PRINCIPAL INVESTIGATOR: Scott Norberg, DO

STUDY TITLE: A Phase I/II Trial of T Cell Receptor Gene Therapy Targeting HPV-16 E7 for HPV-Associated Cancers

STUDY SITE: National Institutes of Health (NIH) Clinical Center

Cohort: *Treatment, Affected Patient*

Consent Version: *12/5/2024*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in the study. For the remainder of this document, the term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

We have developed an experimental therapy that involves taking white blood cells called lymphocytes from you, growing them in the laboratory in large numbers, genetically modifying them to give them new genes (T Cell Receptor (TCR)), which direct them to recognize the cancer, and then giving the cells back to you. In this study, we are modifying your white blood cells with a retrovirus that has the gene for anti-HPV-16 E7 incorporated in the retrovirus. So far, the HPV-16 E7 has been found only on tumor cells. This type of treatment is called cell therapy. We have given other cells modified with similar genes to patients, but this is the first time we have given this type of gene modified cells to patients. Our laboratory studies show that these cells work much like the cells we have given patients in the past and should be just as safe as those cells, but as this is the first time these cells have been given to humans, we can't predict all of the side effects that may occur.

The first few patients enrolled participated 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 the E7 TCR cells. There were 3 dose levels of the E7 TCR cells. The first patient enrolled got the smallest dose and the dose was increased when the level was determined to be safe. This phase was recently completed. A patient treated on this protocol, who had breathing problems from advanced cancer in the lungs, developed severe breathing, blood pressure, and kidney toxicity that required temporary support with a breathing machine, blood pressure medicines, and dialysis and this resulted in injury to her toes and feet. No other patients had intolerable reactions to therapy. Now, we are moving on to the Phase II (second) part of the study. The second part of this study will assess how well the cancer responds to this treatment. These patients will receive a dose that was determined to be safe during the first part of the study. The dose found to be safe was 100 billion E7 TCR T cells.

Before receiving the E7 TCR cells, you will receive 2 FDA approved chemotherapy drugs to temporarily suppress the immune system to improve the chances that the experimental cells will be able to survive in the body. After the cells are given, you will receive aldesleukin (IL-2) to help these cells stay alive longer. The purpose of this study is to evaluate the toxicity of this treatment. Some of your identifiable information will be shared with investigators at Rutgers University to assist with this assessment.

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 an HPV-16 associated cancer such as cervical, vulvar, vaginal, penile, anal, or oropharyngeal cancer. In addition, you completed the screening evaluation and were found to be eligible to participate in this research study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Not everyone screened for the study will be eligible to receive study therapy. It is expected that up to 55 people may receive study therapy in this study.

DESCRIPTION OF RESEARCH STUDY

This study has several stages after screening:

Stage	Timeframe	Location	Comments & Instructions
Baseline	Within 4 weeks prior to starting chemotherapy regimen	Inpatient or outpatient	Optional tumor biopsies, CT of the chest, abdomen and pelvis, labs, PET if needed, other tests as needed.
Leukapheresis before treatment	Within 4 weeks of starting chemotherapy	Inpatient or outpatient	This is a half to full day appointment.
Chemotherapy (day -7 to -3)	1 week	Inpatient	Receive IV chemotherapy to prepare your immune system for the cells.
Cells and aldesleukin (Day 0-4)	1-5 days	Inpatient and possibly ICU	Receive 100 billion E7 TCR cells IV and then high dose aldesleukin about every 8 hours for up to 15 doses.
Recovery	1-2 weeks	Inpatient unit	Recover from the effects of treatment.
Follow -up	Ongoing until disease progression	Outpatient	Return to clinic for physical exam, review of side effects, labs, scans every 1-6 months; optional tumor biopsies.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin study therapy

You will need to supply an updated complete list of your current medications to the study doctor. This includes over-the-counter medications and herbal supplements. Some medications may interact adversely with the study drugs and it is important that your study doctor and prescribing physician be aware of any potential risks so that they can prescribe alternative medications as necessary. If you do not already do so, please carry a list of your medications at all times.

Baseline

Prior to receiving the experimental treatment, you will undergo additional tests. These include imaging procedures, and laboratory tests. You will also have a large catheter inserted into a vein so that leukapheresis can be performed (see below). You may be admitted to the hospital for these tests and procedures.

During study therapy

Cell harvest and growth

You will undergo leukapheresis to obtain white blood cells from you. These cells will be grown in the lab and genetically modified to recognize a protein on your tumor cells. You may have enrolled on protocol 16C0061 to undergo leukapheresis. If you had a leukapheresis procedure and we collected cells on 16C0061, then this initial procedure will not be repeated.

If your cells do not grow, 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.

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, clinically indicated, 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 liquid component of blood), and leukocytes (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 your anticancer 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 treatment to see the impact of this therapy on the immune system and see if cells we gave you are still active.

Chemotherapy Regimen (Day -7 through Day -3)

After we have grown the E7 TCR cells to large numbers in the laboratory, you will be admitted to the hospital to begin your experimental treatment. As clinically indicated, you will be given two chemotherapy medicines, cyclophosphamide and fludarabine, to make space in your immune system so the E7 TCR cells can work without any interference from the cells in your immune system. These medicines may cause your tumor to shrink some, but this shrinkage is anticipated to be only partial and of small duration. The main purpose of the chemotherapy is to see if we can make the cells more effective in fighting cancer tumors. Animal experiments have indicated that chemotherapy can make the infused cells more effective in fighting your cancer, 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.

Cell Infusion and Aldesleukin Regimen (Day 0 through Day 4)

You will be given the 100 billion cells through their IV over 20-30 minutes one to four days after the last dose of chemotherapy. Within 24 hours after your cell infusion you will be given high dose aldesleukin through one of the IVs, as clinically indicated. It will be given as a 15-minute infusion

about every 8 hours for up to five days after the cell infusion. Aldesleukin is a cell growth factor and it is thought that it will help the cells live longer in your body.

The day after your cells are infused, we may give you G-CSF (filgrastim or a filgrastim biosimilar drug) as a shot or injection under the skin every day to stimulate your blood cells until they increase to a sufficient number to help you fight infections. 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 with the T cell treatment

Recovery

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

In addition to the laboratory tests to monitor your condition, we will remove between 1 and 9 teaspoons of blood daily to study the effects of this regimen on your immune system. If you experience side effects in your kidneys, we will collect 1 additional teaspoon of blood and about 6 teaspoons of urine to help us determine the cause of these side effects.

Follow up and Evaluation of Experimental Regimen

You will need to come for a clinic visit approximately 40 days after your cell infusion for a physical examination, blood work, and CT. An MRI or x-ray may also be performed if necessary.

Depending on your response to the treatment, we will ask you to return to the NIH Clinical Center frequently after you are discharged approximately every 3 months (x3), and every 6 months (x5 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.

Re-Treatment

If you received a lower dose of cells and/or your tumor shrinks or disappears following the initial treatment and then recurs you may be able to receive one additional treatment if you tolerated the treatment well and if all the side effects have resolved. You will receive the same medications and cell infusion on the same schedule as with the first treatment, but your dose of E7 cells may be at the higher dose if your first treatment was at one of the lower dose levels used in the Phase I portion of the study. You will be allowed to have second treatment only if we have enough of your cells

left over from the first treatment you had. The study doctors will review this with you. The second treatment will not begin prior to 6-8 weeks after your last dose of aldesleukin.

Birth Control

If you are able to become pregnant or are able to nurse, you may not take part in the study because we don't know how this treatment would affect your baby or your unborn child. If you are able to become pregnant, or are the partner of a participant who can become pregnant, you will need to practice an effective form of birth control and refrain from egg and sperm donation before starting study treatment, during study treatment, and for twelve (12) months after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

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

Gene Therapy Long Term Follow up

You will be followed on a separate protocol once you are off treatment because the Food and Drug Administration (FDA) requires that people who receive gene therapy be watched even after they complete the study, we will ask you to take part in long term follow up for the next 15 years. The separate protocol will provide the details of the required follow-up.

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 lose your fertility following this experimental treatment. It is possible, although unlikely, that this experimental treatment 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.

Blood Samples

The risk for taking blood samples involves the withdrawal of between a few teaspoons and a half-cup of blood and the potential for bruising or infection that occurs with any blood draw.

Each time a blood sample is needed, a needle will be put into a vein in your arm (or into your central venous catheter, if you have one). You may feel pain when the needle goes through the skin. Other side effects associated with drawing your blood for blood tests may include infection, bruising, redness, discomfort or bleeding at the site of the needle stick, and possible

lightheadedness and fainting. Up to 13 tablespoons of blood may be collected at one visit, but no more than 32 tablespoons per 8 weeks period.

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 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, bleeding or bruising where the needles are put in your arms.

Cell Infusion

The cells we will be giving you have a type of virus (retrovirus) put into them that recognizes the HPV E7 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 not been given 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 causing shortness of breath
- Severe reaction to the cells which would include very low blood pressure and damage to your heart, lung, and/or kidneys
- 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.
- Experience with diverse types of cell therapy including tumor-infiltrating lymphocytes, CAR-T cells, and TCR-T cells, indicates that the risk of cell therapy may include cytokine release syndrome (where the T cell therapy causes the release of chemicals called cytokines that aggressively ramp up the immune system), autoimmunity (an immune reaction against normal tissues) and neurotoxicity (damage to the nervous system). Cytokine release syndrome may cause mild symptoms such as fever, fatigue, headache, rash, joint stiffness, and muscle aches, or severe symptoms such as low blood pressure, high fever, uncontrolled systemic inflammatory response, hemophagocytic lymphohistiocytosis (a rare condition in which certain types of white blood cells build up in organs and destroy other blood cells), shock, vascular leakage (where fluids and proteins leak out of small blood vessels and into surrounding tissues), disseminated intravascular coagulation (a serious disorder where proteins that control blood clotting become overactive), and multi-organ system failure.
- A patient treated on the phase I portion of the protocol, who had breathing problems from advanced cancer in the lungs, developed severe breathing, blood pressure, and kidney

toxicity that required temporary support with a breathing machine, blood pressure medicines, and dialysis and this resulted in injury to her toes and feet.

- 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.
- A patient treated on the phase II portion of the study experienced confusion and low blood pressure after E7 TCR T Cells and one dose of aldesleukin that required temporary support with a breathing machine, blood pressure medicine and dialysis. The patient also developed an inflammatory disorder characterized by fevers, prolonged low blood counts, and abnormal blood tests for inflammation that resolved following treatment with steroids. The patient also had delayed recovery of blood counts that was contributed to prior chemotherapy, prior pelvic radiation and poor nutrition.

Other Study Drugs

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

Aldesleukin

Likely	Less Likely	Rare but Serious
• 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 • Low urine output • Swelling in your extremities • Fluid in your lungs that can require oxygen • Dry mouth, nausea, vomiting and diarrhea;	• 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.	• 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

• 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		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.

Cyclophosphamide

Likely, some may be serious	Less Likely, some may be serious	Rare, and serious
• Fever • Infection, especially when white blood cell count is low • Anemia which may cause tiredness or may require transfusion • Brusing, bleeding • Blood in urine • Nausea, vomiting, diarrhea, loss of appetite, pain in belly • Hair loss, skins changes, rash, change in nails • Sores in mouth which may cause difficulty swallowing • Absence of menstrual period which may decrease the ability to have children • Blurred vision, vision changes	• Fluid around the heart • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Loss or absence of sperm which may lead to an inability to father children	• Damage to the heart or heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness • Swelling of the body including the brain which may cause dizziness, confusion • Damage to the lungs or scarring of the lungs which may cause shortness of breath • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Hepatic veno-occlusive disease is a condition that is characterized by damage to blood vessels in the liver and liver cells. Although it may be mild and not require further treatment, sometimes it may cause a severe decrease in liver

Likely, some may be serious	Less Likely, some may be serious	Rare, and serious
		function and may be life threatening or fatal. • Kidney damage which may cause swelling, may require dialysis • A new cancer (e.g., leukemia, lymphoma, sarcoma, etc.) resulting from treatment of a prior cancer • Impaired wound healing • Urinary tract and/ or kidney injury including blood in urine, painful urination, fever, urgency, inability to urinate, loss of bladder control and pain • Abnormal heartbeats: including atrial fibrillation and flutter and ventricular arrhythmias causing your heat to be fast or irregular resulting in a pounding or racing heart, dizziness, weakness, feeling light-headed or shortness of breath • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Decreased levels of sodium in the blood, which can cause confusion, seizures, fatigue and low levels of consciousness.

In addition, because cyclophosphamide may contain alcohol, it may impair a person's ability to drive or operate machinery immediately after the infusion.

Fludarabine

Likely	Less Likely	Rare but Serious
• Low blood counts	• Nausea, vomiting • Diarrhea • Long term reduction of lymphocyte counts which could increase risk of infection • Infection	• Coma, blindness, other neurologic toxicity and even death • Inflammation in the lungs • Kidney damage • Allergic reaction

Supportive Medications

Filgrastim

The risks of filgrastim and filgrastim biosimilars are the same or similar.

Likely	Less likely	Rare but serious
• Bone pain	• Severe headache	• Severe breathing problems • Rupture of your spleen

Fluconazole

Likely	Less likely	Rare but serious
• 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

Likely	Less likely	Rare but serious
	• Temporary decrease in kidney function which may not cause any symptoms	• Skin rash, hives, itching • Tremors, dizziness, confusion, seizures • Fatigue • Blood in the urine

	• Nausea, vomiting, diarrhea, constipation • Pain and irritation at place of injection	

Ondansentron

It can cause headache, dizziness, aching muscles, drowsiness, malaise, and weakness. Less common side effects include chest pain, high blood pressure, itching, constipation and urinary retention.

Trimethoprim and Sulfamethoxazole Double Strength (TMP/SMX DS)

TMP/SMX DS can cause allergies, fever, sensitivity to light, nausea, and vomiting. Neutropenia, a reduction in the number of neutrophils, can also occur.

Mesna

Potential side effects include nausea, vomiting, and diarrhea.

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 (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 watch you for this risk we will be testing your blood as described before.

Study Procedures

Blood Draws

Blood will be drawn frequently during your treatment. Most of the blood draws will be to monitor your health during and after the lymphocyte infusion. In addition, some blood samples will be drawn for research purposes. Additional blood draws might be necessary to investigate T cell responses and serum cytokine levels in cases of clinical events such as rapid regressions of malignancy or toxicity. These samples will be used to study how your immune system is affected by the cell therapy. Some of the samples may be used for other or future research conducted by the investigational team or other researchers. Side effects of repeated blood sampling depend in part on how the blood is drawn. If through a central venous catheter, risks include contamination of the catheter which would result in a serious blood stream infection, requiring admission to the hospital and giving you antibiotics through the vein; if blood is drawn through a needle into your skin, side-effects could include pain and bruising in the area where the blood was drawn. Other side-effects can include lightheadedness, or rarely, fainting. If you have too much blood taken

over a prolonged period, your red blood cell count may drop (this is called "anemia"). As a precaution, we will check your red blood cell level, and give you iron treatment or a blood transfusion if needed.

