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: *Screening*

Consent Version: 11/4/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Scott Norberg, DO
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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 consider joining this study because you have been diagnosed with a stage II or III HPV-16 associated oropharyngeal cancer.

This consent form requests your permission for us to determine your eligibility for our study involving treatment with T Cell Therapy that targets the human papillomavirus (HPV) for oropharyngeal cancer.

We will first do some tests to make sure you qualify for the trial. These will involve blood tests, x-rays, images, and physical exams, etc. Other tests are described further on in this consent form. It is important that you read these.

There is a chance that you may experience side effects from the tests to be done (for example: pain from blood draws where the needle enters the skin). However, these will be rare.

You will not benefit from this screening evaluation.

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

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.

We are asking you to join this research study because you have been diagnosed with a stage II or III HPV-16 associated oropharyngeal cancer.

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.

In order to see if you are able to take part in the research, we are asking you to first take part in this screening.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to take part in this study, you will be asked 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.

- 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: HLA typing
- HPV genotype testing of tumor. Tissue from a previous surgery or biopsy may be used or a new biopsy may be obtained. Results from outside locations may also be used.
- Evaluation of your veins that are used for drawing blood samples
- Routine blood tests
- Electrocardiogram (ECG) – a test for your heart

- As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection (if you have results less than 3 months old, you may not need to have this test redone).
- Other testing for microbes and viruses including Hepatitis B and C infection (if you have results of viral tests that are less than 3 months old, you may not need to have this test redone). If you are found to be positive for Hepatitis B or Hepatitis C then you will be informed of your status, counseled about potential infection of sexual contacts, and will inform about potentially curative treatment options for Hepatitis C.
- Complete physical exam, performance status, vital signs, including the exact size and locations of any lesions you may currently have.
- Imaging (e.g. CT scan, MRI scan, PET scan, Chest X-ray) and/or exam under anesthesia.
- Pregnancy test (blood or urine) if you are a woman of childbearing potential

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this screening, your involvement will last for the length of time to see if you are eligible to take part on the treatment phase of the study. The length of time may range anywhere from a couple weeks to several months. You will be required to come to NIH at least 2 times during screening and each visit may last anywhere from 1 to 4 days.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

As not all persons screened will be eligible for study therapy, up to 180 patients will be enrolled in order to treat about 15 subjects on the study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

There are the following possible risks and discomforts with being in this screening part of the study:

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.

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.

Biopsy

Biopsy of the tumor may be needed to confirm eligibility. They will be done using local anesthesia by an otolaryngologist. In rare 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.

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 scanand 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.

Other

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.

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). 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 will be exposed to radiation from a CT scan, PET, or CT-guided biopsy. The amount of radiation exposure you may receive from these procedures is equal to approximately 3.1 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 PET and CT that you get in this study will expose you to the roughly the same amount of radiation as 10.3 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 capable of becoming 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 will not benefit from this screening evaluation.

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

In the future, other people might benefit from the study because the knowledge gained from this study may be used to help treat others who have this cancer.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

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

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

The results from the evaluations for this screening will be reported to you. You will be informed at that time if you are eligible for the main study at that time. There are no research tests planned as part of screening that there would be any research results to return to you.

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 are ineligible for the study
- if you become pregnant
- if new information shows that another treatment would be better for you
- if the study is stopped for any reason

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 or 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, and will only be used if they are transferred onto protocol 16C0154, if you agree to also take part in this other study. 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. You will receive no financial compensation 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.

The NCI generally does not cover expenses during screening. If you are scheduled for and begin treatment, the NCI will cover the cost for some of your expenses. 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 performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- 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 agai

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: _____.