PRINCIPAL INVESTIGATOR: Scott Norberg, DO

STUDY TITLE: A Phase II Study of E7 TCR Cell Induction Immunotherapy for Stage II and Stage III HPV-Associated Oropharyngeal Cancer

STUDY SITE: NIH Clinical Center

Cohort: *Treatment*

Consent Version: *11/4/2020*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Scott Norberg, DO
Phone: 301-275-9668
Email: scott.norberg@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

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.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you to in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have been diagnosed with Stage 2 or 3, HPV-16 associated oropharyngeal cancer. In addition, you completed the screening evaluation and were found to be eligible to participate in this research study.

The purpose of this study is to determine if E7 TCR cells can be given safely prior to your return to your cancer doctor for further treatment

The use of E7 TCR T cells in this study is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat HPV-associated oropharyngeal cancer. However, the FDA has given us permission to use E7 TCR T cells in this study.

Standard treatment for your cancer consists of chemotherapy with radiation, or surgery with or without radiation. Standard treatment is curative for most patients. However, some patients will have cancer recur at a new location after standard treatment, and when this happens it generally is not curable.

The goal of this study is to find out if it is possible to treat patients with your type of cancer with the experimental treatment (the E7 T cells) prior to getting standard treatment. We hope it will

shrink the cancer and possible prevent it from recurring at a new site later, but we do not know if this will be the case.

The experimental treatment is given before standard treatment and therefore will delay standard treatment. It will require hospitalization, collection of a large volume of blood cells using a procedure called apheresis, optional biopsies of your tumor, and close follow up with visits to the NIH Clinical Center to monitor your cancer and the treatment side effects.

If your cells do not grow, you will not be able to receive the cell infusion. At the time we determine that your cells are not growing, we will inform you and discuss your options with you. The single cycle of chemotherapy that is given as part of the experimental treatment has side effects that may include nausea, vomiting, diarrhea, hair loss, and decreased blood counts. These side effects are similar to the side effects you might experience from the standard chemotherapy you might receive even if your were not in this trial.

As part of the experimental treatment, you will also receive a drug called aldesleukin. The aldesleukin has side effects that may include fever, chills, low blood pressure, high heart rate, body swelling, and fatigue. Aldesleukin may have severe side effects that include lung failure, coma, and kidney failure. A complete list of side effects from the study medications is provided in this consent.

Being in this trial will not prevent you from receiving standard treatment for your cancer, although it will be delayed. If you do not want to delay standard treatment, or undergo any of the research procedures you may not want to join this trial. If you choose not to participate in this study you will receive standard treatment without the experimental treatment.

You might wish to join this trial if you do not mind receiving the experimental treatments and are interested in helping to find new ways to improve the treatment of this type of cancer.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- You may only participate in this study if you have been diagnosed with Stage 2 or 3, HPV-16 associated oropharyngeal cancer. The primary treatment for this condition is either surgery or chemoradiation. Unfortunately, not all patients are cured with this therapy.
- Around 80% of patients with stage II and 65% of patients with stage III oropharyngeal cancer who receive primary treatment are still alive after five years. Receiving experimental therapy may delay your primary treatment. It may also make it more risky or impossible for you to receive it.
- The therapy used in this study is called T cell therapy. Immune cells from your blood will be genetically modified in the laboratory to give them the ability to attack the human papillomavirus which causes oropharyngeal cancer.
- Screening tests are required prior to you receiving the study drug. If you are found eligible for the study, you will undergo a procedure to collect your T cells from the peripheral blood. These cells will be modified in the laboratory and will be given back to you by a one-time infusion into a vein. You will receive chemotherapy prior to getting

the cells and a drug called aldesleukin afterwards. These drugs activate the gene-engineered T cells and help them proliferate. You will stay in the hospital for 2-3 weeks.

- You may experience side effects from taking part in this study. The most common side effects include decreased blood counts requiring transfusions, fevers, chills, nausea, low blood pressure and high heart rate. It is possible that you could develop more serious, temporary, long-lasting or permanent side effects including death.
- If you are a sexually active person with a partner capable of becoming pregnant, it is important that your partner not become pregnant during your participation in this study. You and your partner must agree to use birth control from the time of enrollment on this study to four months after treatment.
- After the study follow-up period has ended, we would like to talk with you for 5 years to see how you are doing.

