INSTITUTE: National Cancer Institute

STUDY NUMBER: 12-C-0003 PRINCIPAL INVESTIGATOR: Thomas A. Waldmann, M.D.

STUDY TITLE: Phase I/II Trial of Yttrium-90-labeled Daclizumab (anti-CD25) Radioimmunotherapy with High-dose BEAM Chemotherapy and Autologous Hematopoietic Stem Cell Rescue in Recurrent and Refractory Hodgkin's Lymphoma

Continuing Review Approved by the IRB on 12/03/18
Amendment Approved by the IRB on 03/07/18 (F) Date posted to web: 12/13/18

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.

Why is this study being done?

Hodgkin's lymphoma (HL) is a highly treatable cancer; however, in persons that have HL that either does not respond to chemotherapy or has responded in the past but has reoccurred, the success in treating HL is greatly lessened. Only 30 – 65% of individuals with HL that has relapsed and been treated with high dose chemotherapy and their own transplanted stem cells (cells that can develop into many different cell types) remain disease free in the long term. Some of the cells within the lymphoma and the surrounding tissue have a molecule called CD25 on the surface. Daclizumab is a monoclonal antibody, a purified protein that attaches to foreign substances in the body or to body tissues. Daclizumab attaches specifically to CD25. Most

monoclonal antibodies are produced from mouse tumor cells, but are the same type of protein that your body produces to fight infection. Basiliximab is a drug that is similar to daclizumab. You may receive basiliximab if unlabeled daclizumab becomes unavailable.

In a study where persons with HL that did not respond to chemotherapy or had relapsed were given daclizumab attached to a radioactive atom called Yttrium 90 on the theory that the radiation would kill the CD25 bearing tumor cells, 63% had their tumors either shrink or disappear completely. In this phase 1/phase 2 study we plan to combine 90Yttrium labeled daclizumab (^{90}Ydaclizumab) with standard high dose chemotherapy consisting of BCNU (carmustine), etoposide, Ara-C (cytarabine) and melphalan (also called the BEAM regimen) and stem cell transplant.

Stem cells are a type of cell that has the potential to develop into several different cell types. We are interested in stem cells that will develop into cell types that fight infection. In this study, we will collect stem cells from your blood before starting the regimen and return them to your body after you have completed chemotherapy. We will attempt to determine:

- the effect of this combination on tumor response and the amount of time participants remain disease free
- the side effects associated with this combination
- the highest dose of ^{90}Y daclizumab that can be given without causing intolerable side effects

Why are you being asked to take part in this study?

You are being asked to participate in this study because you have Hodgkin's lymphoma that has either not responded to chemotherapy or has responded in the past, but has now relapsed.

How many people will take part in this study?

Up to 95 subjects may be enrolled in the study.

Description of Research Study

What will happen if you take part in this research study?

Before you begin the study

All research studies have specific criteria for entry to allow for valid interpretation of the study results and safety of participants, known as eligibility criteria. Before you begin this study, you will need to have some exams and tests to make sure you are eligible for this study. Your doctors and nurses will explain which exams and tests you will have. The exams and tests are part of regular cancer care and may be done even if you do not join the study. You will probably have these tests done while you are on the NCI Screening Protocol. If you recently had some of the tests, they may not need to be repeated. Studies must be completed within 28 days prior to study entry with the exception of the bone-marrow aspirate and biopsy with cytogenetic studies which must be completed within 60 days prior to study entry.

During the study

If you are eligible to participate and agree, you will spend an estimated 6 - 12 weeks in the treatment portion of the study depending on your dose level on the study regimen.

You will receive the following tests to establish a baseline prior to receiving the study regimen:

- Scans and x-rays to measure your disease and an FDG-PET scan
- Routine blood and urine tests
- Pregnancy test if you are a woman that can have children
- Blood test for cytomegalovirus (CMV) infection
- Blood test for to measure your CD25 levels
- Electrocardiogram (EKG)

After you enroll in the study, you will start the preparation of treatment according to the following schedule:

1. You will be given an injection called filgrastim (also called GCSF or neupogen) every day for five to six days in a row.

   a. Filgrastim is used to stimulate the bone marrow to make the stem cells that eventually produce a subgroup of white blood cells called granulocytes.

