INSTITUTE: National Cancer Institute

STUDY NUMBER: 17-C-0116 PRINCIPAL INVESTIGATOR: Christian S. Hinrichs, M.D.

STUDY TITLE: A Phase I Study of Immunotherapy with E6 T Cell Receptor T Cells for Vulvar High-Grade Squamous Intraepithelial Lesions

Continuing Review Approved by the IRB on 09/24/18
Amendment Approved by the IRB on 07/09/18 (C) Date posted to web: 10/04/18

Screening

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. 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 be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, 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). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

This consent form is to determine your eligibility for our study involving treatment with T Cell Therapy that targets the human papillomavirus (HPV) for vulvar high-grade squamous intraepithelial lesion (HSIL).

Why are you being asked to take part in this study?

You are being asked to participate in this study because you have been diagnosed with an HPV-16 associated premalignant condition of the vulva (high-grade squamous intraepithelial lesion (HSIL).

How many people will take part 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 approximately 18 subjects on the study.

Description of Research Study

The purpose of this study is to determine the safe dose of experimental cells (E6 TCR) in combination with aldesleukin to use in patients who have vulvar HSIL.

There will be 2 dose levels of the E6 TCR cells. The first patient enrolled gets the smallest dose and the dose is increased when a level has been determined to be safe. You can discuss this with the study doctors to find out which dose of E6 TCR T cells you will be receiving.

After the E6 TCR cells are given, you will receive up to two doses of aldesleukin (IL-2) to help these cells stay alive longer. The purpose of this study is to evaluate the toxicity of this treatment.

You may not be eligible for our study with E6 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.

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
- 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, if you are at least 50 years of age or older.
- 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

Within 7 days prior to starting the treatment:

- Pregnancy test (blood or urine) if you are a woman of childbearing potential

Additional Blood Samples to be Collected

At the time of HLA typing, which can be done at your local medical doctor's office. your local laboratory or at the NIH, we would also like to draw blood to be processed at the NIH for the following research study:

- HPV-16 tumor genotype test

This test is optional, and if you decline this test, it will not affect your participation in this study.

Assays which could have an impact on both patients and their children, including studies of genetic cancer risk, will not be done. This is a test for research only. Its purpose is to determine the type of HPV that caused your tumor using a blood test. The results of this test will not determine if you are eligible for the study. You will not receive the results of the test. Your research specimens will only be identified by the study code, subject number, and date and time of collection.

Risks or Discomforts of Participation

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.

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.

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.

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.

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.

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.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. 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 Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

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 Cancer Institute Institutional Review Board
- The study Sponsor *(Center for Cancer Research)*

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Stopping Participation

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

- if the screening tests shows that you are ineligible
- if new information shows that another treatment would be better for you

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

Conflict of Interest

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

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

Use of Specimens and Data for Future Research (not required to determine if you are eligible)

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.

OTHER PERTINENT INFORMATION

1. **Confidentiality.** 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.

   The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. **Policy Regarding Research-Related Injuries**. The 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 National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. **Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. **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 S. Hinrichs, M.D., Building 10, Room 4B04, Telephone: 240-760-6059. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM SEPTEMBER 24, 2018 THROUGH APRIL 8, 2019.

Signature of Investigator _____ Date _____ Signature of Witness _____ Date _____

Print Name _____ Print Name _____