INSTITUTE: National Cancer Institute

STUDY NUMBER: 08-C-0121 PRINCIPAL INVESTIGATOR: Steven A. Rosenberg, MD, PhD

STUDY TITLE: Phase II Study of Metastatic Cancer that Expresses NY-ESO-1 Using Lymphodepleting Conditioning Followed by Infusion of Anti-NY ESO-1 TCR-Gene Engineered Lymphocytes

Continuing Review Approved by the IRB on 06/23/16
Amendment Approved by the IRB on 07/22/15 (N) Date posted to web: 06/30/16

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.

### Description of Research Study

You have been diagnosed with metastatic cancer and the standard treatments available have not been effective. We have developed an experimental procedure for treating patients with melanoma that uses blood cells found in their tumors or peripheral blood cells. We genetically modify these cells and grow them in the laboratory. We hope that these cells when infused will decrease the size of your tumors. However, it is possible that these cells will not have this effect. We will be using the anti-ESO-1 gene and a type of virus (retrovirus) in making these special cells (anti-ESO-1 cells). The anti-ESO--1 cells will be given to you as an intravenous (IV) infusion. ESO-1 is a gene present in cancer cells. This type of experimental treatment is called

"gene therapy" and is very closely monitored by the FDA and other regulatory agencies. The risks of gene therapy will be described later in this document.

Our studies in animals of cell transfer have indicated that the administration of a pox virus (a type of virus that cannot reproduce in mammals) in conjunction with cell transfer may increase the effectiveness of the cell transfer. Therefore, we would like to study the combination of anti-ESO-1 cells with an experimental vaccine that includes the NY-ESO-1 gene inserted inside a virus called ALVAC(2) (ALVAC ESO-1 vaccine). This virus, which is used as a vaccine against disease in canaries, cannot reproduce in mammals, so it cannot cause disease in humans. However, when it is injected into a patient, it stimulates specific cells in the immune system.

To date, we have treated 20 patients - 13 with melanoma, 6 with synovial cell sarcoma and 1 patient with breast cancer with the antii-ESO-1 cells (no ALVAC ESO-1 vaccine) and 11 patients have experienced clinical response for a response rate of 45%. We have treated 10 patients with the anti-ESO-1 cells and ALVAC vaccine and of the 8 patients evaluable for response, 4 have experienced clinical responses (50% response rate). Although the response rate seems similar between patients treated with and without the vaccine, we will need to treat many more patients to determine if the vaccine actually makes a difference in the treatment.

There are many steps in the production of the ALVAC ESO-1 vaccine and thus it is not always available to us for clinical trials. Therefore, you will receive the ALVAC ESO-1 vaccine along with the anti-ESO-1 cells when the vaccine is available. If the vaccine is not available at the time that we determine you are eligible for this study, you will receive only the anti-ESO-1 cells.

This highly experimental regimen is explained below.

**Research Study Overview**

**This study has 5 stages outlined below:**

| Stage | Timeframe | Location | Comments & Instructions |
|---|---|---|---|
| Work up | 1-2 weeks | Inpatient and out patient | Scans, x-rays, labs leukapheresis other tests as needed |
| Chemotherapy (day -7 to -1) | 1 week | Inpatient | Receive IV chemotherapy to prepare your immune system for the cells |
| ALVAC ESO-1 vaccine (Days 0 and 14 (when the vaccine is available) | 1 day, then again on day 14 | Inpatient | Receive vaccine under the skin as 4 injections (one in each extremity) |
| Cells, and IL-2 (Day 0) | 1-5 days | Inpatient and possibly ICU | Receive, anti-ESO-1 cells, and then IL-2 every 8 hours for up to 15 doses |
| Recovery | 1-2 weeks | Inpatient unit | Recover from the effects of chemotherapy and IL-2. |
| Follow -up | Ongoing until disease progression | Outpatient | Return to clinic for physical exam, review of side effects, labs, scans every 1-6 months |

**The major side effects of this experimental treatment (described in detail on pages 5-8) 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

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.

Women who are breast feeding or pregnant may not participate in this study because of the unknown effect on a fetus or nursing baby. We also ask that you practice an effective form of

birth control while on this trial from prior to receiving chemotherapy, and for four months after being treated on this trial. Women who think they might have become pregnant while on this trial should notify their doctor immediately.

**Work up**

Prior to receiving the experimental treatment you will under go many tests. These include imaging procedures, heart and lung function tests, eye exams, and laboratory tests. If you have received ipilimumab (also called MDX-010) or ticilimumab, you will have a colonoscopy and biopsies to make sure your colon is normal since these drugs may cause damage to your colon". If you are a woman, you will undergo a pregnancy test. You will also have a large catheter inserted into a vein and leukapheresis will be performed. 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 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 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**

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.

