

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 Institute of Health (NIH) Clinical Center

Cohort: *Screening*
Consent Version: *12/5/2024*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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

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.

PATIENT IDENTIFICATION

Consent to Participate in a Clinical Research Study

NIH-2977 (4-17)
File in Section 4: Protocol Consent (2)
Version Date: 12/5/2024
Page 1 of 11

WHY IS THIS STUDY BEING DONE?

This consent form is to determine your eligibility for our study involving treatment with T Cell Receptor Gene Therapy (called E7 T Cell Receptor, or E7 TCR Cell Therapy) for HPV-Associated Cancers.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 360 individuals may be screened on this study.

DESCRIPTION OF RESEARCH STUDY

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.

You may not be eligible for our study with E7 TCR cell therapy for several reasons, such as the presence of certain other diseases, infections, or blood counts which are not in the correct range to be eligible. Your blood, biopsy or other tissue may also be tested for other factors for research purposes. However, this consent does not permit any additional studies that would test for genes (i.e., tendency for diseases) that might be inherited from you by your children.

Before you begin the study

You will need to supply a 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.

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

Version Date: 12/5/2024

Page 2 of 11



IRB NUMBER: 16C0154

IRB EFFECTIVE DATE: 1/7/2025

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

Blood samples may be drawn at your local medical doctor's office, your local laboratory, or at the NIH. Samples drawn at an outside location will be sent to the NIH. The following tests are needed to determine whether you are eligible for this trial:

Any time prior to starting the treatment:

- HLA typing
- HPV genotype testing of tumor. Tissue from a previous surgery or biopsy may be used or a new biopsy may be obtained.

Within 8 weeks prior to starting the treatment:

- Cardiac evaluation if you are at least 50 years of age or older, or if you have a history of heart disease, chest pain or other risk factors such as diabetes, obesity, hypertension.
- Evaluation of your veins that are used for drawing blood samples

Within 4 weeks prior to starting the treatment:

- History and Physical Examination: A summary of your medical record will be requested from your physician when you are initially referred to the NIH. In addition, a physician or nurse practitioner at the NIH will review your medical history with you, and you will have a detailed physical examination including a neurological assessment.
- EKG
- Pulmonary Function Testing if you have a prolonged history of cigarette smoking (20 pack/year of smoking within the past 2 years) or symptoms of respiratory issues.
- If you have results of a CT of the chest, abdomen and pelvis, and/or brain MRI or PET, we will review them to evaluate the status of your disease. Additional scans, x-rays or tests may be performed if clinically indicated based on your signs and symptoms or to further evaluate the status of your disease.
- HIV testing (if you have results less than a month old, you may not need to have this test redone)
- Viral testing (if you have results of viral tests that are less than 3 months old, you may not need to have this test redone)

Within 14 days prior to starting the treatment:

- Blood tests: Full chemistry panel, thyroid panel, complete blood count (CBC) and other required tests
- Urinalysis and urine culture if necessary

Within 7 days prior to starting the treatment:

- Pregnancy test (blood or urine) if you are able to become pregnant. You may not participate if you are pregnant.

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

Version Date: 12/5/2024

Page 3 of 11



IRB NUMBER: 16C0154
IRB EFFECTIVE DATE: 1/7/2025

RISKS OR DISCOMFORTS OF PARTICIPATION

The possible risks or discomforts of participation include the following:

Study Screening Procedures***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 6 tablespoons of blood may be collected at one visit, but no more than 32 tablespoons per 8 weeks period.

Electrocardiogram (ECG)

An electrocardiogram or 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.

Pulmonary Function Test

Pulmonary function tests are a group of tests that measure how well your lungs work. Pulmonary function tests are usually safe for most people. However, because the test may require you to breathe in and out quickly, you may feel dizzy and there's a risk that you might faint. If you have asthma, this test could cause you to have an asthma attack. In very rare cases, pulmonary function tests may cause a collapsed lung. If you have asthma or feel lightheaded during the test, tell your doctor.

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:

PATIENT IDENTIFICATION**Consent to Participate in a Clinical Research Study**

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

Version Date: 12/5/2024

Page 4 of 11

IRB NUMBER: 16C0154
IRB EFFECTIVE DATE: 1/7/2025

- 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.

Biopsy

Your tumor tissue may be obtained from prior surgeries or from a biopsy that you might elect to have for purposes of determining if you are eligible for this study. Any biopsy or other procedure would be done only if needed and only after you sign an additional informed consent related to the specific procedure.

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 2 CT scans and 1 PET scan. The amount of radiation exposure from these procedures is equal to approximately 2.5 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 scans and PET that you get in this study will expose you to the roughly the same amount of radiation as 8.3 years’ worth of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

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.

Other Risks

It is possible that other side-effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before.

POTENTIAL BENEFITS OF PARTICIPATION

We do not know if you will receive personal medical benefit from allowing us to perform these tests. However, this testing may make you eligible for our trial of treatment with T Cell Receptor Gene Therapy for HPV-Associated Cancers.

PATIENT IDENTIFICATION

Consent to Participate in a Clinical Research Study

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

Version Date: 12/5/2024

Page 6 of 11

If you become eligible for our treatment study and you choose to participate, you would need to give additional informed consent regarding the risks of the treatment.

ALTERNATIVE APPROACHES OR TREATMENTS

You may choose not to be tested for eligibility or to have any other studies done.

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. If you are scheduled for and begin treatment, the NCI will cover the cost for some of your expenses. 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.

PATIENT IDENTIFICATION

Consent to Participate in a Clinical Research Study

NIH-2977 (4-17)

File in Section 4: Protocol Consent (2)

Version Date: 12/5/2024

Page 7 of 11



IRB NUMBER: 16C0154
IRB EFFECTIVE DATE: 1/7/2025

- 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: _____.