CONSENT FOR CANCER RESEARCH

Project Title: The Association between HSD3B1 Genotype and Steroid Metabolism in Normal and Prostate Cancer Tissue of Men with Intermediate and High-risk Prostate Cancer Undergoing Radical Prostatectomy after Treatment with Apalutamide and Leuprolide.

Principal Investigator: Moshe Ornstein, MD, MA 216 445-6592

Coordinating Center: Cleveland Clinic
Funding/Drug Support: Janssen Scientific Affairs, LLC

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC).

One or more of the Investigators conducting this study serve as consultants for the company that makes products used in this study. These financial interests are within permissible limits established by the local institutional Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask you study doctor or call the Cleveland Clinic Institutional Review Board at (216) 444-2924.

1. Introduction

We are asking you to participate in a research study. The purpose of this document is to summarize your discussion with the research team and provide you with written information to help you decide whether you want to participate in research. Your decision is completely voluntary.

Your treating doctor may also be an investigator on this research study. If so, your doctor will have an interest in both your welfare and in the research study. You are not required to take part in this research study offered by your doctor. You may ask for a second opinion from another doctor who is not linked to this study. If you choose not to be in this study, the quality of your regular medical care will not be affected.

Please ask any questions you may have about the study or this consent form before signing it. Please take your time to make your decision. You will be given a copy of this form to keep.

2. Purpose

This is a research study to test Apalutamide given in combination with Leuprolide acetate in men diagnosed with high-risk prostate cancer who have already selected to have surgery to remove their prostate gland as part of their treatment plan. The main purpose of this study is to determine how tumors make androgens (male hormones), which makes these tumors more aggressive and resistant to hormonal therapy and how a short period of treatment with Apalutamide and

leuprolide acetate prior to surgery can affect the production of these hormones in normal and malignant prostate tissue.

Apalutamide is an oral agent (tablet) that has been approved by the FDA for different types of prostate cancer. Some of these types depend on the status of your prostate cancer when you are taking the drug, and factors that make up your cancer. These factors could involve the spread of your cancer (known as metastasis) and how your body responds to hormones related to your prostate. Please speak with your physician if you have additional questions regarding the setting of prostate cancer where Apalutamide is FDA approved. Apalutamide is still considered investigational in this trial because of its use prior to surgery.

Apalutamide works by blocking androgen receptor (AR). Androgen receptor (AR) is like an antenna that when activated by androgens (male hormones) leads to a signal; in the case of prostate cancer, more cancer growth. Leuprolide acetate is an injection, often given intramuscularly (that is in your buttock region) that is FDA approved for the treatment of men with prostate cancer. Leuprolide acetate blocks the production of the male hormone called testosterone in your testicles by inhibiting the signal transmission in your brain responsible for testicular function. The pre-surgical use of Apalutamide plus leuprolide is not a standard treatment for men with prostate cancer.

Because the production of these androgens (male hormones) can be related to one's genetic make-up, this research study will include men with three known genomic variations of a key enzyme in the adrenal gland (glands on top of each kidney also responsible for the production of androgens) called ***HSD3B1.***

Based on the frequency of these genomic variations, we estimate that approximately 120 men will be screened and ultimately a sample size of 57 patients will enroll on this clinical trial. Due to logistical restrictions, and to account for patient drop out/withdrawal, up to 80 male patients may take part in this trial in order to capture all objectives and support the above sample size.

Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

How many people will take part in the study?
A sample size of 57 people will take part in this study. Up to 80 male patients may take part in the study to achieve this sample size.

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

If you decide to take part of this study, the following will occur:

Before you begin the study
You will need to have the following exams or tests to find out if you can be in the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- You will be asked to supply a complete list of your current medications to the study doctor. This includes over-the-counter medications and herbal supplements. Some medications may interact with Apalutamide and it is important that your study doctor and prescribing physician be aware of any potential risks so that they can prescribe alternative medications as necessary. If you do not already do so, please consider carrying a list of your medications at all times.
- Medical History
- Diagnostic prostate biopsy report
- HSD3B1 genotype variant analysis
- Blood sample collection to understand how tumors use and make hormones
- Physical examinations, including height and weight
- Vital signs
- Performance assessment of your ability to do your daily activities
- Routine blood tests (2 tablespoons), including complete blood count, blood chemistry, testosterone level, and Prostate Specific Antigen level. (Also known as “PSA” this is a protein made by prostate cancer cells.) Blood will also be used to obtain DNA and determine baseline hormones (androgens) present in blood for research purposes.