**Chemotherapy Regimen (Day -7 through Day -1)**

After we have grown the anti-ESO-1 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-ESO-1 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. 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 the next five days (Day -5 through Day -1). 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 *with* or *without* the experimental vaccine.**

**Cell Infusion and IL-2 Regimen (Day 0 through Day 4) (No Vaccine)**

One to four days after the last dose of chemotherapy, you will be given the anti-ESO-1 cells. The anti ESO-1 cells will be given in your catheter over 30 minutes. Within 24 hours after the anti-ESO-1 cell infusion, you will be given high dose IL-2 through your catheter. IL-2 is approved by the FDA for treatment of metastatic melanoma and metastatic renal cell cancer. The purpose of giving the IL-2 with this therapy is to keep the cells we give you active for as long as possible so they will fight your tumor. The IL-2 will be given as a 15-minute infusion every 8 hours for up to five days after the cell infusion (maximum number of doses is 15). Doses may be skipped or delayed depending on how well you tolerate the doses. The risks of the cells and IL-2 are described on the following pages.

The day after you receive the anti-ESO-1 cells, we will give you more 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.

**Experimental ALVAC ESO-1 vaccine, Cell Infusion, and IL-2 Regimen (Day 0 through Day 4)**

One to four days after the last dose of chemotherapy, you will be given the ALVAC ESO-1 vaccine and the anti-ESO-1 cells. The ALVAC ESO-1 vaccine will be given as 4 injections, one in each extremity, approximately 2 hours before you receive the cells. If one or two of your extremities is not suitable for vaccination, due to prior radiation, lymphedema or other cause, you may be given the vaccine in the stomach or chest. The anti ESO-1 cells will be given in your catheter over 30 minutes. Within 24 hours after the anti-ESO-1 cell infusion, you will be given high dose IL-2 through your catheter. IL-2 is approved by the FDA for treatment of metastatic melanoma and metastatic renal cell cancer. The purpose of giving the IL-2 with this therapy is to keep the cells we give you active for as long as possible so they will fight your tumor. The IL-2 will be given as a 15-minute infusion every 8 hours for up to five days after the cell infusion

(maximum number of doses is 15). Doses may be skipped or delayed depending on how well you tolerate the doses. The risks of the cells and IL-2 are described on the following pages.

The day after you receive the anti-ESO-1 cells, we will give you more 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.

Two weeks after the anti-ESO-1 cell infusion you will receive one more dose of the ALVAC ESO-1 vaccine, one injection in each of 4 extremities again. If one or two of your extremities is not suitable for vaccination, due to prior radiation, lymphedema or other cause, you may be given the vaccine in the stomach or chest. If you have already been discharged, you will receive this second vaccination during a clinic visit.

**Recovery**

After your last dose of IL-2, you will recover in the hospital until you are well enough to go home. This usually takes 5 to 10 days. 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 (remove a small piece) of your tumor or lymph node after receiving the treatment to look at the effects of the treatment on the immune cells in your tumor. 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 treatment. 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 month for several more months. 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. 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.

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 advise your family of this request.

**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. If you are retreated, you will need to sign a new consent form. The second treatment will not begin prior to 6- 8 weeks after your last dose of IL-2. You may receive up to two retreatments.

**Risks or Discomforts of Participation**

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 loose your fertility following this experimental treatment. It is possible, although unlikely, that this experimental treatment may cause your death.

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.

Discomfort due to a biopsy may include pain at the site of the biopsy, swelling, bruising, and infection.

When IL-2 is given through a 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 IL-2 to over 2,000 patients we have found that these side effects go away within a few days of stopping the IL-2.

**ALVAC ESO-1 vaccine (gene therapy) (only for patients receiving the vaccine)**

This experimental vaccine is made with virus, which is used as a vaccine against disease in canaries. It cannot reproduce in mammals, so it cannot cause disease in humans. This specific vaccine has been given only to a few individuals before so we do not have much information about the side effects, however similar experimental vaccines have been given in other clinical trials and the following side effects have been observed:

**ALVAC ESO-1 Vaccine side effects**

| Common | Less common | Rare |
|---|---|---|
| ▪ Swelling of lymph nodes near the injection site<br>▪ Bruising, pain and redness (inflammation) at the injection sites | ▪ Headache<br>▪ Tiredness<br>▪ Bumps caused by inflammation (granulomas)<br>▪ Skin ulcerations (which may require surgery to be removed)<br>▪ Fever and chills<br>▪ Muscle aches | ▪ Rash, itchy skin<br>▪ Joint pain<br>▪ Allergic reaction |

**Anti-ESO-1 Cell Infusion (gene therapy)**

The cells we will be giving you have a type of virus (retrovirus) put into them along with the anti-ESO-1 protein. 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, such as leukemia or lymphoma. These specific 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
- 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.
- There is no 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.