Just as we do not know what side effects you might have, we cannot know if you may benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

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?

This is a research study. The purpose of this research study is to determine if E7 TCR T cells can be given without delaying your standard treatment whether that is surgery or radiation therapy with chemotherapy unless that delay is because the therapy is shrinking your tumor(s).

We are asking you to join this research study because you have been diagnosed with Stage 2 or 3, HPV-16 associated oropharyngeal cancer. In addition, you completed the screening evaluation and were found to be eligible to participate in this research study.

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 a TCR that recognizes the HPV-16 E7 protein. So far, the HPV-16 E7 has been found only on tumor cells. This type of treatment is called cell therapy. We have given these cells to patients in a previous clinical trial where the goal was to find the most effective yet safe dose of 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. Once you have completed this therapy, you will be seen in our clinic to see if your cancer has grown and whether you are recovering from any toxicities experienced during the trial. If your cancer is getting smaller we will continue to see you in clinic. If your cancer doesn't get smaller or goes away completely you will be referred back to your home oncologist for standard treatment.

WHAT WILL HAPPEN DURING THE STUDY?

This study has several stages after screening:

Stage	Timeframe	Location	Comments & Instructions
Baseline	Within 30 days prior to apheresis	Inpatient or outpatient	Complete physical examination, vein assessment, blood tests
Baseline	Within 4 weeks prior to starting chemotherapy regimen	Inpatient or outpatient	Clinical staging (may include CT scan, MRI scan, PET scan), tumor measurements, tumor biopsy (anytime prior to chemotherapy, biopsy is optional), Chest x-ray, ECG, Cardiac and/or pulmonary testing
Leukapheresis before treatment	At least 11 days prior to cell infusion	Inpatient or outpatient	This is a half to full day appointment.
Chemotherapy (day -6 to -2)	1 week	Inpatient	Receive IV chemotherapy to prepare your immune system for the cells.
Cells and aldesleukin (Day 0-2)	1-3 days	Inpatient and possibly ICU	Receive up to 30 billion E7 TCR cells IV and then high dose aldesleukin about every 8 hours for up to 6 doses.
Recovery	1-2 weeks	Inpatient unit	Recover from the effects of treatment.

Stage	Timeframe	Location	Comments & Instructions
Follow -up	Ongoing until referral for standard of care treatment	Outpatient	Return to clinic for physical exam, review of side effects, labs, scans every 2-4 weeks until referral; tumor biopsy (optional).

Baseline

Prior to receiving the experimental treatment, you will undergo additional tests. These may 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 in less than a week 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

The procedure for obtaining blood cells through leukapheresis is a very common procedure that is done routinely here in the Clinical Center with very few risks. White blood cells (lymphocytes) are removed from you using a serum cell separator machine. This requires putting a needle into your arm to obtain blood to go into the machine. The machine divides whole blood into red cells, plasma (the liquid part) and lymphocytes (white cells). The lymphocytes will be taken out, and the plasma and red cells returned to you through a second needle in your other arm. The procedure takes between 4-6 hours to complete. 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 approximately 4 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.

Intravenous Catheter

In order to receive this treatment, you may need to have a central venous catheter. We will place an intravenous catheter which is a small plastic tube inserted into a vein in your arm using a needle. 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.

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. During that time, we will remove between 1 and 11 teaspoons of blood daily to study the effects of the treatment regimen on your immune system. In addition, some blood samples will be drawn for research purposes. The maximum amount of blood for research is approximately 2.3 cups in 8 weeks. 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.

Chemotherapy Regimen (Day -6 through Day -2)

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. 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 -6 and Day -2) and the fludarabine will be given into your catheter for 30 minutes every day for five days (Day -6 through Day -2). The side effects of these medicines are described on the following pages.