During the study
If the exams and tests show that you can be in the study, and you chose to take part, then you will take one intra-muscular (buttock region) injection of leuprolide acetate and also will be asked to take Apalutamide for about 28 days before your prostate surgery. Apalutamide is an oral medication, and you will take 4 tablets (60 mg) by mouth once a day, with or without food. The tablets should be swallowed whole with liquid. You should receive sufficient medication supply while on study.

The study medication must be stored at room temperature with the cap on tightly and should not be refrigerated. If you miss a dose of study medication, do not try to make it up.

The study medication must be kept out of the reach of children or persons of limited capacity to understand. The study medication must be taken only by you.

The study medication bottle will also include a small sachet, called a desiccant. You should not eat or remove this sachet. It has been placed in the bottle to protect the study medication. You should store your study medication in the study bottle and not place your pills in separate container, such as a pill container. If you have any questions your study doctor will answer them.

Tests and Procedures:

During the week prior to your prostate surgery, you will need to come for an office visit to be evaluated before your surgery. At this visit you will need the following tests and exams as a part of your regular cancer care.

- You will be asked to supply a complete list of your current medications to the study doctor. Physical examinations, including height and weight
- Medical History
- Vital signs
- Performance assessment of your ability to do your daily activities
- Routine blood tests, including complete blood count, blood chemistry, and tests to ensure that clotting function are normal.
- Additional blood tests to look at the level of testosterone, other natural steroids, and PSA in your blood.
- Report any side-effects you are having to your study doctor.
- You may also have an MRI of your prostate (if you didn't have one done recently) to measure the size of the cancer in your prostate and the location of the tumor. Some treating doctors believe ordering this test is important prior to surgery however it is not considered standard or care. Although desired, MRI of your prostate is not mandated for this clinical research study and will be done at the discretion of your treating doctor.

If all the test results and your medical evaluation are satisfactory, you will have your prostate removed on the scheduled date.

Day of prostate surgery

After removal of your prostate by the surgeon, the prostate tissue will be sent to the pathology department for further evaluations as part as the standard and routine management of prostate cancer specimens at the Cleveland Clinic. In addition to necessary evaluations for your routine cancer care, some small pieces of the prostate tissue and an additional sample of blood will be sent to our laboratory for the research study. The samples from your prostate tissue and the DNA from your blood will be used by researchers to determine how prostate cancer becomes resistant to hormonal therapy. Specifically, experiments will be done to evaluate how these tumors make androgens (male hormones), which is required for these tumors to grow. This includes testing how tumors change with various therapies. Although this work does not directly benefit you, it has the potential to improve the treatment of prostate cancer for the patients in the future.

Your surgical and post-surgical care will be conducted as per standard practices at the institution.

Follow up visit

After discharge from the hospital, you will need to come to the clinic for a follow up visit with your surgeon and the research study team. The study team will try to coordinate these visits for the same day, if possible. During this visit you will have the following:

- You will be asked to supply a complete list of your current medications to the study doctor. Physical examinations, including height and weight
- Vital signs
- Performance assessment of your ability to do your daily activities
- Report any side-effects you are having to your study doctor
- Routine blood tests, including complete blood count, blood chemistry, and tests to ensure that clotting function are normal.

How long will I be in the study?

You will be asked to take Apalutamide for about 28 days before your prostate surgery. You also will receive a single one-month intramuscular injection (Buttock region) of leuprolide acetate.
Your last dose of Apalutamide will be taken on the day before your surgery. When you come for your post-surgery follow up visit you will have your final evaluation before finishing your participation in this study.

Can I stop being in the study?

Yes. You can decide to stop/ withdraw from the study at any time without ramifications. Tell your study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the Apalutamide can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

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

The possible discomforts, side effects, and risks from apalutamide are not all known. Some side effects may be serious and require treatment or additional testing. This section describes common side effects from apalutamide.