2. On or about 5 days after filgrastim starts, you will be given an injection of plerixafor.

   a. Plerixafor will help the new stem cells move from the bone marrow into your blood stream so that they may be collected.

3. On or about 6 or 7 days after filgrastim starts, the stem cells will be collected in a procedure called apheresis.

   a. The apheresis procedure involves inserting a catheter (tube) into your vein to allow your blood to be collected. Stem cells will be separated from the rest of your blood and stored until the time they are returned to your body through an IV infusion; and the rest of the blood will be returned to you through the same catheter it came out of. If we are unable to collect enough stem cells during this procedure, you will receive an additional dose of filgrastim and another dose of plerixafor. The apheresis procedure will be repeated. If we are unable to collect enough cells after two apheresis procedures in a row, we will wait a minimum of three weeks then repeat the process once more. If there are still not enough stem cells after this second cycle, you will be removed from the study.

4. Four weeks after your stem cells have been collected and stored, you will be given the radioactive antibody 90Y Daclizumab through an IV (a plastic tube in your vein) over the course of two hours.

5. At the same time, you will receive a low dose Indium 111 labeled daclizumab and unlabeled daclizumab/basiliximab. The Indium 111 labeled daclizumab is used to help us see where the antibodies are binding on CT scan. The unlabeled daclizumab/basiliximab helps to ensure that more the 90Y daclizumab binds to the CD25 target.
6. If you have been assigned to dose level 1 of the Phase 1 portion of the study, you will start BEAM chemotherapy 9 days after you receive the antibody.
7. If you are assigned to dose level 2-7 on the Phase 1 portion, you will receive a second dose of 90Y daclizumab 6 weeks after the first dose.

a. This will help us determine the amount of 90Y daclizumab to be given as the second dose in the Phase 2 portion of the study---this is called the Maximum Tolerated Dose or MTD (highest dose of a drug that will produce the desired effect without unacceptable side effects).

8. If you are assigned to Phase 2, you will receive a dose of 90Y Daclizumab for the first infusion; and then 6 weeks later you will receive a second dose of 90 Y Daclizumab.
9. With each dose of 90Y daclizumab and for two days after (three days total), you will receive an IV dose of Ca-DTPA given over 5 hours to help your body to eliminate the radioactive atom 90Yttrium.
10. After each daclizumab (Indium 111, Yttrium 90 and unlabeled), you will undergo three SPECT scans (CT scans based on the detection of radioactivity) of your chest & abdomen.
    a. The first will be taken 2- 8 hours after the infusion
    b. The second will be done between 1 and three days after the infusion
    c. The third will be taken between 4 and 7 days after the infusion.
    d. These images will tell us where the daclizumab is located in your body at these times and help us make sure the 90 Y Daclizumab is going to all the sites of your disease.
    e. If you are assigned to Phase 1 Dose Level 2-7 or Phase 2, we will also perform a CT scan and FDG PET scan on the day of your second infusion to help us measure any changes in your tumor that may have occurred after the first infusion.
    f. Furthermore, we will draw 12mL of your blood prior to the infusion to test for radiation levels and 8mL of blood at the following intervals: ½ hour, 1 hour, 2 hours, 6 hours, 12 hours, 24 hours and daily up to seven days after the infusion.
11. During this part of the study, starting one week before you receive 90Y daclizumab, you will have weekly physical examinations and blood tests to help us know how you are doing on the medication.
12. Nine days after you have been given the second dose of daclizumab, if you have not experienced intolerable side effects or other problems, you will begin BEAM chemotherapy.
13. Chemotherapy will be given intravenously over the course of 6 days.

a. On the first day, you will receive BCNU (Carmustine) over the course of approximately two hours.

b. On the 2nd through the 5th days of the BEAM protocol you will receive IV infusions of cytarabine (Ara-C) for approximately 30 minutes every 12 hours.

c. On the 2nd through the 5th days of the BEAM protocol, you will also receive etoposide infusions daily over 2-4 hours per day. It is possible that this infusion may take longer.

d. Melphalan will be given by IV on the 6th day of the BEAM regimen over a course of about 30 minutes.

