INSTITUTE: National Cancer Institute

STUDY NUMBER: 11-C-0123 PRINCIPAL INVESTIGATOR: Steven A. Rosenberg, M.D., Ph.D

STUDY TITLE: Prospective Randomized Study of Cell Transfer Therapy for Metastatic Melanoma Using Short-Term Cultured Tumor Infiltrating Lymphocytes Plus IL-2 Following Either a Non-Myeloablative Lymphocyte Depleting Chemotherapy Regimen Alone or in Conjunction with 12Gy Total Body Irradiation (TBI)

Continuing Review Approved by the IRB on 04/09/19

Amendment Approved by the IRB on 05/07/18 (L) Date posted to web:04/12/19

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?

Your doctor has told you that you have been diagnosed with metastatic melanoma. We have developed an experimental therapy that involves taking cells called lymphocytes from patients'

tumors, growing them in the laboratory in large numbers, and then giving the cells back to the patient. These cells are called Young Tumor Infiltrating Lymphocytes, or Young TIL and the therapy is called cell therapy. Before receiving the cells, the patients receive 2 chemotherapy drugs to temporarily suppress the immune system to improve the chances that the tumor fighting cells will be able to survive in the body. In some of our studies using cell therapy, patients have received total body irradiation (TBI) in addition to the chemotherapy in order to increase the length of time that they do not produce white blood cells. Patients who received this regimen seem to have a slightly better response to the treatment – but we do not know if adding radiation to the cell therapy will cause a better response for all patients. In all studies, after the cells are given, the patients receive aldesleukin (IL-2) to help the tumor fighting cells stay alive longer. In this study, we will compare giving cell therapy with the usual chemotherapy to cell therapy with the usual chemotherapy and total body irradiation.

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

You are being asked to participate in this study because you have been diagnosed with metastatic melanoma.

**How many people will take part in this study?**

Up to 118 patients will be enrolled in this study, up to 56 evaluable patients in each group.

**Description of Research Study**

**The Cell protocol has several stages:**

| Stage | Timeframe | Location | Comments & Instructions |
|---|---|---|---|
| Work up | 1-2 weeks | Inpatient and out patient | Scans, x-rays, labs leukapheresis other tests as needed |
| Tumor Resection | 1 day | Inpatient | Cells will be obtained from a tumor biopsy or during surgery. |
| **Stem cell collection** | **1 week** | **Inpatient** | ***For patients in group 2 only*** |
| Chemotherapy (day -7 to -3) | 1 week | Inpatient | Receive IV chemotherapy to prepare your immune system for the cells |
| ***Total Body Irradiation (day -3 to -1)*** | ***3 days*** | ***Inpatient*** | ***For patients in group 2 only*** |
| Cells and aldesleukin | 1-5 days | Inpatient and possibly ICU | Receive the TIL cells IV and then high dose aldesleukin every 8 hours for up to 15 doses |

| | | | |
|---|---|---|---|
| (Day 0) | | | |
| Recovery | 1-2 weeks | Inpatient unit | Recover from the effects of treatment |
| Follow -up | Ongoing until disease progression | Outpatient | Return to clinic for physical exam, review of side effects, labs, scans every 4-6 weeks for the first year, and then every 6 months. |

**The major side effects of this experimental treatment (described in detail on the following pages) that are most severe include:**

- Infection and low blood counts caused by the chemotherapy
- Confusion and changes in mental status caused by the IL-2
- Fluid retention, low blood pressure, and high heart rate caused by the IL-2
- Nausea, vomiting and diarrhea caused by the TBI
- Changes in your vision, and kidney function caused by the TBI
- Side effects may increase by giving both radiation and chemotherapy.

We will discuss the side effects of this experimental treatment with you. You will be given medicines, transfusions, and treatments to prevent or treat the side effects including drugs to prevent and/or treat different types of infections. We will try to make you as comfortable as possible.

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

**Before you begin the study?**

Work-up

We will evaluate you for eligibility for participation on this trial with a physical examination, CT and/or MRI scans, x-rays, EKG, heart and lung function tests, and blood tests. Patients who have a positive HIV blood test will not be eligible for this protocol because it may put them at higher risk of developing infections

Randomization

Once the tests described above show you are eligible for this study, you will be assigned to receive cell therapy with chemotherapy alone (group 1) or cell therapy with chemotherapy plus total body irradiation (group 2) by chance, like a "flip of a coin"; a process called randomization. Neither you nor your doctor can predict which group you will be assigned.

