ID: UMCC 2018.108 NCT03787680

Targeting Resistant Prostate Cancer With ATR and PARP Inhibition (TRAP Trial)

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: A Multi-Center Phase II Study Testing the Activity of Olaparib and AZD6738 (ATR Inhibitor) in Metastatic Castration-Resistant Prostate Cancer

Company or agency sponsoring the study: The University of Michigan along with support from AstraZeneca

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator:
Zachery Reichert, MD, PhD Department of Internal Medicine, Hematology/Oncology, University of Michigan

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains information that will help you decide whether to join the study. All information in this form is important. Take time to carefully review this information. After you finish, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your friends, family, or other doctors about your possible participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you do, be sure you understand what the study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying a new drug in small numbers of people to learn about its safety and its effect on your body at certain doses as a treatment for metastatic-castration resistant prostate cancer. This study will be using the drugs olaparib and AZD6738. These drugs are considered targeted therapy. They work by blocking small molecules in your cancer that are responsible for the growth of your disease. New clinical data from a different trial targeting a different cancer using the same dosing schedule found there is no meaningful difference for a subset of people of one of the treatment arms (people with BRCA1 or BRCA2 loss) between taking olaparib and AZD6738 together compared to taking olaparib by itself. As this was a different cancer and only a subset of patients, there remains potential for clinical benefit in this trial by your participation and olaparib and AZD6738 will continue to be taken together for the remainder of the trial. You will take olaparib orally twice a day, and on certain days you will also take AZD6738 orally for as long as you are tolerating the treatment and your cancer does not get worse. Others procedures that will take place throughout the course of the study include physical exams, blood draws, scans of your cancer, urine collection, tests to measure your hearts health along with other

items listed later in this document. Your health-related information and tumor tissue and/or saliva will be collected for research purposes.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include diarrhea, vomiting, decreased appetite, fatigue, and a decrease in your red blood cell count. More detailed information will be provided later in this document.

This study may not offer any benefit to you now but may benefit others in the future by helping people to live longer or improve the quality of life.

We expect the amount of time you will participate in the study to vary depending on how your disease responds to the study intervention and if you have any major side effects.

You can decide not to be in this study. Alternatives to joining this study include receiving standard of care treatment, participating in other research trials, if one is available or you may also choose not to receive any further treatment.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

Cancer is caused by changes to genes that control how our cells function. Some prostate cancer cells (about one of every five patients) has gene changes resulting in the cancer losing the ability to repair DNA efficiently. These patients are termed to have DNA repair defects. Drugs that stress these damaged DNA repair functions have shown promise and this study will further explore that.

For patients whose cancer does not have these DNA repair defects (about four out of five patients), drugs that affect the normal DNA repair process may work better together than apart. This study will explore that.

The DNA repair status test will be done on a tissue sample of your tumor that was collected previously OR if you don't have tissue, it will be done on a new biopsy or blood sample that you have to provide. This DNA repair status test is not approved by the Food and Drug Administration (FDA) and is still considered investigational.

Overall, the purpose of this study is to test the effectiveness (how well the drugs work), safety, and tolerability of the investigational drug combination of olaparib and AZD6738 for all patients with metastatic castration-resistant prostate cancer.

Olaparib is also known as Lynparza ® and approved by the Food and Drug Administration (FDA) for the treatment of breast cancer and ovarian cancer. Olaparib is being studied in multiple cancers. Olaparib works by blocking proteins called PARP. PARP is important for repairing damage to DNA. When this damage cannot be repaired, the cell dies. Olaparib is not currently approved by the FDA for the treatment of prostate cancer.

AZD6738 is a DNA damage response kinase inhibitor that is currently being tested in combination with olaparib for gastric cancer and breast cancer, however it is not approved by FDA for the treatment of prostate cancer or any other diseases.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Adult men who have adenocarcinoma of the prostate.

There are many other inclusion and exclusion criteria which the doctors will use to determine if you can participate in this study. It is important that you discuss your full medical history and all of your medications with your doctor.

