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Fred Hutchinson Cancer Center
University of Washington

Consent to take part in a research study:

Durvalumab and Olaparib for treatment of biochemically recurrent prostate cancer in men predicted to have a high neoantigen load: a multicenter pilot study

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Request the on-call Oncology Fellow

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully. You may ask any questions about the study. Then you can decide whether or not you want to be in the study.

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to see whether the combination of durvalumab and olaparib can help lower PSA in men who have a rising prostate-specific antigen (PSA) after surgery or primary radiation therapy for prostate cancer.

People who agree to join the study will be asked to attend at least 13 visits over 24 months. The study involves 6 months of therapy with durvalumab (given every 4 weeks into the vein (intravenously)) alone and/or in combination with olaparib (taken orally twice a day) and then study visits to check blood work and fill out questionnaires every 12 weeks until completion of the 24 months.

We do not know if durvalumab and/or olaparib would help treat biochemically recurrent prostate cancer and it could even make your condition/disease worse. Durvalumab can cause side effects such as inflammation of the lungs, skin rash, thyroid hormone deficiency and others as described below in this form. Olaparib can cause side effects such as decrease in number of blood cells, blood cancer, diarrhea, and other side effects described later in this form.

You do not have to join this study. You can choose to receive standard methods to treat biochemically recurrent 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.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have a rising PSA after surgery or primary radiation therapy for prostate cancer – this is known as biochemically recurrent prostate cancer (BCR). Men with BCR may be at higher risk of cancer spreading to other organs. Currently, there is no agreement on what the standard treatment for such men should be. Standard therapy options include lowering testosterone medications, known as androgen deprivation therapy (ADT) or observation. The purpose of the research study is to see whether durvalumab and olaparib will reduce or delay the prostate cancer recurring and also reduce or delay the need to use ADT in certain patients.

Some BCR patients have changes in their tumor DNA - part of every cell containing the blueprints for life. We are looking for men that have particular changes in their DNA called genomic instability. If you decide to join the study we will check if you have any of the three signs of genomic instability that we are looking for: loss of function CDK12 mutations, MMRd/MSI-high (mismatch repair deficiency/microsatellite instability) or HRD (homologous recombination deficiency). If you have one of these three changes you will be eligible to receive study treatment.

We expect that 15 people will be enrolled locally and up to 30 people will join study wide.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say “yes” or “no”, or to drop out after joining. If you say “no,” you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to examine whether the combination of durvalumab (Imfinzi) and olaparib (Lynpraza) helps to treat men with biochemically recurrent prostate cancer and certain changes in their tumor DNA - genomic instability

(manifested by loss of function CDK12 mutations, MMRd/MSI-high or HRD), and to examine the side effects, good and bad, associated with durvalumab and olaparib. We want to know if men with biochemically recurrent prostate cancer will experience a big decrease in prostate specific antigen (PSA) following treatment with durvalumab and olaparib.

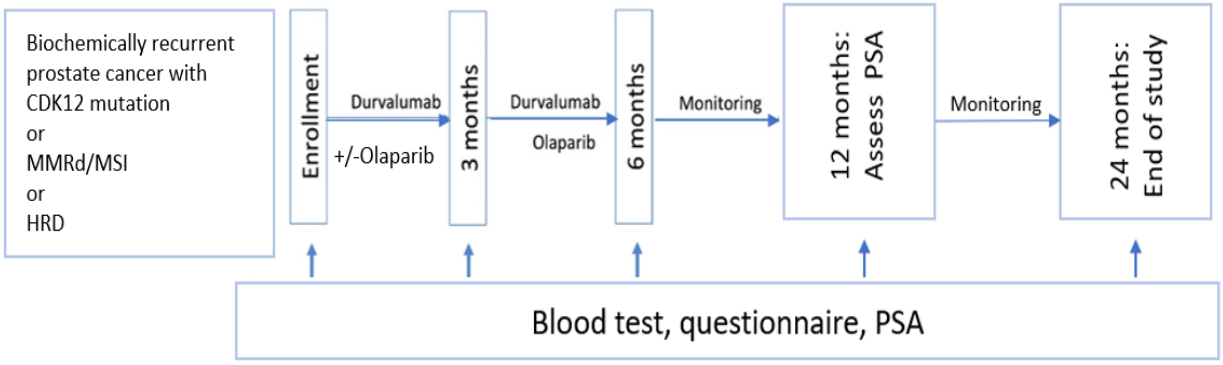
The standard treatment for patients with biochemically recurrent prostate cancer is observation or lowering testosterone medications, also called androgen deprivation therapy (ADT).

