Informed Consent Form

Strategy to Reduce Bladder Activity with rhPSMA 7.3: Comparison of 18F-rhPSMA 7.3 PET/CT with and without Furosemide in Biochemical Recurrence of Prostate Cancer

NCT Number: NCT05779943

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You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study, you may be one of 20 enrolled subjects who will be studied, at Emory, Saint Joseph's, and Johns Creek's Hospitals.

Why is this study being done?

This study is being done to evaluate the effect of a substance (called furosemide IV) in the bladder radioactivity levels, through Positron Emission Tomography (PET) scans, using a radioactive substance (called radioactive tracer rhPSMA-7.3 (^{18}F)). You are being asked to be in this research study because you have had previous surgical treatment for prostate cancer and the study doctor now suspects that the prostate cancer may have come back based on levels of prostate-specific antigen (PSA) in your blood. The standard of care evaluation in this clinical scenario would include imagng evaluation with CT, MRI, bone scan or other PET/CT scans using Ga-68 PSMA-11 or F-18 piflufolastat PSMA at the discretion of your oncologist.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do you have to do if you choose to join this study?

If you are eligible and want to be part of the study, you will participate for the duration of the study (two study visits). The researchers will ask you to do the following: undergo one imaging test called PET-CT scan performed on an individual day without furosemide (Lasix), followed by a second PET-CT with furosemide (Lasix) 2-7 days afterward, or vice versa. The order of these scans will be assigned sequentially. The first set of 10 patients will have the study done without furosemide (Lasix) first followed by the second scan with furosemide (Lasix), and vice versa. The PET-CT scans will be paid for by the study.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question. The information we get from this study may help us to better detect prostate cancer recurrence in real-life practice and may help us to better treat patients with prostate cancer in the future.

What are the risks or discomforts you should know about before deciding?

The study will take time. The procedure that is being tested may not work any better than regular care and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious for this study, these include common risks associated with radiation exposure, allergic or other reactions to furosemide or radiotracers (used for the imaging tests), loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the "What are the possible risks and discomforts?" section of this document.

Alternatives to Joining This Study
Since this is not a treatment study, the alternative is not to participate. You do not have to be in this study.

Costs
You WILL NOT have to pay for the study procedures, such as the experimental PET-CT scan.

There is more information in the "Costs" section further below.

What Should You Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand the research procedures. Take time to consider this and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Strategy to Reduce Bladder Activity with rhPSMA 7.3: Comparison of 18F-rhPSMA 7.3 PET/CT with and without Furosemide in Biochemical Recurrence of Prostate Cancer

IRB #: STUDY00004720

Principal Investigator: David Schuster, MD

Investigator-Sponsor: David Schuster, MD

Study-Supporter: Blue Earth Diagnostics

Introduction

You are invited to take part in a clinical research study.

This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

The study doctor thinks that you might be a candidate for this study because you have had surgery (radical prostatectomy) for prostate cancer and it is now suspected that the prostate cancer may have come back based on levels of prostate-specific antigen (PSA) in your blood. This informed consent describes the research study and your possible role in it.

Before you decide if you want to take part in this study, it is important for you to understand

- why the research is being done,
- how your information will be used,
- what the study will involve, and
- the possible benefits, risks and discomforts for you when you take part.

Please take time to read the following information carefully. Some words may be new to you. If there is anything you do not understand or if you would like a more detailed explanation, please ask the study doctor or study staff. You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate.

You may also discuss the study with family members, friends, and your own doctor, if you wish. If you decide that you want to take part in this study, you will be asked to sign and date the consent statement at the end of this informed

consent form (you will be given a signed and dated copy of this to take home with you). You must not take part in any study procedures until you have read, signed, and dated this form.

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.

What is the purpose of this study?

You are being asked to be in this research study because you have had surgery (radical prostatectomy) for prostate cancer and the study doctor now suspected that the prostate cancer may have come back based on levels of prostate-specific antigen (PSA) in your blood. The purpose of this study is to evaluate whether administering a diuretic substance called furosemide (Lasix) can help your doctors to better detect any recurrent prostate cancer in the structures around the urinary bladder in the pelvis on a PET/CT scan. This will be compared to the PET/CT scan performed without the diuretic substance to see whether there is an advantage in the detection of disease with the administration of the diuretic substance. The diuretic substance administered increases the urine flow into the bladder, thereby decreasing the level of radioactivity within the bladder, which may help to see any abnormal areas that can be masked by the radioactivity within the bladder. The radioactive substance used to perform this PET/CT scan is not FDA-approved but has been shown to be safe in other larger clinical research studies.

What will you be asked to do?

First, you will be asked to sign and date this consent form if you agree to take part in this study. If you take part in this study, you should follow the study procedures and go to all the study visits your study doctor arranges for you. You must tell your study doctor if you have participated in any previous study receiving substances similar to the study agent or if you recently participated in another clinical study.

