PRINCIPAL INVESTIGATOR: Ravi Madan, M.D.

STUDY TITLE: A Randomized Phase II Trial Combining Vaccine Therapy with PROSTVAC /TRICOM and Enzalutamide vs. Enzalutamide Alone in Men with Metastatic Castration Resistant Prostate Cancer

STUDY SITE: NIH Clinical Center

Cohort: *Patients with advanced castration resistant prostate cancer*

Consent Version: 12/04/2019

WHO DO YOU CONTACT ABOUT THIS STUDY?

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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

You have been diagnosed with metastatic, castrate-resistant prostate cancer. There are several therapies available to treat your disease. One of them is Enzalutamide, is a modern hormonal

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therapy that is taken as 4 pills once a day. This agent is FDA approved to treat metastatic prostate cancer.

This study will test a new way of potentially treating prostate cancer using a new vaccine that 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. Laboratory studies show that hormonal therapies can improve the immune system and make it work better. This accomplished by causing the body to produce new immune cells and help them move towards the prostate. That concept is being evaluated in this trial by combining enzalutamide with PROSTVAC-V/F, an immune stimulating therapy.

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. A preliminary study in 125 patients suggested that the vaccine alone may extend survival in prostate cancer patients when compared to a placebo. 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.

All patients in this study will get the FDA-approved therapy, 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.

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

Because you have been diagnosed with metastatic castration-resistant prostate cancer, you are invited to take part in this clinical research. This study is to determine whether the addition of enzalutamide to the vaccine therapy, PSA-TRICOM, prolongs the time to disease progression in patients with disease such as yours.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 72 men with prostate cancer will be enrolled in this study at the National Institutes of Health.

DESCRIPTION OF RESEARCH STUDY

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

Part A: 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 newly diagnosed 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.

Part B: During the study

Once you are found to be eligible for the study and you are willing to participate in this study, you will sign this consent form. Upon signing this consent, you will be registered to this study and randomly assigned to one of 2 arms, in a 1 to 1 ratio: Arm A - enzalutamide alone group; Arm B - enzalutamide plus the vaccine group.

All patients in both Arms A and B:

All patients will receive enzalutamide 160mg once a day orally. The side effects are listed in section *Risks or Discomforts of Participation*. The patients will be evaluated by a physician, with history, physical exams and standard blood tests and blood for research, every two weeks during the first 3 visits (Week 1 (Cycle 1 day1), Week 3 (Cycle 1 day 15), and Week 5 (Cycle 2, Day 1) then every 4 weeks. The restaging CT and bone scans will be obtained every 12 weeks or earlier if your doctor suspects your cancer get worse. Specimens obtained during your participation in this study may be sent for testing to investigators outside of NCI or the NIH.

You will be continued on study drugs as long as you are willing to participate in this study, and you tolerate treatment, and without evidence of disease getting worse based on symptoms or follow-up studies.

For the patients in Arm B:

In addition to enzalutamide, the patients in Arm B will also receive the vaccine, PROSTVAC-V/F. The background information and side effects are listed in section *Risks or Discomforts of Participation*.

The first, priming, vaccine, PROSTVAC-V, is derived from a vaccinia virus, whose genetic information is altered with insertion of 4 human genes encoding Prostate Specific Antigen (PSA) and other immune stimulating molecules. This vaccine is to be administered in Week 1 (Cycle 1 Day 1). The subsequent, booster, vaccines, PROSTVAC-F, are derived from a fowlpox virus, whose genetic information is altered with the insertion of the same human genes as the first, priming, vaccine. PROSTVAC-F is to be administered in Week 3 (Cycle 1 Day 15), Week 5 (Cycle 2 Day 1), then every 4 weeks for subsequent 4 vaccinations (Cycles 3, 4, 5, and 6), then every 12 weeks (every 3 cycles) thereafter.

You will be continued on study drugs as long as you are willing to participate in this study, and you tolerate treatment, and without evidence of disease getting worse based on symptoms or follow-up studies.

Part 3: At the end of Study

When you develop evidence of disease progression by the scans or other clinical findings, or when your study doctor thinks that your participation in this study is detrimental to your health due to your other medical conditions or due to the study drugs, or when you want to withdraw from the study, you will be taken off study drugs and taken off this study. At that time, you will be evaluated by a physician with physical and examination and labs. You will also be offered to take a part in a long-term follow up study. See the section *Gene Therapy Long Term Follow up* below for additional information.

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 treatment. 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 (PROSTVAC)

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 (empty fowlpox vector)

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. 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 the drugs used in this study. The effects of PROSTVAC and enzalutamide, 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 while you are receiving study medications and for a period of at least three (3) months after your last dose of enzalutamide .

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 be more effective at limiting cancer growth than 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 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

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

Please talk to your doctor about these and other options.

RESEARCH SUBJECT'S RIGHTS

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;
- 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.

The National Institutes of Health and the research team for this study are using enzalutamide developed by Astellas Medical and Scientific Affairs through a joint study with your researchers and the company.

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

Only patients who have the HLA-A2 or A3 tissue type will have the possibility of undergoing procedure called apheresis. Those patients will potentially have the apheresis procedure every 12 weeks during the study. During this procedure arm a very small proportion of immune cells will be selectively removed from your blood as it runs through a device. The remaining blood cells are immediately returned to your circulation. In the laboratory, white blood cells will be removed from your blood for further study. Then the remaining parts of your blood will be returned to your body. This procedure will be optional for eligible patients (based on tissue type).

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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

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

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

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

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect

reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

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

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Ravi Madan, M.D., Email: madanr@mail.nih.gov, Telephone: 301-480-7168. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.