INSTITUTE: National Cancer Institute

STUDY NUMBER: 09-C-0082 PRINCIPAL INVESTIGATOR: Steven A. Rosenberg, M.D., Ph.D.

STUDY TITLE: An Assessment of the Safety and Feasibility of Administering T-Cells Expressing an Anti-CD19 Chimeric Antigen Receptor to Patients with B-Cell Lymphoma

Continuing Review Approved by the IRB on 09/15/20

Amendment Approved by the IRB on 06/24/20 (EE) Date posted to web: 09/18/20

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?

We have developed an experimental procedure for patients with cancer that uses their own blood cells. We genetically modify these cells and grow them in the laboratory. We hope that these cells when infused will decrease the amount of cancer you have. However, it is possible that these cells will not have this effect. We will be using the anti-CD19 gene and a type of virus (retrovirus) in making these cells (anti-CD19 cells). The anti-CD19 cells will be given to you as an intravenous (IV) infusion. This type of experimental therapy is called “gene therapy” and is very closely monitored by the Food and Drug Administration (FDA) and other regulatory agencies. The risks of gene therapy will be described later in this document.

With prior treatments, we have given “fresh” anti-CD19 cells, but now we are using “frozen” anti-CD 19 cells, which will be thawed and given to you as an IV infusion.

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

You have been diagnosed with a CD19-expressing B-cell cancer and the standard therapies available have not been effective. CD19 is an antigen (protein) found on the surface of B cells, and this antigen is expressed in the majority of your cancer cells.

How many people will take part in this study?

About 30 patients have been treated with the "fresh cell product"; up to 42 patients may be treated with the "frozen" cell product. This highly experimental regimen is explained below.

Description of Research Study

The study has 5 stages as outlined below:

What	Timeframe	Location	Comments & Instructions
Work up	1-2 weeks	Inpatient and out patient	Scans, x-rays, labs leukapheresis other tests as needed
Chemotherapy (day -5 to -3)	3 days	Inpatient	Receive IV chemotherapy to prepare your immune system for the cells
Cells (Day 0)	1 days	Inpatient and possibly ICU	Receive anti-CD19 cells
Recovery	1-2 weeks	Inpatient unit	Recover from the effects of chemotherapy
Follow -up	Ongoing until disease progression	Outpatient	Return to clinic for physical exam, review of side effects, labs, scans every 1-6 months

This is a phase 1 study, commonly referred to as a "dose finding study", which means that groups of patients treated on this study have received different doses of the cells and chemotherapy in order to find a safe dose of cells that does not result in severe toxicity. These anti CD19 tumor fighting cells appear to be much "stronger" than other cells we have given in other Immunotherapy Surgery Branch protocols. We have treated approximately forty-three patients since the study opened. Some of the patients who were treated in the first few groups had severe side effects and needed to be transferred to the intensive care unit (ICU), these side effects included difficulty breathing, inability to speak, confusion, tremors, and kidney damage. Some patients required breathing tubes and kidney dialysis but all of the patients completely recovered to baseline and were able to be discharged to home.

Because toxicities were observed in the earlier groups of patients, we stopped giving aldesleukin, reduced the cell dose, and reduced the doses of cyclophosphamide and fludarabine. This has decreased the side effects of the treatment. Of the twenty-eight patients treated with the fresh product on this study, 10 patients have had a partial response and 10 have had a complete response to treatment.

We have developed a frozen cell product to be given to patients with reduced doses of chemotherapy and no aldesleukin. The dose we are giving for the frozen cell product is a little higher than the dose we gave with the fresh cells because we think that some of the cells will die off during the freezing and thawing process. Since the start of this new frozen cell product, the first 9 patients treated have experienced neurological toxicities causing confusion, slurred speech, shuffling gait, and tremors. All of the toxicities resolved within about 4 weeks. To potentially reduce the toxicities observed, the cells may be grown in the lab for a longer period of time. We hope that the frozen cell product will work just as well or better than the fresh product and that we will observe the same or fewer side effects as the fresh cell product.

The major side effects of this experimental therapy (described in detail below) that are most severe include:

- Infection and low blood counts caused by the chemotherapy
- Low blood pressure requiring treatment in the intensive care unit
- Neurologic (brain) toxicities which may require intubation for several days

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

Before you Begin the Study

Cell Harvest and Growth

You underwent a process called apheresis, while enrolled on our companion protocol 03-C-0277 (Cell harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols). This process obtained certain types of blood cells from you. These cells (anti-CD19) will be grown in the lab and genetically modified to recognize a protein on your tumor cells. If your cells do not grow, unfortunately, you will not be able to receive the cell infusion. If that happens, we will look at alternative experimental treatments at the NIH Clinical Center or refer you to the care of your referring physician. 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. Several medications are used during the preparation of your cell product, be sure to tell your doctor if you are allergic to any antibiotics.

