary with you. You will also receive low-dose aspirin by mouth to prevent poor function of kidney.

One hour before and 8 hours after your infusion, you will receive famotidine. You will also be given acetaminophen every 6 hours starting one hour before your infusion of Moxetumomab pasudotox-tdfk. These two medications are given to decrease the chance that you will have an allergic reaction to Moxetumomab pasudotox-tdfk.

If there is no detectable disease before your 4 cycles are completed, your study doctor may end study drug administration early. Regardless of your response to the study drug, your study doctor will continue to discuss your options with you during the study and after you have had 4 cycles of study drug. You will have follow-up assessments after the last cycle of Moxetumomab pasudotox-tdfk. After you stop being administered cycles of Moxetumomab pasudotox-tdfk, you will enter a post-treatment follow-up period.

In order to monitor your progress during the study you will need the following tests and procedures:

- History and Physical examination including weight measurement at the beginning of each cycle:
- Vital signs periodically in each cycle including
- Periodic blood and urine specimens will be collected for routine cancer care and also for research purposes to correlate findings with clinical response.
- EKGs before each cycle.

We may access data in your medical record that was collected under other protocols and use it for research in this study, so you do not have to repeat procedures/tests. Also, if you are co-enrolled in another NIH protocol, then research data that is collected in either study may be shared with and used for research in either study, for the same purpose, with IRB approval.

What tests may be performed on the samples that are stored?

Your stored samples may at a later date be examined under a microscope, may be stained so that certain properties of cells are visible under a microscope, or may be used to conduct other laboratory studies of the molecules inside of your cells.

All of your samples collected for research purposes on this study (such as the tumor tissue from bone marrow and normal tissue from blood/urine samples) may 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) in the cells carries genetic information and passes 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 look at your DNA, we may use do what is called "whole genome sequencing." This where we will do special tests in the lab to look at the entire sequence, or order, of how your DNA is put together. This is what makes you unique.

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 tissue from bone marrow and blood/urine samples 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.

However, you should know that 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 or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the next section for "Return of research results."

Return of research results

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.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic 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 that is 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. Once the results are available, we will offer to have you come to NIH (at our expense) to have genetic education and counseling to explain this result.

If you do not want to come to NIH, we will help you find a local genetic healthcare provider who can explain it to you (at your expense).

It is possible that none of the studies described above in this section will be performed.

Note: In order for us to contact you about genetic variants as described above, we must maintain your up to date contact information. This will allow us to contact you at the time findings are discovered.

How long will your samples be stored?

The samples collected during this study will be stored for at least as long as the study is open. If you agree after reading about it later in this form, your samples can be stored after the study closes, for possible use in future research.

When you are finished taking the drugs (treatment)

End of treatment (EOT) visit will occur 28-42 days after the first dose of the last cycle. You will be asked to return to the NIH for a follow up visits at 3 and 6 months after EOT, then every 6 months. The following tests will be performed:

- Medical history and physical exam including vital signs
- Routine blood tests should be done every 3 months until 2.5 year after EOT, then every 6 months.
- Scans if required at 1.5 and 2.5 years after EOT, then every 2 years.
- EKG (at EOT and 6 months after EOT)
- Bone Marrow Biopsy if required at the time of follow-up visit
- Genetic testing of your blood

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 12 months after you finish study treatment. If you are a man, you must use an effective method of contraception from Day 1 for 90 days after receipt of the final dose of Moxetumomab pasudotox-tdfk and rituximab or Ruxience. If you think that you or your partner is pregnant, you should tell your study doctor or nurse.

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

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

The study drugs may cause some side effects. You may experience none, some, or all of those listed below. A study doctor will supervise the administration of study drug, and you will be observed for at least 2-4 hours after each infusion. You will be checked closely by study doctors and nurses to see if you are experiencing a reaction or side effects from the study drug. If you have symptoms, you may be treated to reduce any discomfort, or you may be referred to your own doctor for treatment.

