RTOG FOUNDATION

RTOG 3506

(ClinicalTrials.gov NCT #:* 03809000*)

STEEL: A Randomized Phase II Trial of Salvage Radiotherapy with Standard vs Enhanced Androgen Deprivation Therapy (with Enzalutamide) in Patients with Post Prostatectomy PSA Recurrences with Aggressive Disease Features

Amendment 7: July 12, 2022

Research Study Informed Consent Document

Sponsor / Study Title:	**RTOG Foundation / "A Randomized Phase II Trial of Salvage Radiotherapy with Standard vs Enhanced Androgen Deprivation Therapy (with Enzalutamide) in Patients with Post-Prostatectomy PSA Recurrences with Aggressive Disease Features"**
Study Title for Participants:	**A Study of Salvage Radiotherapy With or Without Enzalutamide in Recurrent Prostate Cancer Following Surgery**
Protocol Number:	**RTOG 3506**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study because you have prostate cancer and your PSA (prostate specific antigen) has recurred after your surgery to remove your prostate. The recurrence has aggressive disease features, which means a greater chance of disease progression. Your doctor is recommending radiation therapy to treat this recurrence. Hormone therapy is also given to improve your chance of remaining cancer free. This study will determine if a new type of hormone therapy improves outcomes for men in this situation.

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 improve the time without disease progression by adding a new hormone drug to the usual combination of hormone drugs 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 after the prostate is removed. The usual approach is defined as care most people get for prostate cancer.

What is the usual approach to my prostate cancer?
The usual approach for patients who are not in a study is treatment with radiation with hormonal therapy. For patients who get the usual approach for this cancer, about 42 out of 100 have no evidence of active cancer (for example, a rising PSA or new tumors) after 5 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 either get radiation therapy and the usual 2 years of hormone therapy, or you will get radiation therapy plus 2 years of the usual hormone therapy and 2 years of hormone therapy with the study drug, enzalutamide.

After you finish your radiation therapy and while you are receiving hormone treatment, your study doctor will continue to follow your condition and watch you for side effects. Your study doctor will check you every 3 months for 2 years and then every 6 months for 3 years. This means you will keep seeing your study doctor for 5 years after you complete radiation, and maybe longer.

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 enzalutamide (study drug) with radiation therapy and hormone therapy may not be as good as the usual approach at increasing your chances of the cancer not coming back.

Some of the most common side effects that the study doctors know about are:
- Weakness or feeling more tired than usual
- Hot flashes
- Diarrhea
- Headache
- High blood pressure

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

Benefits
There is evidence that the combination of radiation therapy and hormone therapy with the study drug increases the time without disease progression in your type of cancer. It is not possible to know now if radiation therapy and hormone treatment that includes study drug will extend your time without disease progression 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. 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 Institutional Review Board (IRB), Food and Drug Administration (FDA), Pfizer/Astellas, or study sponsor, RTOG Foundation. 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? (12-JUL-2022)
The purpose of this study is to compare the usual treatment of radiation and hormone therapy with the usual treatment plus the study drug, enzalutamide. The addition of the study drug to the usual treatment could increase the time without disease progression. 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 than the usual approach. To decide if it is better, the study doctors will be looking to see if the study drug lowers the risk of your cancer returning compared to the usual approach.

This study drug is already approved by the FDA for use in prostate cancer but not until cancer has spread and other hormone drugs stop working. There will be about 170 people taking part in this study.

What are the study groups? (12-JUL-2022)

This study has 2 study groups.

- **Group 1**
  If you are in this group, you will get the usual radiation therapy between 33 and 41 treatments, approximately 7 - 8 weeks, and hormone drugs (an injectable GnRH analog with or without oral bicalutamide) approved by the FDA for treating prostate cancer. You will start hormone therapy with a GnRH analog and will receive it for 2 years. The radiation treatment will start within 70 days after starting hormone therapy.

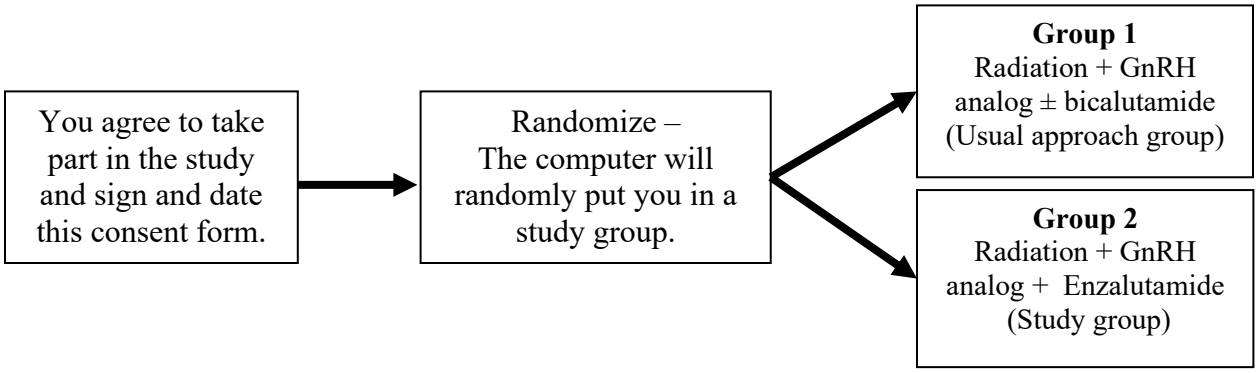
  There will be about 85 people in this group.

- **Group 2**
  If you are in this group, you will get the usual radiation therapy between 33 and 41 treatments, approximately 7 - 8 weeks, and the study drug enzalutamide orally, plus the usual hormone drug called a GnRH analog used to treat this type of cancer. Enzalutamide is also an FDA approved drug for prostate cancer, but the approval is for use in more advanced disease. You will get the study drug enzalutamide and the GnRH analog hormone drug for 2 years. You will start GnRH hormone therapy and will receive the enzalutamide study drug and the injectable GnRH hormone drug for 2 years. The radiation treatment will start within 70 days after starting hormone therapy.

  There will be about 85 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? (20-MAY-2021)

Before you begin the study, your study doctor will review the results of your exams, tests, and procedures. This helps your study 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:

Blood tests to check your liver and kidney 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>Before you begin treatment on the study</u>:

- If you consent to the optional study*, small pieces of cancer tissue removed at the time of your prostatectomy* will be taken for the study *before you begin treatment on this study.* Your study doctor will send this tissue to a laboratory where the tissue will be tested for certain genetic markers. The results from this test will provide what is called the Decipher score and the PAM50 subtype. If your doctor already sent your tumor tissue for this test and you have a Decipher risk score, the report will be submitted for review and a tissue sample will not be required. Please see the Optional Study you can choose to take part in section below for more information.

- Symptoms Survey and Quality of Life
  If you speak and understand English, Spanish, or French, you will be asked to answer questions about side effects and symptoms you may have during the study. This is part of the study that looks at how the study treatment is affecting you. You will be asked questions about side effects like diarrhea and rash. In addition, you will be asked to complete two other questionnaires that will ask you about fatigue and your general wellbeing. Researchers will use this information to learn more about how cancer and cancer treatment affect people, and it may help future patients understand the side effects of treatment. You don't have to answer any question that makes you feel uncomfortable.

