INSTITUTE: National Cancer Institute

STUDY NUMBER: 08-C-0200 PRINCIPAL INVESTIGATOR: Karen A. Kurdziel, M.D

STUDY TITLE: A Pilot Study of ^{18}F- Fluorothymidine (FLT) PET/CT in Lymphoma

Continuing Review Approved by the IRB on 12/16/13
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Early Response

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.

Description of Research Study

You have been invited to participate in this study because you have lymphoma. As standard of care, your doctor will obtain conventional PET/CT scans to evaluate your response to chemotherapy. Conventional PET/CT scans are typically done using a sugar-like radioactive tracer called FDG and low dose x-rays. They are usually performed before treatment and after the completion chemotherapy. Even though, FDG PET/CT is valuable in monitoring treatment response, we hope that a new PET radioactive tracer called ^{18}F- fluorothymidine (FLT) PET/CT will be better able predict final response to treatment. We will work with your clinical provider to see if this early imaging helped predict your response to therapy.

Positron emission tomography/computed tomography (PET/CT) is a type of scan that uses a large donut shaped detection device. The scanner contains crystals that pick up tiny radiation signals given off by radioactive substances (tracers) that have been injected into the vein. The images generated by the scanner show where the radioactive tracer is in the body. The CT portion of the PET/CT is performed with low dose x-rays that go through your body and help us to better localize where the radioactive tracer is concentrating.

FLT is an experimental tracer which has high uptake in tissues involved in cellular division such as tumors. By injecting a small amount intravenously, we can image where FLT accumulates in the body.

Numerous small PET studies using FLT have been performed with no adverse effects ever reported.

By enrolling is this study, you will be asked to undergo an FLT PET/CT scan: before beginning therapy, after 2 cycles of therapy and following completion of your chemotherapy. It is generally standard of care to undergo FDG PET/CT imaging prior to beginning treatment and at the completion of therapy. Some small studies have suggested that FDG PET/CT performed during therapy may be predictive of outcome. For this study, we are asking you to undergo an additional mid-therapy FDG PET/CT study, which will be compared with the mid treatment FLT PET/CT. You will also be giving us permission to collect follow-up information regarding your progress for up to three years after treatment.

There may be additional blood tests performed before the FLT PET scan can be scheduled. These are to be as certain as we can that the injection of FLT will not cause side effects. These tests will be performed to assess your liver function and will require about two teaspoonfuls of blood. Women able to have children will have an additional teaspoonful of blood collected in order to test for pregnancy. Pregnant women cannot participate in this study due to potential negative health effects to the unborn baby.

On each day of your FLT PET/CT studies, you will come to the Nuclear Medicine Department at NIH and an intravenous line will be placed in your arm. You will be asked to lie on your back at the PET/CT scanner table. The table will then be advanced into the scanner. FLT will be injected in the vein over a 10-15 second period. Subsequently, PET/CT imaging over the tumor will be performed for 60 minutes, and immediately afterwards, a whole body scan will be performed (an additional 25-35 minutes). It is important that you remain still during these scans. 120 minutes after the injection, another regional (with your target tumor in the field of view) PET/CT images will be performed in a similar fashion for 10 minutes. Please note that for the additional sets of images re-injection of tracer is not necessary. Doctors and nurses will be supervising the whole procedure and you should ask them any questions you have concerning this study. Additional

blood samples (two teaspoons) will be collected from your vein at 60 and 120 minutes after the FLT injection to determine the amount of FLT that remains in your blood.

For the mid-therapy FDG study, you will also come to the Nuclear Medicine Department at NIH and an intravenous line will be placed in your arm. You will be asked to lie on your back at the PET/CT scanner table. The table will then be advanced into the scanner. FDG will be injected in the vein over a 10-15 second period. One hour after injection a whole body PET/CT will be performed (lasting ~25-35 minutes).

Up to 40 subjects will be enrolled in this arm of the trial. Patients will be enrolled at either the NIH Clinical Center or the Walter Reed National Military Medical Center.

Alternative Approaches or Treatments

You are not obligated to participate in this study. If you decide not to participate, it will not alter your planned treatment.

Risks or Discomforts of Participation

There are a few possible risks of [F-18]FLT PET and PET/CT scans. The most common ones are not considered serious. Any serious risks of [F-18]FLT PET or PET/CT scans are considered very unlikely. All of the known risks are described below.

Possible risks from having an intravenous (IV) injection:

- Bruising, pain, or infection at the injection site
- Leaking of IV fluid into tissues near the injection
- Inflammation of the vein at the injection site
- Allergic reaction, which could be serious or life threatening
- Dizziness if you stand up quickly

Possible risks from having a PET scan in general:

- Claustrophobia (feeling anxious and 'closed in')
- Discomfort from lying still on your back for a total of about 95 minutes during the scans

Possible risks from radiation exposure:

- Each dose of [F-18]FLT will expose you to about [e.g. one-half to three –quarters] of the amount of radiation in a routine CT scan of a large body area such as your

abdomen. Because we also need to do a CT, along with the [F-18]FLT PET, you could get up to another full CT dose of radiation at each scan depending on the scanner used.

A total of 3 FLT PET/CT scans will be performed.

Using the standard way of describing radiation dose, from participating in this study and undergoing all 3 FLT PET/CT scans, you will receive approximately 9.7 rem to your liver, 8.2 rem to your stomach, and your adrenals, 8.1 rem to your pancreas, and 7.9 rem to your small intestines. All other organs will receive smaller amounts of radiation.

Although each organ will receive a different dose, the amount of radiation exposure you will receive from these procedures is equal to a uniform whole-body exposure of 4.2 rem. This calculated value is known as the "effective dose" and is used to relate the dose received by each organ to a single value. The amount of radiation received in this study is within the dose guidelines established by the NIH Radiation Safety Committee for research subjects. The guidelines is an effective dose of 5 rem (or 5,000 mrem) received per year.

For comparison, the average person in the United States receives a radiation exposure of 0.3 rem per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from this research study is about the same amount you would normally receive in 13.7 years from these natural sources.

The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effects were ever observed from the levels of radiation you will receive by taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful at any dose - even low doses such as those received during this research.

If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects.* Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

Experimental FLT PET imaging may reveal new information that would result in further studies (e.g., biopsies) and interventions that might not be necessary. The decision to act on findings on the experimental FLT PET study will be made by you and your referring physician.

It is possible that you may experience some side effects that we cannot anticipate. For that reason, you will be watched closely so that we can treat any side effects early.

Potential Benefits of Participation

As this is NOT a treatment protocol, you are not likely to have any direct benefits.

Research Subject's Rights

Participation in this research study is voluntary and you can withdraw at any time. We encourage you to ask questions so you can make the most informed decisions during your participation in this study. Refusal to participate will not result in penalty or less benefits to which you are otherwise entitled.

It is important to stress that being in this protocol does not promise long-term medical care at the NIH Clinical Center. If there is no further research study that is suitable for you and your state of disease, or if you are not currently on another research study, you will be returned to the care of your referring doctor or institution, or alternative sources of care closer to your home. If you have any questions about your treatment at NIH, you can contact the Principal Investigator, Dr. Karen A. Kurdziel (301-443-0622) or the patient care representative (301-496-2626).

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.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process *http://ethics.od.nih.gov/procedures/COI-Protocol-Review-Guide.pdf*. 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: Karen A. Kurdziel, M.D.; 9000 Rockville Pike, Building 10, Room B3B403, Telephone: (301) 443-0622.

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 DECEMBER 16, 2013 THROUGH DECEMBER 15, 2014.

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

Print Name _____ Print Name _____