INSTITUTE: National Cancer Institute

STUDY NUMBER: 01-C-0158 PRINCIPAL INVESTIGATOR: Robert Yarchoan, M.D.

STUDY TITLE: Protocol to Assess Vascularity in Kaposi's Sarcoma Lesions Utilizing Non-Invasive Imaging Techniques

Continuing Review Approved by the IRB on 09/02/16
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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?

This is a research study to develop noninvasive methods of determining the density of blood vessels and the amount of blood flow in skin that is affected by Kaposi's sarcoma. The intent is to develop techniques that may in the future help us better assess the clinical state of Kaposi's sarcoma lesions.

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

You are being asked to take part in this study because you have Kaposi's Sarcoma.

How many people will take part in this study?

A total of up to 32 people will be enrolled in this study.

Description of Research Study

Kaposi's sarcoma is a tumor that in part depends on the formation of new blood vessels for its growth and purple color. Improvement in Kaposi's sarcoma skin lesions may be accompanied by a decrease in the amount of blood vessels and/or blood flow in the lesions. Some experimental therapies in Kaposi's sarcoma are targeted at decreasing the amount of blood vessels in the Kaposi's sarcoma lesions. Therefore, if measurements could be easily made of the density of blood vessels and blood flow in Kaposi's sarcoma lesions, it could be a useful tool toward helping to assess the effects of both standard and experimental treatments in Kaposi's sarcoma on the skin lesions. This research protocol does not involve any treatment of your Kaposi's sarcoma, but you may be receiving standard treatment for your disease, experimental treatment for your disease on a different research protocol, or perhaps your disease is stable without treatment and you are currently receiving no treatment. While you are on this research protocol, you can begin, change, or stop therapy for your Kaposi's sarcoma at any point, but it is important for us to be able to record these changes if you continue on this protocol.

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

On this protocol, you will have conventional photographs made of your lesions, and four additional experimental methods performed. The four methods are called:

1) laser Doppler imaging
2) multi-spectral imaging
3) infrared thermal imaging, and
4) optical coherence tomography.

In addition, comparisons will be made with normal skin surrounding the lesions or on the opposite side of your body. Laser Doppler imaging takes about 3 minutes to perform on each lesion. It uses a low power laser beam that scans across the skin lesion being measured. The instrument does not touch your skin. You may be asked to have a blood pressure cuff put on your arm and have laser Doppler imaging performed before and after the cuff is inflated for a short time (generally less than thirty seconds).We do not believe that this instrument will harm your skin: in standard practice a similar machine is used to measure how deeply severe burns affect the skin. If you stare at a laser light it could harm your eyes, but precautions will be taken so that you will not stare at it. It is also used to assess allergic responses in the skin. However, its use in Kaposi's sarcoma is experimental. The purpose of this experimental use is to attempt to measure the amount of blood flow through the blood vessels in the Kaposi's sarcoma lesions. It will not have a therapeutic effect on the lesions. The multi-spectral imaging exam should take about 2 minutes to perform on each lesion. It uses principles of the way hemoglobin absorbs light. Hemoglobin is a protein in the blood that carries oxygen to your tissues. The light on the multi-spectral imaging instrument is absorbed differently depending on whether the hemoglobin has oxygen attached to it or not. This will allow an estimate to be made regarding the total blood

volume, and how much of it is carrying oxygen or not. We do not believe that the instrument will harm you. The technique will not make your Kaposi's sarcoma improve. The thermal imaging takes about a minute to perform on each lesion. It uses a special camera to take digital infrared pictures of your skin. This enables us to form a picture of the temperature of your KS lesions and thus assess the blood flow in the Kaposi's sarcoma lesions. We do not believe that the camera and lights will harm you. The spectral domain optical coherence tomography (OCT) exam should take less than 2 minutes per lesion. This technique allows a three dimensional image to be made of the lesion structure. The principle of OCT is based on interference of two light beams, one illuminating and reflecting from the sample and the second one reflecting from a mirror. The light source used is of low power and non-invasive. The system will be placed approximately 4cm away from your skin, and nothing should contact your skin directly. The structural information obtained by this technique will be correlated to the vascular information obtained with the other techniques and will help to further evaluate treatment outcome. We do not believe that the instrument will harm you.