  You will be asked to fill out the symptoms survey at the following times, and each time it will take about 5 to 10 minutes to complete:

  - Prior to randomization
  - At the end of radiation therapy
  - Every 3 months for 2 years and then every 6 months for 3 years

  You will be asked to fill out the two quality of life questionnaires at the following times, and each time it will take about 5 to 10 minutes to complete:

  - Prior to randomization
  - At the end of radiation therapy
  - At years 1 and 2 after the end of radiation therapy

In the past, participants often have filled out these quality of life forms on paper. RTOG Foundation is working with a company, VisionTree Software, Inc., that has a web site where participants can fill out these forms anywhere there is a computer with Internet access. This option is being offered as some participants may find it more convenient to fill out the forms electronically from any location, including home. When you log on to the web site, it will take you through the process of completing the forms step by step. You will need an e-mail address that you agree to use for this purpose. The e-mail address is needed to identify you on the VisionTree web site and for e-mail reminders that will be sent to you when the forms are due. Your e-mail address will only be used for the purpose of this study, not for mail or marketing purposes. If you are interested in filling out quality of life forms electronically but do not have an e-mail address, you may obtain one (quickly and for no charge at web sites such as Yahoo!, Hotmail, or AOL). You will only be sent e-mail reminders at the time that the forms are due (a maximum of 3 e-mail reminders per time point). Your access to the VisionTree web site is password protected and secure. You can use your e-mail address to retrieve your password if you forget it or lose your login card. You will receive a login card either by regular mail or e-mail, and it will include the information you need to log in to the VisionTree web site the first time. All participants will complete the forms before treatment on paper. After that, you can choose to complete the remaining forms online or on paper. The choice is up to you.

Please initial your answer: I choose to use the VisionTree Software. I agree to fill out the Quality of Life forms electronically (after study treatment has started) using the VisionTree web site.

_____ YES _____ NO

If you are having any severe symptoms, health issues or other concerns, please be sure to discuss these with your study doctor or study nurse.

What risks can I expect from taking part in this study? (03-FEB-2022)

General Risks
If you choose to take part in this study, there is a risk that the study drug may not be as good as the usual approach for your cancer in improving the time without disease progression.

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

Side Effect Risks
The study drug 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 study.

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.

Possible side effects of Enzalutamide

VERY COMMON, SOME MAY BE SERIOUS In 10 people receiving Enzalutamide, more than 1 and up to 10 may have:
• Weakness or feeling more tired than usual • Hot flashes • Diarrhea • Headaches • High blood pressure
COMMON, SOME MAY BE SERIOUS In 10 people receiving Enzalutamide, up to 1 person may have:
• Change in taste • Falls • Broken bones • Feelings of anxiety • Difficulty remembering, reduced concentration, forgetfulness, or trouble thinking clearly • Rash • Breast enlargement in men (gynecomastia) • Nose bleeds (epistaxis) • Dry skin • Sensations of whirling and loss of balance (vertigo) • Itching • Restless legs syndrome (an uncontrollable urge to move a part of the body, usually the leg) • Chest pain, heart problems related to a blockage or decreased blood supply to the heart

UNCOMMON, SOME MAY BE SERIOUS In 100 people receiving Enzalutamide, up to 1 person may have:
• Low white blood cell counts • Hallucinations • Seizures • Severe skin rash with blisters and peeling which can involve the mouth and other parts of the body.

Seizure: Some people have had a seizure during treatment with the study drug. Seizure was reported in up to 9 in every 1,000 people taking the study drug who had already received chemotherapy, and 1 in every 1,000 people taking the study drug who had not received chemotherapy. In these studies, patients with known risk factors for seizure were excluded.

If you take the study drug, you may be at risk of having a seizure. You should know that there is a risk in doing any activity where sudden loss of consciousness could cause serious harm to yourself or others. Tell your study doctor right away if you have loss of consciousness (fainting or passing out) or seizure. Also tell your study doctor if you ever had a condition that may give you a higher risk of seizure, including but not limited to past seizure(s), brain injury or tumor, stroke, or history of alcoholism. Your study doctor will stop study treatment if you have a seizure during the study.

In addition, you may experience nausea and vomiting while taking the study drug. It is unknown how common these side effects are.