There may be risks with apalutamide that are not yet known. You will be monitored carefully for side effects. During the study, the sponsor or study doctor may learn new facts about apalutamide. Your study doctor will inform you of any important new information about apalutamide. It is possible that this new information might make you change your mind about being in the study.

Side effects may be mild, moderate, serious or even life-threatening. If you experience any side effects, your doctor may give you medicines to help lessen the side effects. Some side effects may go away soon after you stop taking the study medicine. Other side effects can be serious or long-lasting.

If you experience a side effect, your doctor may temporarily hold the study drug or change the dose of the study drug to help manage the side effect. If severe side effects develop, you and your doctor may decide that it is in your best interest to stop taking the study drug.. In addition, you will be provided with the telephone numbers for people, who can answer any questions about the study, your rights as a study participant and for you to report any side effects.

Risks and side effects that are related to Apalutamide include:

Likely (>10%)	Less Likely (1– 10%)	Rare but serious (<1%)	Frequency unknown*
• Fatigue	• Itching	• Seizure	• Inflammation within the lungs that may lead to permanent damage (Interstitial lung disease)
• Joint pain (Arthralgia) or muscle spasms	• Changes in thyroid function (Hypothyroidism)		• Life-threatening rash with blisters and peeling over much of the body (Toxic epidermal necrolysis)
• Weight Loss	• Increase in cholesterol		
• Skin rash	• Increase in triglycerides		
• Fall	• Change in experience of taste (Dysgeusia)		
• Fracture	• Reduced or blocked blood flow to the heart, including heart attack (Ischemic Heart Disease, including Myocardial Infarction)		
• Increased blood pressure (Hypertension)			

- Hot Flash
- Diarrhea
- Decreased appetite**

* this is information provided voluntarily by doctors using apalutamide in routine clinical practice; not from clinical trials, from a population of uncertain size; therefore, it is not possible to estimate frequency or exclude a causal relationship to apalutamide.

** this is information provided voluntarily by doctors using apalutamide in routine clinical practice where frequency cannot be estimated; however, frequency of this event can be estimated from clinical trials and is assessed as very common.

Seizures have been observed very rarely in patients taking part in apalutamide studies. Your doctor will confirm that you have no history of seizures and will check throughout the study that you are not taking other medications that can increase your risk of seizures. Please inform your doctor of all medications you are taking and any changes in medications. If you think you might have had a seizure, or convulsion, or have lost consciousness (passed out), let your doctor know right away.

More than 1 in 10 patients have developed a rash. Some rashes may need medical attention. The rash may be confined to one area of your body or may spread across your body. Contact your doctor at the first sign of rash or any symptoms of rash (like itching) during the study. Rashes that are painful, blisters on or near the lips, eyes or genitals may need immediate evaluation by your doctor. You may be given medicines to apply to your skin or take by mouth to help the signs and symptoms of rash. Also the study medication may be temporarily held.

Scarring of the inner lining of the lung (Interstitial lung disease) has been observed in patients taking apalutamide. Inform your doctor if you have any history of lung problems. Contact your doctor right away if you experience symptoms such as shortness of breath, breathing difficulty, cough or fever.

The following paragraph only applies to you if you were enrolled in the study before December 1, 2016:

Additional testing by Janssen has found that a chemical impurity was present in very small amounts in some tablets of the study drug. You may have received study drug with this impurity. The impurity is very similar to apalutamide in chemical structure. Studies have shown that the impurity has effects on prostate cancer similar to apalutamide. It is believed that the potential side

effects of the impurity would be similar to apalutamide. The study drug has now been fully replaced with product within standard quality limits.

Leuprolide acetate has been in used for prostate cancer for more than three decades. Although it is safe and well tolerated, potential side effects from this medication are related to the suppression of your testosterone which is the main goal of using this medication. These side effects are also dependent on the length a patient is on treatment and could include:

Likely (>10%)	Less Likely (1– 10%)	Rare but serious (<1%)
• Fatigue • Fluid retention • Nausea • Skin rash • Abdominal pain • Flu-like symptoms • Joint pain • Change in bowel habits • Hot Flashes • Weight gain • Decrease libido • Injection site reaction	• Chest pain • Increased heart rate • Nervousness • Lack of appetite • Breast tenderness • Increase in blood pressure • Increase in cholesterol • Bone loss • Infections	• Decreased pumping power of the heart muscle • Hair loss • Bladder spasms

Are there any additional risks or benefits to taking part in the study?
All hospitals or clinics that do research on people have an institutional review board (IRB). This board reviews all new studies to make sure that the patient's rights and welfare are protected.