Durvalumab is a drug, which is an antibody that attaches to and blocks a molecule called PD-L1. PD-L1 is present on tumor cells and plays a role in shutting down or suppressing the body's ability to detect, attack, and destroy cancer cells. Medications like durvalumab, that target the interaction between PD-L1 and PD-1, have been shown to be effective at treating cancer patients with certain DNA changes (genomic instability). Olaparib is an oral targeted therapy (a pill taken by mouth) that turns off one of the ways cells repair breaks in DNA. Olaparib causes more breaks in the cells, which leads to genomic instability. We think that olaparib will make durvalumab work better. We believe that durvalumab and olaparib will decrease PSA in certain patients with biochemically recurrent prostate cancer, reduce or delay the prostate cancer recurring, and also reduce or delay the need to use ADT.

In this study, we want to learn what effects, good or bad, durvalumab and olaparib have on people with biochemically recurrent prostate cancer. If you join this study, we would give you durvalumab and olaparib 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: Screening/Enrollment, Treatment, and Post-treatment. Below is the schedule of study procedures:



Screening/Enrollment Procedures

You will have the following tests and procedures to make sure you are eligible to be treated on this study; most of those tests are standard of care and are done

regardless of the study. Unless otherwise noted you will have the following procedures within 4 weeks of study entry:

- We will obtain your medical and surgical history.
- We will review all medications you are taking including over-the-counter medicines, vitamins, dietary, and herbal supplements.
- We will do a physical exam.
- We will obtain vital signs (temperature, pulse, and blood pressure), including your height and weight.
- We will conduct an electrocardiogram (ECG) to test the current function of your heart.
- We will evaluate how active you are.
- We will take blood samples for screening tests. We will take about 1 tablespoon of blood. We will use your blood sample to test for the following:
    - complete blood count and chemistries.
    - to check your thyroid function. The thyroid is a gland located beneath your voice box that helps regulate growth and metabolism.
    - to check your adrenal gland function. Your adrenal glands are located on top of each kidney and help regulate your metabolism, sugar levels and blood pressure. The adrenal glands also help regulate how you respond to stress.
    - to check your pancreas function. Your pancreas is located in the back of your abdomen and releases enzymes that help digest food. Pancreas also helps regulate your appetite and blood sugar.
    - additional blood samples will be collected for research to better understand effects of the treatment.
- We will collect a urine sample for a urinalysis.
- We will do a chest, abdomen, and pelvic CT (Computed Tomography- type of x-ray using computers) scan ideally with intravenous (IV) contrast (a type of dye injected into your vein through a special line) and a bone scan to determine the extent of your disease.
- Other routine radiology studies may be needed to assess your cancer if recommended by your doctor.
- We will request your prior tumor tissue, obtained during a standard of care biopsy and/or your surgery, for testing for loss of function CDK12 mutation, MMRs, HRD. This sample is required for you to take part in this study. The local pathologist (doctor that looks at biopsies) will review the sample before you start study treatment to make sure there are enough tumor cells in the sample. The tumor tissue sample will be sent to a central lab for testing of the biomarkers we are looking at in this study. If there is not enough tumor tissue, we will draw additional blood (about 1 tablespoon) to look for tumor DNA in the blood.
- We will ask you to fill out two questionnaires that ask about your quality of life (11 questions) and erectile dysfunction (15 questions) when you join the study

and then every 3 months while you are participating in the study (total of 9 times). Some of the questions may be sensitive. Questions that make you feel uncomfortable would not have to be answered.