We anticipate that the whole exam (involving the four tests) will generally take an hour or less to perform. You may also be asked to have a small amount of blood (less than a tablespoon) drawn from your vein for a complete blood count the days you have the lesion assessments performed. You may occasionally be asked to have two examinations performed the same day if your schedule permits. We do not expect that any of these tests will make your HIV infection or Kaposi's sarcoma improve or become more severe.

During the study

During your participation in this protocol, these experimental imaging techniques will be performed when you begin the study as a baseline evaluation, and then once about every 3 months while you are on the study in order to compare the results of the tests over time. Also, if your Kaposi's sarcoma should improve or worsen, or you change therapy for your KS, the imaging techniques may be repeated in an effort to correlate the findings of the imaging with the clinical changes observed in your KS. In general, we will try to schedule the examinations on this protocol to take place on the same days you are being seen in the clinic for other purposes.

Alternative Approaches or Treatments

The imaging techniques have no therapeutic role. These techniques are being studied to try and determine if they may be useful in assessing Kaposi's sarcoma lesions using non-invasive methods. Patients can elect to not have any imaging performed without jeopardizing their participation in other protocols in the NIH Clinical Center.

Risks or Discomforts of Participation

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

The risks of participating in this study are minimal. There are no invasive procedures involved other than the drawing of a small amount of blood from your vein through a needle, which will be done by standard procedures. The imaging techniques use a variety of methods as described

above to estimate the vascularity in the lesions and blood flow in the lesions. The techniques will require your time, which may be inconvenient to you. The time will vary according to how many lesions are studied by the techniques. If you find that the amount of time you have to spend having the lesions assessed is too great, we will minimize the number of lesions studies by the techniques, if possible.

Potential Benefits of Participation

Are there benefits to taking part in this study?

There are no direct benefits to you of participation in the study. The study is an attempt to develop new methods for assessing Kaposi's sarcoma skin lesions using non-invasive methods.

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.

Participation in this protocol is voluntary you may discontinue your participation in this investigational protocol at any time. You will be given a copy of the consent for your records. There are no penalties imposed on you for withdrawing your participation in the protocol. You may ask questions of the staff, and indeed you are encouraged to do so. Any significant new findings that relate to your treatment will be discussed with you. It is important to stress that participation in this protocol does not constitute a promise of long-term medical care here at the NIH Clinical Center. If there is no research study suitable for you and your state of disease, you will be returned to the care of your private doctor.

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

When we report the results of this research study, we may include photographs and images taken during the course of the study. We will not mention you by name and we will take care so that you will not be recognizable (i.e. no identifiable images of your face will be shown).

Stopping Participation

Your doctor may decide to stop your participation in this study

- if he/she believes that it is in your best interest
- if you do not follow the study requirements

In this case, you will be informed of the reason that 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, according to FDA guidelines, information collected on you up to that point may still be used by the researchers. 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.

Any decisions regarding therapy of your Kaposi's sarcoma will be made by your treating physician using regular clinical information (including counts and measurements of lesions). The results of the non-invasive imaging will not be used to alter your clinical care, as at present these are research tools only. If you are enrolled on a research treatment study for Kaposi's sarcoma, the decisions about your treatment will be made by your treating physician in accordance with the requirements of that study.

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.

This protocol may have investigators who are not NIH employees. Non-NIH investigators are expected to adhere to the principles of the Protocol Review Guide but are not required to report their personal financial holdings to the NIH.

Optional Studies

We would like to keep some of the imaging studies and data that are collected for future research. These imaging studies and data will be identified by a number and not your name. The use of your imaging studies and data will be for research purposes only and will not benefit you. It is also possible that the stored imaging studies and data may never be used. Results of research done on your imaging studies 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 decide now that your imaging studies and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and/or data. Then any specimens that remain will be destroyed and your data will not be used for future research.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My imaging studies and data may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials_____

2. My imaging studies and data may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials_____

3. Someone may contact me in the future to ask permission to use my imaging studies and/or data in new research not included in this consent.

Yes No Initials_____

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, Robert Yarchoan, M.D.; Building 10, Room 6N106, Telephone: 301-496-8959. You may also call the lead research nurse, Ms. Kathleen Wyvill, at 301-496-8959. If you have any questions about the use of your data or imaging studies for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

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 02, 2016 THROUGH SEPTEMBER 01, 2017. _____ _____ _____ _____ Signature of Investigator Date Signature of Witness Date _____ _____ Print Name Print Name	