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

Allergic reaction: Though it may be rare, get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Ischemic heart disease and metabolic syndrome: In clinical studies of enzalutamide, ischemic heart disease occurred more commonly in patients on the enzalutamide arm compared to patients on the placebo arm (2.7% vs 1.2%). Less than 1% of these events resulted in death but appear to be more frequent in patients who received enzalutamide. You should alert your study doctor of any new cardiac symptoms such as chest pain or palpitations. You and your study doctor should carefully monitor and control blood pressure as well as optimize treatment of any pre-existing diabetes or lipid abnormalities (for example, high cholesterol).

Cardiovascular Risk Factors: if you have cardiovascular problems such as hypertension, diabetes, high cholesterol, your study doctor will carefully monitor your condition. If you develop severe symptoms of heart disease, your study doctor will stop the study drug.

Special Handling Instructions: Enzalutamide should not be handled by persons other than the subject and his caregivers, and especially not by females who are or may become pregnant.

Additional Risks

There could be potential interactions with drugs you are taking and radiation therapy. Please discuss further with your study doctor. Share this information with your family members, caregivers, other health care providers, and pharmacists. Rarely, there are problems getting enough supplies of the study drug. If that happens, your study doctor will talk with you about your options.

Possible Side Effects of Bicalutamide

COMMON, SOME MAY BE SERIOUS In 100 people receiving Bicalutamide, more than 20 and up to 100 may have:
• Hot flashes • Breast swelling or pain • Constipation • Pain • Tiredness
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Bicalutamide, from 4 to 20 may have:
• Diarrhea, nausea • Swelling of arms, legs • Liver damage which may cause yellowing of eyes and skin, swelling • Hepatitis (inflammation of the liver) • Infection • Blood in urine • Increased urination at night • Heart attack or heart failure which may cause chest pain, shortness of breath, swelling of ankles, and tiredness
RARE, AND SERIOUS In 100 people receiving Bicalutamide, 3 or fewer may have:
• None

Hormone suppression therapy (GnRH class)
There are a number of different drugs that can be used for hormone suppression therapy. You and your study doctor will choose the regimen 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 drugs selected for your hormone suppression therapy.

COMMON, SOME MAY BE SERIOUS In 100 people receiving hormone suppression therapy, more than 20 and up to 100 may have:
• Hot flashes • Abnormal sexual function • Changes in sexual desire • Tiredness • Loss of bone tissue
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving hormone suppression therapy, from 4 to 20 may have:
• Anemia, which may require blood transfusions • Headaches • Pain • Swelling of the body • Infection • Nausea • Bruising, bleeding • Mood swings, depression • Increased urination • Weight gain • Shrinkage of the testis • Broken bones
RARE, AND SERIOUS 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 • Heart attack, heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Diabetes

Possible Side Effects of Prostate Bed Radiation

COMMON, SOME MAY BE SERIOUS In 100 people receiving prostate radiation, more than 20 and up to 100 may have:
• Need to urinate more often • Urgency with urination • Slower urinary flow • Pain, including with urination and/or bowel movements • Hair loss in the treatment area, may be permanent • Tiredness • Abnormal sexual function, may be permanent
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prostate radiation, from 4 to 20 may have:
• Chronic bowel/bladder symptoms as described above • Blood in urine • Inability to control urine, inability to control bowel movements • Diarrhea • Bleeding of the rectum • Swelling, redness, rash, skin changes, or itching in the area of radiation
RARE, AND SERIOUS In 100 people receiving prostate radiation, 3 or fewer may have:
• Blockage of internal organs that may require surgery • Damage to or bleeding of the rectum requiring surgery • A new cancer resulting from treatment of earlier cancer

Possible Side Effects of Pelvis Radiation

COMMON, SOME MAY BE SERIOUS In 100 people receiving pelvis radiation, more than 20 and up to 100 may have:
• Hair loss in the treatment area, may be permanent • Diarrhea • Need to urinate often • Urgency with urination • Slower urinary flow • Tiredness • Pain, including with urination and/or bowel movements

