INSTITUTE: National Cancer Institute

STUDY NUMBER: 18-C-0141 PRINCIPAL INVESTIGATOR: Jeremy L. Davis, M.D.

STUDY TITLE: Phase II Study Evaluating Confocal Endoscopic Microscopy for Detection of Early Stage Gastric Cancer in Subjects with Hereditary Diffuse Gastric Cancer Syndrome.

Continuing Review Approved by the IRB on 07/22/19
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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?

People with hereditary (passed from parent to child) gastric (stomach) cancer syndrome have a serious lifetime risk of developing cancer in their stomachs. Current international guidelines recommend that these people have regular endoscopies (a procedure using a small tube with a camera at the end that is passed through the throat and into the stomach) and biopsies (a sample of tissue is taken) even if their stomachs appear normal. However, this approach is not good enough to catch early signs of cancer, such as the appearance of tiny cancer cells that signal cancer development. In this study we will use an FDA approved small microscope attached to the endoscope to inspect the stomach lining and evaluate if this device is better than regular endoscopy

in finding the first signs of cancer in the stomach. This special microscopic endoscopy will be performed in addition to the standard endoscopy that would normally be used to evaluate the stomach. The endoscopy itself is not investigational.

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

You are being asked to participate in this study because you have a personal or family history of a hereditary gastric cancer syndrome, OR you have a mutation that is known to lead to gastric cancer.

How many people will take part in this study?

Up to 40 people will take part in this trial.

Description of Research Study

Before you begin the study

You will need to have certain studies done in order to determine whether you meet the criteria to participate in this study. We will ask you questions over the telephone or in person about your medical history and/or the medical history of your family members. We will ask to review your medical records. If you are pregnant, you can only start participation in this trial during your second trimester of pregnancy.

During the study

Endoscopy

Endoscopy, procedure to examine your esophagus and stomach, will be done under general anesthesia.

Before imaging, we will do a physical examination, including weight and vital signs.

During endoscopy a lighted tube will be inserted into your mouth and go down to the stomach. First, we will look at your stomach with regular device and then we will add the microscope.

Before adding the microscope, we will inject you intravenously with a contrast agent called fluorescein. We will not use this agent if you are allergic to it or if you are a pregnant woman.

During the procedure we will collect a small piece of tissue (biopsy) from the different areas of your stomach. The entire procedure will take about an hour, adding a half hour to a standard endoscopy.

After the procedure, we will keep you for observation in the hospital for a few hours. If you live nearby and have someone to accompany you, you can go home on the same day. If you are traveling from a far then you may spend the night in the hospital prior to going discharge.

Follow Up

Approximately 14 days after the endoscopy we would like to invite you to the Clinical Center to discuss results of these imaging procedures and check if you had any side effects from the procedure. If you are not able to come, we can do this over the phone.

If you undergo subsequent gastrectomy (removal of the stomach), we will collect stomach tissue for confirmation of cancer diagnosis.

Risks or Discomforts of Participation

Risks associated with endoscopy and biopsy:

- discomfort in your throat,
- bleeding,
- perforation,
- infection.

Risks associated with general anesthesia:

- temporary confusion and memory loss,
- dizziness,
- difficulty passing urine,
- bruising or soreness from the IV drip,
- nausea,
- vomiting,
- shivering and feeling cold,
- sore throat,
- heart attack,
- pneumonia,
- stroke

Risks associated with fluorescein:

- nausea,
- vomiting,
- headache,
- dizziness,
- fainting,

- low blood pressure

Additional risks for pregnant women:

- loss of baby,
- premature labor and delivery.

You should tell the doctors or nurses about any discomfort you may have. Care will be taken to avoid any complications

Potential Benefits of Participation

The aim of this study is to see if this experimental procedure will help us detect tumors better than we are currently able to. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include detection of gastric cancer at its earliest stage so that it can be cured. Because there is not much information about the procedure's effect on cancer detection, 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

Instead of being in this study, you can get regular endoscopy.

Stopping Study Participation

Your doctor may decide to remove you from this study for the following reasons:

- If he/she believes that it is in your best interest
- If he/she decides to close the study

In this case, you will be informed of the reason why you are being taken off this study.

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 NCI or designated representatives.

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 interventions 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 Institutes of Health Intramural Institutional Review Board

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.

Use of 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 data that we collect and use it for future research and share it with other researchers. We will not contact you to ask about each of these future uses. These 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 data will be used for research purposes only and will not benefit you. It is also possible that the stored data may never be used. Results of research done on your 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 data used for future research, please contact us in writing and let us know that you do not want us to use your data. Then your data will not be used for future research. However, it may not be possible to withdraw or delete data once it has 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, Jeremy Davis, M.D., Building 10, Room 4-3742, Telephone: 240-760-6229. 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 JULY 22, 2019 THROUGH AUGUST 15, 2020.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____