- All through the study you should report any changes to your health, including any side effects, to the study doctor.
- You should tell your study doctor about all medications you are taking at the first Visit and tell the study doctor before you start a new medication or if you stop taking a medication while you are in the study.
- Allow the study staff to call you to ask about your health.
- Agree to follow instructions by your doctor on personal hygiene and other measures to protect against the risk of COVID-19.
- Symptoms of COVID-19 includes cough, fever, and difficulty in breathing. If you experience any of these symptoms in between the study visits or suspect that you may have come in contact with someone infected with COVID-19, please self-isolate yourself at home and contact the study doctor via telephone immediately. If required by the local regulatory authorities, you may also be tested for COVID-19.

You will have a PET-CT scan after intravenous injection of the study agent without furosemide first, followed by a second PET-CT scan with furosemide 2-7 days afterward, or vice-versa. Scanning is done after an uptake period of the study agent of approximately 60-70 minutes. You will be encouraged to void up to 15 minutes before being placed in the scanner for imaging, if possible. You will be encouraged to arrive well hydrated and to drink an additional 500-1000mL of water during the uptake phase. The amount of oral hydration, time and frequency of voiding will be recorded. A PET-CT scan will then be completed from the proximal thigh to skull base (below orbits) at approximately 3 minutes per bed position. Fasting is not required for this study.

Who owns your study data and samples?

If you join this study, you will be donating your study information. You will not receive any compensation if your information is used to make a new product. If you withdraw from the study, data that was already collected may still be used for this study.

What are the possible risks and discomforts?

There may be side effects from the study drug or procedures that are not known at this time.

As with all research studies, the new diagnostic study agent and study procedures may involve unknown risks. Any medication or procedure can have temporary and permanent side effects and can cause unforeseen adverse reactions.

1. Radiation Risks: The principal risk associated with a radiation dose is the possibility of developing radiation-induced cancer later in life. However, the additional risk of radiation-induced cancer from these diagnostic procedures is low compared to the risks from the disease itself. You will be exposed to radiation from nuclear medicine. These procedures are not necessary for your medical care and will occur because you participate in this study. The estimated radiation dose that you will receive is equal to or less than the annual radiation exposure limit allowed for persons who are occupationally exposed to radiation (for example, x-ray technologist, radiologist). The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is minimal.
2. Allergic or other reactions to radiotracer: Although the risk is extremely small, it is possible to develop an allergic reaction to the study agent [5]. This can result in hives, rash, itching, and difficulty breathing which may require emergency medical treatment. There have been no previous instances of allergic reactions. In prior studies where the study agent was used in human subjects, the risk of adverse events which can be attributed to the radiotracer was extremely low, and of minimal medical impact such as burning at IV site or headache.
3. Risks related to IV for PET scan: A small amount of radioactive material will be injected by either a hand-held needle or a machine. Such injections are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery, or vein, or cause infection. The radioactive material could also leak from veins, causing swelling and discomfort.
4. False positive on PET: It is possible that a lesion identified on the experimental PET procedures may be false-positive, thus potentially leading to an inappropriate biopsy. While further evaluation of imaging finding to confirm true positivity may occur according to the standard of care practice, a **biopsy of the imaging-identified lesion is not in the scope of this trial, nor is it a requirement**.
5. Furosemide: The risk from the low dose (20mg) of furosemide is minimal. It will temporarily cause increased urination. Though unlikely, other side effects may include nausea or vomiting, diarrhea, constipation, stomach cramping, vertigo, dizziness, headache, blurred vision, itching or rash.

Researchers may learn something new during the study that may affect your choice to be in the study. If this happens, they will tell you about it. Then you can choose if you want to stay in this study. You may be asked to sign a new form if you choose to stay in the study.

Will you benefit from the study?

There will be no direct benefit to you from participating in this study. You will receive information on your health from the assessments and tests performed during the study. The study doctor will discuss with you the results of any examinations and tests, and may give you health-related instructions and guide you to a healthcare provider for further assessments and treatment, if needed. The study results may be used to help others in the future.

Will you be paid for your time and effort?

You will get $_50_ for each completed study visit, for your time and effort. If you do not finish the study, we will compensate you for the visits you have completed. You will get a travel stipend of $_100_ total, if you complete all study visits. You may be asked to fill out a tax form with your Social Security or Taxpayer Identification Number depending on the amount and method of payment. If your payment will be sent to your house in the mail and could be seen by others in your household you can choose not to be compensated. You can decline payment if you are concerned about confidentiality, or you can talk to the study team if there are other ways to be compensated.

What are your other options?

There is an alternative: you do not have to be in the study. Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns.

