
MEDICAL RECORD	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY	
	• Adult Patient or	• Parent, for Minor Patient

INSTITUTE: National Cancer Institute

STUDY NUMBER: 14-C-0110 PRINCIPAL INVESTIGATOR: Steven A. Rosenberg, M.D., Ph.D

STUDY TITLE: A Phase I/II Study of the Treatment of Metastatic Cancer that Expresses MAGE-A3 Using Lymphodepleting Conditioning Followed by Infusion of Anti-MAGE-A3 HLA-A*01-Restricted TCR-Gene Engineered Lymphocytes and Aldesleukin

Continuing Review Approved by the IRB on 06/28/18

Amendment Approved by the IRB on 05/31/18 (I)

Date posted to Web: 07/04/18

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?

We have developed an experimental therapy for treating patients with cancer that involves taking white blood cells from the patient, growing them in the laboratory in large numbers, genetically modifying these specific cells with a type of virus (retrovirus) to attack only the tumor cells, and then giving the cells back to the patient. This type of therapy is called gene transfer. In this protocol we are modifying the patient's white blood cells with a retrovirus that has the gene for anti-MAGE-A3 incorporated in the retrovirus. So far, MAGE-A3 has been found only on tumor cells. The purpose of this study is to see if these particular tumor-fighting cells can cause tumors to shrink and to be certain the treatment is safe. However, it is possible that these cells will not

PATIENT IDENTIFICATION	CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY
	• Adult Patient or NIH-2514-1 (07-09) P.A.: 09-25-0099 File in Section 4: Protocol Consent (1)

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 2 of 16 pages

have this effect. The first few patients enrolled will participate in the Phase I portion of the study, called the "dose escalation" phase. The purpose of dose escalation is to determine the most effective yet safe dose of anti-MAGE-A3 cells. There will be 5 dose levels of anti-MAGE-A3 cells. The first patients enrolled get the smallest dose and the dose is increased when a level has been determined to be safe. If the first dose has too many side effects, patients enrolled will receive smaller doses. Discuss with your doctor which dose of anti-MAGE-A3 cells you will be receiving. This is the first time these cells will be given to humans. Since this is a phase I/II trial, it is unlikely that you will receive any benefit.

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 cancer that has the MAGE-A3 molecule on the surface of the tumors.

How many people will take part in this study?

Up to 102 patients will be enrolled in this study.

Description of Research Study

This study has several stages as outlined below:

- Stage 1 is performed under the companion protocol, 99-C-0128 (Evaluation for NCI Surgery Branch Clinical Research Protocols), to which you have already enrolled.
- Stage 2 is performed under the companion protocol, 03-C-0277 (Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols), to which you have already enrolled.
- Stages 3-6 are performed under this protocol.

Stage	Timeframe	Location	Comments & Instructions
1. Work-up	1-4 weeks	Inpatient or outpatient	Scans, x-rays, labs, other tests as needed
2. Cell Manufacturing	4-6 weeks	Inpatient or Outpatient	Leukapheresis
3. Chemotherapy (Days -7 to -3)	5 days	Inpatient	Receive IV chemotherapy to prepare your immune system for the cells
4. Cells and aldesleukin (Days 0-5)	1-5 days	Inpatient and possibly ICU	Receive the anti-MAGE-A3 cells IV and then high dose aldesleukin about every 8 hours for up to 15 doses

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 3 of 16 pages

Stage	Timeframe	Location	Comments & Instructions
5. Recovery	1-3 weeks	Inpatient unit	Recover from the effects of treatment
6. Follow -up	Ongoing until disease progression	Outpatient	Return to clinic for physical exam, review of side effects, labs, scans every 1-3 months for the first year.

What will happen if you take part in this research study?**Before you Begin the Study**

The following procedures are conducted under 99-C-0128 or 03-C-0277.

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. Some of these cells will be grown in the lab and genetically modified to recognize a protein on your tumor cells (anti-MAGE-A3). 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 treatment, you will undergo many tests. These include imaging procedures, heart and lung function tests, eye exams, and laboratory tests. If you have received ipilimumab (also called Yervoy, MDX-010) or any antibody therapy that could affect an anti cancer immune response and have experienced any GI toxicities, you will have a colonoscopy and biopsies to make sure your colon is normal since these drugs may have caused damage to your colon that may worsen with aldesleukin treatment. 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 or pass on the days that you are not having tests performed.

Catheter Insertion

Prior to beginning the experimental 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. 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

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 4 of 16 pages

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 and after the treatment, you will have leukapheresis so that we can test your 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 regimen to see the impact of this therapy on the immune system and see if cells we gave you are still active.