*Risk of Cancer:* When retroviral vectors enter a normal cell in the body, the DNA of the vector inserts itself into the normal DNA in that cell; this process is called integration. Most integration is expected to cause no harm to the cell or to the patient. However, there is a chance that there may be some regions of the normal human DNA where integration of the viral vector=s DNA may result in activation of neighboring genes. For example, if one of these genes were a growth factor, this may cause uncontrolled division of the cell, resulting in a cancer. This type of event has occurred in one animal study in mice where the vector integration site correlates with the occurrence of cancer in these mice. Four instances of a similar event have been reported in four children who received a retroviral vector in an experimental gene therapy study for X-linked Severe Combined Immunodeficiency (SCID) conducted in France, not under the jurisdiction of the U.S. Food and Drug Administration (FDA). While most of the children who participated in this clinical trial appear to have been cured of their disease, four children developed leukemia (a form of cancer of the blood) approximately after receiving the gene therapy treatment. The first patient had extensive testing done to determine the cause of the leukemia. A group of experts in this field have looked at all the test results, and concluded that the gene therapy caused the leukemia in the first child. One of the children died as a result of their leukemia. The risk of another cancer developing in you, including leukemia, is unknown, but you need to be aware of this possible risk. 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.

**Medications**

The side effects of cyclophosphamide, fludarabine, IL-2 and some of the other medications you will receive are listed in the tables 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,<br>▪ Diarrhea, stomach pain<br>▪ Mouth sores<br>▪ Hair loss<br>▪ Fatigue<br>▪ Muscle or joint aches | ▪ 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<br>▪ Weakness<br>▪ Hearing loss | ▪ 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 Lymphoma (in patients who have not been exposed to the Epstein-Barr virus). This can be fatal (One patient on another study died as a result of this.)<br>▪ Loss of fertility |

| **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 |

**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 MDX-010. You will have a colonoscopy and biopsy before treatment if you have previously received MDX-010.<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. |

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.

## Alternative Approaches or Treatment

If there are effective salvage regimens (regimens used when standard regimens have failed), you will be directed to undergo these regimens before participating in this protocol.

Other options for treatment of your cancer include:

- standard therapies (such as dacarbazine, or temozolomide for melanoma)
- experimental vaccines;
- experimental chemotherapies or biotherapies (such as ipilimumab or ticilimumab);
- other combination therapies; or
- getting no treatment; getting comfort care, 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.

If you have kidney cancer, you will also have the option of being treated with sorafenib, sunitinib, and temsirolimus. These drugs are FDA-approved for kidney cancer, and have been shown to keep some people with kidney cancer alive, without the disease getting worse. These drugs have different side effects than the drugs used in this study. You can take these drugs by mouth at home.

## Potential Benefits of Participation

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.

## Research Subject's Rights

You should understand that this study involves research and that your participation is voluntary. Unexpected or unforeseeable side effects may also occur. Your participation in this protocol may be terminated without your consent if your physician feels that it would not be safe for you to continue. Any significant new findings that relate to this protocol will be discussed with you.

The sponsor of this study is Dr. Steven A. Rosenberg. Sanofi-Pasteur is providing the ALVAC vaccine. Your records may be reviewed by NIH organizations and by organizations outside the National Institutes of Health, such as the company that supplies the drugs for the study and representatives of the US Food and Drug Administration. Every effort will be made to protect your privacy in any recording or reporting of this information.

## Conflict of Interest:

The National Institutes of Health reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process: http://ethics.od.nih.gov/forms/Protocol-Review-Guide.pdf. You may ask your research team for additional information or a copy of the Protocol Review Guide. It is possible that the information obtained from your participation on this study may become valuable for commercial research and development purposes (including patentable inventions), which may be of significant benefit to society, the sponsor of this study, individual researchers or other third parties. You will not receive direct financial benefit from such research and development. The NIH and two of the investigators on the research team have developed the cell process being used in this research and have a patent pending. This means that it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. If you refuse to participate or withdraw from the protocol or at the completion of the protocol, we will attempt to offer you participation in other NIH protocols if these are available, or will refer you to your home physician for further management.

## Optional Studies

We would like to keep some of the specimens and data that is collected for future research. These specimens and data will be identified by a number and not your name. The use of your specimens and data will be for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you decide now that your specimens and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and/or data. Then any specimens that remains will be destroyed and your data will not be used for future research.

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

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

Yes No Initials_____

2. My specimens and data may be kept for u
se in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials_____

3. Someone may contact me in the future to ask permission to use my specimen(s) and/or data in new research not included in this consent.

Yes No Initials_____

## 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: 301-496-4164. 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 at 301-496-4251.

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**<br>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.<br><br>_____ _____<br>Signature of Adult Patient/ Legal Representative Date<br><br>_____<br>Print Name | **B. Parent's Permission for Minor Patient.**<br>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.<br>(Attach NIH 2514-2, Minor's Assent, if applicable.)<br><br>_____ _____<br>Signature of Parent(s)/ Guardian Date<br><br>_____<br>Print Name |
| **C. Child's Verbal Assent (If Applicable)**<br>The information in the above consent was described to my child and my child agrees to participate in the study.<br><br>_____ _____ _____<br>Signature of Parent(s)/Guardian Date Print Name | |
| **THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JUNE 23, 2016 THROUGH JUNE 22, 2017.**<br><br>_____ _____ _____ _____<br>Signature of Investigator Date Signature of Witness Date<br><br>_____ _____<br>Print Name Print Name | |