

<b>MEDICAL RECORD</b>	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> <ul style="list-style-type: none"> <li>• Adult Patient or                      • Parent, for Minor Patient</li> </ul>
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INSTITUTE:                      National Cancer Institute

STUDY NUMBER:            06-C-0150                      PRINCIPAL INVESTIGATOR:            Robert J.Kreitman, M.D.

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

Continuing Review Approved by the IRB on 04/23/18

Amendment Approved by the IRB on 07/14/18 (K)

Date posted to web: 07/18/18

Standard

### INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, 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). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

#### **Description of Research Study**

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.

PATIENT IDENTIFICATION	<b>CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY</b> <ul style="list-style-type: none"> <li>• Adult Patient or                      • Parent, for Minor Patient</li> </ul> NIH-2514-1 (07-09) P.A.: 09-25-0099 File in Section 4: Protocol Consent (1)
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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)

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- 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 101°F (38.3°C) 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.

*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.

### **Research Subject's Rights**

You will be given a copy of this consent for your records. Participation in this investigational treatment protocol is voluntary, and you can discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. You are free to ask questions of the staff, and are encouraged to do so. Any significant new findings that relate to your treatment will be discussed with you.

If any publications or presentations result from this trial, your anonymity will be protected to the maximum extent possible. However, qualified representatives of the Food and Drug Administration (FDA), and the National Cancer Institute (NCI), may confidentially inspect your patient records during 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 National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board

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.

**What Happens after this Treatment is Completed?**

This depends on how you have responded to the experimental therapy. If you do not have evidence that the disease is worsening, we will schedule periodic visits to the Clinical Center for follow-up examination and tests. 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.

**Certificate of Confidentiality**

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

**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.

Samples to be saved for additional tests:

- 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.

### OTHER PERTINENT INFORMATION

**1. Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

**2. Policy Regarding Research-Related Injuries.** The 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 National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**3. Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

**4. Problems or Questions.** If you have/your child has any problems or questions about this study, or about your/your child's rights as a research participant, or about any research-related injury, contact the Principal Investigator, Robert Kreitman, M.D., Building 37 Room 5124B, Telephone: 301-480-6187. Other researchers you may call are: Wyndham Wilson, M.D., Ph.D., Building 10 Telephone: 240-760-6092. You can contact either one through the hospital page operator 301-496-1211. If you have any questions about the use of your tissue for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

You may also call the Clinical Center Patient Representative at 301-496-2626.

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

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<b>COMPLETE APPROPRIATE ITEM(S) BELOW:</b>			
<b>A. Adult Patient's Consent</b> I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.	<b>B. Parent's Permission for Minor Patient.</b> I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study. (Attach NIH 2514-2, Minor's Assent, if applicable.)		
_____ Signature of Adult Patient/ Legal Representative	_____ Date	_____ Signature of Parent(s)/ Guardian	_____ Date
_____ Print Name	_____ Print Name		
<b>C. Child's Verbal Assent (If Applicable)</b> The information in the above consent was described to my child and my child agrees to participate in the study.			
_____ Signature of Parent(s)/Guardian      Date      Print Name			
<b>THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE          FROM APRIL 23, 2018 THROUGH APRIL 22, 2019.</b>			
_____ Signature of Investigator	_____ Date	_____ Signature of Witness	_____ Date
_____ Print Name	_____ Print Name		