During the Study

The following procedures will be performed under this protocol:

Chemotherapy Regimen (Day -7 through Day -3)

After we have grown the anti-MAGE-A3 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 suppress your immune system so the anti-MAGE-A3 cells can work without any interference from the cells in your immune system. (These medicines will not treat your cancer; although they may cause your tumor to shrink for a short period of time.) 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. The cyclophosphamide will be given into your catheter over 1 hour for two days (Day -7 and Day -6) and the fludarabine will be given into your catheter 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.

After you have completed the chemotherapy regimen you will receive the cell infusion.

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

One to four days after the last dose of chemotherapy, you will be given the anti-MAGE-A3 cells. The anti-MAGE-A3 cells will be given in your intravenous catheter over 30 minutes. Within 24 hours after the anti-MAGE-A3 cell infusion, you will be given high dose aldesleukin through your intravenous catheter. Aldesleukin is approved by the FDA for treatment of metastatic melanoma and metastatic renal cell cancer. The purpose of giving the aldesleukin with this therapy is to keep the cells we give you active for as long as possible so they will fight your tumor. The aldesleukin will be given as a 15-minute infusion about every 8 hours for up to five days after the cell infusion (maximum number of doses is 15). Doses may be skipped or delayed

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 5 of 16 pages

depending on how well you tolerate the doses. The risks of the cells and aldesleukin are described on the following pages.

The day after you receive the anti-MAGE-A3 cells, we will give you G-CSF (filgrastim) as a shot or injection under the skin. This will continue until your white blood cell counts begin to return to normal. 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.

When You are Finished Taking the Drugs (Treatment)**Recovery**

After your last dose of aldesleukin, you will recover in the hospital until you are well enough to go home. This usually takes 7 to 21 days; however, you may need to stay in the hospital for longer than this. 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.

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. 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 3 months x 3, then every 6 months x 2 years 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 tumor shrinks or disappears following the initial treatment and then stops shrinking or recurs, you may receive additional treatments if you tolerated the treatment well and if all the side effects have resolved. The second treatment will not begin prior to 6- 8 weeks after your last dose of aldesleukin.

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 6 of 16 pages

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 your blood tests show no evidence of the cells. In addition, male participants should not donate sperm during this time period. 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 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.

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 7 of 16 pages

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.

Cell Infusion

The cells we will be giving you have been modified with a retrovirus that has the gene for anti-MAGE-A3 incorporated in the retrovirus. The cells could cause you to develop another type of cancer, such as leukemia or lymphoma, although this has never been seen in any gene therapy trial involving lymphocytes. These specific gene-modified cells have not been given to patients and thus we do not know what the specific side effects will be. In 2 prior studies using different parts of the MAGE gene, four patients died. In one of these studies, two patients of 9 who received this treatment died from neurological toxicities, probably due to the treatment. We stopped that study but continued research to try to determine the cause of the side effects from the treatment. In the other study which took place at another institution 2 patients died from cardiac toxicities. The anti-MAGE-A3 is different from the MAGE used in the earlier trials and we do not anticipate that this anti-MAGE-A3 will cause the same side effects.

Potential risks include:

- Fever, chills and shortness of breath, which may last for a few hours (common)
- Lung congestion causing shortness of breath
- 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.
- As this is a new experimental therapy which has not been given to patients, 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.
- 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.

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 8 of 16 pages

Aldesleukin (IL-2)

When aldesleukin is given through an intravenous catheter, it can make you feel like you have the flu. It can also cause confusion and mental status changes making you unable to make sound decisions. Prior to beginning treatment, 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 case you develop these side effects. In our experience giving aldesleukin to over 2,000 patients we have found that these side effects go away within a few days of stopping the aldesleukin.

Medications

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

Cyclophosphamide and Fludarabine Side Effects		
Common	Less Common	Rare
<ul style="list-style-type: none">▪ 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▪ Hair loss▪ Fatigue▪ Muscle or joint aches	<ul style="list-style-type: none">▪ 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	<ul style="list-style-type: none">▪ 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 both died as a result of this disease.)▪ Loss of fertility▪ Death due to complications resulting from suppression of the immune function which resulted in a severe infection