Cell Harvest and Growth

You underwent a procedure, either surgery or a biopsy, to obtain a piece of your tumor either from a biopsy or during surgery, so we can grow TIL from your tumor cells in the laboratory while enrolled on our companion protocol 03-C-0277 (Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols). Sometimes we are unable to successfully grow the cells needed for this procedure. We usually know after about 4 weeks whether the cells will grow well enough to be used as an experimental treatment on this protocol. At the time we determine that your cells are not growing, we will inform you and discuss your options with you.

Catheter insertion

Prior to beginning the experimental cell treatment, you will have an intravenous (IV) catheter placed in your upper chest. The area will be numbed with an anesthetic before the catheter is put in.

Leukapheresis

Leukapheresis is a procedure that allows us to remove certain types of blood cells from you and return the rest of your blood. It is a very common procedure that is done routinely here with very few risks. During leukapheresis, blood is removed from you through a needle in your arm, circulated through a machine that divides whole blood into red cells, plasma (the serum part), and lymphocytes (or white cells), and then the plasma and red cells are returned to you through a second needle in your other arm. The procedure takes between 3-4 hours to complete. Rarely, people may experience lightheadedness or dizziness. We ask that you eat prior to the procedure to prevent this. The white blood cells collected before treatment may be used to help grow the cells and after the treatment, can be tested to see how the therapy has affected your immune system.

Autologous Stem Cell Collection (Group 2 ONLY)

If you are randomized to Group 2 and will receive TBI, we will collect your stem cells during the leukapheresis and freeze them. We will give these cells back to you after you have received treatment in order to help your body recover and produce red cells, white cells and platelets. In order to obtain enough stem cells, we will give you a medication called G-CSF (also known as filgrastim) as a shot or injection under the skin twice every day for 5 days. You will also be given a single dose of plerixafor under the skin at 11 hours prior to the leukapheresis. These medications cause more stem cells to be released into your blood circulation. On the fifth day you will undergo a leukapheresis as described above. We will process them in the laboratory and freeze them until two days after your cell therapy. If we do not collect enough stem cells during the first leukapheresis, we will give you another injection of filgrastim and plerixafor and

do the leukapheresis again on day 6. If after 2 apheresis procedures, we do not have the minimum number of cells, we may ask you to wait approximately 2 weeks and then try the procedure again, to make sure we have adequate cells to regenerate your immune system and your bone marrow. If we cannot obtain enough cells, we will treat you in group 1 of this study and you will not receive radiation.

**During the Study**

Chemotherapy Regimen (Day -7 through Day -3)

After we have grown the cells to large numbers in the laboratory, you will be admitted to the hospital to begin your experimental treatment. You will be given two chemotherapy medicines, cyclophosphamide and fludarabine, to make space in your immune system so the cells can work without any interference from the cells in your immune system. (These medicines will not treat your cancer.) Animal experiments have indicated that this can make the cells more effective in fighting cancer tumors, but it is not known whether this is true in humans. You will receive the cyclophosphamide into your catheter over 1 hour for two days (Day -7 and Day -6) and then the fludarabine will be given for 30 minutes every day for five days (Day -7 through Day -3). The side effects of these medicines are described on the following pages. If you are in group 1, we will ask you if we can collect about 5 teaspoons of blood and 6 teaspoons of urine on day -3 to use in research to compare to samples collected from patients treated in group 2.

Total Body Irradiation (Day -3 through Day -1) – Group 2 ONLY

On the day of the last dose of chemotherapy you will begin receiving three days of high dose radiation in the Department of Radiation Oncology, known as total body Irradiation, or TBI. The doses of radiation will be given twice a day during those three days. TBI is painless but may cause some nausea. Before the radiation, you can receive medicine to control the nausea. It is extremely important that you lie still during the experimental radiation therapy. Like all radiation therapies, you will be alone in the room during the actual experimental therapy, but you will be watched closely on closed circuit television and have a two-way intercom to talk to the therapist. If you are in group 2, we will ask you if we can collect about 5 teaspoons of blood twice (total of 10 teaspoons) and 6 teaspoons of urine on day -3 to use in research to determine what may cause some side effects of radiation. Also, on day -1, we will ask you if we can collect 6 teaspoons of urine.

