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FRED HUTCHINSON CANCER CENTER
CONSENT TO TAKE PART IN A RESEARCH STUDY

TRAMP: Tumor Necrosis Factor- α Blockade and AR Inhibition in Men with CRPC

Short title: TRAMP

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EMERGENCY NUMBER (24 HOURS): 206.606.2284, REQUEST ONCOLOGY FELLOW ON-CALL

KEY INFORMATION

The purpose of this consent form is to help you decide if you want to be in the research study. You should not join this research study until all your questions are answered. Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard care is the treatment normally given for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) drugs, devices or procedures that are being tested for a specific condition or illness. An investigational drug is one that has not been approved by the U.S. Food & Drug Administration (FDA).

- After reading the consent form and talking with the research staff, you should know which parts of the study experimental and which parts are standard medical care. You should also know what parts you would receive even if you weren't in the study.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at or copied by the sponsor of this study. They may also be looked at or copied by government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the study. If your insurance company is billed, then it may have access to the research records. Insurance companies may not pay for treatment that is part of a study. Taking part in a study could affect your current or future insurance coverage.

Research studies include only people who choose to be in them. Please take as much time as you need to make this choice. You can talk with your friends and family about your options. You can also talk with other doctors and nurses you know. If you have any questions, ask your study doctor before making your choice.

This form tells you about the risks and possible benefits of this clinical trial. It explains what will happen if you take part. Your study doctor will also explain the clinical trial to you. After you read this document and have your questions answered, we will ask you to decide if you want to be part of this clinical trial. This process is called informed consent.

You have other options to consider for your cancer. Discuss these options with your study doctor so that you know the risks and benefits of all your choices before you decide.

When you understand the study, including the risks and benefits, you must sign this form if you want to take part in the study. If you take part in this research study, you will be given a copy of this signed and dated consent form. A copy of the consent form for this study will also be placed in your medical record.

SUMMARY

We invite you to join this research study because you have metastatic, castration-resistant prostate cancer.

The purpose of this research is to determine if the addition of a TNF-**α** inhibitor (*i.e.* golimumab) to the androgen receptor (AR) inhibitor, apalutamide, improves your response to therapy.

People who agree to join the study will be asked to attend monthly visits over 6-18 months. The study involves collection of your medical history, physical exams, imaging studies (e.g. bone scans, CT scans, and PSMA PET scans), research blood draws, and metastatic tumor tissue biopsies.

Up to 34 people will join this study.

Based on animal and lab studies, the addition of a TNF-α inhibitor to an AR inhibitor (e.g., apalutmide) resensitized the prostate cancer tumor to AR therapy and led to tumor shrinkage. We are exploring if the combination in patients will achieve the same results and lead to tumor shrinkage, PSA decline, and improve outcomes. We do not know if golimumab, in combination with apalutamide, will help treat metastatic, castration-resistant prostate cancer, it could even make your condition/disease worse. Golimumab could cause side effects such as infections, abnormal liver blood tests, or injection site reactions, as described below in this form.

VOLUNTARY PARTICIPATION

You do not have to join this study. You can choose to receive standard methods to treat metastatic prostate cancer instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

PURPOSE OF THE STUDY

We are doing this study to examine if inhibiting TNF-α allows androgen receptor (AR) inhibitors to be more effective and work longer to treat and control prostate cancer. We want to know if TNF-α inhibitors restimulate prostate cancer cells to AR inhibitors even after patients' PSA levels have increase on those treatments.

We are studying golimumab (Simponi) in combination with apalutamide (Erleada) in metastatic, castration-resistant prostate cancer. Golimumab is an FDA-approved medicine for the treatment of autoimmune diseases (*i.e.* Rheumatoid arthritis, Psoriatic arthritis, etc.). Apalutamide is an FDA-approved medicine for the treatment of men with metastatic hormone-sensitive prostate cancer and non-metastatic, castration-resistant prostate cancer.

In this study, we want to learn what effects, good or bad, golimumab in combination with apalutamide has on people with metastatic, castration-resistant prostate cancer. If you join this study, we would give you golimumab monthly for up to six times total in combination with daily apalutamide and androgen deprivation therapy (ADT) and watch carefully for any side effects.

What research tests, procedures, and treatments are done in this study?

If you join this study, we would do these tests and procedures:

- **Imaging studies.** We would ask you to complete a total of 3 imaging study (*i.e.* PSMA PET scan): once at baseline as standard of care (SOC), a second scan for research after 12 weeks on **combination** treatment, and a final scan at the end of treatment as SOC, if deemed appropriate by your treating physician and/or study investigator.
- **Metastatic tumor biopsies.** We would ask you to have two metastatic tumor needle-core biopsies – one before you start treatment and another 12 weeks after beginning treatment – in order to study the changes in the tumor microenvironment induced by combination treatment.
- **Blood draws.** We would ask you to give extra blood samples for research (*e.g.* 10mL every month) in order to **study** the effects of combination treatment on circulating cytokines.

After you have finished taking golimumab (monthly, up to six times total), you would enter the **follow-up** part of the study and continue on apalutamide daily until disease progression. We would do these tests and procedures:

- **Blood draws.** We would ask you to give extra blood samples for research (*e.g.* 10mL every three months) in order to study the effects of combination treatment on circulating cytokines.

We will also conduct genetic testing on your tissue. Your tissue contains DNA. DNA makes up the genes that serve as the "instruction book" for the cells in our bodies. By studying genes, researchers can learn more about diseases such as cancer. There are many different types of genetic tests. The testing on your tissue samples might include genetic testing called whole genome sequencing. Whole genome sequencing looks at *all* the genetic information in your cells.

DURATION OF PARTICIPATION

If you join this study, you would stay in this study for about 6-18 months depending on how long your prostate cancer remains sensitive to this treatment combination.

You would receive golimumab monthly for six months total in combination with apalutmide and ADT. After that, you would have follow-up exams in the office or clinic every three months and continue daily apalutamide along with ADT injections at pre-determined intervals until you are no longer benefiting from it.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

Long-term follow-up means keeping track of someone's medical condition for a long time. If you join this study, we would contact you via telephone, email, or mail at 6 and 12 months after your end of treatment visit to see how you are doing. We would also ask your doctor to send a copy of your medical records. This information will help us learn about the long-term effects of golimumab in combination with apalutamide.

You do not have to be in long-term follow-up. You could say "yes" or "no". Either way, you could still join this study. If you drop out of the study, you would be asked if we could contact you, as noted above.

If you choose not to join long-term follow-up, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

RISK AND SIDE EFFECTS

Golimumab in combination with apalutamide could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

If you join this study, we would tell you if we discover new side effects that could affect you.

This form lists side effects of *individual* drugs. Other side effects could occur when we use these drugs together. We will monitor this closely as part of this study.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop taking golimumab and/or apalutmide. In some cases, side effects can last a long time or never go away. There also is a risk of death.

GOLIMUMAB

The possible discomforts, side effects, and risks related to golimumab treatment are not all known. Most side effects are not serious. Some may be serious and may require treatment or additional testing. This section describes how frequently side effects occurred in adult patients who were treated with golimumab. The following terms are used:

- Very common: affects 1 in 10 or more patients (10% or more)
- Common: affects between 1 and 10 in 100 patients (between 1% and 10%)
- Uncommon: affects between 1 and 10 in 1,000 patients (between 0.1% and 1%)

- Rare: affects between 1 and 10 in 10,000 patients (between 0.01% and 0.1%)
- Very rare: affects less than 1 in 10,000 patients (less than 0.01%)

You will be told of any new findings that may affect your decision to continue in this study.

Tell your doctors or dentist that you are or have been in a study where anti-TNF alpha is the study drug. This is important if you have any surgery, dental procedures, or receive treatment for any other medical condition.

Infections

You could get more infections while taking golimumab or an existing infection could get worse. Golimumab may keep you from developing a fever if you have an infection and therefore, hide that you may have one.

Upper respiratory tract infections, infections of the nose, and throat have been very commonly seen in patients treated with golimumab.

Infections in other locations of the body and throughout the body have also been reported. Infections could be caused by bacteria, viruses, or fungi.

There have been patients treated with golimumab who have reported serious infections, including pneumonia and sepsis. Some of these infections resulted in death. Pneumonia is an infection in the lungs and has occurred commonly in patients treated with golimumab. It can vary from mild and easy to treat to serious and difficult to treat. Sepsis is an infection of the blood and/or body tissue and has occurred uncommonly in patients treated with golimumab. Patients who have a weakened ability to fight infection are more likely to get pneumonia, sepsis, or other infections than other people.

In studies in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis in which golimumab was given as injections under the skin, serious infections occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab.

Fungal infections have been reported in patients taking golimumab. Some of these fungal infections occur rarely and can be serious and involve internal organs. You should find out from your study doctor which fungal infections are common where you live or travel, and what symptoms they cause. Tell your study doctor and family physician right away if you develop symptoms of such illnesses.

If you never had chickenpox, please tell your study doctor. If you come in contact with someone who has chickenpox or shingles, tell your study doctor right away. Your study doctor may offer you some measures to prevent these diseases or decrease the symptoms of these diseases.

Tell your study doctor if you have a new infection, if an infection keeps coming back, or if you have any signs of infection such as:

Fevers	Chills	Night sweat
Flu-like symptoms	Weight loss	Tiredness
Cold sores	Headache	Coughing (blood)
Congestions	Chest tightness	Shortness of breath
Nausea	Vomiting	Diarrhea
Change in urine frequency or burning while passing urine	Redness or swelling of limbs, skin, or joint	New or worsening of pain in any location

Tuberculosis

Tuberculosis is a type of infection that usually develops in the lungs but can also develop in other areas of your body and throughout the body. Tuberculosis requires prolonged treatment with specific medication. Tuberculosis has been reported in patients who have received TNF-blockers, including patients receiving golimumab. Although a rare event, in studies in which golimumab was given as injections under the skin, tuberculosis occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab or placebo. You may be more likely to get tuberculosis while being treated with golimumab. Tell your study doctor if you develop any of the symptoms noted above, if anybody in your family has ever had tuberculosis, or if you come in contact with anyone who has tuberculosis while you are participating in this study.

Your study doctor or qualified staff will do a blood test to see if you have come in contact with tuberculosis. A chest CT scan will be done to see if there is or has been tuberculosis in your lungs. If you have a CT scan that shows signs of tuberculosis, or a positive blood test you cannot be in this study.

Cancer

Cancers have been reported in patients who have received golimumab and other TNF-blockers, and lymphoma (a cancer of lymph nodes) has been reported in these patients more frequently than expected for the general population. A type of lymphoma, mycosis fungoides, has been reported in a child treated with golimumab. Cases of leukemia (a cancer of the blood) have also been reported in patients taking TNF-blockers, including golimumab. Leukemia has occurred rarely in patients treated with golimumab. There have been cases of unusual cancers in children, teenage, and young adult patients taking TNF-blockers that sometimes resulted in death. It is known that patients who have had inflammatory diseases for a long time (such as rheumatoid arthritis, Crohn's disease or ulcerative colitis) and who use immunosuppressive therapies for a long time (such as methotrexate or azathioprine) may have a higher risk of developing cancer even if they

never received a TNF-blocker. For children and adults taking TNF-blockers, the chances of getting lymphoma or other cancers may increase.

In larger clinical studies of golimumab, the frequency of patients developing cancer was similar in the golimumab and the placebo groups, with the exception of lymphoma in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, which although a rare event, occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab or placebo given as injections under the skin. Most of the patients with lymphoma in golimumab clinical trials had rheumatoid arthritis. In a smaller study in patients with severe asthma, there were more patients that developed cancer in the golimumab group than in the placebo group. A similar finding has been observed with another TNF blocker in patients with another lung disease that is often caused by smoking called COPD (Chronic Obstructive Pulmonary Disease). If you have asthma or COPD, discuss with your study doctor if taking part in this clinical study is right for you.

Rarely, patients who received golimumab developed skin cancers, including melanoma and Merkel cell carcinoma. Melanoma was observed more frequently in clinical trial patients receiving golimumab than placebo. Merkel cell carcinoma and melanoma may result in death if not discovered early. If you notice an unusual or discolored skin bump or lesion, contact your doctor.

If you take part in a clinical study with golimumab, your risk for developing lymphoma or other cancers may increase. You should tell your study doctor prior to participating in this study if you have a history of lymphoma or cancer, and if you develop lymphoma or cancer, including skin cancer, during or after you have participated in this study.

You should also regularly discuss cancer screenings, including skin examinations, with your study doctor, and the impact of life-style choices (for example, smoking) on the risk of developing cancer.

A very aggressive type of lymphoma, called hepatosplenic T-cell lymphoma, has occurred rarely in patients who have been treated with TNF-blockers similar to golimumab. This type of cancer usually causes death. Nearly all of these cases have occurred in patients with Crohn's disease or ulcerative colitis. The majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine in combination with a TNF blocker at or prior to diagnosis. It is unclear what role golimumab may have in the development of the lymphoma. No patients treated with golimumab have developed this type of lymphoma.

Liver

It has been common for patients treated with golimumab to develop abnormal liver blood tests. Your study doctor will monitor the results of tests done on your blood during the

study. If liver blood tests are abnormal, your study doctor may stop your treatment for a while or permanently, and may perform more tests to find the cause of abnormal liver blood tests. In most cases in studies with another TNF-blocker (REMICADE®), the liver blood tests return to normal after stopping the drug.

TNF-blockers, including golimumab, may reactivate the hepatitis B virus in patients who have been known to carry the virus. Reactivation of the hepatitis B virus has occurred rarely in patients treated with golimumab. If you now or anytime in the past, have had any liver problems, including hepatitis B and hepatitis C, you should tell your study doctor right away. You will have a blood test to see if you have hepatitis B or C prior to treatment with golimumab.

There have been cases where patients taking TNF-blockers, including golimumab, have developed serious liver problems, sometimes fatal. Signs that you could be having a problem include:

- skin and eyes turning yellow
- dark brown urine
- right-sided stomach pain
- nausea
- vomiting
- loss of appetite
- fever
- extreme tiredness

If you develop any of these symptoms, tell your study doctor right away.

Infusion Site Reactions and Allergic Reactions

In patients treated with golimumab, when injected under the skin, common reactions seen at the injection site were:

- hives
- swelling
- pain
- bruising
- skin irritation
- tingling or burning
- itching
- redness

The majority of the injection site reactions have been mild or moderate.

Any drug may cause an allergic reaction in some people. The following can be signs of an allergic reaction:

- fever
- chills
- hives
- rash
- headache
- nausea
- flushing
- light-headedness
- shakiness
- irregular heartbeats
- chest tightness
- shortness of breath
- wheezing
- difficulty in swallowing or breathing
- low blood pressure

These reactions are usually mild to moderate.

Serious allergic reactions called anaphylaxis have occurred during administration of golimumab and other drugs made from proteins and can be life threatening.

If you have an allergic reaction your study doctor may give you a medication used to treat allergic symptoms (such as an antihistamine), or to reduce aches, pains, and fever (such as acetaminophen or paracetamol).

Another type of allergic reaction, called serum sickness-like reaction, has occurred in some patients 1-14 days after receiving TNF-blockers, including golimumab. The symptoms of this type of allergic reaction may include fever, rash, muscle aches and joint pain.

Latex Allergy

The needle cover for the prefilled syringe that contains study drug may contain dry natural rubber (a form of latex). This may cause allergic reactions in people who are sensitive to latex. Please tell your study doctor if you have ever had an allergic reaction to latex.

Heart

Congestive heart failure (CHF), a disease where the heart's pumping action is weakened, has been reported in patients who have received TNF-blockers, including golimumab. In some patients with known CHF, worsening of their CHF occurred. Rarely, patients treated with golimumab have developed worsening CHF or developed CHF for the first time. Some of these patients died. If you have a history of CHF or have received treatment for CHF, you are not allowed to participate in this study. Signs of CHF may include shortness of breath or swelling in your ankles and/or feet; tell your study doctor right away if you have had these symptoms or if they develop.

Lung

Interstitial lung disease is the name for diseases that inflame or scar the lungs. The inflammation and scarring may make it difficult to breathe and get enough oxygen in your blood.

Patients treated with golimumab have uncommonly developed interstitial lung disease.

Nervous System

Commonly, patients treated with golimumab experienced dizziness, numbness, or tingling.

Rarely, in studies with TNF-blockers, including golimumab, cases of multiple sclerosis and similar disorders have been observed. These events occurred more frequently in patients receiving higher golimumab doses. Multiple sclerosis is a serious disease of the

central nervous system which may cause muscle weakness, difficulties in walking, visual problems and symptoms of pins and needles. If you have any personal or family history of nervous system disorders, tell your study doctor. Signs of nervous system disorders include:

- changes in vision
- weakness in arms and/or legs
- numbness or tingling in any part of the body

Tell your study doctor right away if you experience any of these symptoms.

Blood

In studies with TNF-blockers, including golimumab, sometimes the body fails to make enough white blood cells that help the body fight infection or fails to make enough red blood cells, resulting in anemia. In addition, sometimes the body fails to make enough blood cells that help you stop bleeding. Some patients have died from this failure to produce blood cells. Your study doctor will monitor the results of tests done on your blood during the study. If you develop a fever that does not go away, bruise or bleed very easily, look very pale or become tired easily tell your study doctor right away.

Patients treated with TNF-blockers including golimumab commonly developed abnormal blood tests called ANA (anti-nuclear antibodies); some of these patients rarely developed symptoms that look like a disease called lupus. Lupus-like symptoms may include:

- muscle aches
- joint pain
- fever
- rash on the cheeks or arms that gets worse in the sun
- chest discomfort
- shortness of breath

You should tell your study doctor if this happens.

Skin

Rashes and hair loss have occurred commonly in patients treated with golimumab.

Some patients treated with golimumab may uncommonly develop fluid-filled blisters on the skin.

Uncommonly, patients treated with TNF-blockers, including golimumab, may develop worsening of psoriasis or new onset psoriasis, including a type called pustular psoriasis. Symptoms may include dry, red skin with yellow blisters, often on the palms of the hands or soles of the feet, although it can occur elsewhere.

Rarely, a type of rash called vasculitis resulting from inflammation of blood vessels in the skin can occur in patients treated with golimumab. You should tell your study doctor if you develop any of the symptoms above.

Rarely, scaly, peeling skin can occur in parts or all over your body.

Rarely, lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes) have occurred in patients treated with TNF-blockers, including golimumab.

Antibodies to Golimumab

Sometimes the body can make special antibodies that may increase the risk of an allergic reaction to either golimumab or other antibody medicines. If you have an allergic reaction, you may not be able to have these types of medications in the future. You should always tell your doctors that you have been treated with human antibodies in this study.

Vaccinations/Therapeutic Infectious Agents

Vaccines are made to help protect people from certain illnesses. Some vaccines are made from live bacteria or live viruses. You cannot receive this kind of live vaccine (for example, nasal flu vaccine, BCG) during this study or for 3 to 6 months after the last study drug administration. You could get sick from this kind of vaccine while on golimumab. Other kinds of vaccines, like tetanus and flu shots, are allowed but it is not known if golimumab may interfere with these vaccines and prevent them from working. Tell your study doctor before getting any vaccines while you are in this study. If you do get a live vaccination during this study, you should tell your study doctor, as you may no longer be allowed to receive any more study medication.

You could also get sick if you receive treatments that include live organisms (a therapeutic infectious agent) while on golimumab. An example of this type of treatment is BCG that is put into the bladder for the treatment of cancer. Tell your study doctor if you have received or are scheduled to receive treatment with a therapeutic infectious agent.

Other Medications

Tell your doctor about all the medicines you take, especially if you take any medications that affect your immune system. Taking those medications at the same time as golimumab may increase your chance of getting an infection; therefore golimumab should not be taken together with some medications that affect your immune system.

Other Risks

It was common for patients treated with golimumab to have elevated blood pressure or fever. Uncommonly, patients treated with golimumab can have constipation.

Rarely, patients treated with golimumab develop an immune disorder called sarcoidosis that could affect the lungs, skin, and lymph nodes.

Rarely, a serious inflammation of the blood vessels called systemic vasculitis may occur and in severe cases may result in permanent damage of the affected internal body organs.

There may be other discomforts or risks to you from this study that are not yet known. Your study doctor and staff will ask you about any side effects you may have at every visit. **If you have any side effects or problems, you should let your study doctor know right away.**

APALUTAMIDE

Potential Discomforts, Side Effects, and Risks Associated with Apalutamide

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

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

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

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

Risks and side effects that are related to apalutamide include:

Very Common (≥10%)	**Common (≥1% - <10%)**	**Uncommon (≥0.1%-< 1%)**	**Rare (≥0.01%-<0.1%**
Fatigue	Itching	Seizure	***Life-threatening rash with blisters and peeling over much of the body (Stevens-Johnson syndrome/Toxic epidermal necrolysis)

Skin rash	Changes in thyroid function (Hypothyroidism)	*Inflammation within the lungs that may lead to permanent damage (Interstitial lung disease)	***Skin rash with fever, and blood cell abnormalities including increase in white blood cells (lymphocytes and eosinophils), a decrease in platelets and potential life-threatening inflammation of internal organs (Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
Joint pain and Muscle spasms (Arthralgia)	Increase in cholesterol		
Weight loss	Increase in triglycerides		
Fall	Change in experience of taste (Dysgeusia)		
Fracture	Reduced or blocked blood flow to the heart, including heart attack (Ischemic Heart Disease, including Myocardial Infarction)		
Increased blood pressure (Hypertension)	Reduced or blocked blood flow to the brain, including stroke (Ischemic Cerebrovascular Disorders)		
Hot flush	Alopecia (hair loss)		
Diarrhea			
Decreased appetite**			

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

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

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

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

More than 1 in 10 patients have developed a rash. Some rashes may need medical attention. The rash may be confined to one area of your body or may spread across your body. Contact your doctor at the first sign of rash or any symptoms of rash (like itching) during the study.

Rashes that are painful, blisters on or near the lips, eyes or genitals; peeling of areas of skin surface, may need immediate evaluation by your doctor. If you develop rash with fever at the same time; contact your doctor immediately for evaluation. You may be given medicines to apply to your skin or take by mouth to help the signs and symptoms of rash. Also, the study medication may be temporarily held.

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

Reproductive Risks

The effects of golimumab and apalutamide on human sperm or unborn babies is not known. It is very important that men taking part in this study do not get a woman pregnant while participating in this study.

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

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

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

You should inform your study doctor if you father a child while participating in the research project. The doctor will advise you on any appropriate medical attention for your partner should this be necessary. The sponsor may ask you and your partner to allow him/her to collect information about her pregnancy and the health of the baby. You should also notify your partner's childbirth doctor that the father received an experimental drug (apalutamide and golimumab).

Certain Drugs May Interact With Apalutamide

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

Radiation risks

Undetectable Risk (more than background radiation): 3-50 mSv per year

Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called "background radiation". This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below. The risk to your health from this level of radiation exposure is too low to be detectable and may be nonexistent.

- PSMA PET scan: 4.3 mSv
- CT Attenuation scan: 4.5 mSv
- CT-biopsy: 5 mSv

Non-physical risks

If you join this study, non-physical risks are:

- You might not be able to work.
- Results of genetic tests might be released by accident. This risk is very low, because we keep personal information private. If these results became known, you could have problems from others knowing about your genetic test results. For example, the results could cause stress or anxiety in family members who learn about their own risk of developing disease, or you could have problems with insurance because of your health status. There is also a risk that these test results could be combined with other information to identify you.

POTENTIAL BENEFITS

We do not know if this study would help you. We are testing the combination of golimumab and apalutamide in men with metastatic, castration-resistant prostate cancer. You might get better if you receive golimumab in combination with apalutamide, but your condition could stay the same or even get worse. We hope the information from this study will help other people with metastatic, castration-resistant prostate cancer in the future.

ALTERNATIVES TO PARTICIPATION

You do not have to join this study. You are free to say "yes" or "no". Your regular medical care would not change if you decide to say "no".

You have other choices for treatment. Each of these choices has risks and benefits. By participating in this study, you may be forgoing approved therapies with potential survival benefit such as taxane, lutetium Lu 177 vipivotide tetraxetan, and PARP inhibitor if you

have BRCA-mutated mCRPC. You should talk to your doctor or healthcare provider about these choices.

Other choices include: chemotherapy, another research study, metastasis-directed therapy with radiation therapy, no treatment, or comfort care.

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Janssen pharmaceuticals (providing drug and funding support) and their affiliates.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center and University of Washington.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be disclosed if required by law. For example, we are required to report certain diseases and infections to public health authorities. We are also required to report suspected abuse or neglect of children and vulnerable adults. Workplace safety rules may require health workers to contact you about lab tests. Or a court may order that study information be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or

- Using genetic information when making decisions regarding your eligibility or premiums

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

If you join this study, you may have some extra costs. Your insurance company might pay these costs, but some insurance policies do not cover these costs. We could help find out whether your insurance company would cover these costs.

The extra costs might be:
- Cost of tests that are given for the study more often than for standard care.
- Cost of LHRH agonist/antagonist (i.e. Lupron or hormone shots).
- Cost of any other medical care needed because of this study.

If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study.

You would **not** be billed for:
- Golimumab
- Apalutamide

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact the FHCC study team. They will treat you or refer you for treatment.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study. The investigators will be closely examining changes in prostate cancer tumor microenvironment and RNA transcription comparing pre-treatment samples to on-treatment samples.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, we do not expect any test results that would affect your care, so we do not plan to return results to you.

Will my information and/or tissue samples ever be use for future research?

After we do tests on tissue in this study, some tissue may be left over. We invite you to donate this leftover tissue for future research. This may include genetic research. We also would like to use your information for future research.

If you join this study, you would not have to donate tissue or information for future research. You would be free to say "yes" or "no." Regular medical care would not change if you say "no."

If you say "no," your tissue and information (even if made anonymous) will not be used in future research.

If you donate tissue and information, it would be stored in a secure location. If we want to use your tissue for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated tissue and information would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with tissue and information might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the tissue.

If you donate tissue and information for research, you could withdraw the donation at any time by calling Dr. Ruben Raychaudhuri at 206-606-7400. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated tissue to you or your doctor, but we might be able to destroy the donated tissue. We could not destroy tissue if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

Future genetic research databases

Several genetic databases are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases.

As part of this study, we would like to release DNA code and information about your medical condition into a genetic database in order to help future research. The genetic database would not contain names, addresses, or other information that could be used to identify you.
The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

Your rights

- You do not have to join this study. You are free to say "yes" or "no".
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping golimumab and apalutamide. You and the doctor could talk about the follow-up care and testing that would help the most.
- Before you leave the study, the doctor might ask you to continue in the long-term follow-up part of the study.

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.

Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

For more information

All hospitals or clinics that do research on people have an institutional review board (IRB). This board reviews all new studies to make sure that the patient's rights and welfare are protected. The IRB at Fred Hutchinson Cancer Center has reviewed this study.

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206.606.2284 (Dr. Ruben Raychaudhuri)
If you get sick or hurt in this study	206.606.2284 (Dr. Ruben Raychaudhuri)
Your rights as a research participant	206.667.5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206.543.0098 (Human Subjects Division, University of Washington)

EMERGENCY NUMBER (24 HOURS): 206.606.2284

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Do you agree to donate your tissue and information to study cancer? (circle one) **YES** **NO**

Do you agree to donate your tissue and information to study other health problems, such as diabetes, Alzheimer's disease, or heart disease? (circle one) **YES** **NO**

Is it OK if someone contacts you in the future to ask you to donate more tissue or information for research? (circle one) **YES** **NO**

Is it OK if we send your genetic information to one or more databases for future research? (circle one) **YES** **NO**

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant:

Printed Name	Signature	Date

If you were a witness for a participant who was not able to read this written consent form, sign below to indicate (1) you were present at the consent discussion in person, (2) you witnessed the verbal presentation of the written consent form, and (3) the participant had the opportunity to ask questions and agreed to take part in the study.

Impartial Witness:

Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	Signature	Date

Protocol: 56021927PCR2051
Current consent version date: December 19, 2024
Previous consent version date: July 10, 2024
Copies to: subject; subject medical record