3.2 How many people (subjects) are expected to take part in this study?

A total of approximately 47 subjects at several institutions will take part in this study, including approximately 36 from the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

The study team will explain the research study and answer any questions you have about the study. If you want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Many of the procedures that will be performed during the study, including routine blood tests, disease evaluations, physical examinations, vital signs (blood pressure, heart rate, breathing rate, and temperature) and measurement of height and weight, would normally be done as part of your standard of care regardless of study participation. However, some of these may be done more frequently as a result of your participation in this study.

Tests and procedures that are done more often than your regular medical care because of your study participation and that are solely for research purposes will be identified below. The study staff will inform you of the types of tests and procedures you have to undergo during the study.

During the study you must:

- Follow the instructions you are given.
- Come to the study center for your visits with the study doctor. Virtual (by phone or computer) clinic monitoring will be allowed as indicated by the enrolling physician, depending on your willingness and/or availability. Tell the study doctor or study staff about any changes in your health and/or medications you are taking.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

Before starting the study: Some exams, tests, and procedures will be required to find out if you can be in this study. If you have had some of the tests recently, they may not need to be repeated. The screening tests and procedures do not have to be completed in one day and you are allowed to take breaks if you have multiple procedures in one day.

The following tests and procedures will be performed during screening and/or at one or more study visits. Refer to the study calendar below for information about which procedures will be performed at certain study visits.

- **Medical history**: including any past treatments, surgeries, infection and autoimmune diseases.

- **Medications**: It is important that you tell your doctor about all of the medications that you have been taking, including over the counter medicines, vitamins or herbal treatments.

- **Physical exam/Vital Signs**: including measurement of your height, weight, blood pressure, heart rate, respiratory rate and temperature. For virtual clinic visits, the physical exam and collection of vital signs will not be required.

- **Performance status**: Your ability to perform day to day activities and care for yourself

- **Routine blood tests (approximately 2 teaspoons)**: will be drawn for tests to check blood counts, chemistry, and blood markers for cancer (PSA, testosterone). For certain visits blood tests may not be collected if the local lab is closed.

- **Urinalysis**: A urine sample for standard laboratory tests to check your general health.

- **Electrocardiogram:** An ECG is a recording of the electrical activity of your heart.

- **Scans of your cancer**: these could include Computed tomography (CT) of the chest, CT or magnetic resonance imaging (MRI) of the upper and lower belly or bone scan.
    - A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the Radiology Department and takes about half an hour.
    - A MRI scan takes an image of your head or body to observe the location and size of your tumor. For the MRI scan, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). You will be asked to lie down on a narrow bed which will slide into a tunnel that is 6 feet long by 22 inches across and is open at each end. You will be asked to lie quietly for about one hour, during which time you will hear a loud machine-like noise. A MRI scan takes about an hour and a half to complete.
    - Bone scan. A bone scan is a procedure in which a very small amount of radioactive material is injected into a vein in your arm. The radioactive material is then transported by your blood into your bones. This will allow the doctor to monitor the cancer in your bones before, during, and after you receive the study treatment.

- **Toxicity evaluation:** You will be asked about any side effects or illnesses you experience.

- **Tumor tissue:** Your doctor will check to see if you have had certain tests performed on a tissue sample of your tumor that was collected previously. If you have not had these tests, you will be asked to undergo a fresh tissue biopsy. If the biopsy doesn't have enough tissue for testing or you can't have a biopsy for safety reasons; we will collect an additional blood sample for testing. You must have tissue or blood for

this testing for you to participate in this study. *This tumor tissue biopsy/additional blood sample is for research purposes.*

- **Blood for Research (approximately 3-5 tablespoons):** Will be drawn for testing for biomarkers (testing of substances such as proteins that tell us how the drug is working in your body). *This is for research purposes.*

- **Saliva for Research:** You will be asked to spit into a small bottle. Saliva will be used along with your tumor tissue and blood to help researchers better understand the reasons for cancer development, growth, spread and its response.

