PRINCIPAL INVESTIGATOR: Robert Kreitman. M.D.

STUDY TITLE: A Phase II Clinical Trial of Anti-Tac(Fv)-PE38 (LMB-2) Immunotoxin for CD25 Positive Hairy Cell Leukemia

STUDY SITE: NIH Clinical Center

Cohort: *Standard*

Consent Version: *02/09/2021*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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

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

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

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

This is a clinical trial for the treatment of hairy cell leukemia (HCL) with an experimental drug called LMB-2. LMB-2 is a recombinant immunotoxin that has been shown to kill leukemia and lymphoma cancer cells that have a protein on their surface called "CD25". To be eligible for treatment on this study your leukemia cells must have CD25 on their surface. However, the

presence of CD25 on your leukemic cells does not ensure enrollment on the protocol. We plan to include at most 27 patients on this trial.

LMB-2 is an experimental drug that is considered to be a recombinant immunotoxin. Each LMB-2 molecule is made up of two parts: a protein part that binds or targets a cancer cell and a toxin (a type of poison) part that kills the cancer cell to which it binds. The binding part is derived from a protein that is naturally produced by mice. The toxin portion of LMB-2 is naturally produced by bacteria. LMB-2 is a protein that is produced by connecting the part of the mouse gene responsible for producing the binding protein to part of the toxin gene. We believe that the binding part of LMB-2 will selectively target and kill the cancer cells that have CD25 on their surface. In laboratory experiments, LMB-2 has been shown to kill CD25-containing cells outside a human body and it has caused a significant decrease in the size of tumors in mice that were given doses similar to those used in the first human trial of LMB-2.

A preliminary study of LMB-2 has been performed at the National Cancer Institute (NCI) in which 39 patients with various leukemias and lymphomas were treated. In that trial, a partial response was observed in 1 of 8 patients with CLL. Patients with other cancers including hairy cell leukemia (4 patients), cutaneous T cell lymphoma (1), adult T-cell leukemia/lymphoma (1), and Hodgkin's lymphoma (1) had reduction in their tumors also.

LMB-2 Treatment

LMB-2 will only be given to patients at the NIH Clinical Center. Patients must have received prior cladribine at least 4 weeks prior to enrollment, and have either received or demonstrated ineligibility for BL22. Each cycle of LMB-2 is given by an intravenous (into a vein) infusion every other day for 3 doses (days 1, 3, 5). You will receive up to 6 cycles of LMB-2 every 4 weeks unless you develop worsening of disease, serious side effects, or voluntarily withdraw.

A small amount of blood (up to 10 teaspoons) will be drawn before, during, and after treatment. These blood tests allow us to measure how much LMB-2 is in your blood, the effects of LMB-2 on your cancer cells in your blood, and monitor for side effects. We will also do blood tests prior to each cycle and during each cycle to know how your immune system is interacting with LMB-2.

Before each cycle and in follow-up visits you will undergo repeat disease evaluation. This will include a careful physical examination, blood tests, chest X-ray, and electrocardiogram (test of your heart). Prior to the first cycle you will have a computed tomography (CT) scan and an echocardiogram (ultrasound of your heart). You will also have a bone marrow biopsy. If these studies help us understand how your leukemia is reacting to LMB-2, we may ask for your permission to repeat these tests again prior to other cycles.

The infusion of LMB-2 takes 30 minutes. You will also receive a liter (about 8 cups) of fluid through an IV or central venous catheter before and after each dose of LMB-2. A central venous catheter (CVC) is a plastic IV tube that is placed in a large vein that leads to the heart. You may already have a CVC in place. If not, depending on the size of your arm veins, one may need to be placed prior to treatment. A CVC makes treatment on this study easier and less painful by decreasing the need for IVs and needle sticks to draw blood. If a CVC is required or requested, you will be asked to review another consent form and give consent prior to its placement.

You will receive the first cycle as an inpatient (admitted to the hospital). Subsequent cycles may be given as outpatient (not admitted to the hospital). If the infusions are well tolerated, you may return home after about 1 week (possibly longer if complications occur). After returning home, you will have blood tests done weekly and the results will be faxed to us by your local physician. During the course of this study, you may also require other treatments such as transfusions and antibiotics. Hospitalization may be needed if complications develop. If there is evidence that therapy with LMB-2 is no longer effective, it will be discontinued. Blood will be checked prior to each cycle of LMB-2 to determine if the level of neutralizing antibodies is too high to give the cycle of LMB-2. If it is too high, further LMB-2 will be discontinued.

Risks or Discomforts of Participation

In order to determine if you are eligible for this experimental therapy, several tests will have to be done. This period of evaluation may take several weeks and will most likely be done as an outpatient. These tests may include standard blood and urine tests, an electrocardiogram test of your heart, a chest X-ray, an echocardiogram, which is an ultrasound of the heart, computerized tomography (CT or CAT) scans, X-rays, nuclear medicine studies, and a bone marrow biopsy.

