# Research Study Informed Consent Document

**Study Title for Participants:** Testing the addition of the drugs, abiraterone acetate with prednisone and apalutamide , to the usual hormone therapy and radiation therapy after surgery for prostate cancer

**Official Study Title for Internet Search on http://www.ClinicalTrials.gov:** Protocol NRG-GU008, Randomized Phase III Trial Incorporating Abiraterone Acetate with Prednisone and Apalutamide and Advanced Imaging into Salvage Treatment for Patients with Node-Positive Prostate Cancer after Radical Prostatectomy (INNOVATE*) (NCT #04134260)

** **IN**tensifying treatment for **NO**de positive prostate cancer by **VA**rying the hormonal **Th**e**r**apy*

## Overview and Key Information

## What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services and funding support from Janssen Scientific Affairs, LLC. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have prostate cancer that has spread to your lymph nodes.

## Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

## Why is this study being done?

This study is being done to answer the following question:

Can we lengthen the time without your prostate cancer spreading by adding two new hormone therapy drugs to the usual combination of hormone therapy and radiation therapy?
We are doing this study because we want to find out if this approach is better or worse than the usual approach for your prostate cancer. The usual approach is defined as care most people get for prostate cancer that has spread to the lymph nodes.

## What is the usual approach to my prostate cancer?

The usual approach for patients who are not in a study is treatment with Food and Drug Administration (FDA)-approved hormone drugs and radiation therapy after surgery to remove the prostate. For patients who get the usual approach for this cancer, about 75 out of 100 are free of cancer after 4 years.

## What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

## What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get either:

- the usual hormone drugs for up to 24 months plus the usual radiation therapy for 7-8 weeks, or
- you will get the usual hormone drugs for up to 24 months, the usual radiation therapy for 7-8 weeks, and the study drugs, apalutamide and abiraterone acetate, for 24 months. Abiraterone acetate must be taken with a steroid called prednisone. Both apalutamide and abiraterone acetate are approved by the FDA for use in prostate cancer that does not respond to hormone therapy, but are not approved for your type of prostate cancer.

After you finish your study treatment your doctor will continue to follow your condition and watch you for side effects. They will check you every 6 months for 3 years after treatment, then annually for your lifetime.

## What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

**Risks**

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer at stabilizing your cancer and preventing your cancer from spreading.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Tiredness
- Rash
- Itching
- Pain
- Weight loss
- Swelling
- High blood pressure
- Fall
- Broken bone
- Hot flashes
- Diarrhea

There may be some risks that the study doctors do not yet know about.

**Benefits**

There is evidence that the study drugs are effective in stabilizing your type of cancer. It is not possible to know now if the study drugs will extend your time without disease spreading compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

## If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. When you stop abiraterone acetate with prednisone you will have to slowly decrease the dose of prednisone under the direction of your physician. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

## Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Central Institutional Review Board (CIRB), Food and Drug Administration (FDA), or study sponsor, National Cancer Institute and NRG Oncology. The study sponsor is the organization who oversees the study.

**It is important that you understand the information in the informed consent before making your decision.** Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

## What is the purpose of this study?

The purpose of this study is to compare the use of hormone therapy and radiation therapy (usual treatment) to the use of apalutamide and abiraterone acetate with prednisone plus the usual treatment. The addition of apalutamide and abiraterone acetate with prednisone to the usual treatment could stabilize your cancer and prevent it from spreading. But it could also cause side effects, which are described in the risks section below.
This study will help the study doctors find out if this different approach is better, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if the study approach increases the time without prostate cancer spreading compared to the usual approach.

The study drugs, apalutamide and abiraterone acetate with prednisone, are already approved by the FDA for use in prostate cancer. But, most of the time abiraterone acetate with prednisone is not used until hormone drugs stop working and apalutamide is not used until hormone drugs stop working and after prostate cancer has spread. There will be about 586 people taking part in this study.

## What are the study groups?

This study has 2 study groups. You will know which group you are in.

- **Group 1**

  If you are in this group, you will get the usual approach, hormone therapy and radiation therapy, to treat this type of cancer. You will get FDA-approved hormone therapy for 24 months, and you and your doctor will decide which hormone regimen is best for you.