Study Intervention (for Research):
If you qualify to participate in the study based on the results of the screening tests and procedures, you will return to the study doctor's clinic. You may receive your study medications (olaparib and/or AZD6738) directly at home, per local study team instructions. The medications will be shipped to you using an overnight delivery courier that will require a signature when the package is delivered.

Olaparib:
You will take olaparib twice a day by mouth – once in the morning and once in the evening (approximately 12 hours apart) on days 1-28 of a cycle.

AZD6738:
You will take AZD6738 once a day by mouth –on days 1-7 of the 28-day cycle.

For your morning dose:
- Fast for 2 hours before and for 1 hour afterwards.
- You should take olaparib and AZD6738 at the same time each morning on days 1-7

For your evening dose:
- You should take only olaparib and it can be taken with or without food

Below are general rules for taking the study drugs:
- Swallow whole (do NOT break, chew, crush, dissolve or divide the tablet)
- The medication SHOULD NOT be ingested if broken, cracked or otherwise not intact.
- If you miss a dose (i.e. you do not take it within 2 hours of the scheduled time) DO NOT "make it up". Skip the missed dose and start taking the study drug(s) with the next scheduled dose.
- If you vomit after you take the tablet(s), and you can see that the study drug tablet appears to be complete you can attempt to take the dose for up to 2 hours after the scheduled time. If you cannot take it within 2 hours of the scheduled time DO NOT "make it up". Skip the missed dose and start taking the study drug(s) with the next scheduled dose.
- You should not consume grapefruit juice or Seville oranges (including marmalade, juice, etc.) while participating in the study.
- You should avoid sun exposure and it is recommended that you use sunscreen
- You should be careful with driving within the first few days of starting therapy (cycle 1 only) due to the risk of low blood pressure since tolerance is unknown.
- Olaparib has concomitant drug interactions and may require dose reduction if a strong or moderate CYP3A is required for a short period while on study.

You will be required to keep a drug diary to track when you take the olaparib and AZD6738. Bring your drug diary and medication bottles (empty and/or with extra tablets), with you when you return for each appointment.

If you experience adverse events, you might have to stop taking all or some of the study drugs and if you recover from your adverse events, you may be able to restart the study drug(s).

You may continue to receive olaparib and AZD6738 as long as you are tolerating the treatment and your disease has not progressed.

Follow-up:
If you stop the study intervention for any reason you will be asked to return for end of treatment visit 30 days after your last dose of study intervention.

If you have been diagnosed with Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) or another malignancy, a questionnaire may be sent to you for further information. This will continue for 5 years after you complete the study treatment.

See the table for a summary of the study intervention and procedures.

Study Procedures Table:

Procedures	Screening	Cycle 1, 2*		Cycle 3+*	End of treatment Visit	Long-term Follow up
		Day 1	Day 8	Day 1		
Medical History	X					
Medication Review*	X	X	X	X	X	
Physical Exam/Vital Signs*	X	X	X	X	X	
Performance status*	X	X	X	X	X	
Routine Blood tests**	X	X	X	X	X	
Urinalysis	X					
ECG	X	X				
Scans/Imaging of your Cancer	X***			X***		
Research Blood*	X	X		X (Cycle 3 Day 1 only)	X	
Tumor Tissue/Biopsy/Saliva	X					
Study Drug Administration		X	X	X		
Toxicity Evaluations		X	X	X	X	
Long-term follow-up for MDS/AML or new malignancy						X

*Virtual visits (by phone or computer) will be allowed at the discretion of your oncologist as described below:

- Physical Exam/Vital signs will not be required for virtual visits
- Cycle1 Day8 – Visit window ±3 days
- Cycle2 Day1 – Visit window ±3 days

- Cycle2 Day8 – Visit window at your physician's discretion
- Cycle3+ Day1 – Visit window up to -5 days to + 3 days

**For certain visits blood tests may not be collected if the local lab is closed.
*** To accommodate biopsy timing, the screening CT and bone scans to enroll will allow for scans up to 6 weeks prior to Cycle 1 day 1. If by the time therapy starts (to accommodate delays) prior scans will be >4 weeks from the planned start date of treatment, they must be repeated prior to Cycle 1 day 1 (≤4 weeks). While receiving treatment, scans are performed every 8 weeks (±1 week) from Cycle 1 day 1. After the 3rd scanning timepoint (about 6 months), scans can be performed every 12 weeks (±1 week) from Cycle 1 day 1.

OPTIONAL Research Samples Stored for Unspecified Future Research:

Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens. We would also like your permission to keep some of your blood, tumor tissue, saliva and medical information collected in the main study, so that we may study it in future research. The future research may be similar to this study or may be completely different.

You can take part in the main study even if you decide not to let us keep your blood, tumor tissue, saliva and medical information for future research.

If you give us permission, we will use your blood, tumor tissue, saliva and medical information for future research. Even if you give us permission now to keep some of your blood, tumor tissue, saliva and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your blood and tumor tissue, we may not be able to take the information out of our research.

We may share your blood, tumor tissue, saliva and medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your blood, tumor tissue, saliva and medical information with other researchers, we will not be able to get it back. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your blood, tumor tissue and saliva samples. If you have the screening biopsy, the results of the tests run on the tumor tissue sample will be released to your treating doctor. Allowing us to do future research on your blood, tumor tissue, saliva and medical information will not benefit you directly.

With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the future research on your blood, tumor tissue, saliva and medical information. You will not have rights to these discoveries or any proceeds from them.

You can make your choice about whether to participate in the Optional substudy (storage of research samples for future use) in Section 12 of the consent.

4.2 How much of my time will be needed to take part in this study?
The initial screening visit will take approximately 2-5 hours. Each study visit is expected to take approximately 4-6 hours.

4.3 When will my participation in the study be over?
The maximum time you will be in the study will depend on how your disease responds to the study intervention and if you have any major side effects. After you stop taking the study intervention you will be asked to come back for an end of treatment visit. Your participation may end sooner if you decide to no longer participate, your study doctor feels it is in your best interest to stop your study participation, your disease progresses or the study is ended. You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular physician first.

4.4 What will happen with my information and/or biospecimens used in this study?
Your collected information and biospecimens may be shared with AstraZeneca. Your collected information and biospecimens may also be shared with other researchers, both here or around the world, or with companies. Any sharing is subject to contractual obligations with AstraZeneca.

Additionally:

- With appropriate permissions, your identifiable collected information and biospecimens may be shared, and/or,
- Without your additional consent, your identifiable private information and identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?
The drugs used in the study may cause certain side effects and discomforts. You may have all, some, or none of the known side effects. There is also a risk that other rare or unknown side effects may occur. Your doctors and nurses will check you closely for side effects, and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study medication is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death. If you have any side effects, it is important that you report them to your study doctor or research staff.

These risks will be minimized by monitoring you carefully. We will provide the usual supportive care that would be routinely given to someone with your condition. If you have side effects from the study intervention, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the study intervention if the side effects are too serious.

The known or expected risks are:

Side Effects ASSOCIATED WITH OLAPARIB

Common Side Effects (> or equal to 10% of study subject)

- Diarrhea
- Nausea/vomiting
- A change in the sense of taste
- Acid or upset stomach (heartburn)
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- Decreased appetite
- Headache
- Dizziness
- Shortness of breath
- Cough
- Extreme tiredness (fatigue) and weakness
- Low number of red blood cells that can causes tiredness and shortness of breath (Anemia)
- Condition in which the number of white blood cells circulating in the blood is abnormally low (Leucopenia). This increases the risk of infection, which may be serious or life threatening
- Condition in which the number of white blood cell called neutrophils is abnormally low. This increases the risk of infection, which may be serious or life threatening (Neutropenia)
- Low number of platelets which may cause bleeding and bruising (Thrombocytopenia). Bleeding may be serious, or life threatening and may require a blood transfusion.
- Venous thromboembolism (VTE), also known as blood clots, is a disorder that includes deep vein thrombosis and pulmonary embolism. A deep vein thrombosis (DVT) occurs when a blood clot forms in a deep vein, usually in the lower leg, thigh, or pelvis. A pulmonary embolism (PE) occurs when a clot breaks loose and travels through the bloodstream to the lungs
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Occasional Side Effects (> 5% of study subjects)

