INSTITUTE: National Cancer Institute

STUDY NUMBER: 09-C-0025 PRINCIPAL INVESTIGATOR: Robert J. Kreitman, M.D.

STUDY TITLE: Phase II Trial of LMB-2, Fludarabine and Cyclophosphamide for Adult T-Cell Leukemia

Continuing Review Approved by the IRB on 01/19/21

Amendment Approved by the IRB on 10/15/18 (P) Date Posted to Web: 01/27/21

Eligibility Screening

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 consent form is to allow drawing blood and sending samples to determine your eligibility for our study involving a recombinant immunotoxin for the treatment of cancer. The recombinant immunotoxin is a protein containing a toxin part and an antibody part. The antibody part binds to a surface protein (also called antigen) on the surface of the cancer cell and then the toxin goes inside the cell and kills it. In this study the recombinant toxin is called LMB-2 and the antigen it binds to, CD25, is often present on the malignant cells. To determine your eligibility for LMB-2, we would first need to test your tumor or other tissue for the presence of CD25 on the surface of your cancer cells. You will be informed if CD25 is found and if several other requirements are met, you may be eligible for our recombinant immunotoxin study. Whether or not you are eligible for our study, we may obtain follow-up data on your outcome from you or your physician. This includes, if they occur at all, the date of tumor recurrence, tumor progression, and possibly death. However, this consent does not permit any additional studies that would test for genes (i.e. tendency for diseases). Other tests to determine if you are eligible 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.

Tests needed to determine whether you are eligible for this trial:

- Flow cytometry of the blood. Requires about 1/2 tablespoon.
- Neutralizing antibodies: Antibodies a patient might make to certain protein drugs which block their effect against cancer cells. You may or may not consider receiving these protein drugs in the future. Requires about 1 teaspoon.

Alternative Approaches or Treatments

You may choose not to be tested for CD25 or to have any other studies done.

Risks or Discomforts of Participation

The risk involves the withdrawal of between a few teaspoons and a half-cup of blood and the potential for bruising or infection that occurs with any blood draw. Your tumor tissue may be obtained from prior surgeries or from a biopsy that you might elect to have for purposes of determining if you are eligible for this study. Any biopsy or other procedure would be done only

if needed and only after you sign an additional informed consent related to the specific procedure.

Potential Benefits of Participation

There may be no direct benefit from allowing us to test your blood or other tissue for CD25 or other factors. However, this testing may make you eligible for our recombinant immunotoxin protocol. If you become eligible for our treatment study you would need to give additional informed consent regarding the risks of the treatment.

Consent for Participation

Upon completion of this study, you may be given the option of participating in additional research protocols if such protocols exist. If they do not, you will be returned to the care of your referring physician. It is important to stress that participation in this protocol does not constitute a promise of long-term medical care here at the NIH Clinical Center. If there is no research study that is suitable for you and your state of disease, you will be returned to the care of your referring doctor or institution, or to alternative sources of care closer to home. It is conceivable that participation in this study may make you ineligible to participate in certain other research protocols. You may decide now not to participate in this protocol, or you may choose at any time to withdraw from the protocol.

Optional Studies (not required)

We would like to keep some of the specimens and data that are collected for future research. These specimens and data will not be identified by name when sent outside the NIH or stored, only by number. The use of your specimens and data will be 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 decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and/or data. Then any specimens that remain will be destroyed and your data will not be used for future research.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My specimens and data may be kept for use in research to learn about, prevent, or treat cancer or other health problems.

☐ Yes ☐ No Initials_____

2. Someone may contact me in the future to ask permission to use my specimens and/or data in new research not included in this consent.

☐ Yes ☐ No Initials_____

Optional Studies (not required to determine if you are eligible)

- Soluble CD22, CD25, CD30, 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. Soluble CD25 may also be measured in your tumors if they need to be removed as part of your medical care, or if tumors can be easily and safely removed like with a skin biopsy.
- Skin biopsy: To determine whether skin lesions have ATL cells, and if so, to determine the extent to which ATL cells are cleared with FC or FC/LMB2.
- HLA typing to better understand the immune system in patients getting LMB-2. HLA is the human leukocyte antigens, a complex of proteins on your white blood cells which allow your body to determine whether the cell is yours or not. Requires about 1 teaspoon.
- PAX-gene tube: To obtain RNA to study tumor markers, and an assay called micro-arrays, to study why some patients do not respond as well as others to LMB-2. PAX-gene tubes contain a special liquid that keeps RNA in the blood stable, and it mixes with your blood only after it is drawn. Requires about 1/2 teaspoon.
- DNA samples to look for abnormalities which might make a patient more susceptible to toxicity. The genes to look at would include those that trigger cells to die, and those that help make hormones which cause inflammation. Requires about 1/2 teaspoon.

- Assays to identify genes in your DNA which would have significant risk to you, including how likely you or your children might be to get cancer, will not be done.
- Samples to determine levels of LMB-2 in the blood, urine, and other tissues by activity or immuno (ELISA) assays.
- Flow cytometry assays to quantify tumor markers on the malignant cells. In flow cytometry, your blood after being drawn goes into a tiny tube where lasers determine whether the tumor markers are present if so how much. Requires about 1/2 tablespoon.
- Cytotoxicity assays. Leukemia or lymphoma 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.

Disclosure of potential conflict of interest:

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

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

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.

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 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.; Building 37, Room 5124b, Telephone: 301-496-6947. Other researchers you may call are: Theresa Yu, R.N., Telephone: 301-496-9458. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

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.

Signature of Adult Patient/ Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

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 Parent(s)/Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

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 _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JANUARY 19, 2021 THROUGH JANUARY 18, 2022.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____