INSTITUTE: National Cancer Institute

STUDY NUMBER: 18-C-0032 PRINCIPAL INVESTIGATOR: Julius Strauss, M.D.

STUDY TITLE: Phase I Trial Using a Multi-Targeted Recombinant Ad5 (CEA/MUC1/Brachyury) Based Immunotherapy Vaccine Regimen in Patients with Advanced Cancer

Continuing Review Approved by the IRB on 11/19/18
Amendment Approved by the IRB on 06/12/18 (A) Date posted to web: 12/01/18

Standard

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 research study is being done to test the safety of combination of three therapeutic vaccines (ETBX-011, ETBX-061, and ETBX-051) and to study their effects on the immune system.

The goal of cancer vaccines is to teach the immune system to target and then kill cancer cells. The targets of these vaccines are proteins called carcinoembryonic antigen (CEA), MUC1, and brachyury which are found on many types of cancer.

Similar vaccine therapies which have targeted one or two of these proteins have been very well tolerated, and had few side effects. Data in animal studies suggests that targeting all three of these proteins may lead to better results than targeting just one or two of these proteins. Therefore, this trial aims to target all three of these proteins in unison.

ETBX-011 has been studies in humans and has been found to be safe with few side effects, however, the combination of ETBX-011, ETBX-061, and ETBX-051 vaccines has not been tested in humans. This study will be the first time the vaccine combination has been given to humans. This vaccine combination is an investigational agent that has not been approved by the US Food and Drug Administration (FDA).

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

You are being invited to participate in a research study because you have been diagnosed with advanced cancer that has not responded to standard cancer therapies.

How many people will take part in this study?

Up to 32 people will be enrolled in this study.

Description of Research Study

What will happen if you take part in this research study?

Before you begin the study

You will need to have the following exams, tests and procedures to find out if you can be in the study. These exams, tests and procedures are part of regular cancer care and may be done even if you do not join the study. However, there are some extra exams, tests and procedures that you will need to have if you take part in this study. If you have had some of them recently, they may not need to be repeated. You will be removed from the study if you are not eligible.

These tests include:

- History and physical evaluation including vital signs
- Routine blood tests
- Urine tests
- Pregnancy test (if you are female and can have children)
- CT or MRI scan
- Hepatitis B and C screening test
- HIV Testing
- Electrocardiogram (ECG) to test the function of your heart

During the study

Once it has been determined that you are eligible and agree to participate in the study, you may need to have some of the tests that were done at screening repeated depending on how much time has passed. Your study team will let you know if any of the above tests need to be repeated.

You will receive ETBX-011, ETBX-51 and ETBX-61 vaccines by subcutaneous injections (three shots under the skin) every 3 weeks for 3 doses, and then every 8 weeks for up to a year.

We will give you a diary card after your first vaccine so you can record any symptoms you might have at the site of injection. Please bring the card with you at the next visit.

You will have blood drawn for safety every time you get your vaccinations. This includes a pregnancy test if you are a woman who can have children. We will also take scans and other measurements to test the effect, if any, the vaccines have on your tumor.

Research blood samples:

Research tests will be done on blood taken at various times during your participation in this study: baseline (before you have received any vaccines), Weeks 6, 14, 30 and end of treatment. The total amount of blood we will draw for research in this study is about 350ml (25 tablespoons).

When you are finished taking the treatment

You will return to the clinic for an evaluation within 90 days after your last treatment, whenever that occurs. You will have the following tests done: physical exam, vital signs, routine blood tests and urine tests. If you have ongoing significant side effects, you will continue to be followed until the side effects end or they are not changing. If you are unable to come to this visit, we will call you to find out if you are having side effects and will try to reschedule the blood tests for another time if possible.

After this visit, we will continue to call you every 3 months for the first year, every 6 months for the next two years, and every 12 months for another two years to find out how you are doing and if you have started any new anti-cancer therapy.

At the end of this study, we would still like to follow you for any late side effects and to see how you do on other treatments. We would request that at that time you enroll onto our Long-Term Follow-up Study 04-C-0274 which the study team can go over with you.

Birth Control

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for one month after you finish study treatment. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Acceptable birth control options for you and your partner include:

- abstinence
- surgical sterilization (you and/or your partner)
- approved hormonal contraceptives or therapies (such as birth control pills, Depo-Provera, or Lupron Depot)
- barrier methods (such as a condom or diaphragm) used with a spermicide
- an intrauterine device (IUD)

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

Risks from study vaccines

The combination of the ETBX-011, ETBX-061, and ETBX-051 vaccines has not been previously given to humans before, so risks and discomforts may occur that we cannot predict. While in the study, you may have side effects. They may be mild or very serious. Please tell your nurse or doctor about any side effects you experience. Your study doctor may give you medications to try to help lessen some of the side effects. All subjects in the study will be monitored for side effects.

The side effects listed below have occurred in people receiving ETBX-011. ETBX-061 and ETBX-051 have not been tested in humans.

Likely

- Pain, tenderness, swelling or redness at the injection site

Less Likely

- Fever
- Flu-like symptoms
- Anorexia
- Chills
- Nausea
- Headache

Risks from blood collection

The risks from drawing blood may include discomfort from insertion of the needle, bruising, pain, redness or swelling at site of blood drawing, fainting and rarely, infection at the site of blood drawing.

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to find the maximum safe dose of a combination of three immunotherapeutic vaccines (ETBX-011, ETBX-061, and ETBX-051). We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Alternative Approaches or Treatments

What other choices do I have if I do not take part in this study?

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

Stopping Therapy

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

- if he/she believes that it is in your best interest
- if you become pregnant
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if the investigator decides to end the study
- if new information shows that another treatment would be better for you

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 Etubics or designated

representatives. 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 cannot be recalled and destroyed.

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
- Qualified representatives from Etubics, the pharmaceutical company who produces ETBX-011, ETBX-061, and ETBX-051.

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.

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 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.

The National Institutes of Health and the research team for this study are using drugs developed by Etubics through a joint study with your researchers and the company. The company also provides financial support for this study.

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.

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, Julius Strauss, M.D., Building 10, Room 13N240A, Telephone: 301-480-0202. 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 NOVEMBER 19, 2018 THROUGH DECEMBER 3, 2019.

Signature of Investigator | Date | Signature of Witness | Date

Print Name | Print Name