- Constipation
- Swelling of arms or legs
- Fever
- Rash

Rare Side Effects (<5% of study subjects)

- Cancer of the bone marrow (for example leukemia or myelodysplastic syndrome). Myelodysplastic syndrome is a condition that can occur when the blood-forming cells in the bone marrow become abnormal. This leads to low numbers of one or more types of blood cells.
- Irreversible damage to bone marrow which may cause infection, bleeding or require transfusion
- Inflammation of lungs that may cause shortness of breath
- Itchy rash on swollen skin (dermatitis)

Some patients who took olaparib after it was approved to use by the FDA experienced an allergic reaction that could include rash, itchy rash or swollen skin (dermatitis), and/or a severe allergic reaction that could include rapid build-up of fluid under the skin, in the face, in the lining of the intestine, and possibly in the throat or swelling of the tongue which could make it difficult to breath and rarely can be life threatening (angioedema).

Side Effects ASSOCIATED WITH AZD6738

Common Side Effects (> 10% of study subject)

- Low number of red blood cells that can causes tiredness and shortness of breath (Anemia)
- Fatigue

Occasional-Rare Side Effects (<10% of study subjects)

- Nausea
- Vomiting
- Diarrhea
- Loss of appetite and weight loss (Anorexia)
- Condition in which the number of white blood cells called neutrophils is abnormally low. This increases the risk of infection, which may be serious or life threatening (Neutropenia)
- Condition in which the number of white blood cells circulating in the blood is abnormally low (Leucopenia). This increases the risk of infection, which may be serious or life threatening
- Low number of platelets, which may cause bleeding and bruising (Thrombocytopenia). Bleeding may be serious or life threatening and may require a blood transfusion.
- Dizziness
- Dehydration
- Fainting (Syncope)
- Increase in creatinine
- Feeling week and having no energy (Asthenia)
- Build-up of fluid in the abdomen, which causes bloating and discomfort (Ascites)
- Abdominal pain
- Large intestinal blockage (Obstruction)

Risks of CT Scan

The contrast substance injected during the CT scan may cause pain, burning feeling, sweating and rarely a serious allergic reaction that can be serious. If you know you're allergic to iodine you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated and if you're older. In addition, your thyroid function may be affected. Please inform your doctor if this is the case.

CT imaging uses ionizing radiation, which increases your risk to develop cancer. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation. The estimated additional lifetime risk of developing a fatal cancer from a standard CT scan is approximately 1 in 2,000.

Risks of MRI Scan

Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks of MRI include: feeling fearful of being in a small enclosed space (claustrophobia) when you are lying inside the MRI scanner, feeling uncomfortable because of the loud noises made by the machines, and feeling uncomfortable with the physical sensations you may feel during the process. You are also exposed to some risk because of the injected contrast, gadolinium-DTPA, which may cause headache, nausea, and local burning sensation.

The contrast agent, gadolinium has been linked to development of Nephrogenic Fibrosing Dermopathy (NFD) (also known as Nephrogenic Systemic Fibrosis (NSF) This causes a thickening of the skin, organs and other tissues, and is a rare complication in patients with kidney disease that undergo an MRI with contrast material. To help prevent this, we will check how well your kidneys work before you have any MRIs. Because of the use of contrast, all female subjects who are able to have children will be required to use adequate birth control. If you have implanted metal objects such as a pacemaker, artificial limbs, or metal joints, you will not be able to have an MRI done, and may not be able to take part in this research.

Bone Scan
During a bone scan, you will be injected with radioactive material which collects in your bones and then shows up on a special camera. This means that you will be exposed to a low level of radiation. The tracer contains about the same amount of radiation as an x-ray. The injection of radionuclide may cause some discomfort and bruising.

Electrocardiogram (ECG)
An ECG shows the electrical activity of the heart by placing several small adhesive pads that are attached to wires on your chest and limbs (called leads) and connecting them to a machine that reads the signal. There may be minor discomfort, similar to removing a bandage, when the electrodes taped to your chest are removed.