14. In order to prevent dehydration, you will receive IV fluids during BEAM therapy; you will also receive medication to help prevent nausea and vomiting.

15. On the day following the last day of chemotherapy, the stem cells we collected and stored will be returned to you through an IV infusion.

16. During your treatment, you will receive several medications to prevent or treat side effects of the stem cell transplantation regimen, including:

    a. medication to help prevent the infections that can result from bone marrow depletion.

    b. medication to help prevent or treat fungal and viral infections starting with the first dose of 90Y daclizumab.

    c. medication to help prevent mouth sores.

    d. If needed, you will be given antibiotics to treat bacterial infections.

17. Five days after the stem cell transplant, you will be given daily injections of filgrastim to help stimulate the growth of cells in your bone marrow.

    a. You will continue to receive these injections until the number of a certain type of white blood cell, granulocytes, reaches an acceptable level.

18. You will have daily physical examinations and your blood will be sampled for testing twice daily to help us assess your health during the chemotherapy and transplantation portion of the study. This assessment schedule will continue until your granulocyte count is adequate.

When you are finished taking the drugs (treatment)

Following completion of the study regimen and recovery of your neutrophil count, we will assess your condition with physical examinations and blood tests at a minimum of every week for one month, then at a minimum of every 2 weeks for one month.

One hundred (100) days after the stem cell transplant:

- We will measure the size of your tumor using a CT scan of your chest, abdomen and pelvis and an ^{18}FDG-PET scan.

- We will take a sample of your bone marrow (bone marrow biopsy).
- We will perform tests for lung function (PFTs).

After Day 100, you will come to the NIH Clinical Center at the following times: 4, 6, 9, 12, 16, 20, 24 (± 14 days) months after the end of treatment. During the 3rd, 4th and 5th year, you will return to the NIH clinic every 6 months (± 28 days) and then yearly for regular physical and laboratory examinations.

Birth Control

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

Effective forms of birth control include:

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

Risks or Discomforts of Participation

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

The main risks of this study come from the side effects of the drugs you will be given, some of the procedures you will undergo and from radiation exposure.
Listed below are the side effects of the agents used in this study:

Filgrastim

Likely	Less Likely	Rare but Serious
• Itching • Joint pain • Muscle pain • Bone pain • Rash • Headache	• Increase in white blood cells • Pain and bleeding at injection site	• Bleeding from the lungs • Coughing up blood • Enlarged or ruptured spleen

Plerixafor

Likely	Less Likely	Rare but Serious

Likely	Less Likely	Rare but Serious
• Joint pain • Dizziness • Trouble sleeping • Low energy • Nausea • Vomiting • Gas • Diarrhea • Pain and bleeding at injection site • Headache	• Dry mouth • Indigestion • Constipation • Redness of skin • Muscle pain • Excessive sweating • Numbness • Swelling of the abdomen • Not feeling well • Abdominal pain • Hives	• Trouble breathing • Decreased platelets • Low oxygen levels in blood or tissues • Increased white blood cells • Fainting • Low blood pressure

BCNU

Likely	Less Likely	Rare but Serious
• Nausea • Vomiting • Flushing • Pain and burning at the injection site • Low white blood cells count with increased risk of infection • Low platelet count with increased risk of bleeding • Diarrhea • Loss of appetite • Headache • Fetal abnormalities if pregnancy occurs while on drug	• Scarring of lung tissue, with cough and shortness of breath, which can happen years after treatment • Flushing of skin • Redness of the eyes (just after infusion) • Low energy • Loss or thinning of hair • Low red blood cell counts (anemia) causing tiredness and other symptoms	• Temporary kidney damage • Hardening of the vein used for injection • Death due to lung damage or other problems • Temporary decrease in liver function

Etoposide

Likely	Less Likely	Rare but Serious
• Low white blood cell count with increased risk of infection • Low blood platelet count with increased risk of bleeding • Low red blood cell count (anemia) causing tiredness and other symptoms • Nausea • Vomiting • Loss of appetite • Hair loss	• Constipation • Diarrhea • Fever and chills	• Sores in mouth and throat • Rash, which can become serious • Itching • Numbness and tingling in hands and/or feet • Allergic reactions (may include chills, fever, rapid heart rate, trouble breathing, dizziness) • Increased risk of a second • cancer

Cytarabine

Likely	Less Likely	Rare but Serious
• Low white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Low red blood cell count (anemia) with symptoms like weakness, tiredness, shortness of breath • Nausea • Vomiting • Stomach pain • Tiredness • Sores in mouth or on lips	• Diarrhea • Loss of appetite • Rash • Hair loss or thinning • Fever • Muscle and bone aches • Liver damage • Blood clots and inflammation of the vein where the drug was given	• Kidney damage • Fetal changes that may lead to birth defects, prematurity, or serious illness in the newborn if you become pregnant while taking this drug • Allergic reaction with itching, dizziness, trouble breathing, or swelling of the face, mouth, or throat • Death due to infection, bleeding, or other causes

Melphalan

Likely	Less Likely	Rare but Serious
• Nausea • Vomiting • Low white blood cell count with increased risk of infection • Low platelet count with increased risk of bleeding • Anemia (low red blood cell count) with symptoms like tiredness, paleness, or trouble catching your breath	• Weakness • Inability to have children	• Severe allergic reaction • Scarring or inflammation of lungs • Second type of cancer (may happen years after treatment) • Death from lung damage or other causes

Daclizumab/Basiliximab

Likely	Less Likely	Rare but Serious
	• High blood pressure • Low blood pressure • Fluid in the lungs • Fever • Increased heart rate • Trouble breathing • Chest pain • Nausea • Vomiting • Diarrhea • Fluid retention in the legs, feet, arms or hands	• Abnormal heart rhythm – which can lead to complete stoppage • Swelling of vocal cords • Loss of consciousness • Increased blood sugar • Decreased oxygen in blood or other tissues • Allergic reaction • Kidney damage

CaDTPA:

Side effects of CaDTPA include nausea, vomiting, diarrhea, chills, fever, itching and muscle cramps. These side effects are observed in fewer than 10% of persons using this drug.

Other:

Other side effects seen with the chemotherapy treatment may include ovarian function changes in women, including hormonal changes with menopausal symptoms (such as hot flushes) or early permanent menopause (also known as ovarian failure).

Procedure Risks:

Bone Marrow Biopsy: This procedure is performed to collect cells from your bone marrow. Your hipbone will be numbed with a small needle containing a local anesthesia, and then a needle will be put into the hipbone, and about two tablespoons of bone marrow will be taken out through the needle. This procedure usually causes some pain. Very rarely, infection or bleeding may occur at the needle site.

Lymph node biopsy: This test involves taking a small tissue sample from one or more of your lymph nodes. The lymph nodes are small, oval-shaped glands found throughout the body, interconnected by lymph vessels. To obtain the sample, a local anesthetic is injected under the skin over the lymph node. A biopsy needle is placed through the skin and into the lymph node. A small tissue sample is removed when the needle is withdrawn. Tissue can also be drawn up into the needle by suction; this is called fine needle aspiration (FNA). The risks of the biopsy procedure include pain at the biopsy site, bleeding from the skin, bruising, and infection of the biopsy site.

ECG: The ECG (electrocardiogram) is a procedure that requires you to lie still for a few minutes while adhesive pads are attached to your chest to record the activity of your heart. The ECG leads may cause slight discomfort during their placement on and removal from your skin.