Cell Infusion and Aldesleukin Regimen (Day 0 through Day 5)

All patients will be given the cells through their IV over 20-30 minutes one to four days after the last dose of chemotherapy. Within 24 hours after your cell infusion you will be given high dose aldesleukin through one of the IVs. It will be given as a 15-minute infusion every 8 hours for up to five days after the cell infusion. Aldesleukin is a cell growth factor and it is thought that it will help the cells live longer in your body.

The day after your cells are infused, we will give you G-CSF (filgrastim) as a shot or injection under the skin every day to stimulate your blood cells until they increase to a sufficient number. We will watch you closely during this entire time for any side effects of this experimental regimen. We will discuss the side effects below and we will include in your care all the medicines and treatments to prevent as many of these side effects as we can and to make you as comfortable as we can.

If you are in group 2, we will give you back your autologous stem cells (those we obtained from you during leukapheresis in Department of Transfusion Medicine) to regenerate your immune system and bone marrow. And then give you the filgrastim as described above.

**When you are finished taking the drugs (treatment)**

Recovery

You will recover in the hospital until you are well enough to go home. This usually takes 7-12 days after you have received cells or your last dose of IL-2; however, you may need to stay in the hospital for longer than this before you are well enough to go home. We will continue to give you support medications, do laboratory tests, and watch you closely for any side effects until we feel your condition is stable.

In addition to the laboratory tests to monitor your condition, we will remove between 1 and 9 teaspoons of blood daily to study the effects of this regimen on your immune system. If you experience side effects in your kidneys, we will collect 1 additional teaspoon of blood and about 6 teaspoons of urine to see if we can determine the cause of these side effects. Also, at two times (prior to the chemotherapy, and at about 10 days after you receive TIL) and at follow-up visits, we will remove about 8 teaspoons of blood to study your immune cells, and vitamin A levels. In an animal model, we have observed that some immune cells and vitamin A levels are changed after the immune system is suppressed with chemotherapy or radiation. We would like to study if these changes also happen in patients on this study. The maximum amount of blood for research is approximately 2.3 cups in 8 weeks.

Follow up and Evaluation of Experimental Regimen

You will need to continue to take Bactrim, an antibiotic, for at least 6 months following your treatment to prevent you from catching a certain type of pneumonia seen in patients who have low white blood cell counts. We will ask you to return to NIH 4-6 weeks after completing your regimen for evaluation. This visit will probably take 2 days. If your tumor shows evidence of shrinking, we will ask you to return for evaluation every 4-6 weeks for 1 year and then every six months after that for up to 5 years, and then yearly thereafter. If your tumor appears to be growing, we will look for other investigational therapies you may be eligible for, or refer you back to the care of your local physician. We will continue to contact you every 3-6 months for the first 2 years, and yearly thereafter to request information about your disease, and any additional treatments you may have received after treatment on this study. At some of your

follow up visits, you may undergo leukapheresis so that we can see the effect this therapy has had on your immune system and if the cells we gave you are still alive.

**Birth Control**

If you are a woman who is breast feeding or pregnant, you may not participate in the study because we don't know how this medicine would affect your unborn child or your baby. 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 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 risks and discomforts of this research study can be significant. This experimental treatment can lead to long-term decrease in your immune function. It is also possible that you may lose your fertility following this experimental treatment. It is possible, although unlikely, that this experimental treatment may cause your death.

**Catheter Insertion**

Although rare, putting these catheters in can sometimes cause collapse of a lung or cause bleeding. Lung collapse is treated by putting a tube into your chest for a few days to allow your lung to expand. Pressure is placed on any area that might bleed. Other IVs may be needed in one or both of your arms if we to give you extra fluids, medicines, or nutrition.

**Leukapheresis**

The risks of leukapheresis include

- Tingling in the face or neck, lightheadedness, dizziness
- Fainting, bleeding and infection
- You may also have pain or bruising at the needle sites

| **Total Body Irradiation side effects** | | |
|---|---|---|
| Common | Less Common | Late effects of total body radiation |
| ▪ **Loss of appetite, nausea, vomiting, weight loss which is frequently severe**<br>▪ Diarrhea, stomach pain<br>▪ Mouth sores, difficulty swallowing, dry mouth, metallic taste, sticky saliva<br>▪ Fatigue<br>▪ Skin changes including pinkness, dryness, and itching<br>▪ Hair loss<br>▪ Inflammation of the lung, dry cough or difficulty breathing which may or may not require a breathing tube<br>▪ Fever<br>▪ Prolonged changes in the blood counts caused by the cyclophosphamide and fludarabine | ▪ Loss of skin color (vitiligo)<br>▪ Hearing loss (which may be temporary)<br>▪ Vision changes<br>▪ Damage to the liver which may result in changes in your liver tests or severe liver failure.<br>▪ Increase severity of the breathing problems caused by the IL-2 | ▪ Changes in kidney function that may or may not cause symptoms or require treatment<br>▪ Scarring of the lung causing shortness of breath<br>▪ Cataract formation<br>▪ Risk of developing a secondary cancer.<br>▪ Early onset of sterility {you may wish to consider banking sperm/eggs prior to starting on this study.} |

In two previous studies, we have used this approach to treat patients with melanoma using either 200 cGy TBI (25 patients) or 1200 cGy TBI (25 patients). Patients who received 1200 cGy TBI usually took longer to recover their blood cells and required more transfusions compared to patients who received 200 cGy. One patient who received 200 cGy TBI and four patients who received 1200 cGy TBI required intubation for drowsiness. Four patients who received 1200 cGy TBI developed severe kidney problems which eventually resolved. One patient in the 1200 cGy TBI group developed uveitis (inflammation of the eye) that did not respond to treatment. There was one experimental therapy-related death in the 200cGy TBI protocol due to a severe infection.

If you develop severe kidney problems, you may be asked to undergo a biopsy of our kidney in order to determine why you are having kidney problems.

**Cell Infusion**

Based on our experience giving similar types of TIL cells grown in the laboratory, you may experience the following side effects:

- Fever, chills and shortness of breath, which may last for a few hours (common)

- Lung congestion, which could be mild (shortness of breath) to severe (difficulty breathing – possibly needing a breathing tube and breathing machine for a few days)
- Autoimmune reaction such as loss of skin pigment (known as vitiligo) or inflammation of the eye (uveitis) which may require the use of steroid eye drops. You may also experience other side effects that we don't yet know about

Because a significant number of people receiving high-dose aldesleukin are, at some point in the treatment, unable to make sound decisions for themselves, we will ask you to complete a Durable Power of Attorney so that a person of your choosing can make health care decisions for you in the event that you are no longer capable of doing so.

The risks and discomforts associated with the experimental cell therapy can be significant. It is possible, but extremely unlikely, that this experimental treatment may cause your death. Side effects that can occur from a biopsy include infection or bleeding. If your tumor specimen is obtained during a surgery, the risks and side effects of the surgery will be explained to you by the surgeon.

**Medications**

The side effects of cyclophosphamide, fludarabine, high dose IL-2 and some of the other medications you will receive are listed below:

**Cyclophosphamide and Fludarabine side effects**

| Common | Less Common | Rare |
|---|---|---|
| ▪ Changes in blood counts including: low red cell count (causing fatigue and shortness of breath), low platelet count (increasing the risk of bleeding and bruising), decrease in white blood cells (increasing the risk of infection and the need for treatment with antibiotics or other treatment)<br>▪ Loss of appetite, nausea, vomiting, | ▪ Bleeding<br>▪ Infection<br>▪ Bladder irritation with bloody urine<br>▪ Severe allergic reaction (difficulty breathing/swelling)<br>▪ Headache or dizziness<br>▪ Sweating<br>▪ Swelling of arms or legs<br>▪ Skin changes, rash, blisters | ▪ Heart damage<br>▪ Lung damage<br>▪ Kidney damage<br>▪ Inflammation of the eye resulting in blindness<br>▪ Inflammation of nervous system resulting in death<br>▪ Epstein Barr Virus Lymphoma. This can be fatal (Two patients on other studies in the Surgery Branch developed EBV lymphoma, and one died as a result of this disease.)<br>▪ Loss of fertility<br>▪ Two out of the first 81 patients enrolled on the initial young TIL study died from complications resulting from |

| | | |
|---|---|---|
| ▪ Diarrhea, stomach pain<br>▪ Mouth sores<br>▪ Hair loss<br>▪ Fatigue<br>▪ Muscle or joint aches | ▪ Weakness<br>▪ Hearing loss | suppression of the immune function which resulted in a severe infection (one of these patients also received radiation as part of their treatment regimen). |