You will receive radiation therapy 5 days a week for 7-8 weeks. See the study chart below for more information.

There will be about 293 people in this group.

- 
- **Group 2**

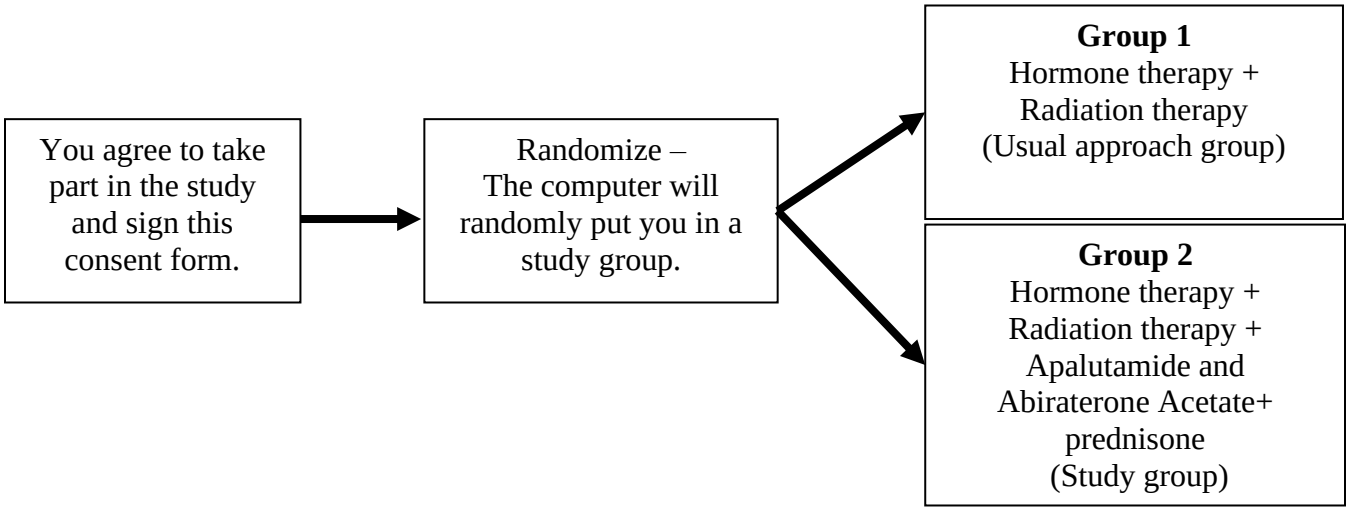
If you are in this group, you will get a study drugs, apalutamide and abiraterone acetate with prednisone, plus the usual approach used to treat this type of cancer (hormone therapy and radiation therapy). You will get the hormone and radiation therapy as described above for Group 1. In addition, you will receive both study drugs, apalutamide and abiraterone acetate with prednisone, as pills you take by mouth once a day for 24 months. You will take 8 pills (4 pills to receive the total daily dose of apalutamide and 4 pills to receive the total daily dose of abiraterone acetate) every day. Abiraterone acetate must be given with prednisone. You will take prednisone every day as long as you are taking abiraterone acetate. See the study chart below for more information.

You will not be able to get additional doses of the drugs after your complete study treatment.

There will be about 293 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



## What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

For participants receiving apalutamide and abiraterone acetate with prednisone:

- Blood tests to monitor liver function every 2 weeks for the first 3 months and then every month.
- Blood tests within 2 weeks of starting treatment and then every 3 months to monitor for side effects, thyroid function, and kidney and liver function.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

<u>Quality of Life</u>

If you speak and understand English, French, and Spanish and choose to take part in this study, you will be asked to fill out 4 forms with questions about your physical and emotional well-being. Researchers will use this information to learn more about how cancer and cancer treatment affects people.

Since these forms are being used for research, the responses you provide will not be shared with your study doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

You will be asked to fill out the forms at 6 times:

- Before you start treatment
- 6 months after you start radiation
- 12 months after you start radiation
- 18 months after you start radiation
- 2 years after you start radiation and at the time you end hormone therapy
- 5 years after you start radiation

Each form will take about 10 minutes to complete for a total of 40 minutes to complete the forms each time. The forms will ask about things like your general health, your urinary and bowel symptoms, as well as sexual and hormonal symptoms. You don't have to answer any question that makes you feel uncomfortable.
You will have the option of completing the questionnaires by paper or by an electronic device (See *Section Below).

**Option for completing Quality of Life Questionnaires and Symptoms Survey with a personal electronic device*

If you speak and understand English, French, or Spanish, you will have the option of completing the questionnaires and survey by paper or by an electronic device. If you choose to complete the questionnaires and survey with an electronic device, you will enter your answers to the questionnaires and survey via a personal electronic device such as your smart phone or tablet. In some cases, a tablet may be provided to you at your health care institution. The use of your own electronic device on a cellular network may result in a nominal cost to your data plan. Regardless of the device you use, your answers and personal information will not be stored on the device. Your survey answers will be sent to the research database and will be kept private in the same way listed in the later section about who will see your medical records. Your e-mail address will only be used for this survey study and will not be used for mail or marketing purposes. NRG Oncology will not keep your e-mail address

If you need help using the survey application on your phone or tablet, ask for help at your study site. You don't have to answer any question that makes you feel uncomfortable. Someone may help you enter your answers in the device if you need.

All patients will complete the questionnaires and survey before treatment on paper. After that, you can choose to complete the remaining forms online or on paper. The choice is up to you. If you choose to complete questionnaires using an electronic device, see Appendix I of this document for more information.

Please circle your answers:

I choose to use the electronic software for completing the Quality of Life Questionnaires. I agree to fill out the Quality of Life forms electronically (after treatment has started).

YES NO

## What risks can I expect from taking part in this study?

### General Risks

If you choose to take part in this study, there is a risk that the study approach may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. From when you start taking the study drug until 3 months after your last dose of the study drugs, you must use a condom and another effective method of birth control even if you have had a vasectomy when you have sex with a woman of child-bearing potential or use a condom if you are having sex with a woman who is pregnant while on study drugs. The type of birth control you use must be discussed with, and approved by, the study doctor before you begin the study. 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.

**Risks of Blood Draws**

The most common risks related to drawing blood from your arm are brief pain and possibly a bruise. Rarely, an infection can occur.

**Side Effect Risks**

The study hormone drugs, apalutamide and abiraterone acetate with prednisone, used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the radiation therapy and hormone therapy.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

**Drug Risks**

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

**Study Group 1 and Group 2** – Possible side effects of hormone therapy are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

**Possible Side Effects of Hormone Therapy**

There are a number of different drugs that can be used for hormone suppression therapy. You and your doctor will choose the drug that is best for you. The risks below describe the side effects of hormone suppression therapy, in general. Your study doctor will discuss any side effects specific to the drug selected for your hormone suppression therapy.

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving hormone suppression therapy, more than 20 and up to 100 may have: |
|---|
| • Hot flashes<br>• Abnormal sexual function<br>• Change in sexual desire<br>• Tiredness<br>• Breast tenderness or enlargement<br>• Diarrhea<br>• Loss of bone tissue |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving hormone suppression therapy, from 4 to 20 may have: |
|---|
| • Anemia, which may require blood transfusions<br>• Headache<br>• Pain<br>• Liver damage which may cause yellowing of eyes and skin<br>• Swelling of the body<br>• Infection<br>• Nausea<br>• Bruising, bleeding<br>• Mood swings, depression<br>• Increased urination<br>• Weight gain<br>• Shrinkage of the testis<br>• Broken bone |

| **RARE, AND SERIOUS**<br>In 100 people receiving hormone suppression therapy, 3 or fewer may have: |
|---|
| • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat<br>• Heart attack, heart failure which may cause shortness of breath, swelling of ankles, and tiredness<br>• Diabetes |

**Study Group 2** - In addition to side effects listed above, people who are in Group 2 may also have some side effects from apalutamide and abiraterone acetate with prednisone. These side effects are listed below.

**Possible Side Effects of Abiraterone Acetate (18-SEP-2020)**

| **FREQUENT, SOME MAY BE SERIOUS**<br>In 100 people receiving abiraterone acetate, more than 20 and up to 100 may have: |
|---|
| • Low potassium that may cause abnormal heart rate or rhythm<br>• High blood pressure |

| **VERY COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving abiraterone acetate, from 10 to 19 may have: |
|---|
| • Swelling |

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving abiraterone acetate, from 5 to 9 may have: |
|---|
| • Change in liver function<br>• Urinary tract infection which may cause painful or frequent urination<br>• Indigestion<br>• Blood in urine<br>• Broken bone |

| **LESS COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving abiraterone acetate, less than 5 may have: |
|---|
| • High levels of fat in the blood<br>• Chest pain<br>• Abnormal or fast heart beat |

| **UNCOMMON, SOME MAY BE SERIOUS**<br>In 1,000 people receiving abiraterone acetate, from 1 to 9 may have: |
|---|
| • Heart failure which may cause shortness of breath, swelling of ankles, and tiredness<br>• Changes in heart rhythm<br>• Adrenal insufficiency, or lack of stress hormones, that can cause tiredness, weakness, low blood pressure, nausea, vomiting, diarrhea, and low blood sugar<br>• Muscle weakness or muscle pain<br>• Loss of strength of bones |

There is a small chance of severe allergic reaction to the drug which may be life-threatening and cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat.

Abiraterone acetate may cause harm to the liver. Approximately 13 out of 100 patients taking abiraterone acetate have had abnormal blood levels of liver enzymes. Rarely, failure of the liver to function may occur, which can lead to death. In the majority of these cases liver enzymes returned to normal after delaying or stopping treatment with abiraterone acetate.

If you have diabetes, your blood sugar may drop if you take abiraterone acetate plus prednisone/prednisolone with some medicines for diabetes such as pioglitazone or repaglinide. Tell your healthcare provider if you monitor your blood sugar while taking a medicine for diabetes and notice a drop in your blood sugar.

Other risks that have been reported but with an unknown relationship to abiraterone acetate are swelling and irritation of the lung, a type of abnormal heart rhythm called Torsade's de Pointes, and muscle injury.

**Possible Side Effects of Prednisone**

Prednisone is given with abiraterone acetate to reduce or stop some of the side effects of abiraterone acetate, such as high blood pressure, low blood potassium, and swelling of the legs.

You should tell the study doctor if you have ever had a reaction to prednisone.

Prednisone can weaken your body's ability to fight off infection, and can make infections hard to diagnose or treat. If you develop fever, or suspect you have an infection, you should alert your study doctor right away.

Prednisone should never be stopped suddenly. If you need to stop your doctor will advise on how to slowly cut down the dose and stop the drug.

**Possible Side Effects of Prednisone** (Table Version Date: September 22, 2017)

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving Prednisone, more than 20 and up to 100 may have: |
|---|
| • High blood pressure which may cause headaches, dizziness, blurred vision<br>• Pain in belly<br>• Loss of bone tissue<br>• Mood swings<br>• Swelling of the body, tiredness, bruising<br>• Increased appetite and weight gain in the belly, face, back and shoulders<br>• Difficulty sleeping<br>• Skin changes, acne |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving Prednisone, from 4 to 20 may have: |
|---|
| • Blood clot which may cause swelling, pain, shortness of breath<br>• Infection<br>• Kidney stones<br>• Diabetes<br>• Glaucoma<br>• Cloudiness of the eye, visual disturbances, blurred vision<br>• A tear or a hole in the bowels which may cause belly pain or that may require surgery<br>• Heartburn<br>• Damage to the bone which may cause joint pain and loss of motion<br>• Numbness and tingling of the arms, legs and upper body<br>• Muscle weakness<br>• Non-healing wound |

| **RARE, AND SERIOUS**<br>In 100 people receiving Prednisone, 3 or fewer may have: |
|---|
| • Bleeding from sores in the stomach<br>• Broken bones |

**Possible Side Effects of Apalutamide (18-SEP-2020)**

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving apalutamide, more than 10 and up to 100 may have: |
|---|
| • Fatigue<br>• Skin rash<br>• Joint pain or muscle spasm<br>• Weight Loss |

- Fall
- Fracture
- Increased blood pressure
- Hot flush
- Diarrhea

**OCCASIONAL, SOME MAY BE SERIOUS**
In 100 people receiving apalutamide, from 1 to 10 may have:

- Itching
- High levels of fat in the blood
- Changes in thyroid function. Signs and symptoms may include: extreme tiredness or changes in mood or behavior; decreased sex drive; weight gain.
- Change in taste
- Decreased or blocked blood flow to the heart, heart attack
- Reduced or blocked blood flow to the brain, stroke

**RARE, AND SERIOUS**
In 100 people receiving apalutamide, fewer than 1 may have:

- Seizure

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 or stopped.

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.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

**Additional Drug Risks**

The study drugs could interact with other drugs. Apalutamide may have a stronger effect or apalutamide may decrease the effectiveness of other drugs. Abiraterone acetate may increase the strength or side effects of other drugs.

There are a number of drugs that are not allowed to be taken while receiving apalutamide and abiraterone acetate. If you are taking one of these drugs, your treating physician will discuss your options and the possibility of taking a different medication.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

**Radiation Therapy Risks**

**Study Arm 1 and Arm 2** – Possible side effects of prostate and pelvis radiation are listed in the tables below. Radiation to both the prostate and pelvis is part of the usual approach for treating this type of cancer:

**Possible Side Effects of Radiation Therapy to the Prostate (excluding pelvis)**

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving prostate radiation, more than 20 and up to 100 may have: |
|---|
| • Need to urinate more often<br>• Urgency with urination<br>• Slower urinary flow<br>• Pain, including with urination and/or bowel movements<br>• Hair loss in the treatment area, may be permanent<br>• Tiredness<br>• Abnormal sexual function, may be permanent |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving prostate radiation, from 4 to 20 may have: |
|---|
| • Chronic bowel/bladder symptoms as described above<br>• Blood in urine<br>• Inability to control urine, inability to control bowel movements<br>• Diarrhea<br>• Bleeding of the rectum<br>• Swelling, redness, rash, skin changes, or itching in the area of radiation |

| **RARE, AND SERIOUS**<br>In 100 people receiving prostate radiation, 3 or fewer may have: |
|---|
| • Blockage of internal organs that may require surgery<br>• Damage to or bleeding of the rectum requiring surgery<br>• A new cancer resulting from treatment of earlier cancer |

**Possible Side Effects of Pelvis Radiation**

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving pelvis radiation, more than 20 and up to 100 may have: |
|---|
| • Hair loss in the treatment area, may be permanent<br>• Diarrhea<br>• Need to urinate often<br>• Urgency with urination<br>• Slower urinary flow<br>• Tiredness<br>• Pain, including with urination and/or bowel movements<br>• Nausea, vomiting<br>• Abnormal sexual function, may be permanent (men) |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving pelvis radiation, from 4 to 20 may have: |
|---|
| • Chronic bowel/bladder symptoms as described above<br>• Blood in urine<br>• Inability to control urine, inability to control bowel movements<br>• Mucous-like stools<br>• Bleeding of the rectum<br>• Swelling, redness, rash, skin changes, or itching in the area of radiation |

| **RARE, AND SERIOUS**<br>In 100 people receiving pelvis radiation, 3 or fewer may have: |
|---|
| • Weight loss<br>• Blockage of internal organs that may require surgery<br>• A tear or hole in internal organs that may require surgery |

| **RARE, AND SERIOUS**<br><br>In 100 people receiving pelvis radiation, 3 or fewer may have: |
|---|
| • Bladder shrinkage, discomfort, or bleeding which may require medication or surgery, including removal of the bladder.<br>• Internal bleeding which may cause bleeding of the rectum, black tarry stool, blood in vomit, blood in urine, and may require surgery.<br>• Infection which may cause painful and frequent urination<br>• A new cancer resulting from treatment of earlier cancer |

## What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home and the number of pills you take.
- You will be provided with a patient clinical trial wallet card. The wallet card contains important information such as the study number you are currently enrolled in; study drugs; and the study doctor contact number. You must carry this card with you all the time and show it to your other healthcare providers or when you present to the emergency room.