Work-up

Prior to receiving the experimental therapy, you will undergo many tests. These include imaging procedures, laboratory tests, and a bone marrow aspirate and biopsy. Bone marrow is spongy tissue found inside some of your larger bones. Bone marrow has a fluid portion and a more solid portion. A bone marrow biopsy removes a small amount of the more solid portion while a bone marrow aspiration removes the fluid portion. Both can be done during the same procedure. The procedure consists of putting a needle about ¾ of an inch deep into a bone (usually the hip bone or sternum, also known as the breast bone) after numbing the area, and removing small samples of your bone marrow. As part of your workup you will also have a large catheter inserted into a vein and leukapheresis will be performed. If you are a woman, you will undergo a pregnancy test. You may be admitted to the hospital for these tests. However, you will be allowed to leave on pass on the days that you are not having tests performed.

Catheter Insertion

Prior to beginning the experimental therapy, 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. 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 need to give you extra fluids, medicines, or nutrition.

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 at the NIH 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 white blood cells may be used to help grow the cells. In addition to the leukapheresis you will undergo as part of your work up, we will also ask you to undergo one additional pheresis procedure between 4 and 6 weeks after your cell therapy to see the impact of this therapy on the immune system and see if cells we gave you are still active.

Lumbar Puncture

Before starting your chemotherapy, we may ask you to have a lumbar puncture (LP) so that we can see if there are any white blood cells in your spinal fluid. If you have neurologic side effects following treatment you may also have a LP to see if there are any white blood cells in your spinal fluid. Knowing whether or not you had white blood cells before starting treatment may help us to learn more about what causes the neurologic side effects caused by this treatment. The LP prior to treatment is optional; if you have neurologic side effects, the FDA requires that this procedure be performed as soon possible after the side effects start as long as it is safe for you.

A lumbar puncture is a procedure in which a thin needle called a spinal needle is put into the lower part of the spinal column to collect cerebrospinal fluid or to give drugs. This is also called spinal tap. You will be asked to lie in a curled position on a table. After a small area on your lower back is numbed, a spinal needle (a long, thin needle) is inserted into the lower part of the spinal column to remove cerebrospinal fluid. The fluid will be sent to a laboratory for testing. You will be asked to sign a separate consent for the lumbar puncture.

During the Study

Chemotherapy Regimen (Day -5 through Day -3)

After we have grown the anti-CD19 cells to large numbers in the laboratory you will be admitted to the hospital to begin your experimental therapy. You will be given two chemotherapy medicines, cyclophosphamide and fludarabine, to make space in your immune system so the anti-CD19 cells can work without any interference from the cells in your immune system. These medicines may have an effect on your cancer; however, the dose and schedule used in this experimental study are not intended to treat your cancer. Animal experiments have indicated that making space for the cells you will receive can make them more effective in fighting cancer cells, but it is not known whether this is true in humans. The cyclophosphamide and fludarabine will be given into your catheter one following the other for three days (Day -5 through Day -3). The side effects of these medicines are described on the following pages.

Cell Infusion (Day 0)

You will be given the cryopreserved (frozen) anti-CD19 cells two - four days after the last dose of chemotherapy. The cryopreserved anti-CD19 cells will be given in your catheter over 30 minutes.

We will give you G-CSF (filgrastim) as a shot or injection under the skin the day after you receive the cells if your white blood cell count is low. This is used to stimulate your white blood cells to grow again and will continue until your white blood cell counts begin to return to normal.

When you are Finished Taking the Drugs (Treatment)

Supportive Therapy – Allopurinol (Aloprim™ or Zyloprim™) for Tumor Lysis Syndrome

Anti-cancer treatment sometimes kills leukemia or lymphoma cells so rapidly that the body cannot get rid of the waste products fast enough. This is known as tumor lysis syndrome and it requires special attention and treatment to decrease the chance of kidney damage and other side effects. If tests suggest that you might be at risk, we will watch closely for this problem. In addition, a medication called allopurinol will be given to try to prevent kidney problems from developing. It is given by mouth three times a day and continuing until it appears that the risk of tumor lysis syndrome is low. Allopurinol is usually well tolerated. Possible side effects are described in detail on page 10.