Administration of LMB-2 will be through a central venous catheter or a peripheral I.V. The CVC is inserted by experienced staff using local anesthesia. The risks associated with the procedure include pain, bleeding, infection, and development of air in the chest. However, these complications are rare. Air in the chest outside the lung may require temporary placement of a chest tube by a surgeon. The risks of chest tube placement include pain, bleeding, and infection. Other risks of the catheter include infection and clotting of your veins, which could require removal of the catheter for treatment. These risks will be explained to you in more detail at the time of insertion. When a peripheral line is used, there is a small risk of infection, clot or bleeding at the site of the IV line. There is also a risk of some of the drug leaking out, or extravasating. If that occurs there may be some destruction of skin tissue in a limited area. Patients are urged to alert the study physicians at the first sign of any skin changes, for example redness or tenderness, around the infusion site but also with any discomfort in the involved extremity as well. If there is any evidence of toxicity from leaking, the infusion will be held until a central line can be placed for the infusion of drug. In addition, any toxic effects to the skin will be treated to the fullest extent possible.

LMB-2:

There is limited experience with LMB-2 in humans. In the Phase I trial, a total of 39 patients received 65 cycles of LMB-2. On that trial, all side effects of LMB-2 went away when LMB-2 was stopped. In some cases this required additional medical treatments. The following list of side effects includes those seen on the LMB-2 trial in adults and those seen with similar immunotoxin drugs.

Possibly related to LMB-2:

- Anemia which may require blood transfusion
- Heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Fluid in the body which may cause low blood pressure, shortness of breath, and swelling of ankles

- Abnormal heart beat
- Bloating
- Decrease in heart's ability to pump blood during the "active" phase of the heartbeat (systole)
- Diarrhea
- Nausea or the urge to vomit
- Vomiting
- Swelling of the body
- Fatigue or tiredness
- Fever
- Abnormal reaction of the body to substances, called allergens, that are contacted through the skin, inhaled into the lungs, swallowed, or injected (allergic reaction) which may cause rash, low blood pressure, wheezing, shortness of breath, and swelling of the face or throat
- Bruising or bleeding
- Pain
- Increased blood level of a liver enzyme (ALT/SGPT)
- Increased blood level of a liver or bone enzyme (alkaline phosphatase)
- Increased blood level of a liver enzyme (AST/SGOT)
- Increased blood level of enzyme (creatine phosphokinase) from muscle
- Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)
- Decreased number of a type of blood cell that help to clot blood (platelet)
- Weight gain, loss of appetite
- Dizziness, headache
- Decreased levels of a blood protein called albumin
- Muscle pain
- Blood in the urine
- More protein in the urine than usual, often a sign of kidney disease
- Shortness of breath
- Increase in the number and size of the pores in the capillaries (small blood vessels) which causes leakage of fluid from the blood to the tissue spaces, resulting in dangerously low blood pressure, swelling and multiple organ failure
- Low blood pressure which may cause feeling faint

A common side effect of immunotoxin drugs similar to LMB-2 is vascular leak syndrome, where fluid leaks out of blood vessels into the skin, lungs, and other organs. Symptoms include swelling, decreased blood pressure, or difficulty breathing. This can be severe, and although vascular leak syndrome usually gets better, it may require intubation and can be fatal. Other side effects associated with immunotoxins include edema (swelling), aches and pains of the muscles, joints, and/or bones, headache, fatigue, dizziness, blurred vision, lowering of normal blood cells including the red cells (with risk of anemia), white cells (with risk of infection), and platelets (with risk of bleeding), abnormal blood clotting tests and risk of bleeding, muscle damage, diarrhea, constipation, stomach or intestinal ulcers, stomach pain, indigestion, dehydration, kidney damage, abnormal blood salt levels, fluid leak in the lungs with shortness of breath, inflammation of the pancreas gland (the organ involved in diabetes), chills, decreased function of the thyroid gland, and neurologic problems including sleepiness, decreased level of alertness, weakness, painful tingling ("pins and needles"), numbness (decreased feeling), and coma.

A condition known as hemolytic uremic syndrome (HUS) has been seen with related immunotoxin drugs. HUS is a potentially fatal problem that can cause fever, anemia (low red blood cell count), thrombocytopenia (low platelet count), bleeding, stroke, and kidney failure. Treatment of severe HUS includes a procedure known as plasma exchange or plasmapheresis, where the liquid portion of the blood (plasma) is removed from the body and replaced with plasma from blood donors using a special machine. Even with treatment, HUS may lead to death or permanent kidney and/or brain damage. Adverse reactions associated with plasmapheresis are rare, and are generally mild. They include pain and bruising at the insertion site of the intravenous line, and a temporary decrease in the platelet count and/or red blood cell count. Fainting episodes related to needle insertion can occur, and skin tingling caused by low calcium levels can rarely occur. Interrupting the plasmapheresis procedure can reverse this latter reaction. During plasmapheresis, at least two nurses will be present, and a blood bank physician will be available in the clinic area where the procedure is performed.