Echocardiogram: The echocardiogram is an ultrasound of your heart. Sticky patches or electrodes are attached to the chest and shoulders and connected to electrodes or wires. These help to record the electrocardiogram (ECG) during the echocardiography test. The ECG helps in the timing of various cardiac events (filling and emptying of chambers). A colorless gel is then applied to the chest and the echo transducer is placed on top of it. There may be slight discomfort in the application of the gel and during the placement and removal of electrodes.

Pulmonary Function Tests (PFTs): These tests, performed to test your lung function, involve inhaling and exhaling forcefully through your mouth and into a tube. There is relatively little discomfort associated with this test; however, the tests may be tiring.

Blood sampling: Local pain, bruising, bleeding, blood clot formation, and, in rare instances, an infection might occur at the site where blood is drawn. There is also the possibility of dizziness or fainting while your blood is being drawn. The decision to use a catheter (a thin tube) for

blood collecting is made by the study staff. The study staff will explain the catheter to you if its use is necessary.

FDG-PET and CT scans: Though the scanning itself causes no pain, there may be some discomfort from having to remain still for several minutes. If you have a hard time staying still, are claustrophobic or have chronic pain, you may find scanning procedures somewhat uncomfortable. You will also be exposed to radiation during the scan.

Radiation Risk from Research Procedures:

This research study involves exposure to radiation from 90Y daclizumab and 111Ind daclizumab as well as the SPECT scans you will undergo. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation you will receive in this study is from 2 injections (scans or repetitions) of 5 millicuries 111Ind daclizumab and 15 - 90 millicuries of 90Y daclizumab in addition to two series of 3 SPECT scans. The NIH Radiation Safety Committee has reviewed the use of radiation in this research study and has approved this use as involving acceptable risk and necessary to obtain the research information desired.

Using the standard way of describing radiation dose, from participating in this study, you will receive a total of 1600 rad to your liver, 1000 rad to your red bone marrow, and 710 rad to your bone surfaces. All other organs will receive smaller amounts of radiation (whole body dose of 200 rad). The amount of radiation received in this study exceeds the dose guideline established by the NIH Radiation Safety Committee for research subjects (this radiation is therapeutic so it is deemed reasonable). The guideline is an effective dose of 5 rad (or 5,000 mrad) received per year.

The possible side-effects from the exposure to radiation are:

- Low white blood cell count with increased risk of infection
- Low platelet count with increased risk of bleeding
- Anemia (low red blood cell count) with symptoms like tiredness, paleness, or trouble catching your breath
- Damage to the bone marrow which may cause myelodysplastic syndrome (a group of disorders caused by poorly formed or dysfunctional blood cells)

The average person in the United States receives a radiation exposure of 0.3 rad per year from natural sources, such as the sun, outer space, and the earth's air and soil.

If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*. Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant or breast feeding, you will not be permitted to participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aims of this study are to find the highest dose of 90Y daclizumab that can be given with BEAM chemotherapy and stem cell transplant and to determine if this experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Alternative Approaches or Treatments

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

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

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

Please talk to your doctor about these and other options.

Stopping Therapy

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

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

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

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

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

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. 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 Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

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.
- Qualified representatives from Hoffmann-La Roche, the pharmaceutical company who produced daclizumab.

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.

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.

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 method for joining radioactive atoms and molecules to daclizumab. Two agents developed in this process, ^{90}Y daclizumab and ^{111}Ind daclizumab are 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 ^{90}Y daclizumab and ^{111}Ind daclizumab.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the

information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect, use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used.

Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

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, Dr. Thomas Waldmann, M.D., Building 10, Room 4N115, Telephone: 240-760-6091. 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: 240-760-6070.

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 DECEMBER 03, 2018 THROUGH DECEMBER 17, 2019. _____ _____ _____ _____ Signature of Investigator Date Signature of Witness Date _____ _____ Print Name Print Name	