Cell Infusion and Aldesleukin Regimen (Day 0 through Day 2)

You will be given up to 30 billion cells through the IV over 20-30 minutes one to four days after the last dose of chemotherapy. Within 24 hours after your cell infusion you will be given high dose aldesleukin through one of the IVs. It will be given as a 15-minute infusion 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) 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 supportive 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. 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 come to the NIH for a clinic visit approximately 14 days after your cell infusion for a physical examination and blood work. You will also need to come for a clinic visit 28 days after your cell infusion to evaluate the response of the tumor to treatment. The timing of your next clinic visit will depend on whether the tumors are getting smaller. If your tumor appears to be growing or has disappeared entirely, we will refer you back to the care of your local physician.

At each safety visit, you will have lab tests, an exam by ENT, and a physical examination performed. These visits are to make sure you are recovering from the treatment. At each response assessment 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.

Gene Therapy Long Term Follow up

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. We can obtain the blood needed for these studies at your regular follow-up visits as long as you are on the study. If you are removed from the study, we still need to conduct these gene-therapy follow-up visits according to FDA regulations and will request your permission to enroll you in a protocol that would allow us to follow you for this reason only. If you return to your referring physician after receiving therapy here, we will ask you to have your physician send your blood specimens here for this testing, which will decrease the inconvenience to you. This testing will determine if the cells have grown or changed in your body. We will test your blood immediately before you receive the cells, and then at 3, 6, and 12 months. 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 therapy approach. Please discuss this request with your family to inform them of your wishes.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement will last for up to 5-years*:*

- After you receive E7 T cells, you will be seen in the clinic every 2-weeks. This will continue until the disease either stops shrinking, goes away completely or gets bigger. At this time, you will be referred back to your home doctor to receive standard of care definitive treatment. We will then contact you once a year to ask you questions about your disease and any treatments for the disease that you have received. This will happen for a total of 5 years.

Your involvement on the Gene Therapy Long Term Follow Up Study will be 15 years once you receive the E7 T cells.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

Not everyone screened for the study will be eligible to receive study therapy. It is expected that up to 15 people may receive study therapy in this study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE 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.

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

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.

Leukapheresis

The risks of leukapheresis include pain, bruising, lightheadedness or dizziness, nausea, vomiting and chills. Bruising may last up to 72 hours.

Tingling around the mouth, fingers, or toes and mild muscle cramps may develop from slight lowering of the blood calcium by the blood thinner used during the procedure. These symptoms can be treated by either temporarily stopping the procedure or by giving Tums. Leukapheresis uses a completely closed sterile system. The risk of infection is minimized by cleaning the skin

before the needle stick. No infections from leukapheresis have been noted in thousands of such procedures performed over the last 10 years at the NIH.

Rarely, there can be a malfunction of the apheresis machinery that might prevent the return of your blood being processed in the machine. The amount of blood lost would be very small and not harmful. It is also rare for people to faint, have seizures, or have air trapped in the bloodstream.

Temporary or permanent nerve damage may occur at the needle placement sites. This is very rare. At the NIH, to this point, there have been no cases of permanent nerve damage with leukapheresis.

During the leukapheresis procedure, your platelet count may decrease because platelets are collected with the white blood cells. Platelets are cells that help your blood to clot. Taking aspirin in combination with a lowered platelet count may increase your chance of developing bleeding. Therefore, you should not take aspirin or aspirin-containing drugs for 2 weeks after the procedure without physician approval.

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 been given to only a few 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.
- A patient treated with E7 TCR T cells on another 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.

Other study drugs:

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

Potential side effects from 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; • 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	• 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 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.

Potential side effects from cyclophosphamide and fludarabine

Likely	Less Likely	Rare but Serious
• 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	• Bleeding • Infection • Bladder irritation with bloody urine • Severe allergic reaction (difficulty breathing/swelling) • Headache or dizziness • Sweating • Swelling of arms or legs • Skin changes, rash, blisters • Weakness • Hearing loss	• Heart damage • Lung damage • Kidney damage • Inflammation of the eye resulting in blindness • Inflammation of nervous system resulting in death • Epstein Barr Virus Lymphoma. This can be fatal (Two patients on other studies in the Surgery Branch developed EBV lymphoma, and one died as a result of this disease.) • Loss of fertility • Death due to complications resulting from suppression of the immune function.