LMB-2 and other similar drugs can cause allergic reactions that may range from mild to severe. Symptoms of allergic reactions may include hives (red rash with bumps, wheals, or welts), and other skin rashes, swelling, itching, fever, chills, low blood pressure, fast heart rate, wheezing, shortness of breath, and rarely, death. In an attempt to decrease the risk of such reactions, you will be given a number of additional medications ("Premedications") before and after each dose of LMB-2.

Patients with HCL often have low blood counts and require red blood cell and/or platelet transfusions, with associated risks including transfusion reactions and infections (such as HIV and hepatitis). Prior treatment may have weakened your immune system. It is possible that LMB-2 may also weaken your immune system. Infections that develop in individuals with cancer can be very serious. You should seek immediate medical attention for fever over 101ºF (38.3ºC) or any signs of infection.

Risks Associated with Routine Procedures:

Blood Drawing: To monitor the effects of therapy frequent blood tests will be necessary. Up to a one unit (about 50 teaspoons) of blood, may be drawn every 6 weeks for research purposes while you are participating in the study. Every effort will be made to keep blood tests to a minimum. You will be monitored for anemia and given blood transfusions if needed. Side effects of blood

draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting.

Bone Marrow Tests: If a bone marrow aspiration is done, your hipbone will be numbed with anesthesia, a small needle will be inserted into the hipbone, and about two tablespoons of bone marrow will be removed through the needle. This procedure usually causes only brief discomfort. Very rarely, infection or bleeding may occur at the needle site.

Imaging/scans: You may receive a contrast agent injected into your arm as part of your scan. Contrast agents can cause allergic reactions and kidney damage. Allergic reactions can include mild itching associated with hives but can also result in a serious life-threatening emergency from difficulty breathing. If this occurs, it is treatable. You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach. Please ask the study doctor if you have questions about the risks of these scans.

MRI: Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the body. We will obtain pictures of your chest, abdomen and pelvis for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. 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 from Gadolinium: During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (IV) catheter (small tube). It will be done for both research and medical purposes.

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

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

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

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

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body.

What are the risks of radiation from being in the study?

During your participation in this research study, you may be exposed to radiation from up to 4 CT scans each year. The amount of radiation exposure from these procedures is equal to approximately 5.2 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 scans that you get in this study will expose you to the roughly the same amount of radiation as 17.3 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.5 out of 100 (0.5%) and of getting a fatal cancer is 0.3 out of 100 (0.3%).

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.

Premedications:

Acetaminophen (Tylenol): side effects are extremely unlikely. Regular use of acetaminophen can cause liver damage especially at high doses (more than 4000mg/day or 12 regular strength tablets per day). To minimize this possibility, you should not take over-the-counter products containing acetaminophen and should avoid alcohol during the time periods you are taking scheduled acetaminophen doses on this study.

Ranitidine (Zantac): possible side effects include tiredness, dizziness, headache, and diarrhea.

Hydroxyzine (Atarax): Possible side effects include sleepiness, dizziness, restlessness, and irritability.

Dexamethasone (Decadron): To be given only before the first of the 3 doses, only for retreatment (cycles 2-6) cycles. Side effects of a single dose of dexamethasone might include difficulty sleeping, increased hunger, and increased blood glucose. Steroids are associated with an increased risk of infection although this is more common when they are used more frequently.

Patients infected with HIV will be excluded from this trial because the effect of LMB-2 on HIV replication and/or the immune system is unknown and potentially harmful. Patients with hepatitis C surface antigen positivity are excluded from this trial because the effect of LMB-2 on hepatitis C and/or the immune system is unknown and potentially harmful. Patients that are pregnant or breast-feeding will be excluded from this trial because the effect of LMB-2 on a developing fetus or a nursing infant is unknown and potentially harmful. Patients with childbearing potential should use adequate birth control measures while on the study, until 30 days after the last dose of LMB-2.

We will carefully monitor you to detect any of these side effects; in addition, you will be taught about side effects, which you may experience and must report immediately. Although side effects of this treatment usually last for a short period of time and completely resolve, you may experience side effects that are permanent. Although not expected, death could occur from this experimental treatment. It is very important that you notify us as soon as possible if you experience any type of side effect so that you can be carefully examined. All precautions will be taken to prevent these side effects and you will be treated promptly (if treatment is required and possible) if they occur. Treatment on this study will require a significant amount of your time and may be stressful. Participating in this study may prevent you from being in other research studies in the future.