The IRB at the Cleveland Clinic has reviewed this study.

Taking part in this study may improve your condition. None of these benefits are guaranteed to happen. There may be no benefit to you by being in this study. During the study your condition may remain the same or get worse. While you are in this study, the study doctor will follow your condition closely. By taking part in the study you may help future patients.

Alternatives to Participation
Your other choices may include:
- Getting treatment or care for your cancer (including immediate surgery) without being in a study
- Taking part in another study
- One alternative is not to participate in this study.

You should discuss treatment alternatives with your physician

Certain drugs may interact with Apalutamide

Some medications can affect the level of study drug in your blood. You need to tell your study doctor of all the medications and supplements (e.g., herbs, vitamins) you are taking, as well as any changes in medications. Your study doctor can determine if these medications or supplements interact with the study drug.

Surgery related risks:

Because of participating in this study, you might have an increased risk for the following side effects of surgery. You should discuss these with your study doctor, your urologic surgeon and your regular healthcare provider.

The potential risks associated with prostate surgery, regardless of participating in this trial, include but are not limited to:

- Infection
- Bleeding
- Tissue-organ damage
- Bowel perforation (damage to digestive organs)
- Respiratory depression (from intravenous sedatives)

Reproductive risks:

The effect of the study drug on your semen is unknown. To avoid risk of drug exposure to your partner through the semen (even in men with vasectomies (tubes that carry semen from the testicles have been cut), patients must use a condom during sexual activity while on study and drug and for 3 months following the last dose of study drug.

Apalutamide may cause harm to the unborn child. From when you start taking the study drug until 3 months after your last dose of study drug, you must use a condom and another effective method of birth control when you have sex with a woman of child-bearing potential. The type of birth control you use must be discussed with, and approved by, the study doctor before you begin the study. This is done to prevent pregnancy. If your partner becomes pregnant in the time between when you start taking the study drug until 3 months after your last dose of drug, you must tell the study doctor immediately.

Donation of sperm is not allowed during the study and for 3 months following the last dose of study drug.

You should advise your study doctor if you father a child while participating in the research project. The doctor will advise you on any appropriate medical attention for your partner should this be necessary. The study doctor may ask you and your partner to allow him/her to collect information about her pregnancy and the health of the baby.

Risks of MRI

If you take part in this research, you might have an MRI (magnetic resonance imaging and/or magnetic resonance spectroscopy). If done, the MRI can be completed at any time prior to start Apalutamide and leuprolide acetate.

MRI uses a magnet and radio waves to make images (pictures) of the inside of the head and/or body. There have been no ill effects reported from exposure to the magnetism or radio waves used for these studies; however, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal that may cause injury to you. We will ask you about metal within your body (this includes certain dyes used in tattoos and body piercings). If there is any question about potentially hazardous metal within your body, you will not be able to participate in this research study. We will also keep the MRI room locked so that no one carrying metal objects enters the room while you are having this scan performed. In addition, the MRI scanner makes a loud buzzing noise that could affect hearing ability. You will be provided with earplugs and assistance in their use in order to protect your hearing. You will be able to communicate with the scanner technologist using an intercom and/or signaling device. The technologist will try to help you feel as comfortable as possible in the scanner. You can ask to stop the scan and be removed from the scanner at any time by using the intercom or signaling device.

There is a very slight risk of an allergic reaction if contrast material is injected. Such reactions usually are mild and easily controlled by medication. If you experience allergic symptoms, a radiologist or other physician will be available for immediate assistance.

Gadolinium-based contrast agents (dyes) may increase the risk of a rare but serious disease called nephrogenic systemic fibrosis in people with poor kidney function that will further hurt their kidneys. Nephrogenic systemic fibrosis triggers thickening of the skin, organs and other tissues. There is no effective treatment for this debilitating disease.

Loss of personally identifiable genetic material:

Your prostate tissue and DNA will be stored in a secured area with access limited to the research staff and personnel assigned to tissue and DNA storage laboratories. However, it is possible that tumor tissue, DNA, or information regarding either will be lost.

