INSTITUTE: National Cancer Institute

STUDY NUMBER: 14-C-0107 PRINCIPAL INVESTIGATOR: Baris Turkbey, MD

STUDY TITLE: Evaluation of Ferumoxytol Enhanced MRI for the Detection of Lymph Node Metastases in Genitourinary (Prostate, Bladder And Kidney) Cancers

Continuing Review Approved by the IRB on 01/08/18

Amendment Approved by the IRB on 01/18/17 (D) Date posted to web: 01/24/18

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.

Purpose of the Study

The purpose of this study is to help researchers determine how well Ferumoxytol can detect lymph node metastases in patients with prostate, bladder, or kidney cancer. Ferumoxytol is an FDA-approved iron replacement therapy agent. However, it is NOT approved by the FDA as an imaging agent. So the use Ferumoxytol in this protocol is experimental.

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

You are being invited to take part in a research study because you have one of the following types of cancers: prostate, bladder, or kidney and you may have surgery to remove your cancer or a biopsy to remove some tissue from your lymph nodes here at the Clinical Center. The decision to have surgery or a biopsy will not be made as a part of this study.

This study will not affect your ability to take part in other research protocols or receive medical care.

How many people will take part in this study?

Up to 56 people will be included in this study.

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

Before you begin the study

For your safety, and to help make sure the results of this trial are scientifically meaningful, your medical history will be reviewed to make sure you are eligible to take part.

At your first study visit, three vials of blood will be drawn for a panel of routine blood tests, you will have a physical exam, and your vital signs (blood pressure, heart rate, breathing rate and temperature) will be measured. If you are a woman able to get pregnant, you will also have a pregnancy test done. You will also answer questions about your medical history and current medications.

During the study

If you are eligible for this study and wish to participate, you will then be scheduled for study procedures including ultrasonography, MRI imaging and Ferumoxytol infusion. These activities will be performed in the NCI Molecular Imaging Clinic except for the ultrasonography, which will be performed in the Radiology and Imaging Sciences Department of Clinical Center, NIH.

If you are women, an additional pregnancy test will also be done within 48 hours prior to Ferumoxytol infusion if more than 48 hours have passed since the screening test.

The first MRI before Ferumoxytol infusion will take approximately 1 hour, whereas the first ultrasound examination will take about 10-15 minutes. Twenty-four hours after Ferumoxytol infusion, you will have a second MRI scan and an ultrasound examination, which will again take approximately 1 hour and 10-15 minutes, respectively. Finally, forty-eight hours after Ferumoxytol infusion, you will have a third MRI scan and an ultrasound examination.

Ultrasonography is a medical imaging technique used to visualize internal organs to capture their size, structure and any pathological lesions with real time images. This technique uses harmless sound waves to provide pictures of organs or tissues inside the body.

During the MRI scan, a standard sensor, which is like a small blanket with wiring inside, will be wrapped around your lower torso to improve MRI quality. The MRI scan usually takes less than

an hour. You will need to lie still on the scanning table during that time. An intravenous line (IV; a very thin catheter inserted into a vein with a tiny needle) will be started after your first MRI scan and Ferumoxytol will be injected into your system as an IV infusion. You will receive more information about your MRI scan when you visit the Molecular Imaging Clinic and you may ask questions at any time. In addition, you should ask your doctor or the study doctor any questions you have concerning this study.

After imaging has been completed, your referring physician will treat your disease per the treatment protocol you are enrolled on.

If you have surgery to remove lymph nodes or a biopsy after the MRI scan, your tissue will be reviewed in the NCI pathology department to determine if the imaging agent was able to detect involvement of your lymph nodes.

If you do not have surgery to remove lymph nodes or a biopsy, the research team will review your medical records to determine if the imaging agent was able to detect involvement of your lymph nodes.

Birth Control

If you are a woman who is breast feeding, pregnant, or planning to become pregnant during the study, 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 1 day after you finish study related imaging. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- tubal ligation
- vasectomy

Some methods of birth control will not work when you are taking certain drugs. You can still become pregnant even if you use an acceptable birth control method.

Women who become pregnant during the study will have to leave the study. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with the sponsor and the institutional review board/research ethics board that reviews this study.

If you are a woman of childbearing potential:

By signing this consent form, you confirm to the best of your knowledge that you are not pregnant now and you do not intend to become pregnant during this study.