Recovery

After your dose of cells, you will recover in the hospital until you are well enough to go home. This usually takes 5 to 10 days; however, you may need to stay in the hospital for longer than 10 days 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 approximately 9 teaspoons of blood three times per week to study the effects of this regimen on your immune system. The maximum amount of blood for research is approximately 2.3 cups in 8 weeks.

We may ask you to allow us to perform a biopsy of your lymph node after receiving the therapy to look at the effects of the therapy on the immune cells in your cancer. However, this biopsy is not required for you to participate in this experimental study. To obtain cells by a biopsy, a small area of skin is numbed with an anesthetic and a small piece of your tumor is removed, either with a needle or by a small cut in the tumor. The area is covered with a bandage for a day or two, during which time we will ask you to keep it dry.

Follow-up and Evaluation of Experimental Regimen

You will need to continue to take Bactrim, an antibiotic, for at least 6 months following your therapy. We will ask you to return to the NIH Clinical Center frequently after you are discharged approximately 6 and 12 weeks following treatment and then if you are responding to the treatment, every 1-3 months for the first year following treatment, every 6 months for the second year and then as determined by your physician. The follow up visits will probably take 1-2 days. At each visit you will have lab tests, imaging studies and a physical examination. At some of your follow up visits, you may undergo leukapheresis or have about 8 tubes of blood drawn (4 tablespoons) 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. If you are unwilling or unable to travel to the NIH Clinical Center we will contact you by phone or e-mail and we may ask you to send us lab, imaging, and physical exam reports. 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.

Retreatment

If your disease grows after experiencing tumor shrinkage or disappearance or if you have residual disease at the second or subsequent assessments following the initial treatment you may receive one additional treatment if you tolerated the treatment well and if all the side effects have resolved. If you are retreated, you will receive the currently enrolling dose level.

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 therapy and for four months after you finish study therapy. 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

Gene Therapy Long-Term Follow-up (Retroviral Vectors)

Because we do not know the long-term side effects of gene therapy, we will collect your blood over the next several years, frequently at first and then less frequently. If you return to your referring physician after treatment here we will ask you to have your physician send your blood specimens here for this testing. This testing will determine if the cells have grown or changed in your body. We will test your blood immediately after you receive the cells, and then at 3, 6 and 12 months (2 teaspoons each time). If all of the tests are normal and show no change, we will collect blood from you every year after that to store in case you develop symptoms later. According to FDA requirements, we need you to return annually to the NIH for a physical examination for five years after you receive the cells. After that time, we will be sending you a questionnaire to get information regarding your health for the next ten years, for a total follow up time period of 15 years. For this reason, we ask that you continue to provide us with a current address and telephone number, even after you complete this research study. At the time of your death, no matter the cause, we may request permission for an autopsy in order to obtain vital information concerning the safety of this experimental treatment approach. Please discuss this with your family to inform them of this request.

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 therapy can lead to long-term decrease in your immune function. It is also possible that you may lose your fertility following this experimental therapy. It is possible, although unlikely, that this experimental therapy may cause your death.

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. You should talk to your study doctor about any symptoms that you experience while taking part in the study.

Leukapheresis

During the leukapheresis procedure, you may have some tingling in your face and lips due to the medicine used to keep your blood from clotting during the procedure. The nurses may give you a calcium containing antacid, like TUMS to chew that takes away this tingling. Rarely, people may experience lightheadedness or dizziness. We ask that you eat prior to the procedure to prevent this. Rare complications of this procedure are lowered blood pressure or bleeding.

Lumbar Puncture

Lumbar puncture (LP) is a very common and safe procedure. The most common side effect from a lumbar puncture is a headache which can last from several hours to several days. You will be asked to lie flat for several hours following the procedure in order to decrease the chance of you getting a headache. The other less common side effects include bleeding and back discomfort. In extremely rare situations, removing the spinal fluid could cause compression of your brain stem. This causes increased pressure within your skull and is a medical emergency.