Apalutamide and abiraterone acetate may cause harm to the unborn child. Tell your study doctor right away if you think your partner has become pregnant during the study or within 3 months after your last dose of study treatment.

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

## What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the hormone therapy ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include: the quality of life forms and if you agree to participate in the optional specimen collection studies.

You or your insurance provider will not have to pay for the apalutamide, abiraterone acetate, and prednisone while you take part in this study. Janssen Scientific Affairs, LLC is providing the study drugs and prednisone.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. Contact information for your study doctor is listed on the consent cover page. The study sponsors and the company supporting the trial will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

No funds have been set aside to compensate you in the event of injury.

## Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- Montana Cancer Consortium
- NRG Oncology and, Janssen, the company supporting the study, or any company supporting the study in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research
- The NCI and the groups it works with to review research, including the Cancer Trials Support Unit (CTSU).
- The NCI's National Clinical Trials Network and the groups it works with to conduct research including the Imaging and Radiation Oncology Core (IROC).

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

## Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

## Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

## Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

**Known future studies**

Tissue Laboratory Study for Decipher Score

If you choose to take part in this study, the study doctor for the main study would like to collect a small piece of the cancer tissue that was removed at the time of your surgery. This tissue will be sent to a laboratory where it will be tested for certain genetic markers. The results from this test will provide what is called the Decipher score and the PAM50 subtype. The results may provide useful information about your response to the treatment

Blood Laboratory Study for Circulating Tumor Cell Analysis.

If you choose to take part in this study, the study doctor for the main study would like to collect blood for research on cancer cells that may be in your bloodstream. These circulating tumor cells (CTCs) may give the study doctors additional information about your cancer. They would like to see if it is possible to get the same information from your blood that they can get from the molecular test of your prostate tissue.

Blood Laboratory Study for Genetic Changes

If you choose to take part in this study, the study doctor for the main study would like to collect blood for research on genetic changes in your blood that may give the study doctors additional information about your cancer.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be

coded. Research results will not be returned to you or your doctor. See *What Are the Possible Risks* below for further details.

**Unknown future studies**

If you choose to take part in this optional study, blood, urine, and a sample of tissue from your previous biopsy will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG Oncology and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood, urine, and tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

**What is involved in this optional sample collection?**

If you agree to take part, here is what will happen next:

1. About 3 tablespoons of blood will be collected from a vein in your arm before you begin treatment, at the end of treatment, and if your tumor comes back. A sample of your urine will be collected before you begin study treatment. A sample from the tissue that was collected at the time of your surgery will be sent to a laboratory and the biobank.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

**What are the risks in this optional sample collection?**

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. *For non-US participants, adapt the following two sentences as needed.* There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

**How will information about me be kept private?**

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.

3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

**What are the benefits to taking part in this optional sample collection?**
You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

**Are there any costs or payments to this optional sample collection?**
There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

**What if I change my mind about this optional sample collection?**
If you decide you no longer want your samples to be used, you can call the study doctor who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

**What if I have questions about this optional sample collection?**
If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer below to show if you would or would not like to take part in each optional study:

**Samples for known future studies:**
I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

**Samples for unknown future studies:**
I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

## Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

**This is the end of the section about optional studies.**

## My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)

## Appendix I: Patient Instructions for Accessing the Patient Cloud Using Your Personal Device

### Downloading the Patient Cloud ePRO App

If you are using your personal device, and you do not have the Patient Cloud ePRO app, use the following instructions. When downloading the app, you must use the Apple ID or Google account associated with the device. If the Patient Cloud ePRO app is already on the device, or if you are using the study team's device, you can skip this section.

You will need an email address that you agree to use for this purpose. The e-mail address is needed to identify you on the Patient Cloud Application and for you to receive notifications to let you know when forms are due. Your e-mail address will only be used for this survey study, and will not be used for mail or marketing purposes.