Important Identified and Potential Risks Associated with Moxetumomab pasudotox-tdfk

Moxetumomab pasudotox-tdfk can produce unwanted side effects or symptoms. Side effects may range from mild to severe. Your health care team may give you medicines to help lessen side effects. Many side effects or symptoms go away shortly after the administration of study drug has stopped. In some cases, side effects can be serious, long-lasting, or may never go away. Study doctors may not know all the side effects that may happen. Please tell the study doctor if you experience any side effects as a result of participation in this study.

The following have either been seen in subjects on moxetumomab pasudotox-tdfk or are known to happen with administration of similar drugs**:**

Common (More than 10% of subjects)	**Rare but Severe (generally in less than 10% of subjects, but can be severe in nature)**
Blood and lymphatic system disorders: • Febrile neutropenia (fever and a low number of certain type of white blood cell) ***General disorders:*** • Infusion-related reactions may range from local skin reactions at the IV site (redness, swelling, pain, infection), fever and flu-like symptoms to severe allergic reactions. They usually occur within the first 2 hours after the infusion but may be less common and less severe after the second or third infusion. • Allergic reactions may range from mild to severe but if not treated can become life-threatening. Symptoms may include hives (red rash with bumps, wheals, or	• Pneumonia, respiratory infections and difficulty breathing • Abnormalities like QTc prolongation (an abnormality in heart rhythm that can be fatal) has been observed in a few subjects on moxetumomab pasudotox-tdfk, however, these subjects either had prior heart conditions, were on other medications known to cause prolonged QTc interval or had blood electrolyte or other heart problems. • Eye disorders such as inflammation of the optic nerve and retinal detachment, which may result in loss of vision. • Thrombotic microangiopathy/ including HUS is an illness that causes

Common (More than 10% of subjects)	Rare but Severe (generally in less than 10% of subjects, but can be severe in nature)
welts), other skin rashes, swelling, itching, low blood pressure, wheezing, and shortness of breath. • Chills, fatigue (tiredness), swelling, fever, accumulation of fluid, increases in weight • Immune complex disease: antibodies may cause the body to make anti-drug antibodies, which may cause such signs and symptoms as joint pain, serum sickness (syndrome with rashes, itching, fever and rarely kidney failure), inflammation of blood vessels, change in drug levels in the blood or change in the activity of moxetumomab pasudotox-tdfk. ***Vascular disorders*** • Capillary leak syndrome (CLS) is a known risk (identified risk) of moxetumomab pasudotox-tdfk. Capillary leak syndrome can result in fluid leaking into the lungs, drop or increase in blood pressure, and kidney failure. In serious cases, this can lead to difficulty breathing. There have been a few serious cases reported, including life-threatening CLS observed in studies with moxetumomab pasudotox-tdfk. Pulmonary edema due to CLS causes fluid accumulation in the lungs. This fluid accumulation in acute form can lead to respiratory failure, respiratory distress, cardiac arrest due to hypoxia (not enough oxygen in the blood) and death. You will be monitored closely for any early signs of CLS by additional exams and methods to ensure the safety of subjects in study. • The other most frequent treatment related effects-you may experience are very high albumin levels in your blood, decrease in the level of lymphocytes, elevated liver	the destruction of red blood cells and platelets in the blood, and can cause kidney damage, or rarely, death. Serious cases have been reported in study subjects. Additional treatments and methods to look after you have been put in place to ensure safety of subjects in study. • Tumor Lysis Syndrome is a condition in which your metabolism may be affected when many cancer cells are killed rapidly, resulting in life-threatening complications and death if left untreated. A few cases of tumor lysis syndrome have been reported with moxetumomab pasudotox-tdfk. • A few serious cases of kidney failure/abnormal kidney function have been reported with moxetumomab pasudotox-tdfk. We recommend that you pay attention to the amount of urine you pass every day. If you are not passing enough water or see a decrease in the amount of water you pass, please report this to the doctor immediately. • PML – progressive multifocal leucoencephalopathy is a rare and severe opportunistic infection that has occurred in patients on other similar drugs used to treat cancer. Although no cases of PML have been observed with moxetumomab pasudotox-tdfk, it may be a potential risk. • Pulmonary edema is a fluid accumulation in the lungs which can lead to respiratory failure, respiratory distress, cardiac arrest, low oxygen levels and death.

Common (More than 10% of subjects)	Rare but Severe (generally in less than 10% of subjects, but can be severe in nature)
enzymes, swelling, pain in muscles, headache, and hypotension. • Injection site reaction, including infection, redness, swelling, pain and hardening of the skin at the site where the drug was given.	

Risks and discomforts of Rituximab

Common, some may be serious (Occurring in 20% -100% of subjects)
• Nausea • Reaction during or following infusion of the drug (Reactions may include fever, chills, nausea, itching, rash, swelling of the hands, feet or face, low blood pressure, dizziness, headache and difficulty breathing. Reactions can be treated and are usually temporary.) • Infection, especially when white blood cell count is low • Numbness and tingling of the arms and legs • Tiredness

Occasional, some may be serious (Occurring in 4% -20% of subjects)
• Anemia which may require blood transfusions • Bruising, bleeding • Abnormal heartbeat • Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Sores in eye • A tear or a hole in the stomach that may require surgery • Diarrhea, vomiting • Pain • Swelling of the body • Hepatitis which may cause yellow eyes and skin • Dizziness, headache • Kidney damage which may require dialysis • Cough • Scarring of the lungs • Stuffy nose • Blockage of internal organs which may cause shortness of breath, wheezing, vomiting • Increased sweating • Itching, rash, blisters on the skin

Occasional, some may be serious (Occurring in 4% -20% of subjects)
• Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Low blood pressure which may cause feeling faint

Rare, but serious (< 3% of subjects)
• Damage to the brain which may cause changes in thinking • Heart stops beating

Risks and discomforts of Ruxience

- Infusion-related reactions
- Fever
- Lymphopenia (low number of certain type of white blood cells)
- Neutropenia (low number of certain type of white blood cells)
- Chills
- Infections
- Tiredness
- Nausea
- Diarrhea
- Headache
- Muscle spasms
- Swelling of lower legs and/or hands
- Hepatitis B reactivation (which may cause yellow eyes and skin)
- Progressive Multifocal Leukoencephalopathy (PML) (brain infection)
- Mucocutaneous reactions (Severe skin rash with blisters and peeling which can involve mouth and other parts of the body)
- Kidney damage which may require dialysis
- Heart attack or heart failure
- Abdominal pain, bowel obstruction and perforation

Risks Associated with Routine Procedures

Blood collection

In this study, blood samples will be collected from you. Your study doctor will ensure that the maximum volume of blood drawn per day meets your hospital's institutional guidelines and that blood samples are prioritized according to your needs.

You may feel some pain when the blood samples are taken, but attempts will be made to take them through your central venous access IV line (if you have one) to prevent this. Sometimes a bruise may develop and, occasionally, infection or bleeding may develop at the place where the needle was put in. There is a rare possibility that you will faint while having blood drawn.

The amount of blood to be drawn at any one visit is up to about 8 ½ tablespoons and no more than 21 ½ tablespoons in an 8 week period. This includes testing for standard of care tests (i.e., complete blood counts) as well as blood for research.

Urine collection

There is no physical risk involved with urine collection.

Electrocardiogram

Some skin irritation can occur where the ECG/EKG electrodes are placed. The test is completely painless, and generally takes less than a minute to perform.

Echocardiogram

There is no physical risk involved with echocardiogram.

Abdominal ultrasound

There is no physical risk involved with abdominal ultrasounds.

Stress test

A stress test is generally safe, and complications are rare. Risks of complication include hypotension, arrhythmias, or myocardial infarction.