Cryopreserved Anti-CD19 Cell Infusion (Gene Therapy)

The cells we will be giving you have a type of virus (retrovirus) put into them along with the anti-CD19 gene. Although this retrovirus is not active, there is the rare possibility that it may cause infection. The cells could also cause you to develop another type of cancer in your blood cells. Other gene-modified cells have been given only to a few individuals before so we do not have much information about the side effects. Potential risks include:

- Fever, chills and shortness of breath, which may last for a few hours (common)
- Lung congestion
- Rash
- Low blood pressure sometimes requiring treatment in the intensive care unit
- Minor neurological side effects including, facial droop, dizziness and difficulty finding words
- Major neurological complications that may require intubation including: becoming difficult to arouse and tremors
- Immune-mediated toxicity, from targeting of the B cells in your blood, which may increase the risk of infection. *Note:* In similar clinical trials with cells targeting a melanoma protein, we have observed the following immune-mediated toxicities: loss of skin pigment (known as vitiligo), inflammation of the eye (uveitis), hearing loss, and dizziness. The skin, the eye, and the ear are all sites that contain the melanoma protein

used in these trials. Since B cells do not have this protein we do not expect these toxicities to occur with the anti-CD19 cell infusion.

- You will be treated on this gene transfer protocol with a viral vector that was manufactured at the NCI Surgery Branch Vector Production Facility before May 2016. An internal review of the facility that made the vector for this protocol determined that the facility needed to be closed due to manufacturing issues. We know of no additional risks related to the previously produced vector for patients who have received cells with vectors made in this facility as the vectors were extensively tested by outside experts. Therefore, the IRB has determined that the potential benefit to you outweighs the potential risks.
- There is little data available at this time to guide us in how humans might respond to this type of cell infusion. As this is a new experimental therapy, side effects that we do not anticipate that may cause your condition to deteriorate may be encountered. Any new information that becomes available during the course of this study will be shared with you.

Medications

The side effects of cyclophosphamide, fludarabine, and some of the other medications you may receive are listed in the tables on the next pages.

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) ▪ Loss of appetite, nausea, vomiting, ▪ Diarrhea, stomach pain ▪ Mouth sores	▪ Bleeding ▪ Infection* ▪ Bladder irritation with bloody urine ▪ Severe allergic reaction (difficulty breathing/swelling) ▪ Headache or dizziness ▪ Sweating ▪ Swelling of arms or legs ▪ Skin changes, rash, blisters ▪ Weakness ▪ Hearing loss	▪ Heart damage ▪ Lung damage ▪ Kidney damage ▪ Inflammation of the eye resulting in blindness ▪ Inflammation of nervous system resulting in death ▪ 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.)

▪ Hair loss ▪ Fatigue ▪ Muscle or joint aches	*One patient who received anti-CD19 cells died of pneumonia caused by an infection with H1N1 18 days after cell infusion.	▪ Loss of fertility ▪ Myelodysplastic Syndrome

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

	▪ Pain and irritation at place o injection	
Allopurinol (To prevent Tumor Lysis Syndrome)		
▪ Skin rash or sores ▪ Hives ▪ Itching	▪ Drowsiness (patient should not drive or use machines until they feel alert again)	▪ Chills ▪ Fever ▪ Joint pain ▪ Muscle aches or pains ▪ Sore throat ▪ Nausea or vomiting

Prior to and throughout this study you will undergo many tests to determine the extent of your cancer, as well as the impact of the therapy. If your disease progresses or recurs after this experimental therapy then you will no longer receive therapy in this protocol, though you may be eligible to be considered for other protocols at the National Cancer Institute, NIH or referred elsewhere for therapy.

Gene Therapy Risk of Cancer and Other Diseases

We are unsure if this type of gene therapy will cause you to become sick in the future. It is possible that it may cause your immune system or nerves not to work well or cause a sickness of your blood cells or even a cancer. We do not know if you will develop any of these disorders, but you need to be aware of this possible risk. Children in France and England received gene therapy for a particular disease of the immune system. Most of the children were cured but 5 children out of 22 later developed leukemia and one died. Experts who looked at these cases thought that the gene therapy caused the leukemia in these children. To monitor you for this risk we will be testing your blood 3 months after cell infusion, then at 6 and 12 months, and then annually thereafter. If we find that the cells we have given you grow out of control, chemotherapy will be given to you to kill the cells, given their risk of causing leukemia or a second cancer.

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to see 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 effect of this treatment on 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?

Other options for treatment of your cancer include:

- 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.
- Allogeneic transplantation (curative option for some patients)

Please talk to your doctor about these and other options.

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
- The study Sponsor (Center for Cancer Research) or their agents
- Kite Pharma

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 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.

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 are working with Kite Pharma to see if this type of study could be done at institutions other than the NIH Clinical Center. Kite Pharma 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 CRC, Room 3-3940, Telephone: 240-760-6218. 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 SEPTEMBER 15, 2020 THROUGH SEPTEMBER 14, 2021.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____