How will your private information be protected?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you) may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data from this study may be useful for other research being done by investigators at Emory and its affiliates Saint Joseph and Johns Creek or elsewhere. To help further science, we may provide your de-identified data to other researchers. If we do, we will not include any information that could identify you. If your data is labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

We will use your data only for research. The data will be shared with Blue Earth Diagnostics Ltd, which is a company sponsoring this study. We will not sell your data. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

In general, we will not give you any individual results from the study . If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Medical Record

If you have been an Emory and Saint Joseph's/Johns Creek's Hospital patient before, then you already have an Emory and Saint Joseph's /Johns Creek's Hospital medical record. If you have never been an Emory and Saint Joseph's /Johns

Creek's Hospital patient, you do not have one. An Emory and Saint Joseph's/Johns Creek's Hospital medical record will be made for you if an Emory and Saint Joseph's/Johns Creek's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Saint Joseph's/Johns Creek's Hospital medical record you have now or any time during the study.

Emory and Saint Joseph's/Johns Creek's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Saint

Joseph's/Johns Creek's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and **may or may not be placed** in your medical record. For this study, those items include:

- rhPSMA-7.3 (^{18}F) PET scan results (besides basic documentation of scan completion).

Tests and procedures done at non-Emory and Saint Joseph's/Johns Creek's Hospital places may not become part of your Emory and Saint Joseph's/Johns Creek's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

The data collected during this study, including your personal data, may be further used in analyses by the Sponsor or other researchers to answer additional scientific questions related to the study procedure/prostate cancer. Sponsor will take appropriate measures to protect your information and will only use and share coded data for such additional research.

In Case of Injury

If you believe you have become ill or injured from this research, you should contact Dr. David Schuster at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory, Johns Creek Hospital and Saint Joseph's Hospital will help you to get medical treatment. Neither Emory, Johns Creek Hospital or Saint Joseph's Hospital nor the sponsor have set aside money to pay for this medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

For Emory and Saint Joseph's Hospital, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory and Saint Joseph's Hospital employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

Withdrawal from the Study

Taking part in this study is your choice. The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you. Your decision will not result in any penalty or loss of benefits to which you are entitled.

If you choose to take part, you may change your mind and choose to leave the study at any time for any reason.

The study doctor can withdraw you from the study at any time if he or she feels it is in your best interest or if you cannot meet the study requirements.

Your participation in the study may also be stopped by the Sponsor or by the regulatory authorities or an independent ethics committee or Institutional Review Board (IRB) at any time without your consent. In this event, the reason(s)

for stopping the study will be explained to you, and you will be given advice about continued care for your condition, if this is appropriate.

If you leave (or withdraw from) the study, you will be asked to go through study withdrawal procedures detailed below and information about you will be handled as detailed below.

If you withdraw voluntarily or are withdrawn involuntarily after rhPSMA-7.3 (18F) PET scan, your study doctor will ask you to come to the study center for a follow-up visit to review your health. You have the right to choose not to take these tests and examinations.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, authorized personnel from the Sponsor and its representatives, regulatory authorities such as FDA, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:

By signing and dating this form, you consent to the study doctor and study staff collecting and using your personal and study data for the study.

- Personal data include: your gender, your ethnic origin, your date of birth (day, month and year, information on your physical or mental health or condition.
- Study data are information collected from you including results from the tests and examinations performed during this study.

By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The study doctor, authorized personnel from the Sponsor and its representatives, regulatory authorities such as FDA, and members of the ethics committees will be able to inspect confidential data that identify you by name under certain circumstances. This will be done without violating your confidentiality to the extent permitted by the applicable laws and regulations.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Other researchers and centers that are a part of this study.
    - Government agencies that regulate the research including Office for Human Research Protections, Food and Drug Administration.
    - Public health agencies.
    - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: David Schsuter, MD, Division of Nuclear Medicine and Molecular Imaging, Department of Radiology and Imaging Sciences, Emory University Hospital, 1364 Clifton Road NE, Room E152, Atlanta, GA 30322, Dene Anastasia Voisin, CRC II, and/or Bridget Fielder, Department of Radiology and Imaging Sciences, Emory University, 1365 Clifton Road, Clinic A, AT 600, Atlanta, GA 30322.

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Once you have withdrawn your consent for participating in the study, no further data will be collected about you for the purposes of this study.

A copy of this ICF will be available in either one of the following public federal websites:

- http://www.ClinicalTrials.gov or
- Docket folder on Regulations.gov (docket ID: HHS-OPHS-2018-0021)

Other Items You Should Know about Your Privacy

Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. David Schuster (Principal Investigator) at [redacted], Dene Anastasia Voisin (Study Coordinator) at [redacted], and/or Bridget Fielder (Study Nurse) [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

This study has been reviewed by an ethics committee to ensure the protection of research participants. If you have questions about your **rights as a research participant**, or if you have **complaints** about the research or an issue you would rather discuss with someone outside the research team, contact the Emory Institutional Review Board at [redacted] or [redacted]

To tell the IRB about your experience as a research participant, fill out the Research Participant Survey at https://tinyurl.com/ycewgkke.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Print your name, **sign**, and **date** below if you choose to be in this research study. You will not give up any of your legal rights by signing this form. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____
Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion **Date** **Time**