Since the main factor determining whether you can join this study is finding out whether or not you have one of the required gene changes in your tumor, we may start with this test before completing all of the other tests we list here. If you have any of the gene changes we are looking for, we will proceed with completing this list of tests to complete the check to see that you can join.

Treatment Procedures

If you are found to be eligible, you will start treatment. If you are enrolled into the study, you will start the study medications (durvalumab and olaparib).

During the treatment period, you will be asked to come to the clinic to receive the study drug (durvalumab) every 4 weeks for total of 6 months. Before receiving each treatment, you will be asked about any new problems that may have occurred since your last visit. Durvalumab will be given as an IV infusion (into your veins) over approximately 60 minutes.

Depending on what gene changes you have, you will take olaparib for total 6 months (patients with HRD) or for total of 3 months (patients with MMRd/MSI-high and CDK12 mutations). Patients who are planned to receive 6 months of olaparib will start it at the same time as durvalumab. Patients who are planned to receive only 3 months of olaparib will start it with the 4th cycle (dose) of durvalumab. You will take two 150 mg tablets of olaparib twice daily (300 mg total). A 4-week supply of the oral drug (olaparib) will be provided at the beginning of each month of the trial. You will be given a diary to record your olaparib dosing. Study staff will instruct you on how to fill out your diary. Olaparib must be taken only by you. It must also be kept out of the reach of children or persons of limited capacity to understand.

Certain drugs may interact with durvalumab and/or olaparib. You need to tell your study doctor of all medications and supplements (e.g., herbs, vitamins) you take.

You will be evaluated for side effects and asked about all medications you are taking throughout the study. Below are time points and the tests and procedures that will be done during these time points. The study doctor may perform more tests and procedures if they feel it is necessary to monitor your safety and evaluate your cancer.

During each of the treatment visits, you will have the following tests, procedures, and assessments done:

- We will review all medications you are taking including over-the-counter medicines, vitamins, dietary and herbal supplements.
- We will do a physical exam.

- We will obtain vital signs (temperature, pulse, and blood pressure), including weight. These will also be done before and through your infusion.
- We will evaluate how active you are.
- We will take blood samples for complete blood count and chemistries. We will take about 1 tablespoon of blood each visit.

Before the 4th infusion visit, after 6th infusion visit, and at the 12- and 24- month time points we will do more assessments:

- In addition to the assessments, tests, and procedures above, we will collect additional blood specimens to check your PSA as well as your thyroid, adrenal and pancreas function, and blood sample for research. We will take about 2 tablespoons of blood during these visits.
- We will ask you to fill out the same two questionnaires that you filled out when you joined the study that ask about your quality of life and erectile function. We will compare them to answers you gave before treatment to evaluate if treatment affected your quality of life.

How long would you stay in this study?

If you join this study, you would stay in this study for 24 months. You will receive durvalumab every 4 weeks for total 6 doses. Depending on particular DNA changes your tumors have, you will start oral tablets of olaparib at the time of 1st or 4th infusion visit. You will continue taking olaparib twice a day every day for 3 or 6 months. You will have a total of 6 months of treatment: 3 months of durvalumab, followed by 3 months of a combination of olaparib and durvalumab or 6 months of durvalumab and olaparib combination therapy. You will then have follow-up exams every 3 months for at least 2 years after enrollment to check on your health and any other anti-cancer therapies you may have taken or are taking.

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.

You may withdraw from the study for any reason. If you withdraw from the study, 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.

Once you are no longer receiving study medications, or if you withdraw from the study at any time, we will follow-up either during a routine clinic visit or by phone call to see how you are doing and to learn about any other anti-cancer therapies you may have taken or are taking. This will occur approximately every 3 months for a maximum of 24 months after you join the study or until the study closes.

Afterward, you will continue to be monitored at regular intervals as per standard practice to ensure that the cancer does not come back. We will ask you permission to access your clinical chart after you completed study participation to follow up on your health for up to 5 years. With your permission, 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 durvalumab and olaparib

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 call you as often as every 3 months to see how you are doing.