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 9 of 16 pages

Aldesleukin (IL-2) Side Effects

Common	Less Common	Rare
<ul style="list-style-type: none"> ▪ Fever, chills, and fatigue ▪ Lowered platelet and red blood cell levels that may require transfusions ▪ Significant fluid retention causing weight gain (as much as 20 pounds). ▪ Low blood pressure ▪ Increased heart rate ▪ Shortness of breath ▪ Low urine output ▪ Swelling in your extremities, ▪ Fluid in your lungs that can require oxygen ▪ Dry mouth, nausea, vomiting and diarrhea; ▪ Rash, itching; and changes in skin or hair pigmentation, called vitiligo; ▪ Changes in mental status, including confusion, difficulty sleeping or vivid dreams; this can be severe and require sedation and monitoring in the ICU 	<ul style="list-style-type: none"> ▪ Decrease in thyroid function that may require daily thyroid hormone replacement. ▪ Abnormal kidney and liver function that can be severe. ▪ Abnormal heartbeats or low blood pressure that may require treatment in the ICU. ▪ Breathing problems which may need monitoring in ICU and insertion of a breathing tube. 	<ul style="list-style-type: none"> ▪ Bowel perforation (a hole) requiring longer hospitalization or surgery. ▪ 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. ▪ Damage to the heart muscle or heart attack ▪ 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. ▪ Aldesleukin 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

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD**CONTINUATION SHEET for either:**

NIH 2514-1, Consent to Participate in A Clinical Research Study

NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER:14-C-0110

CONTINUATION: page 10 of 16 pages

		<ul style="list-style-type: none">▪ Rupture of your spleen
Bactrim (To prevent a specific type of pneumonia)		
	<ul style="list-style-type: none">▪ Fever▪ Nausea, vomiting▪ Skin rash with itching▪ Reduced number of white blood cells▪ Allergic reaction	
Fluconazole (To prevent fungal infections)		
<ul style="list-style-type: none">▪ Headache▪ Nausea, vomiting, diarrhea, abdominal pain▪ Itching		<ul style="list-style-type: none">▪ A skin disorder called Stevens Johnson Syndrome, which can be fatal▪ Liver damage which may be permanent
Acyclovir and Valacyclovir		
	<ul style="list-style-type: none">▪ Temporary decrease in kidney function which may not cause any symptoms▪ Nausea, vomiting, diarrhea, constipation▪ Pain and irritation at place of injection	<ul style="list-style-type: none">▪ Skin rash, hives, itching▪ Tremors, dizziness, Confusion, seizures▪ Fatigue▪ Blood in the urine

Prior to and throughout this study you will undergo many tests to determine the size and extent of your tumor, as well as the impact of the treatment. Multiple blood tests will be performed and some of your serum and lymphocytes will be stored for future testing. Blood and tissue samples collected from you may be stored and used in the future to study scientific questions related to this protocol. If there are any risks to you or your family associated with these future scientific studies which are not covered in this consent form, your consent will be obtained before such studies are performed.

If your disease progresses or recurs after this experimental treatment, then you will no longer receive treatment in this protocol, though you may be eligible to be considered for other protocols at the National Cancer Institute, NIH or referred elsewhere for treatment.

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

PATIENT IDENTIFICATION**CONTINUATION SHEET for either:**

NIH-2514-1 (07-09)

NIH-2514-2 (10-84)

P.A.: 09-25-0099

File in Section 4: Protocol Consent

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 11 of 16 pages

your blood cells or even a cancer (for example leukemia). 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. This testing will be conducted on our protocol 09-C-0161, "Follow up Protocol for Subjects Previously Enrolled in NCI Surgery Branch Studies" to which you will be enrolled following treatment.

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 no treatment or 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.

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

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 12 of 16 pages

- 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.

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.
- NCI Institutional Review Board

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 13 of 16 pages

- The study Sponsor, Center for Cancer Research or their agents
- Our research collaborator, Kite Pharma, Inc.

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 Website 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.

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

MEDICAL RECORD	CONTINUATION SHEET for either: NIH 2514-1, Consent to Participate in A Clinical Research Study NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study
-----------------------	--

STUDY NUMBER:14-C-0110

CONTINUATION: page 14 of 16 pages

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 using the cell product developed by the NCI Surgery Branch through a joint study with your researchers and the company (Kite Pharma, Inc.). The company also provides financial support for this study.

Use of Specimens and Data for Future Research

Blood and tissue 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.

PATIENT IDENTIFICATION	CONTINUATION SHEET for either: NIH-2514-1 (07-09) NIH-2514-2 (10-84) P.A.: 09-25-0099 File in Section 4: Protocol Consent
-------------------------------	--

STUDY NUMBER: 14-C-0110

CONTINUATION: page 15 of 16 pages

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, Room 3-3940, Telephone: 240-760-6218. 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. You may also call the Clinical Center Patient Representative at 301-496-2626.

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

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 JUNE 28, 2018 THROUGH DECEMBER 27, 2018.**

Signature of Investigator

Date

Signature of Witness

Date

Print Name

Print Name