PRINCIPAL INVESTIGATOR: William D. Figg, PharmD, MBA

STUDY TITLE: A Pilot Study to Evaluate the Effects of Castration on the Pharmacokinetics of Zolpidem After Single Dose Administration in Men with Prostate Cancer Undergoing Androgen Deprivation Therapy Compared to Normal Healthy Females

STUDY SITE: NIH Clinical Center

Cohort: *Affected Participants*

Consent Version: *02/08/2022*

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: William D. Figg, PharmD, MBA

[redacted]

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.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

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?

Insomnia, which is a condition associated with difficulty sleeping, is a common problem for many, and recently zolpidem has been widely prescribed. However, some participants feel the effects of the drug for a long time, mainly drowsiness when they wake up the following morning. Zolpidem is currently approved for the treatment of participants who have difficulty sleeping. Because women and elderly more often report difficulty with the sleep, studies need to be conducted to further study the effects of zolpidem.

Women have reported more adverse effects from zolpidem than have men. The studies that followed, showed that levels of drug in the blood in women are higher than those in men. Further studies revealed that zolpidem stays longer in the bodies of both women and elderly. A possible conclusion is that the effects of the drug depend on male hormones which are usually higher in younger males. As a result, the recommended dose of zolpidem has been reduced to half for women and elderly. In this study, we would like to further study how zolpidem affects bodies of males who have been diagnosed with prostate cancer before they are castrated and after. We will compare these results to healthy women.

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

You have been asked to take part in this study because you are either a man who has been diagnosed with prostate cancer and is planning to receive androgen deprivation therapy (ADT) or a healthy woman.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

We are planning to enroll up to 15 males with prostate cancer and up to 15 healthy female volunteers for a total of 30 participants.

DESCRIPTION OF RESEARCH STUDY

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

Before you begin the study

Before you begin this study, you will have several exams and tests to make sure you are eligible. Most of the tests needed would be part of your routine medical care. They include blood tests, a physical examination and an EKG. If you are a male participant, we will need a sample of your tumor tissue left over from a previous surgery or a report from your doctor that confirms you have a prostate cancer. If you are a woman who can become pregnant, you will also have a pregnancy test.

If it is determined that you are not eligible, you will be removed from the study. Otherwise, you will continue with the assessments described below.

During the study

All participants

You will have to be admitted to the Clinical Center on Day 1 in the evening and spend a night at a hospital. You should have an early dinner, at approximately 6 pm, and fast for at least four hours before taking zolpidem. You will receive a 5 mg zolpidem tablet on an empty stomach at approximately 11 pm. We will then collect your blood to measure the amount of the drug in your blood starting at 15 minutes after you have taken zolpidem. We will collect blood every 15 - 30 minutes for two hours, and after that we will collect blood every hour for three hours. We will collect the last blood sample eight hours after you have taken zolpidem.

You will be discharged from the hospital once the sampling is complete.

Male participants only

You will receive androgen deprivation therapy (ADT) as part of standard treatment for your cancer here are NIH. Treatment with ADT is not experimental. Your doctors will describe your treatment plan to you in detail before asking you to sign this consent form. After this has been completed, we will measure the levels of testosterone in your body. When these levels drop to a certain point, you will have the same tests performed before you received the first dose of zolpidem repeated and you will be re-admitted to the hospital for a second 5 mg dose of zolpidem followed by blood collection as described in the section above. The same fasting instructions and collection times will apply.

When you are finished taking the drugs

Each time you are discharged from the hospital, a member of a research team will contact you one day later to ask about any symptoms that you have.

Study Chart

Procedure	Screening/ Baseline	Period 1		Period 2*	
		Day 1	Day 3	Day 1	Day 3
Blood tests, physical examination and EKG	X	X		X	
Blood collection to measure levels of zolpidem		X		X	
You will be asked about symptoms you are experiencing		X	X	X	X
You will be asked about medications you are taking		X		X	
Follow up phone call			X		X

* applies to male participants only

PREGNANCY

If you are a woman who is pregnant or had a labor or miscarriage within 12 weeks of enrollment onto this study, you may not take part in the study. If you are breastfeeding at time you enroll onto this study, you will need to discard breastmilk for 24 hours following zolpidem.

RISKS OR DISCOMFORTS OF PARTICIPATION

The discomforts involved will be related to the withdrawing of blood from a vein, through a needle ("venipuncture"), which will be performed by standard procedures. The risks of venipuncture include minor discomfort and a rare risk of bruising, infection, or dizziness. The samples may be stored for a long period of time without any additional identifying information.