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.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Durvalumab and olaparib could cause additional side effects we do not know about yet. We will 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.

You may experience all, some, or none of the side effects described below. Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Some side effects may not show up until several weeks after treatment is given. Many side effects may go away soon after you stop taking the medications. In some cases, side effects can last a long time or never go away. There is also a risk of death.

Risks and side effects that may or may not be related to the study drugs given in this study may include:

Durvalumab

Durvalumab works by helping your immune system to fight your cancer. However, durvalumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking durvalumab. Durvalumab side effects are often treated with steroids. About 30 in 100 treated patients require steroids therapy. The study doctor believes that the following side effects may be caused by durvalumab.

Common durvalumab side effects (greater than 10 in 100 chance this will happen) include:

- Itching of the skin
- Rash
- Cough
- Loose or watery stools
- Joint pain
- Fever
- Back pain
- Low level of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps, and/or feel sick to your stomach
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools

Less common durvalumab side effects (1 in 100 to 10 in 100 likelihood this will happen) include:

- Inflammation of the lungs so you may feel short of breath and cough. Sometimes this condition might lead to death
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection. These severe conditions can sometimes lead to death.

Rare durvalumab side effects (out of 100 people who receive durvalumab, less than 1 person may have) include:

- Immune-mediated Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs,

arms and upper body leading to severe muscle weakness and possible temporary paralysis

- Inflammation of the muscles so you may feel weak or have pain in your muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Inflammation of the pituitary gland or hypothalamus (both glands in the head), which may cause problems with how your kidneys process fluids and lead to increased urinary frequency and thirst
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, lose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots.
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting. Sometimes this condition can lead to death.
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy.
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing.
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs.

- Inflammation of the brain with confusion and fever. This may also include disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness.
- Pancreatitis is an inflammatory condition of the pancreas that frequently includes low-grade abdominal pain with accompanying fever and a general feeling of discomfort, illness, or uneasiness.
- Encephalitis is a rare event resulting in the inflammation of the brain with consequent neurologic dysfunctions. Encephalitis frequently causes only mild flu-like signs and symptoms, such as a fever or headache, or no symptoms at all. Sometimes though, the flu-like symptoms can be more severe. Encephalitis is possibly associated with confusion, seizures, or problems with the motor and sensory systems. In some cases, encephalitis may be life-threatening.
- Low platelets due to an auto-immune effect

Olaparib

Very common (affects more than 1 in 10 patients) side effects that may occur are:

- Feeling sick (nausea)
- Being sick (vomiting)
- Tiredness/weakness (asthenia)
- Loss of appetite
- Headache
- Change in taste of foods (dysgeusia)
- Dizziness
- Diarrhea. Your doctor may prescribe a medicine to treat this. If it gets severe, tell your doctor straight away.
- Cough
- Indigestion/heartburn (dyspepsia)
- Difficulty breathing (dyspnoea)

The following side effects are very commonly (1 in 10 patients) shown in blood tests:

- Decrease in the number of red blood cells (anemia), which can be associated with symptoms of shortness of breath, fatigue, pale skin or fast heartbeat
- Decrease in the total number of white blood cells (leukopenia) and in certain white blood cells (neutropenia) that protect from infection, which can be associated with symptoms of fever

Olaparib less common side effects (1 to 10 in a 100 chance this will happen) include:

- Venous Thromboembolism includes PTs of deep vein thrombosis, embolism, pulmonary embolism, thrombosis, vena cava thrombosis and venous thrombosis.
- Sore mouth (stomatitis)
- Pain in the stomach area under the ribs (upper abdominal pain)
- Rash

The following side effects are commonly (1 to 10 in a 100 chance this will happen) shown in blood tests:

- Decrease in the number of platelets in blood (thrombocytopenia) which can be associated with symptoms of bruising or bleeding for longer if injured
- Increase in blood creatinine seen from a laboratory test showing how your kidneys are working
- Decrease in the number of white blood cells that support the immune system (lymphopenia) which can be associated with increased susceptibility to infection

Olaparib uncommon side effects (up to 1 in 100 chance this will happen) include:

- Hypersensitivity
- Mean cell volume elevation (an increase in size of red blood cells). This will be monitored by the laboratory safety tests that will be done in this study because this doesn't normally have any symptoms.
- Allergic reactions
- Itchy rash on swollen, reddened skin (dermatitis)
- Tender bumps under the skin (Erythema nodosum)
- Swelling under the skin (Angioedema)
- Myelodysplastic syndrome: a pre-cancerous condition where the bone marrow isn't as good at producing blood cells as it was before (red blood cells and/or white blood cells and/or platelets). This condition has the potential to transform into acute myeloid leukemia.
- Acute myeloid leukemia: a cancer of the bone marrow where many abnormal and immature white blood cells (blast cells) are made while normal functioning blood cells are not made.

Other potential risks of olaparib

Other side effects have been seen in previous studies, but it is not yet known if these were related to olaparib, or if they were unrelated events possibly due to the patient's cancer or other cause. Assessing the full range of side effects of olaparib is an important part of this study.

Pneumonitis: (lung inflammation) has been reported in a small number of patients treated with olaparib in previous studies, and has led to death in some reports. It is not known if olaparib caused the pneumonitis in these patients as they might have had other possible causes such as lung cancer

and/or metastases in the lungs, pre-existing lung disease, were smokers, or had been treated previously with chemotherapy or radiotherapy. If you experience any new or worsening symptoms of shortness of breath, cough and fever, you should contact your study doctor as soon as you can.

Driving and using machines

The study drug may affect your ability to drive or use machines. If you feel dizzy, weak, or tired while taking your study treatment, take special care when driving or using tools or machines.

The study doctor may decide to interrupt and/or reduce your olaparib dose if you experience certain side effects. If your dose is reduced, you will be given a new bottle of tablets.

Drug interactions

Combination of olaparib and durvalumab safety

Combination of olaparib and durvalumab was studied in phase I/II study (NCT03810105). In this trial most common side effects were decreased red blood cells (4/17 patients), decrease in certain immune cells (lymphopenia 2/17 patients), infection (2/17 patients) and nausea (2/17 patients). Four patients had immune-related side effects, including 2 with sudden hearing loss on one side, one with eye nerve inflammation, and one who developed joint inflammation and swelling. All immune related side effects were treated with high-dose steroids. After treatment, symptoms disappeared completely or close to completely in 3 patients. Patient with hearing loss required use of a hearing aid.

Durvalumab and Olaparib taken in combination with other medicines may be associated with other risks that are unknown at this time. If any physician other than the study doctor prescribes medication for you for another condition or you are taking over-the counter medications, vitamins, dietary or herbal supplements, you must inform the study staff.

You may not take certain medications or receive certain medical treatments without the permission of the study staff during the study and for up to 30 days after the last dose of durvalumab or olaparib. This includes other anti-cancer treatments, other medications that can suppress your immune system (i.e., prednisone greater than 10 mg) and live vaccines.

Other risks and discomforts

The risks of having blood drawn and/or inserting the needle in your vein, include fainting, bleeding, bruising at the place on your arm where the blood was drawn or needle inserted, pain, swelling and rarely, infection or nerve damage.

Radiation risks

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.

There is minimal risk to your health from the amount of radiation you will receive in this study. The usual lifetime risk of getting cancer is 42%. For every 10 mSv you receive, your risk may increase 0.1%. If you have more procedures that expose you to radiation, your risk will go up. For comparison, the estimated radiation dose from each of these tests is listed below:

- CT chest: 7 mSv
- CT abdomen: 8 mSv
- CT pelvis: 6 mSv
- Bone Scan: 5.3 mSV

Reproductive risks If you are a sexually active male and your partner is of childbearing potential, from the time of screening throughout the total duration of the drug treatment and the drug washout period (90 days after the last dose of durvalumab), you must agree to use a medically acceptable form of birth control, as determined by your study doctor in order to be in this study. Male patients should refrain from sperm donation throughout this period and for 3 months following the last dose of olaparib or durvalumab. Female partners (of childbearing potential) of male patients must use two highly effective methods of contraception in combination throughout this period and for 3 months following the last dose of olaparib or durvalumab. It is important that you tell your doctor if your female partner becomes pregnant during the course of the study or within 7 months of the last dose of durvalumab. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, she should promptly notify her doctor and that the study team will request her permission to receive information on the outcome of her pregnancy.

Non-physical risks In addition to the physical risks/discomforts associated with this study, there may be psychological, emotional, financial, social, and legal risks that might result. There may be financial risks related to reimbursement for study procedures. If you join this study, non-physical risks are:

- You may get tired or bored when we are asking you questions, or you are completing questionnaires. You do not have to answer any question you do not want to answer.
- There is risk that information about you may become known to people outside this study.
- 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 with family members or insurance.
- There may be psychological, emotional, financial, social, and legal risks that might result. These risks include change in emotional state, anxiety, or depression associated with taking the study drugs. There may be financial risks related to reimbursement for study procedures.

What are the benefits?

We do not know if durvalumab and olaparib will help treat your cancer. Durvalumab and olaparib have been used before in treatment of prostate cancer and showed activity in certain patients. Potential benefit to you could be postponing starting ADT and side effects associated with it, but your condition could stay the same or even get worse. If effective, patients enrolled to this study would benefit by receiving an effective combination therapy that is otherwise unavailable. There may be no direct benefits to participants in this study, however, participants and others may benefit in the future from information learned from this study. Specifically, information learned in this study may lead to the development of a safe and effective treatment of biochemically recurrent prostate cancer with genomic instability. We hope the information we learn will help people with biochemically recurrent prostate in the future.

You have other choices besides this study.

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. You should talk to your doctor or healthcare provider about these choices.

Other choices include:

- Standard therapy which may include other FDA-approved available therapies for your cancer such as androgen deprivation therapy (ADT).
- Taking part in another research study.
- Close observation with no therapy, also called “watch and wait” approach if you don’t want treatment at this time despite discussion with your doctor.
- Supportive 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.
- AstraZeneca Pharmaceuticals (the sponsor of the study) and their agents.
- 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
- 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 given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to 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.

Financial conflicts of interest

The study team and the University of Washington are receiving financial support and study drugs from AstraZeneca for the time spent completing study-related duties.

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 would 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 are:

- Cost of tests that are given more often than usual.
- Cost of people and equipment to give durvalumab and olaparib. There is no charge for durvalumab or olaparib itself.
- Cost of standard doctor visits and lab tests.
- 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:

- Study drugs, durvalumab and olaparib.
- Testing for genomic markers: loss of function CDK12, MMRd/MSI-high, HRD.
- Submission and storage of tumor samples obtained from prior biopsy or surgery.
- Collection and storage of research blood samples.

If durvalumab and/or olaparib are approved as a treatment while this study is still going on, you or your insurance company might have to pay for durvalumab and olaparib in order to complete this study.

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 Dr. Michael Schweizer. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

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

You would not lose any legal right to seek payment for treatment if you sign this form.

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.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you.

Your information biospecimens collected as part of this research study will not be used or distributed for any research other than the study presented.

Commercial Profit

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.

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 durvulamab and/or olaparib. 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 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 Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website 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

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)	206-606-6252 (Dr. Michael Schweizer)
If you get sick or hurt in this study	206-598-6190 (Oncology Fellow on call)
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)
Your bills and health insurance coverage	206-598-8260 (UWMC Patient Financial Services) 206-606-1091 (Fred Hutchinson Cancer Center Patient Financial Clearance)

Emergency number (24 hours): 206-598-6190

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 served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

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: V8 (11OCT2022)
Current consent version date: 11OCT2022
Previous consent version date: 30JUN2022
Copies to: Researcher and Subject