Potential Benefits of Participation

While we hope that LMB-2 treatment will be beneficial to you, we do not know if you will receive personal, medical benefit from this treatment. LMB-2 treatment may cause improvement in your leukemia such as reduction in cancer-related symptoms. Your participation in this study may help us advance the understanding of the use of biologic agents in the treatment of HCL.

Alternative Approaches or Treatments

You may decide now not to receive treatment in this protocol or you may choose at any point in time to stop the drug and withdraw from the protocol. In either case you would be returned to the care of your referring physician.

Because of the type and extent of your tumor, chemotherapy is felt to be more beneficial than surgery or radiation alone. Alternative approaches that could be used may include:

1. Other forms of treatment:

   a. Several drugs besides cladribine, which you have already been treated with, can be useful in patients with HCL. Rituximab is a monoclonal antibody which has been reported to produce responses in patients with HCL. Pentostatin, fludarabine and interferon are also drugs which can produce responses in HCL, but they also can hurt the immune system.

   b. Radiation treatment, which sometimes can control tumor growth in local areas such as lymph nodes, spleen and bones. However, this approach will not effectively treat disease that has spread beyond the areas that are irradiated.

   c. Surgery, which can be used to remove the spleen (if this has not already been done).

2. Other experimental agents.

3. Getting no treatment; getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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What Happens after this Treatment is Completed?

Once you complete the study treatment , you may have periodic visits every 3-12 months at the NIH Clinical Center or at your local provider for follow-up examination and tests (i.e. blood tests and imaging). The maximum amount of blood we may draw for research in each follow-up visit is 2 teaspoons. If the disease worsens then you may need other therapy. At that time you will be given the opportunity of participating in additional research protocols that may be appropriate for you. If no such protocols are available, you will be returned to the care of your local physician. It is important to stress that participation in this protocol does not constitute a promise of long-term medical care here at the Clinical Center. If there is no research study that is suitable for you and your stage of disease, you will be returned to the care of your private doctor or to a clinic in your local community. It is conceivable that participation in this study may make you ineligible to participate in certain other research protocols because the requirements for entry onto these protocols may disallow patients who have already been treated with certain drugs or who have had certain side effects from previous treatment. You may decide now not to receive treatment on this protocol, or you may choose at any point in time to stop the treatment and withdraw from the protocol; in either case you will be returned to the care of your referring physician.

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.

The National Institutes of Health and the research team for this study have developed a drug, being used in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of LMB-2.

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 the 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 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.

<u>Samples to be saved for additional tests:</u>

- Neutralizing antibodies: Antibodies a patient might make which block the effect of certain recombinant immunotoxins like LMB-2. Requires about 1 teaspoon of blood.
- Flow cytometry assays to quantify tumor markers on the malignant cells. Requires about 1/2 teaspoon of blood.
- Bone marrow biopsy samples, whether they obtained at NIH or elsewhere, and whether the bone marrow test has already been done or not yet done.
- Cytotoxicity assays. Leukemia cells from the blood, bone marrow, or other tissues may be tested with LMB-2 and related drugs to determine if the malignant cells can be killed outside the body. Requires 1-3 tablespoons of blood.

- Soluble CD25, CD22, and other tumor markers: To estimate the amount of cancer cells in the body by measuring proteins which fall off cancer cells and go into the blood. Requires about 1 teaspoon of blood.
- HLA typing to better understand the immune system in patients with hairy cell leukemia. Requires about 1 teaspoon of blood.
- PAX-gene tube: To obtain RNA to study the mechanism of how leukemia cells form, and to detect very low levels of leukemia cells in patients. Requires about 1/2 teaspoon of blood.
- RNA samples can also be used, in an assay called micro-arrays, to study why some patients may not respond as well as others to recombinant immunotoxins like LMB-2. Taken with PaxGene tube.
- Samples of blood to study how hemolytic uremic syndrome (HUS), a major toxicity of a recombinant immunotoxin called BL22, which is similar to LMB-2, occurs and might be prevented. Requires about 1/2 teaspoon of blood.
- DNA samples to look for abnormalities which might make a patient more susceptible to HUS. Requires about 1/2 teaspoon of blood.
- Assays which could have an impact on both patients and their children, including studies of genetic cancer risk, will not be done.
- Samples to determine levels of immunotoxin in blood, urine, and other tissues.

Your research blood samples will only be identified by the study code, subject number, visit number and date and time of collection.

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?

Participants will be reimbursed for hotel, travel, meals (government rate). Receipts must be provided for all expenses.

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.

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

COSTS

Will taking part in this research study cost you anything?

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

- 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 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, Robert Kreitman, kreitmar@mail.nih.gov, at 301-480-6187. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

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

Signature of Research Participant	Print Name of Research Participant	Date

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

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Signature of Witness*	Print Name of Witness	Date

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

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

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