Genetic Studies

The privacy of the research information generated from your DNA (gene) sample will be protected as much as possible. If this information were released to you, your family, or third parties, there could be adverse psychological effects for you or your family members. There could also be

undesirable effects on you or your family members' ability to obtain a job or insurance. In order to minimize these risks, every effort will be made to keep all genetic research information obtained from your blood sample confidential. But absolute confidentiality cannot be guaranteed.

The results of the analysis of your DNA done as part of this study will not be given to you. Your DNA (genes), or your cells that can be used to make your DNA, will be stored for research purposes.
Your DNA samples may be used for any scientific purpose involving this project and/or any other project.

At any time, you may ask to have your samples that were collected for research testing be destroyed by contacting the study doctor. If you do this, all of the remaining samples will be destroyed so that no more research can be done. However, any information collected from your samples before your request to destroy them will be kept by the Cleveland Clinic. If you decide to stop participating in the study, but do not request destruction of your samples, Cleveland Clinic may continue to use your samples for this project as well as any other projects.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), effective May 21, 2010, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Psychological or Social Risks Associated With Loss of Privacy

- Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all the safety measures that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify your relatives.

- While neither the public nor the controlled-access databases developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or Social Security number, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a relative) in another database and be able to identify you. It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.
- Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a relative) carry a genetic disease.

The information obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, locked file at Cleveland Clinic, and will not be disclosed to third parties except with your permission or as may be required by law. If your genetic testing information is released to an employer or insurance company, it could have an impact on your ability to acquire or maintain life, health, or long-term care insurance.

Will my 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. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- Janssen Scientific Affairs, LLC

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Moshe Ornstein, MD, MA and the research staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study sue~ as the Cleveland Clinic Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for People;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards;
- Janssen Scientific Affairs, LLC will receive your safety-related information, but it will not include PHI.

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosure-s at any time by writing to:

Moshe Ornstein, MD, MA
9500 Euclid Ave. CA-60
Cleveland, OH 44195

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study.

This Authorization does not have an expiration date.

What are the costs of taking part in this study?

The study will pay for some procedures/devices/drugs that are directly associated with this research study. This includes the Apalutamide for the duration of treatment in this study. Leuprolide is considered standard of care and will be billed to your regular insurance.

Routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. Treatments to help control side effects could result in added costs.

This includes additional imaging studies, pre-surgery evaluations and blood work, and your prostate surgery and follow up visits.

Allowing for the storage and future testing of tissue and blood samples will involve no cost to you. Your tissue will be used only for research and will not be sold. The research done with your tissue and blood may lead to the development of new products in the future, You will not receive, either now or in the future, any compensation, royalty, or any other financial benefit which might result from any product, procedure, or other items that may be developed from studying your samples or any information or data that is derived from such research.

For more information on clinical trial and insurance coverage, you can visit the National Cancer Institute's (NCI) website at

http://cancer.gov/clinicaltrials/understanding/insurance-coverage

You can print a copy of the 'Clinical Trials and Insurance Coverage' information from this website. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask NCI for a free copy.

You will not be paid for taking part in this study.

What happens if I am injured because I took part in this study?

It is important that you tell the study doctor, Moshe Ornstein, MD, MA if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 216-445-6592.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

If you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic or elsewhere; however, the Cleveland Clinic has no plans to provide free care or compensation for lost wages.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924.

Voluntary Participation

Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study contact your study doctor Moshe Ornstein, MD, MA at 216-445-6592.

For questions about your rights while taking part in this study, call the Cleveland Clinic

Institutional Review Board (a group of people who review the research to protect your rights) at 216-444-2924.

*You may also call the Operations Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only).

If you have any questions, you can ask the Principal Investigator, Moshe Ornstein, MD, MA and/or research staff.

Emergency and After-hours Contact Information

If you are a Cleveland Clinic patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

If you have questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

Where Can I Get More Information?

You may call the National Cancer Institute's Cancer Information Services at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615
You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database

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.

Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	***Date***	***Printed Name of Participant***

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____
Signature of Person Obtaining Consent	***Date***

_____

Printed Name of Person Obtaining Consent