PRINCIPAL INVESTIGATOR: Christian Hinrichs, MD

STUDY TITLE: A Phase II Study of Immunotherapy with E7 T Cell Receptor T Cells for Vulvar High-Grade Squamous Intraepithelial Lesions

STUDY SITE: NIH Clinical Center

Cohort: *Screening*

Consent Version: *4/27/2020*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Christian Hinrichs, MD
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KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes the 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 human papillomavirus (HPV)-16 associated premalignant condition of the vulva (high-grade squamous intraepithelial lesion (HSIL).

This consent form requests your permission for us to determine your eligibility for our study involving treatment with T Cell Therapy that targets the HPV for vulvar HSIL.

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

You may only participate in this study if you have vulvar HSIL that cannot be removed with surgery without causing disfigurement or functional impairment that you would consider unacceptable, or if you have already had surgery but it failed to control your vulvar HSIL.

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.

The remaining document will now describe this 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 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.

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

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 receive care 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 THIS STUDY IS BEING DONE?

This is a research study. The purpose of this research study is to determine whether experimental cells (E7 TCR) can make your HSIL lesions go away. E7 TCR T cells are made by removing a specific type of immune cell called T cells from the peripheral blood and genetically engineering them in the lab to recognize and kill the virus that causes HSIL. The E7 TCR T cells are considered investigational, which means it has not been approved by the US Food and Drug Administration (FDA) to treat HSIL.

We are asking you to join this research study because you have been diagnosed with an HPV-16 associated premalignant condition of the vulva (high-grade squamous intraepithelial lesion (HSIL).

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.

WHAT WILL HAPPEN DURING 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.

Laboratory results performed outside of the NIH may be accepted if they have been performed recently. Otherwise, you will have the following standard, clinical tests performed at the NIH to determine whether you are eligible for this trial:

Any time prior to starting the treatment:

- HLA typing (this blood test determines if E7 TCR T cells can recognize vulvar HSIL)
- We may need to do a PAP-smear test. We will know if we need to do a PAP-smear by reviewing your most recent one. This will be performed by a gynecologist.
- HPV testing
- If we cannot get a copy of your test results that show you have vulvar HSIL, or if we can't read your results, we will need to do a vulvar biopsy so we are sure of your diagnosis and you are eligible to participate in this study
- Evaluation of your veins that are used for drawing blood samples

Within 4 weeks prior to starting the treatment:

- ECG
- Chest x-ray
- Cardiac stress test and/or tests of your lung function if you have history of heart or lung problems.
- HIV Testing: 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 viral testing 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, including the exact size and locations of any lesions you may currently have.
- Medical history

Within 14 days prior to starting the treatment:

- Blood tests: Full chemistry panel, thyroid panel, complete blood count (CBC) and other required tests
- 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 determine eligibility to participate 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 3 days.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

As not all persons screened will be eligible for study therapy, up to 200 patients will be enrolled in this study in order to treat up to 16 subjects on the study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN 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.

Vulvar biopsy risks

The risks of a vulvar biopsy include bruising and discomfort at the biopsy site and rarely bleeding and infection.

Cardiac Stress Test

Stress tests pose little risk of serious harm. The chance of these tests causing a heart attack or death is about 1 in 5,000. More common, but less serious side effects linked to stress testing include:

- An arrhythmia (irregular heartbeat). Often, an arrhythmia will go away quickly once you're at rest. But if it persists, you may need monitoring or treatment in a hospital.
- Low blood pressure, which can cause you to feel dizzy or faint. This problem may go away once your heart stops working hard; it usually doesn't require treatment.
- Jitteriness or discomfort while getting medicine to make your heart work hard and beat fast (you may be given medicine if you can't exercise). These side effects usually go away shortly after you stop getting the medicine. Sometimes the symptoms may last a few hours.

Pulmonary Function Tests

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.

Pap Smear

A Pap smear is a gynecological test used to evaluate cervical cells in women. During this cervical cancer screening test, which is also called a Pap test, a small number of cells are removed from your cervix using a tiny brush. These cells are then examined in a laboratory for any type of abnormalities. While Pap smears typically do not cause complications, it is possible to have temporary discomfort or bleeding after this test. Most women do not experience pain after a Pap smear. In certain cases, however, you may feel slight sensations of pelvic discomfort, pressure or pain while your doctor removes cervical cells. Such complications are temporary and typically resolve as soon as the Pap smear is completed. Mild abdominal cramping can occur as a possible complication of a Pap smear. You may experience abdominal cramping during or immediately after a Pap smear. This possible complication of a Pap smear is temporary and typically subsides shortly after the test is complete.

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.

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 able to become 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. Please discuss with the research team how long you need to wait before becoming pregnant after completing the course of this study drug or procedures on this study.

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; however, if eligible for the study protocol the potential benefit to you might be that your lesions could go away or get smaller. The treatment could also decrease some of your symptoms, including pain, that are caused by your lesions.

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

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 precancer.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

You may choose not to be tested for eligibility or to have any other studies done. Instead of being in this study, you could:

- Get treatment or care for your precancer without being in a study, such as surgery to remove the lesion(s). This is called *surgical excision*. Another treatment option for some individuals is topical imiquimod, a cream that is applied directly to the lesions.
- Take part in another study

Please talk to your doctor about these and other options.

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.

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 your participation is being stopped.

You can stop taking part in the study at any time.

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.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

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 will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding vulvar HSIL, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the 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.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will Your Specimens or Data Be Shared for Use in Other Research **Studies?**

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. 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.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

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 samples. For example, if some research with your specimens

and data has already been completed, the information from that research may still be used. Also, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

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

If you are eligible for the study, your specimens and data will be stored at 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 samples/data, we will do everything we can to protect your identity by removing 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 data or samples.

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 screening.

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 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 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.

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 website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website 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 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 Cancer Research) or their agent(s)

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 or 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 information that 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 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, Christian Hinrichs, MD, hinrichs@nih.gov, 240-764-6059. *Other researchers you may call are: Scott Norberg, DO, at 240-858-3303.* 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 medical and 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 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.

_____	_____	_____
Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION: TO BE COMPLETED BY NIH STAFF IF INTERPRETIVE SUPPORT IS USED. PLEASE CHECK THE BOX THAT APPLIES:**

___ 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 the witness. The name or ID code of the person providing interpretive support is: _____.