Blood tests
Collection of blood samples may cause pain, bleeding, bruising or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having your blood drawn at any time during your study participation.

Tumor Biopsy
A piece of a tumor will be removed for testing. Potential risks and discomforts that you may experience as a result of the procedure depend upon the location of the tumor. The more common risks/discomforts include pain, bleeding, infection, damage to tissues, and healing complications. Your doctor will further explain any specific risks that may apply based on the procedure, and you will sign a separate consent for the procedure which will provide risk information in more detail. In order to make the procedure more comfortable, you will get a local anesthetic to numb the area. A mild sedative may also be given to you.

- Genetic material, including DNA and RNA, will be obtained from samples, stored in freezers, and used for profiling and analyzing your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison. The goal is to identify key changes in the genes important to cancer cells that could potentially influence clinical decision making for your cancer. However, success or clinical benefits from the profiling of your cancer DNA is not guaranteed.

- Some cells from your tumor may be grown and used to create cell lines that can be used as an ongoing source of genetic material or used for laboratory research. Additional analysis of the sequencing data will be used for research purposes, for example to discover new, unknown associations between genes and cancer. This type of research may affect the lives of future patients with cancer.

- Since these tests are not approved or cleared by the FDA, there is a chance of a false positive or a false negative result. A “false positive” refers to the identification of a genetic change that is not present. A “false negative” is the failure to find a genetic change that indeed exists. The tests have been designed to ensure that the possibility of incorrect results is low. Since the results of this genetic test will not change your treatment on this study, the risks of inaccurate test results are the risks of receiving genetic results

that that may not be accurate, causing psychological or emotional distress for you or for a biologically related family member.

- The researchers may discover that you have a gene that, if inherited by biologically-related family members, could increase their risk of cancer. These family members may or may not have the gene; they would need to be tested to find that out. Your study doctor will discuss this result with you. If your test results show that you have gene mutations that are inherited, your doctor will recommend that you meet with a genetic counselor. This referral is considered standard care and is not part of this study. This is typically covered by most insurance agencies. If this is not covered, you may have to pay out of pocket for this service. Speak with your doctor if you have any questions.

Research samples/Loss of Confidentiality
Your samples will be coded, however, there is a risk of loss of confidentiality of your information. If your samples are provided to research collaborators the following information may be made available: your diagnosis and treatments, the time the samples were collected in relation to your study regimen, your disease status, and demographic data (for example gender, race, age, etc.). See section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

Pregnancy
MEN
All men must use an acceptable form of birth control while taking part in the study and for 6 months after treatment has stopped because the effects on sperm are not known. Acceptable forms of birth control are male latex condom (with spermicide) or vasectomy. Also, men should not donate sperm or semen while taking part in the study and for 6 months after treatment because the effects on sperm are not known.

FEMALE PARTNERS
Female partners of male subjects should also use a highly effective form of contraception if they are of childbearing potential.

Primary forms
• tubal sterilization (tubes tied)
• partner's vasectomy
• intrauterine device
•hormonal contraceptives - (includes transdermal patch, injectables, implantables)

Secondary forms
•diaphragm with spermicide
•cervical cap with spermicide
•vaginal sponge (contains spermicide)

The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished.

You should advise your study doctor if you father a child while participating in this study. The doctor will advise you on medical attention for your partner should this be necessary. We will ask for your partner's permission to collect information about the pregnancy and health of the baby. The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any direct personal benefits from being in this study. However, others may benefit from the knowledge gained from this study.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?
You do not have to be in this study to get treatment for your cancer. Other possible options include:

- Treatment with standard of care drugs such as: enzalutamide, abiraterone + prednisone, chemotherapy such as docetaxel or cabazitaxel, radium-223 or sipuleucel-T
- You could participate in other research trials, if one is available
- You may also choose not to receive any further treatment.

You may have received one of these drugs already, but here is more detail regarding the most common standard of care options.

