PRINCIPAL INVESTIGATOR: William D. Figg, PharmD, MBA

STUDY TITLE: A Bioequivalence Study to Compare Capsule and Liquid Formulations of Enzalutamide After Single Dose Administration Under Fasting Conditions in Prostate Cancer

STUDY SITE: NIH Clinical Center

Cohort: *Affected Participants*

Consent Version: *03/11/2020*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: William D. Figg, PharmD, MBA
Phone: 240-760-6179
Email: figgw@mail.nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Enzalutamide is a modern hormonal therapy that is approved by the FDA for the treatment of metastatic prostate cancer. Unfortunately, the current 4 pills required to deliver the desired 160mg treatment causes problems for patients. Due to the number of capsules necessary for the current enzalutamide therapy, it can be difficult for cancer patients that already have multiple drugs to take. Additionally, some patients may have difficulty with swallowing, therefore an alternate method of oral administration is necessary.

For these reasons, this study will test the new way to give enzalutamide by mouth using a test formulation of liquid enzalutamide removed from the standard gelatin capsules compared to

standard 4 gelatin capsules of enzalutamide to find out whether they are handled by the body in the same way.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

Because you have been diagnosed with prostate cancer, you are invited to take part in this clinical research.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 14 men with prostate cancer will be enrolled in this study.

DESCRIPTION OF RESEARCH STUDY

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

Before you begin the study

Certain criteria have been established to ensure that you are a medically appropriate candidate for this trial. These criteria also make sure that the results of this study can be used to help make decisions about treating other patients. Before beginning the study, you will need to have tests and/or procedures to help your doctor decide whether you can take part in the study. This is called screening. Most of the exams, tests, and procedures you will have are part of regular cancer care. However, there are some extra tests that you will need to have if you take part in this study. If you have had some of them recently, they may not need to be repeated.

These tests include:

- Review of your previously collected tissue or a laboratory report to confirm your diagnosis
- History and physical evaluation including vital signs
- Routine blood tests
- ECG
- Testosterone and prostate-specific antigen (PSA) levels
- ECOG performance status

You will be removed from the study if these tests indicate that you may not be a suitable candidate.

During the study

If you are eligible for the study, some of the tests that were performed for screening may need to be repeated depending on when they were done. Your study doctor will let you know. In addition, you will have a routine urine test. You will be randomized (selected by a procedure similar to a flip of a coin) to receive treatment of either standard capsule enzalutamide treatment (Arm A) or the test liquid formulation enzalutamide (Arm B). This is period 1 of the study. In period 2 of the study, 42 days after you have received your first dose of enzalutamide, you will switch arms and receive a second dose. That is, if you were initially assigned to take capsules in period 1, you will take the liquid in period 2. If you were initially assigned to take the liquid during period 1, you will take the capsules in period 2.

On the days (Day 1 of each period) you receive enzalutamide, you will be admitted as an inpatient to the NIH Clinical Center and will be asked to stay for about 24-36 hours. After receiving

enzalutamide, we will sample your blood periodically over the next 24 hours. You will be required to avoid eating or drinking for 2 hours before taking the enzalutamide and for 2 hours after taking the enzalutamide. You may resume your normal eating and drinking patterns 2 hours after taking the enzalutamide. On the day you take the liquid formulation, you will be asked to fill out a questionnaire, it will take 10 minutes to complete.

At the end of each study period, we will repeat blood and urine tests, history, physical exam as well as the ECG. You will return to the Clinical Center on Day 3, Day 8 and Day 42 of each period for additional blood draws. For these visits you will be at the Clinical Center as an outpatient for about 4 hours.

BIRTH CONTROL

Your study doctor will discuss the risks to unborn children for the drugs used in this study. The effects of the study drugs, if any, on unborn children are unknown. If your partner is capable of becoming pregnant and you wish to participate in this study, then you must use a medically acceptable method of birth control while you are receiving study medications and for 3 months after your last dose of study medication.

If your partner becomes pregnant during the course of treatment, you must inform your doctor immediately. Your doctor will ensure that you and your partner receive information about options available to you in relation to pregnancy and that you and your partner are fully supported in whichever option you chose.

Effective forms of birth control for you and your partner include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

Possible side effects of enzalutamide*:*

Likely:

- Ankle swelling.
- Fatigue
- Headache
- Hot flashes
- Diarrhea
- Low blood counts
- Back pain
- Upper respiratory tract infection

Less Likely:

- High blood pressure
- Dizziness, anxiety
- Dry skin

- Blood in urine
- Jaundice
- Weakness of muscles

Rare but Serious:

- Seizures
- *Posterior reversible encephalopathy syndrome (PRES)

*There have been rare reports of posterior reversible encephalopathy syndrome (PRES), a rare, reversible condition involving the brain, in patients treated with enzalutamide. If you have a seizure, worsening headache, confusion, blindness or other vision problems, please contact your doctor right away. Your doctor will stop enzalutamide if you develop PRES.

Other Risks Related to Research Tests

The study treatment may involve risks to you that are currently unknown. Your cancer may not get better or may become worse while you are in this study.

Blood draws: There may be some side effects associated with the procedures for drawing blood in this study, but the person drawing your blood will attempt to minimize this discomfort. Side effects include pain and bruising in the area where the needle is inserted, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) is a risk.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to determine whether your body handles the experimental liquid formulation of enzalutamide similarly to the standard gel capsule, and to evaluate if it is safe and tolerable. You will not receive personal, medical benefit from taking part in this study. However, the knowledge gained from this study may help others in the future who have cancer

ALTERNATIVE APPROACHES OR TREATMENTS

What other choices do I have if I do not take part in this study?

Instead of being in this study, you have these options**:**

- Choose to not participate
- Take part in another study

Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if you have side effects from the treatment that your doctor thinks are too severe

In this case, you will be informed of the reason therapy 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. 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.

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.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens 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 do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be compensated for your time and inconvenience as follows:

- $20 for the pre-dose PK sample
- $20 for the 30 minutes post dose PK sample
- $20 for the 1 hour post dose PK sample
- $20 for the 2 hours post dose PK sample
- $20 for the 4 hours post dose PK sample
- $20 for the 8 hours post dose PK sample
- $20 for the 24 hours post dose PK sample
- $20 for the 48 hours post dose PK sample
- $20 for the 168 hours (Day 8) post dose PK sample
- $20 for the Day 42 post dose PK sample

For each PK sample, 4 mL will be drawn one time for a total of 10 samples and 40 mL (just over 8 teaspoons) of blood.

Total compensation of $200 will be in the form of a check issued through standard NIH compensation procedures.

If you are unable to finish the study, you will receive no future compensation, but prior compensation for the parts you completed will not be taken back.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Review Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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 NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

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.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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: William D. Figg, 240-760-6179, figgw@mail.nih.gov. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.