Intravenous Catheter

In order to receive this treatment, you may need to have a central venous catheter. This catheter is placed under the skin of the chest wall and enters a major vein in the chest. The area will be numbed with an anesthetic before the catheter is put in. There are several types of catheters including those which must be removed after each cycle of chemotherapy (temporary type) and those which may be kept for the duration of therapy (permanent type). These options will be discussed with you. The risks associated with placing some catheters include pain, bleeding, infection and collapsed lung. 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. The long-term risks of the catheter include infection, and clotting of your veins. If these occur, it may be necessary to remove the catheter. These risks will be explained to you in more detail at the time of insertion.

CT and PET Scans

During a CT scan and PET, you're briefly exposed to much more radiation than you would be during a plain X-ray. Radiation exposure potentially increases your risk of developing cancer. Although rare, the intravenous (IV) contrast material involved in some CT and PET scans causes medical problems or allergic reactions in some people. Most reactions are mild and result in hives or itchiness. In rare instances, an allergic reaction can be serious and potentially life threatening. Make sure to tell your study doctor if you've ever had a prior reaction to contrast material during medical tests.

MRI & Gadolinium-enhanced MRI

MRI:

You might be at risk for injury from the MRI magnet if you have some kinds of metal in your body. It may be unsafe for you to have an MRI scan if you have:

- pacemakers or other implanted electrical devices,
- brain stimulators,
- some types of dental implants,
- aneurysm clips (metal clips on the wall of a large artery),
- metal prostheses (including metal pins and rods, heart valves, and cochlear implants),
- permanent eyeliner,
- tattoos,
- an implanted delivery pump,
- or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye.

You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should tell us. You will be asked to fill out an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before you enter the MRI scan room.

If you are afraid of confined (small, cramped) spaces, you may get anxious during an MRI. If you have back problems, you may have back pain or discomfort from lying in the scanner.

The noise from the scanner is loud enough to damage your hearing, especially if you already have hearing loss. We will give you hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Gadolinium-enhanced MRI:

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

Optional Biopsies

The risks associated with the biopsies include pain and bleeding at the biopsy site. Sometimes a CT scan may be needed to identify the right tumor to biopsy. In this situation, there is the risk of exposure to radiation associated with the CT scans.

What are the risks of radiation from being in the study?

During your participation in this research study, you may be exposed to radiation from 5 CT scans and 2 PET scans. The amount of radiation exposure from these procedures is equal to approximately 5.8 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scan and PET that you get in this study will expose you to the roughly the same amount of radiation as 19.3 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.6 out of 100 (0.6%) and of getting a fatal cancer is 0.3 out of 100 (0.3%)

Radiation Exposure in People Capable of Becoming Pregnant

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if this new 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 E7 TCR therapy effect on your type of cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may benefit others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

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

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

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat

the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

STOPPING THERAPY

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

- if he/she believes that it is in your best interest
- if your disease comes back during treatment and you are not eligible for retreatment
- 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
- If your disease gets worse
- if you become pregnant
- if the study is ended early by the PI

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 Kite Pharma or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect 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

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive compensation for participation in this study.

REIMBURSEMENT

Will you receive reimbursement or direct payment by NIH as part of your participation?

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

COSTS

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs.

CONFLICT OF INTEREST (COI)

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The National Institutes of Health and the research team for this study are using E7 TCR (biological product) developed by Center for Cancer Research through a joint study with your study team and Kite Pharma. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of E7 TCR.

A research partner not associated with the NIH working on this study has a financial association with Neogene Therapeutics, Pact Pharma, and the National Cancer Institute, and may receive payments or benefits, limited by the rules of their workplace.

Kite Pharma will provide financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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 NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor (Center for Clinical Research) or their agent(s)
- Qualified representatives from Kite Pharma, the pharmaceutical company who is a collaborator in the production of the E7 TCR T cells
- Investigators at Rutgers University

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or

2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, Scott Norberg, DO, scott.norberg@nih.gov, 301-275-9668. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness	Print Name of Witness	Date

NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.