Abiraterone: This is a drug taken by mouth every day that has been shown to make people live longer an average of ~4 months when it is given before or after chemotherapy for prostate cancer like yours. Several important side effects of abiraterone include high blood pressure, low potassium, liver injury, swelling, fatigue or shortness of breath.

Enzalutamide: This is a drug taken by mouth every day that has been shown to make people live longer an average of ~4 months when it is given before or after chemotherapy for prostate cancer like yours. Several important side effects of enzalutamide include seizures and fatigue.

Docetaxel: This is a chemotherapy given through a vein every 3 weeks. It has been shown to make people live longer an average of ~3 months for prostate cancer like yours. Several important side effects of docetaxel

include low blood counts, fatigue, numbness or tingling in the hands or feet, hair thinning, allergic reactions, swelling and nail changes.

You should talk to your study doctor and your regular physician about each of your options and their risks and benefits before you decide if you want to take part in this study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
If you decide to leave the study early, please notify someone on the study team. They will instruct you on how to stop the study safely and you will be advised whether any additional test may need to be done for your safety.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You will not be billed for the research tissue biopsy or the processing, storage, or the DNA sequencing.

Olaparib and AZD6738 will be provided by AstraZeneca free of charge.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices (such as the cost of the infusion)
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services
- Treatment of complications

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Reichert, at (734) 764-3066 or (734) 936-4000 (Hospital Operator- 24-hour paging) . The doctor will either treat you or send you to another doctor for treatment.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
You will not be paid to take part in this study.

8.3 Who could profit or financially benefit from the study results?
Information obtained from this study may help the supporter AstraZeneca and/or the University of Michigan learn more about the causes, risks, treatments, or how to prevent this and other health problems. AstraZeneca, the University of Michigan, and/or physicians at the university could profit financially from this information.

In the interest of transparency, we would like to disclose that Dr. Alva participated in advisory board meetings as a paid consultant on 6/22/2018 and 11/1/2019; he also entered into a 2-year consulting agreement with AstraZeneca, the sponsor on 10/19/2019. He is not likely to benefit financially from the results of this study.

A. Alva is prohibited from participating in the informed consent process as of 1/23/2020 per his Conflict Management Plan.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?
The University of Michigan has rules to protect information about you. Federal and state laws also protect your privacy. Upon enrolling in this study, you will be assigned a unique identification number. All records related to the study will use this identification number instead of your name or other personally identifying information whenever possible. We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file.

You have the right to request access to your protected health information that is used or shared during this research and that is related to your study treatment for your disease, but you may access this information only

after the study is completed. To request this information, please contact the researchers listed in Section 10 "Contact Information" (below).

Genetic Risks:

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

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.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease or other communicable disease status
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.

- The researchers may need the information to check your test results or look for side effects.
- University of Michigan, Food and Drug Administration (FDA), and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- AstraZeneca, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular University of Michigan medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?
As a rule, the researchers will not continue to use or disclose information about you but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help the University of Michigan and government officials make sure that the study was conducted properly

9.4 When does my permission expire?
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?
Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

- Principal Investigator: Zachery Reichert, MD, PhD
- Mailing Address: University of Michigan
- 1500 East Medical Center Drive
- Ann Arbor, MI 48109
- Telephone: 734-764-3066
- Emergency Contact: 734-936-4000 (Hospital Operator – 24-hour paging)
-
- You may also express a concern about a study by contacting the Institutional Review Board listed below.
- University of Michigan Medical School Institutional Review Board (IRBMED)
- 2800 Plymouth Road
- Building 520, Room 3214
- Ann Arbor, MI 48109-2800
- Telephone: 734-763-4768
- Fax: 734-763-1234
- e-mail: irbmed@umich.edu

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received signed and dated copies of all of the following documents:

- This "Consent to be Part of a Research Study" document.
- Other (specify):_____

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent to Collect and Store OPTIONAL Research Samples for Unspecified Future Research
This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to take part in this optional research. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep and store my blood tumor tissue and saliva samples for future research.

_____ No, I do not agree to let the study team keep and store my blood, tumor tissue and saliva samples for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____