• Nausea, vomiting • Painful sexual intercourse (women) • Abnormal sexual function, may be permanent (men)
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pelvis radiation, from 4 to 20 may have:
• Chronic bowel/bladder symptoms as described above • Blood in urine • Inability to control urine, inability to control bowel movements • Mucous-like stools • Bleeding of the rectum • Swelling, redness, rash, skin changes, or itching in the area of radiation
RARE, AND SERIOUS In 100 participants receiving pelvis radiation, 3 or fewer may have:
• Weight loss • Blockage of internal organs that may require surgery • A tear or hole in internal organs that may require surgery • Bladder shrinkage, discomfort, or bleeding which may require medication or surgery, including removal of the bladder. • Internal bleeding which may cause bleeding of the rectum, black tarry stool, blood in vomit, blood in urine, and may require surgery. • Infection which may cause painful and frequent urination • 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 study 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 study drug diary when you take the study drug at home.

What are the costs of taking part in this study?

The study drug will be supplied by Pfizer at no charge while you take part in this study. The cost of getting the study drug ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that the study drug may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your insurance plan will need to pay for the costs of medical care as you would when getting the usual care for your prostate cancer. This includes:

- The costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, as well as prevent and treat side effects.
- 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 research study. Also, find out if you need approval from your plan before you can take part in the study.

Ask your study 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 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. The study sponsors 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.

Who will see my medical information?(16-MAR-2021)

Your privacy is very important to us. The study doctors will make every effort to protect it. However, some of your medical information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. 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 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:

- RTOG Foundation, Pfizer/Astellas, and any company supporting the study now or in the future
- The 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 and similar one if other countries are involved in the study.

Your study records also will be stored for future research. If data are entered into any other study database, your name and other personal information will not be associated with your study data (it will be "anonymized"). Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. We don't know what research may be done in the future using your anonymized information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your anonymized 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 anonymized information.
- The permission to use your study data, including biospecimens, will last as long as we have a scientific and research need.

[Sites in Canada please add: Any study-related information and/or samples sent outside of Canadian borders will be coded (this means it will not contain your personal information such as your name, address, or contact information). Any information will be transferred in compliance with Canadian privacy laws.]

By signing and dating this consent form, you consent to the collection, access, use and disclosure of your information as described in this form.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for 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.

Whom to contact about this study

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 the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

For questions about your rights while in this study, call the *study doctor/organization* at _____ *(insert telephone number) or* Institutional Review Board at _____ *(insert telephone number).*

Optional study that you can choose to take part in (16-MAR-2021)

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

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

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

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.

Decipher Prostate RP Testing (20-MAY-2021)

If you choose to take part in this optional study, researchers will collect tumor tissue for research on certain genomic markers, such as your Decipher Score and PAM50 subtype. The tissue will be collected at the time of your prostatectomy and will be sent to Decipher Biosciences for testing. The results can be provided by your study doctor upon request.

What is involved in this optional sample collection? (03-FEB-2022)

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

1. A sample from the tissue that was collected at the time of your prostatectomy will be sent to Decipher Biosciences.
2. There is no limit on the length of time Decipher will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. 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?

- 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 Decipher Biosciences 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. 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? (20-MAY-2021)

Your privacy is very important to the study researchers and Decipher Biosciences. 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?
If you are in the US, the Decipher test will be considered standard of case and will be billed to your insurance company. If you are in Canada, the cost of the Decipher test will be covered by the RTOG foundation. 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? (20-MAY-2021)
If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let Decipher Biosciences know. 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, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

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 study described above.

YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from this study.

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's Printed Name _____

Participant's signature_____

Date of signature_____

Witness signature for subjects who cannot read

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date

Printed name of person conducting the informed consent discussion_____
Signature of person conducting the informed consent discussion_____

Date of signature_____