If you decide to use the electronic method to complete the questionnaires, and do not have an e-mail address, you may sign up for one at no charge at many different websites. A few sites that are commonly used and will allow you to create an email address very easily are Yahoo, Gmail, and Outlook.

For iOS:

1. An Apple ID is required for downloading the Patient Cloud ePRO app.
2. Tap the *App Store* icon.
3. Search for *Medidata Patient Cloud* and follow the installation instructions.

Note: Patient Cloud ePRO is listed as an iPhone App in the App store. When using an iPad, please view the search results under iPhone apps.

For Android:

1. A Google account is required for downloading the Patient Cloud ePRO app
2. Tap the *Play Store* icon.
3. Search for *Medidata Patient Cloud* and follow the installation instructions.

### Registering

You must register in order to complete and submit your study forms. When you register, you will create a username, which is your email address, and a password that allows you to log in to the Patient Cloud ePRO app.

Note**:** You must have an activation code to begin this process. If you do not have an activation code, please contact your study team.

There are two possible ways to register. Your study team may have sent you a link to a web address where you may register from any web browser, including the one on your device. The other way to register is on the Patient Cloud ePRO app.

1. If registering from the Patient Cloud app, tap Register on the bottom of the log in page. If registering on the web, open the URL shield.imedidata.com on a web browser.
2. Enter your activation code and tap Activate.
3. On the next page, read the instructions and tap Next.
4. Read the privacy notice and tap I agree. Then tap OK to confirm.
5. Enter and confirm your email address. Tap Next.
6. Enter and confirm your password. Tap Next.
7. Choose a security question by scrolling through the dropdown menu to display the question of your choice.
8. Enter your security question response.
9. Tap Create my account to complete your registration.

If you registered on the Patient Cloud ePRO app, it automatically logs you out. If you registered on the web, you are presented with the option to download the Patient Cloud ePRO app. You can then proceed to log in with the credentials you created.

## Logging in to the App

1. Enter your Email and Password that you created during the registration process. (If you previously set a PIN code, just enter your four-digit PIN.)
2. Tap Log in.

Note: If you do not remember your password, tap **Forgot Password**, and follow the instructions provided.

## Setting a PIN Code

The first time you log in to the Patient Cloud ePRO app, you are given the option to create a PIN code. A PIN code allows you to bypass the step of entering your email and password every time you need to log in to the Patient Cloud ePRO app. Instead, you can enter a four-digit PIN.

1. If you wish to set a PIN code the first time you log in, tap Yes when prompted.
2. Note: You can also set your PIN at a later time by tapping the options menu on the top left of most pages and selecting Set PIN.
3. Enter a four-digit PIN.
4. Re-enter the four-digit PIN to confirm.

If you forget your PIN code, tap **Forgot PIN** and you can access the app using your email and password. You may reset your PIN by tapping the options menu on the top left of most pages and selecting Set PIN.

### Resetting Your Password

You can reset your password by using the options menu at the top left of most pages.

1. Tap the options menu icon.
2. Tap Reset Password.
3. Follow the instructions to reset your password.

### Completing and Submitting Forms

Once logged in, forms related to your study display on the Tasks page. If you are enrolled in multiple studies, select the appropriate study first, and then select a form. New forms can appear on the Tasks page at any time, depending on how the study is designed.

There are two types of forms displayed on the Task List page:

- *Scheduled Forms* (with a  icon): These forms have a "Due Date" indicator in them so you are aware of the last day by which you will need to complete the form. If the form is due in less than one day, you will see the due time in hours.
- *Anytime Forms* (with a  icon): These forms have "Last Completed Time" indicator on them which tells the most recent date or time when you completed the form. If you start a form, but do not complete it, you will see an 'Incomplete" status beneath the form name, along with a half-moon icon.

1. Select the appropriate form.
2. Follow the on-screen instructions until you reach the end of the form where you are given the opportunity to review and change your responses prior to submitting.
3. Review your responses by scrolling down the list.
4. If you need to change an answer, tap the question to go back and change the answer.
5. When you are ready to submit, tap Submit Your Data.

Note: Once a form is submitted, you will be unable to edit any of your responses. In some cases, you may be asked to acknowledge your submission by entering your password.