A serum (blood draw) or urine pregnancy test will be done to confirm that you are not pregnant 48 hours prior to any imaging session. If you are found to be pregnant, you will not be given the infusion or undergo imaging and you will be removed from the study.

If at any later time during this study you think you might be pregnant, or later learn that you were pregnant during the study, you must contact the study doctor immediately for further instructions about your participation in this study and what to do next

How long will you be in the study?

Participation in this study will last until you have had the forty-eight hour ultrasonography and MRI completed. The active part of the study, (Ferumoxytol infusion, ultrasonography, and MRI scanning) will last a few days.

However, patients that do not undergo surgical excision or a biopsy to remove lymph nodes will remain on study for a minimum of 12 months.

It is expected to take approximately 24 months for this study to enroll all patients.

What do I have to do?

Read this informed consent and take the time to get answers to all your questions. You will be provided a copy of this consent once you, the investigator and a witness have signed the form.

You will need to provide your doctor with a listing of all your current medications as certain medications may react with the study infusion.

What are the possible risks / discomforts?

Risk from Blood Draws

The risks associated with the blood draws and IV insertion includes:

- pain at the needle site;
- bruising;
- possible dizziness if you stand up quickly; and
- possible inflammation of the vein or infection at the needle site.

Risks from Ultrasonography

The ultrasonography procedure will take about 10-15 minutes. Ultrasonography has no known risks with no use of ionizing radiation or adverse heating or pressure effects in tissue.

Risks from MRI

Having an MRI requires that you lie still with part of you or all of you inside a tube shaped machine for about 45 minutes to an hour. Even with the ear plugs we give you it can be noisy with loud clicking and thumping sounds, which bothers some people. Some people may feel 'closed in' or 'trapped' (even though they being closely watched and are quite safe). This is

called claustrophobia. Cool air will surround you, and the room is large and brightly lit to help avoid claustrophobia. You may ask your physician for a mild sedative for the procedure if you think it will help. If you take a sedative you must not drive a vehicle until it wears off after the MRI.

MRI scans cannot be done on people who have:

- a cardiac pacemaker,
- neural pacemaker,
- surgical metal clips in the brain or on blood vessels,
- cochlear implants,
- or foreign metal objects within the eye.

At the time of your MRI, you will be asked about these things.

Risks from Ferumoxytol

Ferumoxytol has been generally safe when given to people for its FDA approved purpose of iron replacement therapy. Side effects, some of which can be serious or life threatening, may sometimes occur. These side effects, though rare, may happen in this trial. If they do happen it is usually right around the time that Ferumoxytol is injected, which is why you will be closely watched at that time, and promptly treated if necessary. These effects include:

- whole body allergic reactions, which can range from mild to serious or life threatening (this is called anaphylaxis),
- low blood pressure, which can lead to becoming unconscious (fainting, passing-out)
- iron overload.

One person who took part in a prior study in NCI experienced a mild allergic reaction while the Ferumoxytol was being given. It was promptly treated and got better right away. Again, you will be closely observed during and right after the Ferumoxytol is given so that if any reaction occurs it can be immediately treated. The dose used in this study is less than that used for iron replacement therapy. It is always possible that you may experience some side effects that we cannot anticipate.

What are the possible benefits of taking part?

There is no anticipated direct benefit to participating in this study, but you may help others that have cancer by contributing to cancer research.

What are the alternatives for diagnosis or treatment?

This is not a treatment trial. The alternative is not to participate. If you do not consent to this trial, you will not be deprived of any treatment for which you are otherwise entitled.

Stopping Participation in this study

Your study doctor may remove you from the study if:

- they think it is in your best interest;
- if you do not follow the study instructions; or
- if you are found to be pregnant before you receive Ferumoxytol
- for administrative reasons

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. 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, any data generated from the scans that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

What if relevant new information becomes available?

If new information that might affect your decision to be in the study becomes available, your physician will tell you about it and discuss whether you want to continue on the study. If you decide not to carry on, this will not influence your care. If you decide to continue in the study you will be asked to sign an updated consent form.

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.

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.

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

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.

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, Dr. Baris Turkbey; Bldg 10, Room B3B69, 10 Center Drive, Bethesda, MD 20892; Telephone: 240-760-6112. You may also call the Clinical Center Patient Representative at 301-496-2626.

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 JANUARY 08, 2018 THROUGH JANUARY 07, 2019. _____ _____ _____ _____ Signature of Investigator Date Signature of Witness Date _____ _____ Print Name Print Name	