**IL-2 (aldesleukin) side effects**

| Common | Less common | Rare |
|---|---|---|
| ▪ Fever, chills, and fatigue<br>▪ Lowered platelet and red blood cell levels that may require transfusions<br>▪ Significant fluid retention causing weight gain (as much as 20 pounds).<br>▪ Low blood pressure<br>▪ Increased heart rate<br>▪ Low urine output<br>▪ Swelling in your extremities,<br>▪ Fluid in your lungs that can require oxygen<br>▪ Dry mouth, nausea, vomiting and diarrhea;<br>▪ Rash, itching; and changes in skin or hair pigmentation, called vitiligo;<br>▪ Changes in mental status, including confusion, difficulty sleeping or vivid dreams; this can be severe and require sedation and monitoring in the ICU | ▪ Decrease in thyroid function that may require daily thyroid hormone replacement;<br>▪ Abnormal kidney and liver function that can be severe;<br>▪ Abnormal heartbeats or low blood pressure that may require treatment in the ICU.<br>▪ Breathing problems which may need monitoring in ICU and insertion of a breathing tube. | ▪ Bowel perforation (a hole) requiring longer hospitalization or surgery. This is more common in patients who have previously received anti-CTLA-4 antibody. You will have a colonoscopy and biopsy before treatment if you have previously received anti-CTLA-4 antibody.<br>▪ Autoimmune disease, where your immune system attacks cells in organs of your body. Should this occur, you will be treated with steroids to stop the immune response.<br>▪ Damage to the heart muscle or heart attack<br>▪ Loss of blood flow to the extremities due to medicines used to treat very low blood pressure and shock. In one instance a patient had to have her lower arm amputated after treatment with these medicines.<br>▪ IL-2 is mixed with human albumin which could cause an allergic reaction or potentially transmit viral infections, although we have not had this occur. |

| **Support Medications – side effects** | | |
|---|---|---|
| Common | Less common | Rare |
| **Filgrastim (To increase production of white blood cells)** | | |
| ▪ Bone Pain | ▪ Severe headache | ▪ Severe breathing problems<br>▪ Rupture of your spleen |
| **Bactrim (To prevent a specific type of pneumonia)** | | |
| | ▪ Fever<br>▪ Nausea, vomiting,<br>▪ Skin rash with itching<br>▪ reduced number of white blood cells<br>▪ Allergic reaction | |
| **Fluconazole: (To prevent fungal infections)** | | |
| ▪ Headache<br>▪ Nausea, vomiting, diarrhea, abdominal pain<br>▪ Itching | | ▪ A skin disorder called Stevens Johnson Syndrome, which can be fatal<br>▪ Liver damage which may be permanent |
| **Acyclovir and Valacyclovir** | | |
| | ▪ Temporary decrease in kidney function which may not cause any symptoms<br>▪ Nausea, vomiting, diarrhea, constipation<br>▪ Pain and irritation at place of injection | ▪ Skin rash, hives, itching<br>▪ Tremors, dizziness, Confusion, seizures<br>▪ Fatigue<br>▪ Blood in the urine |

**Potential Benefits of Participation**

**Are there benefits to taking part in this study?**

It is possible that your tumors may shrink as a result of this experimental regimen, but it is not possible to predict whether this will occur.

**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:

- Taking part in another study
- Getting treatment or care for your cancer without being in a study
- Getting comfort care which is 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.

Please talk to your doctor about these and other options.

**Research Subject's Rights**

**What are the costs of taking part in the 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
- The study Sponsor (Center for Cancer Research) or their agents
- University of California at Berkley
- Lion Biotechnologies

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.

**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 become pregnant
- 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 the Sponsor. 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.

**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 are working with Lion Biotechnologies to see if this type of study could be done at institutions other than the NIH Clinical Center. Lion Biotechnologies also provides financial support for this study.

**Use of Specimens and Data for Future Research**

Specimens and data collected during the course of this study will be used for future research and will be stored, tracked and disposed of under our companion protocol 03-C-0277, (Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols) on which you have already been enrolled.

In addition, 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 and 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, Steven A. Rosenberg, M.D., Ph.D., Building 10 CRC, Room 3-3940, [redacted] 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, [redacted].

You may also call the Clinical Center Patient Representative [redacted].

**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 APRIL 09, 2019 THROUGH MAY 06, 2020.**

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____