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.

Intravenous Catheter

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.

Biopsies

Biopsy of the primary tumor is optional and will be performed before getting the cells and approximately 4 weeks following T cell infusion. They will be done using local anesthesia by an otolaryngologist. In cases where the tumor cannot be seen using the instruments in the clinic, you might have the biopsy performed in the operating room under general anesthesia. Risks associated with the biopsies are pain and bleeding at the biopsy site. Although rare, serious risks associated with general anesthesia include an adverse drug reaction, stroke, heart attack or death. You will be asked to sign a separate consent prior to each procedure involving anesthesia.

Electrocardiogram (EKG)

An EKG (also referred to as ECG) is a test that records the electrical activity of the heart. It is used to measure the rate and regularity of heartbeats as well as the size and position of the heart chambers, and the presence of any damage to the heart. For this test, you will be asked to lie down, and small patches that have an adhesive edge with a gel in the middle, called electrodes, will be placed on your arms, legs, and chest. The areas where the electrodes are placed will be cleaned and, if needed, some hair may be shaved or clipped to allow for better attachment of the electrodes. The adhesive from the patches may irritate your skin.

X-ray examination

An x-ray examination exposes you to a small amount of radiation, corresponding to one-fifth of the dose a person gets each year from natural sources, such as the sun and the ground. This small amount of radiation is not considered dangerous.

CT scan, MRI and PET

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, PET and MRI 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.

Risks for gadolinium enhanced MRI scans:

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" which 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 not normal or if you received gadolinium within the previous month.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA recently 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 than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before starting this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 4 months after you finish study treatment (the restricted period). Adequate contraception includes intrauterine device, hormonal or barrier method of birth control; abstinence; tubal ligation or vasectomy. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the study team as soon as possible..

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 up to two CT scans, two PET scans, or two CT-guided biopsies. The amount of radiation exposure you may receive from these procedures is equal to approximately 6.2 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." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The PET and CT scans that you may get in this study will expose you to the roughly the same amount of radiation as 20.7 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.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study. However, the potential benefit to you might 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.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because the knowledge gained from this study may help in developing treatments for those who have oropharyngeal cancer.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss the other options that are available to you. Instead of being in this study, you could:

- choose to be treated with surgery, radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

We do not plan to return research results to you. A summary of the research results will be posted on Clinicaltrials.gov at completion of the study.

EARLY WITHDRAWAL FROM THE STUDY

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

- if he/she believes that it is in your best interest
- if you start a new treatment for your cancer

- if new information shows that another treatment would be better for you
- if you become pregnant
- if the study is ended early by the investigator

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 our collaborators and designated representatives.

WILL YOUR SPECIMENS OR DATA BE SAVED FOR USE IN OTHER RESEARCH STUDIES?

As part of this study, we are obtaining specimens and data from you. We plan to use these specimens and data for studies going on right now, as well as studies in the future. These studies may provide additional information that will be helpful in understanding HPV-Associated Oropharyngeal Cancer, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you. By agreeing to let us use your specimens and data, you give the NIH any rights you may have in the specimens and data.

We may share your specimens and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or industry sponsors of research.

In addition to the use and sharing of your specimens and data described above, we might remove any information from your specimens and data that can identify you such as name, address, or medical record number, and then use the specimens and data for additional research studies at the NIH or other places. If we do this, we might not contact you to ask your permission or otherwise inform you.

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw the specimens and data.

Please place your initials in the blank next to Yes or No for each of the questions below:

My specimens and data may be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

My specimens and data may be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

How Long Will Your Specimens and Data be Stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

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

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

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. Someone will work with you to provide more information.

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 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 NIH Clinical Center.

- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (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 NIH 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.

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

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, the Center for Cancer Research or their agent(s)
- Qualified representatives from Kite Pharma, the pharmaceutical company who is working with us on sample analysis

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens and data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

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.

POLICY REGARDING 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

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

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: _____.