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Department/Section of *Hematology and Oncology*

EVALUATING THE POTENTIAL OF ADRB2 BLOCKERS AS THERAPY FOR PROSTATE CANCER

Informed Consent Form to Participate in Research
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INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are having a prostate biopsy or prostatectomy as a part of your normal care as indicated by your doctor. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out how reducing stress by using medication changes your cancer cells. Epinephrine, a molecule your body makes when you are stressed, can prevent cancer cells from dying in laboratory experiments. The study is designed to determine how the signals in cells that cause survival and death are affected by certain drugs like propranolol. Propranolol is FDA approved for use in hypertension, angina and anxiety.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 60 people will take part in this study. The study will be conducted only at Wake Forest Baptist Medical Center and all 60 people will take part at this location.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. Group 1 will involve taking propranolol prior to prostate biopsy or Group 2 will involve prostate biopsy only. You will have an equal chance of being placed in any group as a part of the research study, when you come to the clinic or hospital for your prostate biopsy or prostatectomy, you will fill out 2 stress surveys so we can assess how you are feeling and depending on which group you are randomized to, you may be asked to take a propranolol tablet (40 mg) 2 hours before you have your procedure. You will also provide approximately 2 teaspoons of blood prior to your procedure to test plasma epinephrine level and propranolol level. You will remain at the facility 4 hours post the dose of propranolol, to make sure your blood pressure is not too low. The prostate biopsy itself and any biopsy -related procedure outside of those mentioned above, are not a part of the research. This is a part of your care. However, a small sample of your prostate tissue will be used for research.

If you take part in this study, you will have the following tests and procedures:

Prostate biopsy or prostatectomy will be performed as a normal part of your care (standard of care). Your doctor would have already recommended this procedure, and you should be scheduled or will be scheduled to have it done.

On the day of your procedure, approximately 2 teaspoons of blood will be taken for research.

You may be asked to take a medication called propranolol, a 40mg tablet, by mouth, one time, 2 hours before your procedure. This is a part of the research study.

Storage of Biological Tissue

If you agree to participate in this study, we will draw two teaspoons of blood and use some of the removed prostate tissue for future research. This sample will be kept, used for this study and remaining portions may be used in future research to learn more about other diseases. Your sample will be obtained at the Comprehensive Cancer Center at Wake Forest University Baptist Medical Center. The sample will be stored ***In the Tumor Tissue Core Laboratory*** and it will be given only to researchers approved by Ashok Hemal, M.D. or George Kulik, D.V.M, Ph.D.

Tumor Tissue Core

An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research.

Your blood and tissue (prostate) sample will be stored de-identified, which means that no identifying information will be stored with it. Researchers will not know the name, date of birth, medical record number, social security number, etc., of the person who donated the sample.

The research that may be performed with your blood/prostate sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood /prostate sample will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/prostate sample will not affect your care.

Your blood/prostate sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

How Long Will I Be in the Study?

This study is only 1 day, which is the day of your prostate biopsy or prostatectomy.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the propranolol we are studying include:

Risks associated with the stress surveys:

As part of this study, you will be asked questions about how you are feeling emotionally. Filling out this form may increase those feelings you are being questioned about.

Risks of Propranolol

Below are side effects and how common they are that have been observed in people while taking propranolol. You will only receive 1 dose of this medication.

Common side effects of propranolol:

- Feeling Weak
- Low Energy

Infrequent side effects of propranolol:

- Bronchospasm
- Dizziness
- Diarrhea
- Throwing up or feeling like throwing up
- Stomach Cramps

Rare side effects of propranolol:

- A Spasm of the Larynx
- Abnormal Heart Rhythm
- Abnormally Low Blood Pressure
- Acute Respiratory Distress Syndrome
- Blood Pressure Drop Upon Standing
- Complete Stoppage of the Heart
- Confusion
- Constriction of Blood Vessels of the Extremities
- Hallucination
- Hives or rash
- Insufficient Blood Supply to the Colon
- Large Purple or Brown Skin Blotches
- Life Threatening Allergic Reaction
- Slow Heartbeat
- Throat Irritation
- Fever

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Risks of Blood Draws

You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

This is not a treatment study. Your alternative is to not participate in this study.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a

court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by Wake Forest Baptist Health Comprehensive Cancer Center which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a research study. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive a $50 gift card as payment for taking part in this study and parking will be validated for research related visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by The Comprehensive Cancer Center of Wake Forest Baptist Hospital. The sponsor is providing money or other support to help conduct this study.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and

the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Ashok Hemal, M.D. or George Kulik, D.V.M, Ph.D.at [redacted] or [redacted], respectively.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** your health history, how you respond to study procedures, laboratory and other test results, and physical examinations.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.
We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis

centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

1) Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

2) Representatives from government agencies such as the US Food and Drug Administration (FDA).

3) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

4) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished
You can tell Ashok Hemal, M.D. or George Kulik, D.V.M, Ph.D. that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Ashok Hemal, M.D. or George Kulik, D.V.M, Ph.D.
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be at the Principal Investigator's discretion and may include any medical reason the Investigator may find it inappropriate for your care to be in the study.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Ashok Hemal, M.D. or George Kulik, D.V.M, Ph.D.at [redacted] or [redacted], respectively.

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm