INSTITUTE: National Cancer Institute

STUDY NUMBER: 13-C-0153 PRINCIPAL INVESTIGATOR: Ravi Madan, M.D.

STUDY TITLE: A Phase II Trial of Enzalutamide in Combination with PSA-TRICOM in Patients with Non-Metastatic Castration Sensitive Prostate Cancer

Continuing Review Approved by the IRB on 10/16/17
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Standard Cohort 1

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

Androgen deprivation therapy (ADT) and close clinical monitoring are standard therapy for prostate cancer patients who have biochemical progression (rise in PSA) after local radiation or surgery therapy. This group of patients is also referred to as non-metastatic castration sensitive prostate cancer (nmCSPC) or as D0 prostate cancer. These patients cannot be cured of prostate

cancer and the primary therapeutic goal is to control the disease with ADT, which lowers testosterone. ADT consists of an injection (shot) of a normally occurring hormone called gonadotropin-releasing hormone. The injection is given under the skin of the abdomen once every three months. Alternative approaches include intermittent use of ADT and other hormonal therapies called androgen receptor antagonists (ARAs). Enzalutamide is a modern ARA. This agent is FDA approved to treat metastatic prostate cancer after chemotherapy. Enzalutamide treatment consists of four pills taken together once a day.

In addition to the direct anti-cancer effect of enzalutamide, there is evidence that hormonal therapies like enzalutamide enhance the immune system. This study will also test a new way of potentially treating prostate cancer using a PSA-targeted immunotherapy vaccine product called PROSTVAC-V/F in combination with enzalutamide. This combination may help cells from your own body to recognize and kill the cancer cells. The study will test how safe it is to receive this vaccine and how well it works in prostate cancer in combination with enzalutamide.

All patients in this study will get enzalutamide. Half of the patients will receive enzalutamide only and half of the patients will receive enzalutamide plus PROSTVAC-V/F vaccine. Your treatment is determined by a randomization process (chosen as if by the flip of a coin). You have an equal chance of being randomized to any of the two groups.

Clinical development of PROSTVAC-V/F is based on the idea that the immune system (group of cells and organs in the body that recognize and fight infection) can be taught to find and kill certain cancer cells, in this case prostate cancer cells. This is an investigational vaccine regimen, which means that it is not yet approved by health authorities and can be used only in a research study. In September of 2017, it was reported that a large (phase III) study of PROSTVAC alone did not show that this treatment could improve survival in advanced prostate cancer. However, the scientific reasoning to combine PROSTVAC with enzalutamide remains sound, and this study will continue. Furthermore, at this point neither this trial or the phase III trial have suggested a safety concern for PROSTVAC.

The goal of this study is to determine if the short-term benefits of enzalutamide (lowering of PSA/disease control) can be improved when used with PROSTVAC-V/F, resulting in a slower PSA rise after enzalutamide.

Patients will be randomly assigned to either one of two main study groups. One group will receive only enzalutamide and the other group will receive enzalutamide and PSA-TRICOM vaccine. Random assignment will be done with the help of a computer and patients will be informed on the day of their start about their respective group.

Why are you being asked to take part in this study?

You are being asked to participate in this study for three reasons: 1) You had received local therapy for prostate cancer and now your PSA is rising 2) You do not have tumor anywhere else in the body that can be seen on imaging 3) you have normal levels of testosterone, all of which indicate that you have nmCSPC or D0 prostate cancer.

How many people will take part in this study?

We plan to enroll 38 patients.

Description of Research Study

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

Before you begin the study
Certain standards (criteria) have been established to ensure that you are a medically appropriate candidate for this trial. These criteria also make sure that the results of this study can be used to help make decisions about treating other patients. We will record your medical history and give you a physical examination. You will undergo standard blood tests including a complete blood count, chemistry panel, and prostate-specific antigen (PSA) levels, and scans and x-rays as part of the NCI Screening Protocol. One test of your immune system will be a blood test that checks for the presence of the human immunodeficiency virus (HIV), the cause of acquired immunodeficiency syndrome (AIDS). HIV infection may disqualify you from this study. If you test positive for HIV, we will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection. We will do other blood tests to look for infection with hepatitis B and C. If these tests are positive, you will not be eligible to participate in the study because of the potential harm the vaccine may cause. Altogether, these tests will require about 100 cc (6 to 7 tablespoons) of blood.

During the study
Once you agree to participate in this study, you will be assigned to 1 of 2 groups: the enzalutamide only group or the enzalutamide plus PSA-TRICOM vaccine group

<u>All patients will receive the enzalutamide.</u> You will receive enzalutamide (Arm A and B) at a dose of 160 mg daily orally for 3 months. You may receive a second course of enzalutamide if at any time after you have been on the study for 7 months, your PSA level rises higher than what it was at the beginning if the study.

For most patients, if you do not receive a second course of enzalutamide, you will be followed for up to 1 year total, potentially 9 months after completing enzalutamide therapy. If you receive a second course, you will be followed for 9 months after completing your second course of enzalutamide therapy.

Patients randomized to receive enzalutamide and vaccine. If you are randomized to enzalutamide plus vaccine arm (Arm B), you will receive PSA-TRICOM. It will be administered as a shot under the skin on week 1 (vaccinia version of PSA-TRICOM) and then week 3, 5 and then monthly (fowl-pox version of the same vaccine) until week 21. For description of the versions of the vaccine and explanation of why there are two versions, see pages 6-8, under Vaccinia Virus and Fowlpox Virus.

At each visit, we will give you a physical exam and standard blood tests, and ask you how you are feeling. This is standard care you would receive as part of your cancer treatment, whether you were participating in a study or not.

Research Tests

An important part of this study is testing the effects of this treatment on your tumor and immune system. The following blood samples and tests will be done while you participate in this study:

Research blood samples

Research tests will be done on blood obtained by apheresis and on blood taken at various times during your participation in this study and for as long as we continue to follow you. If research blood needs to be drawn on the same day as apheresis, it will be taken at the same time. Each of these blood draws will take about 6 tablespoons of blood. The NIH has set a limit on the maximum amount of blood that can be taken for research. This limit is based on your age. For adults, no more than 37 tablespoons can be taken over an 8-week period. Specimens obtained during your participation in this study may be sent for testing to investigators outside of NCI or the NIH.

Scans and x-rays

As part of this study, we will look for any signs that your cancer is recurring or getting worse:
1. Your PSA level will be checked at each visit when blood is taken for standard laboratory tests.
2. Bone scan will be done at baseline and as needed.
3. CT scan of the chest, abdomen, and pelvis will be done at baseline and as needed.

These tests will be initially done before your treatment begins. The bone and CT scans will be repeated if the doctor suspects your cancer has gotten worse. PSA level will be checked frequently throughout the study.

When you are finished taking the drugs (treatment)

You will be followed for a total of 52 weeks from the start of study if you receive one course of enzalutamide. If you receive a second course, the follow up period extends for up to 9 months after you have completed the second enzalutamide course. You will finish your first course of enzalutamide in 12 weeks and those in Arm B will finish vaccine in 21 weeks. The second course of enzalutamide (if given) will be completed 12 weeks after it has begun.

However, if you have rising prostate-specific antigen (PSA) but have not required additional therapy, you may continue to be seen on this study beyond the treatment period.

What Do I Have To Do?

It is important that you inform your trial doctor of any changes in your health, whether or not you think that it is related to the trial drug.

You must tell your trial doctor about all medications you are currently taking. This includes both medications prescribed by your regular doctor and medications you obtain without prescription, (e.g., from a pharmacy or health food shop, including herbal medication and vitamin supplements). Your trial doctor will inform you whether you can continue taking these. You must tell your trial doctor before making changes in to your existing medications or taking any new medication. Always follow your trial doctor's instructions during the trial.

If you are involved in any other clinical trials, you should inform your trial doctor. You cannot be involved in another clinical trial during your participation in this trial.

In case you need to contact your trial doctor in an emergency, you will be given a contact card with all the relevant contact information. **It is important that you follow your trial doctor's instructions throughout the trial. If you have questions or want further information, contact your trial doctor.**

Gene Therapy Long Term Follow Up

You will be followed on a separate protocol once you are off study. The Food and Drug Administration (FDA) requires that people who receive gene therapy be watched even after they complete therapy. Once you have finished therapy, you will be watched for up to 15 years to see how well you are doing. At least, you will be asked to have a routine physical exam each year for five years following your last vaccination. You will be asked questions about your health such as whether you have developed any new cancers or problems with your blood or immune system (the organs and cells that defend your body against infections and other diseases). You will also be asked whether you have had a hospital stay for something you did not expect and the medicines you are taking. You will be called by telephone for more information about your health each year for 15 years following your last treatment. The FDA will have access to this information. For this reason, we ask that you continue to provide us with a current address and telephone number, even after you complete this research study.

Risks or Discomforts of Participation

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

As with all treatments, there are several side effects or risks from the treatments provided in this study. However, doctors don't know all the side effects that may happen with this combination

of drugs, so it is important to report any changes that you notice, even if your study team does not ask specifically about them. Side effects may be mild or severe. Your study team will give you medicines to help lessen side effects. Many side effects go away with those medicines and others may go away soon after you stop treatment. In some cases, side effects can be serious, long-lasting, or may never go away. In very rare instances, they could cause death.

Possible side effects of enzalutamide:

Likely	Less Likely	Rare but Serious
• Ankle swelling. • Fatigue • Headache • Hot flashes • Diarrhea • Low blood counts • Back pain • Upper respiratory tract infection	• High blood pressure • Dizziness, anxiety • Dry skin • Blood in urine • Jaundice • Weakness of muscles	• Seizures • *Posterior reversible encephalopathy syndrome (PRES)

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

Risks to be considered with PSA-TRICOM

Vaccinia Virus

The first vaccine injection you will receive will be PSA-TRICOM vaccinia (PROSTVAC-V). It is derived from the vaccinia virus. Vaccinia virus has been given to hundreds of millions of people worldwide to prevent the disease smallpox. Vaccinia immunization has resulted in the worldwide elimination of smallpox. It is a live replicating virus that infects large mammals and rodents, and usually causes only a self-limited skin infection in humans. The virus stimulates a strong immune response, which results in the body eliminating the virus. However, caution is required in its use, in that subjects or their contacts may experience inadvertent spread of vaccinia, or worse may experience more severe rare infections. The potential for these risks, and the precautions necessary to minimize these risks, are discussed further below.

Importantly, in order to be in this study, you must have been previously vaccinated with vaccinia for smallpox (this was probably done when you were a child or possibly as a young adult). Immunity induced by vaccinia lasts decades, and the chances for complications are markedly reduced.

In clinical studies of PSA-TRICOM, the vaccine is given by injection under the skin. Most subjects experience some redness and diffuse swelling in the surrounding area, approximately 1-4 inches (2-10 centimeters) in diameter. This lasts for 7-14 days and may be accompanied by itching and soreness. There is typically full healing and no residual scarring from subcutaneous administration. On average, vaccinia stays active in your body for approximately 10-14 days. Prior to receiving your next vaccine, you will be evaluated for evidence of bacterial infection, blisters, vesicles, (lesions seen on your skin at or around your vaccine site) or evidence of persistent vaccinia infection.

When vaccinia is given to protect against smallpox, it is usually scratched into the outer layers of the skin with a two-pronged needle. A normal reaction after this administration in a person who has been previously vaccinated with vaccinia includes appearance of a small bump (papule) in 3 days, a small blister or cluster of blisters in 5-7 days, and healing with little scarring within 2 to 3 weeks. Swollen lymph nodes ("swollen glands") and/or fever are infrequent.

You would receive your investigational vaccine by a shot under the skin rather than by scratching it onto the skin the way a traditional smallpox vaccination is given. Therefore, you may have less of a skin reaction; however, vaccination with PSA-TRICOM may produce reactions similar to those seen with the smallpox vaccine.

A potential problem associated with vaccinia vaccination is accidental spread of the virus to another area of your body. This occurs rarely (incidence 1 in 4000 in some reports), however, it is very important to protect against. You can transfer the virus to your eye and mucous membranes (inner lining) of the nose, mouth or genitals by scratching the vaccination site and then rubbing the eye or an open skin area. If you participate in this study you will have to take special care of your vaccination site and wash your hands often to prevent spreading of the virus. You will be provided with written instructions with details about the vaccination site and how to care for it, as well as how to contact the study staff if you have questions or concerns.

Because you may "shed" live virus from the vaccination site after vaccination until the vaccination site heals completely, and could spread the virus to others, you must avoid close contact with the following people for approximately 3 weeks after the first vaccination only:

- persons with weak or suppressed immune systems such as individuals with leukemia or lymphoma, individuals with AIDS, or those receiving treatment to suppress their immune system (for example, after organ transplantation).
- individuals with eczema or other significant skin rashes, itching infections, burns, chicken pox, or skin injury
- pregnant or breast-feeding women
- or, children under 3 years of age

"Close contact" means that these people share your house with you, are in physical contact with you, come in contact with your bed linens or clothes, and/or you take care of them and touch them.

For every 1 million people vaccinated with vaccinia scratched into the outer layer of the skin, the vaccinia virus was transmitted to roughly 75 of their contacts (In this study, the investigational vaccine will be injected under the skin which minimizes this risk). A dressing will be placed over the vaccination site to reduce the risk of accidental spreading. It is very important that you keep the vaccination site covered. Hand washing is also necessary.

During the reintroduction of smallpox vaccination in the past decade, several individuals thought to be at risk for heart disease experienced inflammation around the heart (myopericarditis). With careful monitoring it was noted that approximately 1/2000 subjects, who had not been previously vaccinated, developed this condition. The incidence was lower in re-vaccinees. The symptoms of myopericarditis were typically mild and transient. If you have poor heart function requiring treatment, you will not be able to participate in this study.

Possible adverse reactions can also be related to allergic responses the vaccine itself. An allergic reaction to the study vaccine may be development of a rash or hives within 7 to 10 days of vaccination, which usually gets better within 2 to 4 days. Rarely, a serious allergic reaction requiring hospitalization may occur.

Generalized vaccinia may be characterized by several small blisters around the vaccination site or by widely distributed lesions developing 7-12 days after immunization. This is also known as a disseminated vaccinia infection. These tend to follow a course of healing similar to that of the inoculation site.

Serious side effects from the vaccinia vaccine are most common in young children, subjects with disorders of the immune system, and individuals with skin disorders. That is why precautions are taken to exclude such individuals from exposure.

Serious reactions such as post-vaccinia encephalomyelitis ("brain inflammation"), which can lead to coma and death, or progressive vaccinia which leads to a large unhealing sore and death are the most severe complications after vaccination. They occur almost exclusively in very young children who are exposed to vaccinia for the first time, or in subjects with impaired immunity; such individuals are not eligible for this study and must be avoided after vaccination. The death rate for people receiving revaccination with vaccinia for smallpox is about 1 in 10 million.

These serious reactions have not been seen in any subjects treated with PROSTVAC-V to date.

Vaccinia Immune Globulin (VIG) has been successful as a therapy for some but not all of these complications. VIG is an injectable antibody preparation made from the plasma of people vaccinated with the vaccinia vaccine. If symptoms develop suggestive of one of the previously described vaccinia complications, or a close contact occurs between a recently vaccinia-vaccinated subject and a susceptible person with one of the pre-existing medical conditions described above, the subject should report the findings immediately to the protocol investigator or other established contact, for consideration for VIG therapy, since VIG may work better if given early.

There are other anti-viral treatments with activity against vaccinia virus. Cidofovir, FDA approved for use in treating cytomegalovirus infections, has antiviral activity against poxviruses. However, the drug is only given intravenously under careful monitoring as it has some side effects, in particular risk for kidney toxicity.

Fowlpox Virus

PROSTVAC-F (the second and subsequent doses of PSA-TRICOM) is based on fowlpox virus. Fowlpox virus naturally infects birds, not mammals, and has been researched and used in other vaccines for at least twenty years. The virus does not grow (replicate) in human cells and is not known to cause human disease. Previous studies have indicated that using the fowlpox-based vaccine after the vaccinia-based vaccine induces a better clinical response than either virus used alone or fowlpox followed by vaccinia. The vaccines including fowlpox virus have been given in research studies to both animals and humans for HIV, malaria and cancer. Side effects from fowlpox are mild and could include injection site reactions, fever, fatigue, anemia (low red blood cell count) and leucopenia (low white blood cell count). With any experimental compound, there is the risk of unexpected and serious or deadly complications even if they have not been seen previously.

Additional risks and side effects related to the vaccine therapy with PROSTVAC-V/TRICOM and PROSVTAC-F/TRICOM

Likely:
- Injection site reaction (pain, swelling, itching, induration, and redness)
- Tiredness, weakness
- Fever
- Shaking chills
- Nausea
- Glands, (lymph node) enlarge and become tender

Less likely:
- Headache
- Allergic reaction
- Sweating
- Wound complication

• Vomiting
• Confusion and disorientation
• Loss of appetite
• Yeast infection
• Constipation
• Cough
• Diarrhea
• Indigestion
• Fatigue
• Facial tingling
• Muscle ache
• Nausea
• Facial numbness
• Pruritus (itching)

Rare but serious:

• An uncommon blood condition called thrombotic thrombocytopenic purpura (TTP). One patient treated with this vaccine developed TTP. It is not known if this was related to the vaccine or from something else. This is a serious disease that is associated with low blood counts (both red blood cells that carry oxygen and platelets that help your blood clot), bleeding, fever, neurologic symptoms (such as changes in level of alertness including coma, headache, difficulty speaking confusion or paralysis) and kidney dysfunction. The symptoms are due to the formation of clots that form or spread to many organs. This can usually be treated with exchange plasmapheresis, a therapy that removes and replaces plasma the protein containing fluid from a patient's blood. Should you go on this trial, we will follow you closely for any signs or symptoms of this disease.
• Leg weakness

Other Potential Side Effects

Additional adverse effects could be related to the immune response to the PSA and/or TRICOM proteins that are part of the vaccines. Some normal human cells (such as normal prostate cells) have these proteins on their surface. If the vaccine causes an immune reaction against these normal cells, you could develop swelling or inflammation of these tissues. While unlikely, it is also possible that if you develop a very active antibody (immune) reaction after the vaccination, you could develop an immune complex disease (or serum sickness) which can cause fevers, rashes, joint pains, and less commonly, kidney failure and severe allergic reaction inside blood vessels (vasculitis) or any part of your body. None of these symptoms have been observed to date in subjects receiving Bavarian Nordic's vaccines, but the possibility of their occurrence exists.

Risks to an Unborn Child and Sexual Partner

Birth Control

Your study doctor will discuss the risks to unborn children for drugs other than PROSTVAC or GM-CSF that may be used in this study. The effects of PROSTVAC, if any, on unborn children are unknown. If your partner is capable of becoming pregnant and you wish to participate in this study, and you have not had your prostate or testicles removed, or you are not receiving continuous hormone therapy, then you must use a medically acceptable method of birth control.

You should refrain from fathering a child or donating sperm during the study and for 3 months after you finish study treatment. If your partner becomes pregnant during the course of treatment, you must inform your doctor immediately. Your doctor will ensure that you and your partner receive information about options available to you in relation to pregnancy and that you and your partner are fully supported in whichever option you chose.

Acceptable birth control options for you and your partner include:

- surgical sterilization (you and/or your partner)
- approved hormonal contraceptives or therapies (such as birth control pills, Depo-Provera, or Lupron Depot)
- barrier methods (such as a condom or diaphragm) used with a spermicide
- an intrauterine device (IUD)

Other Risks

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

Risks from X-rays and / or Scans: Radiological testing, such as CT scans, MRIs, X-rays and/or radioactive drugs may be used to assess the treatment of your disease at various times during therapy. The cumulative radiation exposure from these tests is considered very small and is unlikely to adversely affect you or your disease. Because some of these tests require administration of contrast you could experience pain, bruising, and/or infection at the site of injection, or an allergic reaction to the contrast agent. Please notify the investigator if you know or suspect you are allergic to contrast dye.

EKG: There are no significant risks or discomforts associated with an EKG. Some patches will be adhered to your skin that may cause some reddening or slight itching.

Blood draws: There may be some side effects associated with the procedures for drawing blood in this study, but the person drawing your blood will attempt to minimize this discomfort. Side effects include pain and bruising in the area where the needle is inserted, lightheadedness, and

rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) is a risk.

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to see if enzalutamide with PROSTVAC vaccine will cause your tumor growth rate to decrease as compared to enzalutamide alone. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include delayed relapse or progression of your tumor. Because there is not much information about the vaccine's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Alternative Approaches or Treatments

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

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

- Taking part in another study
- Getting treatment with standard therapy outside this study.
- Observation only, where your doctor, depending on his clinical judgment and your opinion, follows your PSA and watches you for cancer recurrence.

Please talk to your doctor about these and other options.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board
- The study Sponsor (Center for Cancer Research) or their agent(s)
- Qualified representatives from Bavarian Nordic and/or Medivation and Astellas, Inc., the pharmaceutical companies who produce the study drugs.

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Stopping Therapy

How long will I be in the study?

You will continue to receive therapy and medical follow-up until:

- The study is completed;
- You decide that you no longer wish to participate in the study;
- You experience unacceptable side effects;
- Your cancer gets worse;
- You need to start another kind of therapy (called androgen deprivation therapy) for your cancer
- The doctor feels that it is unsafe for you to continue;
- New information becomes available that suggests another treatment would be better for you; or
- The study is stopped.

You can stop taking part in the study at any time. However, if you are thinking about dropping out of the study, please tell your research team so they can tell you how to end your participation safely.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Bavarian Nordic, Inc. and/or Medivation and Astellas, Inc. or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study are using vaccine developed in collaboration with the National Cancer Institute under a Cooperative Research and Development Agreement with Bavarian Nordic, Inc. The company also provides financial support for this study.

Use of Specimens and Data for Future Research

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

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Apheresis

You will undergo a procedure called apheresis to collect certain blood cells for immune studies to measure your immune response to the vaccine. This test will be of no benefit to you, but is part of the experimental portion of this study. Apheresis will be done at several different points for each course of enzalutamide treatment: before treatment begins, 13 weeks after treatment the treatment course has begun and at about 25 weeks after the treatment course has begun. Apheresis is a very common procedure at the Clinical Center and has very few risks. A needle is inserted into a vein in your arm to obtain blood that then goes into an apheresis machine. This machine divides whole blood into red cells, plasma (serum), and lymphocytes (white cells). The

sample cells are taken out and the rest of the blood is returned to you through a second needle in your other arm. A total of 2 Liters of blood will undergo this process.

A separate consent form will be provided to you at the time of the apheresis for you to grant permission to that procedure if you agree to the apheresis. You can participate in the study even if you decide not to undergo the apheresis procedure.

Risks of Apheresis

You may have pain or bruising where the needle is inserted. There is a very small chance of introducing infection at the needle site. There is a slight chance of blood infections from contamination of the apheresis machine, but this has never occurred at the NIH. Some patients feel weak or dizzy during apheresis. Some have tingling or numbness in their lips, fingers or toes. These symptoms don't last long, and they often stop when the procedure is slowed down.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Ravi Madan, M.D., Building 10, Room 13N240, Telephone: 301-480-7168. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM OCTOBER 16, 2017 THROUGH OCTOBER 15, 2018.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____