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

Likely	Less Likely	Rare
• Abnormal movements • Confusion • Elevated feeling of well being • Headache • Inability to sleep • Head spinning • Increased acidity in stomach • Hiccups • Nausea • Lung infection • Double vision • Abnormal vision • Urinary tract infection	• Increased sweating • Pale skin • Feeling dizzy when you rapidly stand up from sitting or lying down • Fainting • Swelling • Falling • Body weakness • Fever • Trauma • Disease of brain blood vessels • Increased blood pressure • Increased heart rate • Agitation • Anxiety • Decreased cognition • Feeling separated • Difficulty concentrating • Slurred speech • Uncontrolled change of emotions • Hallucination • Reduced sensation to touch • Illusion • Leg cramps • Migraine • Nervousness • Burning in limbs • Sleeping (after daytime dosing) • Speech disorder • Feeling unconscious • Body shivering • Anorexia • Constipation • Dysphagia	• Inability to maintain eye focus • Disturbed salivary secretion • Flushing • Glaucoma • Swelling • Low blood pressure • Impotence • Increased saliva • Pain in rectum • Allergic reaction • Increased allergy • Anaphylactic shock • Hot flashes • Abnormal tests of the red blood cells • Pain • Restless legs • Chills • Tolerance increased • Weight decrease • Chest pain • Abnormal heart rhythm • Inflammation of arteries • Circulatory failure • Abnormal electrical activity in heart • Increased blood pressure • Heart attack • Inflammation of veins • Clot in lungs • Swelling of lungs • Protruded veins • Increased heart rate • Loss of balance • Abnormal thinking • Aggressive reaction • Lack of interest

Likely	Less Likely	Rare
	• Gas • Irritation of stomach and intestines • Vomiting • Infection • Abnormal function of liver • Increased liver enzymes • Increased blood sugar • Thirst • Arthritis • Menstrual disorder • Inflammation of vagina • Bronchitis • Coughing • Shortness of breath • Stuffy nose • Skin itching • Eye irritation • Eye pain • Inflammation of eye sclera • Taste alterations • Ringing in the ear • Inflammation of the bladder • Inability to control bladder	• Appetite increased • Decreased sexual desire • Delusion • Dementia • Feeling disconnected or detached from your body and thoughts • Impaired speech • Feeling strange • Loss of muscle movement • Low muscle tone • Feeling uncontrollably excited • Change in personality • Nerve pain • Inflammation of nerves • Numbness of fingers and toes • Mental disturbances • Panic attacks • Muscle weakness due to nerve damage • Personality disorder • Sleepwalking • Suicide attempts • Muscle spasms • Yawning • Inflammation of intestines • Belches • Spasms of esophagus • Gastritis • Hemorrhoids • Intestinal obstruction • Rectal bleeding • Tooth caries • Low red blood cells count • Abnormal white blood cells count • Blood clots • Collection of pus

Likely	Less Likely	Rare
		• Cold sores • Painful rash caused by herpes zoster virus • Inflammation of middle ear • Inflammation of outer ear • Increased liver enzymes • Inflammation of joints • Increased cholesterol levels • Increased fats in blood • Increased liver enzymes • Increased kidney function test • Joint wear • Muscle weakness • Leg pain • Inflammation of tendons • Breast lumps • Breast cancer • Breast pain • Spasms in bronchi • Low entry of air into lungs • Bleeding from nose • Low oxygen levels • Laryngitis • Pneumonia • Acne • Blisters on the skin • Skin inflammation • Infection of hair follicles • Injection-site inflammation • Reaction to sun burn • Hives • Inflammation of eye conjunctiva • Ulceration of the cornea of the eye

Likely	Less Likely	Rare
		• Abnormal eye tearing • Alterations in smell • Lightening visual effects • Acute renal failure • Painful urination • Excessive urination at night • Frequent urination • Kidney scarring • Kidney pain • Inability to urinate

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

There will be no direct benefit to you by participating in this study and no research results will be returned to you.

ALTERNATIVE APPROACHES OR TREATMENTS

You will receive ADT treatment as part of this protocol for your disease. You can receive ADT without participating in this study.

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**:**

- Getting treatment or care for your cancer without being in a study.
- Taking part in another study.
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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 you are not eligible to participate in the study
- when you complete all study procedures
- if you have side effects from the treatment that your doctor thinks are too severe
- if he/she believes that it is in your best interest

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.

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.

Study participants will be compensated for each blood sample collected for PK analysis as follows:

- $20 for the 1st pre-dose PK sample
- $20 for the 2nd (0.25 hours) PK sample
- $20 for the 3rd (0.5 hours) PK sample
- $20 for the 4th (1 hour) PK sample
- $20 for the 5th (1.5 hours) PK sample
- $20 for the 6th (2 hours) PK sample
- $20 for the 7th (3 hours) PK sample
- $20 for the 8th (4 hours) PK sample
- $20 for the 9th (8 hours post dose) PK sample

For each PK sample, 4 mL will be drawn one time for a total of 9 samples and 36 mL (just over 7 teaspoons) of blood.

Total compensation of up to $180 will be in the form of a check issued through standard NIH compensation procedures.

You will only be compensated if samples are collected solely for research purposes.

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, [redacted], figgw@mail.nih.gov. You may also call the NIH Clinical Center Patient Representative at [redacted], or the NIH Office of IRB Operations at [redacted], 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 should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

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: _____.