Pulmonary function tests (PFTs)

PFTs are usually safe for most people. Risks of complication include dizziness, asthma attack, or collapsed lung.

Bone marrow aspirate and/or biopsy

Your study doctor may need to take bone marrow samples from you to study how your disease is responding. Your hipbone will be numbed with anesthesia, a small needle will be put into the hipbone, and about 10 mL (2 teaspoons) of bone marrow will be taken out through the needle. A bone marrow biopsy may also be obtained. This procedure usually causes some pain. Very rarely, infection or bleeding may occur at the needle site.

Computed tomography scan

During this study you may have several Computerized tomography (CT) scans of your chest, abdomen and pelvis in order to determine disease status. A CT scan is an x-ray test that may use a dye (contrast material) to enhance visualization of the areas being studied. The dye is put into a needle in the vein of your arm (IV). You could have an allergic reaction to the dye that is used and if you have had a previous reaction to the dye, you may be given premedication with an antihistamine (diphenhydramine / Benadryl) and steroids (such as prednisone) to prevent the reaction. These same medications may be administered if you develop a reaction to the dye. The dye may also cause problems for people who are diabetic or have kidney problems in which case the scans may be done without injection of dye, and the study doctor will discuss this with you.

Risks from radiation

During your participation in this research study, you may be exposed to radiation from up to 3 CT scans each year. The amount of radiation exposure from these procedures is equal to approximately 3.9 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." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans that you get in this study will expose you to the roughly the same amount of radiation as 13 years' worth of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation

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.

Risks of MRI

The MRI examination poses almost no risk to the average patient when appropriate safety guidelines are followed. Although the strong magnetic field is not harmful, implanted medical devices that contain metal may malfunction or cause problems during an MRI exam. You will be asked if you have any such devices implanted prior to the exam.

Having an MRI requires that you lie still with part of you or all of you inside a tube-shaped machine for about 45 minutes to an hour. Even with the ear plugs we give you it can be noisy with loud clicking and thumping sounds, which bothers some people. Some people may feel 'closed in' or 'trapped' (even though they are being closely watched and are quite safe). This is called claustrophobia. Cool air will surround you, and the room is large and brightly lit to help avoid claustrophobia. You may ask your physician for a mild sedative for the procedure if you think it will help. If you take a sedative, you must not drive a vehicle until it wears off after the MRI.

MRI scans cannot be done on people who have:

- a cardiac pacemaker,
- neural pacemaker,
- surgical metal clips in the brain or on blood vessels,
- cochlear implants,
- or foreign metal objects within the eye.

If you have any of the above, please discuss this with your study team before signing the consent.

Risks from Gadolinium

Gadolinium is an FDA-approved medication used to improve MRI images. About 98% of patients receiving gadolinium have no symptoms related to the injection of this medication. Mild symptoms that may occur include: coldness in the arm at injection, a metallic taste, headache, and nausea. In an extremely small number of patients, more severe symptoms have been reported including: shortness of breath, wheezing, and lowering of blood pressure.

MRI contrast agents containing gadolinium can cause a rare disease known as Nephrogenic Systemic Fibrosis (NSF) mostly in patients with severe kidney disease. NSF has been nearly eliminated by screening kidney function prior to MRI. To try and avoid NSF, we do not give gadolinium to patients with severe kidney disease in this research study. NSF can cause tight rigid skin, trouble bending joints, pain, weakness, and can scar body organs. NSF is debilitating and may cause death.

Recent reports indicate that some gadolinium may be retained in the brain, bone, and skin. In May 2018, the FDA stated that no harmful effects have been identified related to gadolinium in the brain, but it is continuing to study the issue. You will receive additional information called a "medication guide" about the contrast medication you will receive.

Gadolinium will be administered for research purposes and as clinically indicated. We will check your kidney function before giving you any gadolinium contrast.

Privacy Risks Associated with Genetic Testing

It may be possible that genetic information from you could be used by law enforcement agencies or other entities to identify you or your blood relatives.

Psychological or Social Risks Associated with Return of Incidental 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.

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 this experimental treatment is safe. 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 combination'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 Innate Pharma or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved by the study team for use in other studies?

As part of this study, we are obtaining specimens and data from you. We plan to store and use these specimens and data for studies other than the one described in this consent form that are going on right now, as well as studies that may be conducted in the future. The specimens and data will be kept in a way that we will still know that they came from you (i.e., they will be identifiable to us). If we use your identifiable specimens or data for future research, our study will be reviewed and approved by an Institutional Review Board who will make sure that we are protecting your confidentiality. These future studies might help us better understand HCL or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my identifiable specimens and data to be stored and used by the study team for future studies as described above.

_____ Yes _____ No

Initial Initial

Will your specimens or data be shared with other researchers for use in other studies?

We may share your specimens and data with other researchers. The other researchers may be doing studies in similar areas to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or at commercial entities.

One way that we may share your data is by putting it into a large database called a repository, which is a way to make it widely available to the research community. If we do place your data in a repository, it will be labeled with a code, (not with your name or other information that could be used to easily identify you). Even though it will only be labeled with a code, some types of data, in particular data about your genes (called genetic or genomic data), can be used to figure out who you are, although this is difficult to do, and we think it is unlikely to happen.

The data in the repository will be widely available to anyone who wants it.

If we do share your specimens or data, we will know that the specimens and data came from you. However, the other researchers will not know that they came from you (i.e., they will be de-identified).

I give permission for my **de-identified** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

In some cases, it may help other researchers to know that the specimens or data were collected from you (i.e., they will have your identifiers). If we share your identity with other researchers, their study will be reviewed and approved by an Institutional Review Board who will make sure that the study team is protecting your confidentiality.

I give permission for my **identifiable** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

Information about all the people (including you) in this study may be combined to create what is called summary information. The summary information may be placed in a database and shared in scientific publications. This information will help the researchers understand if some patterns are more common than others among everyone who was a part of this study. The summary information will be available to anyone without the need for any permission. The risk of anyone identifying you based on this information is very low.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others who should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or that no one will gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

Can you change your mind about use and sharing for future research?

If you change your mind and do not want us to store and use your specimens and data for future studies, you should contact the study team. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data is already complete, the information from that research may still be used. Also, if the specimens and data have been shared already, it might not be possible to withdraw them.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

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.

- The study agent, Moxetumomab pasudotox-tdfk, will be provided to you by the NCI. Even though it probably won't happen, it is possible that the Innate Pharma may not continue to provide Moxetumomab pasudotox-tdfk to the NCI for some reason. If this would occur, other possible options are:
    - If there is no moxetumomab pasudotox-tdfk available at all, no one will be able to get more, and the study would close.
    - If a problem with getting moxetumomab pasudotox-tdfk occurs, your study doctor will talk to you about these options.
- If some tests and procedures performed outside the NIH Clinical Center, you may have to pay for these costs.

CONFLICT OF INTEREST (COI)

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

The NIH and the research team for this study are using moxetumomab pasudotox-tdfk developed by Innate Pharma through a collaboration between your study team and the company. The company also provides financial support for this study.

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

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

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 National Cancer Institute 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 Innate Pharma, the pharmaceutical company who produces Moxetumomab Pasudotox-tdfk.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

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

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

Certificate of Confidentiality

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

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

The Certificate does not protect your information when it:

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

3. is for other research;
4. is disclosed with your consent.

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

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

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

RESEARCH-RELATED INJURIES

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

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Robert J. Kreitman, M.D, kreitmar@mail.nih.gov, 301-648-7375. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

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

Signature of Research Participant	Print Name of Research Participant	Date

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

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either::

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

Signature of Witness	Print Name of Witness	Date

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

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

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