Olaparib in Men With High-Risk Biochemically-Recurrent Prostate Cancer Following Radical Prostatectomy, With Integrated Biomarker Analysis

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If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Phase II Study of Olaparib in Men with High-Risk Biochemically-Recurrent Prostate Cancer Following Radical Prostatectomy, with Integrated Biomarker Analysis**

Application No.: **IRB00114635**

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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

2. Why is this research being done?

This aim of this research is to find out if the study drug olaparib leads to lowering of PSA levels in men experiencing biochemical recurrence (a rise in your PSA after surgery) of prostate cancer. The research will also examine if olaparib is safe in individuals with early prostate cancer.

For some men who have undergone surgery for prostate cancer, a rise in the PSA is the only sign that there are cancer cells remaining in the body. A PSA that is rising quickly means that the patient has a high risk of the cancer showing up in areas outside the prostate like bones or lymph nodes that can be identified on a CT scan or bone scan in the coming years. For men with a rapidly rising PSA and no signs of cancer spread on scans, the standard treatment options are either ongoing surveillance (continuing to monitor PSA and look for areas of cancer) or medicines to lower testosterone. This trial is testing whether an alternate approach – administration of olaparib – results in lowering of the PSA, and if so, how low and for how long.

Olaparib capsules are approved by the Food and Drug Administration (FDA) and other countries for the treatment of certain types of ovarian cancer and breast cancer. . It is a new formulation which is more convenient for patients than the approved capsule formulation because fewer tablets of olaparib need to be taken daily than with capsules. Olaparib is not approved for use in prostate cancer. The FDA is allowing the use of olaparib in this research study.

Olaparib is a type of drug called a PARP (poly [adenosine diphosphate-ribose] polymerase) inhibitor. PARP inhibitors can destroy cancer cells that are not good at repairing DNA damage.

Olaparib has been tested in some men with advanced prostate cancer and resulted in lowering of PSA in some of the participants. In the setting of advanced prostate cancer, Olaparib appeared to benefit certain participants with specific altered genes (specific gene mutations). However, it is unknown whether Olaparib will have the same benefit for men with a rise in PSA after surgery. This study will not pre-screen participants to be tested for specific gene mutation.

Men with PSA that is rising after surgery for prostate cancer, with a PSA that is doubling in less than 6 months, with a PSA greater than or equal to 1.0, and no evidence of cancer in areas outside the prostate on CT scans and bone scans, may join the study.

How many people will be in this study?

Up to 50 participants are expected to enroll in this study. About 42 of these participants are expected to be enrolled at Johns Hopkins.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

You will have a clinic visit where the study's screening procedures will take place. The study team will ask you questions about your medical history and health, review your medical record, and perform a physical exam. The study team will order blood tests (3 tablespoons of blood) and a urine test, an EKG (an electrical heart tracing), and a CT scan and bone scan (if these have not been performed in the past 4 weeks). A sample of your (archived) prostatectomy tumor tissue will be requested and tested for genetic mutations in your cancer cells. Since this is being done in a clinical lab, the results will be returned to you and your doctor.

If you are eligible for the study and choose to participate, then you will be scheduled for a clinic visit after which you will start on the olaparib regimen. All participants who enroll in the study will have the same procedures and receive the same study drug (olaparib).

You will take two doses of study drug at the same time each day, morning and evening, about 12 hours apart, with one glass of water and with or without food. The tablets should be swallowed whole and not chewed, crushed, dissolved or divided.

If vomiting occurs shortly after the study drug tablets are swallowed, the dose should only be replaced if all of the intact tablets can be seen and counted. Should you miss a scheduled dose for whatever reason (e.g., as a result of forgetting to take the tablets or vomiting), you will be allowed to take the scheduled dose up to a maximum of 2 hours after that scheduled dose time. If greater than 2 hours after the scheduled dose time, the missed dose is not to be taken and you should take your next dose at the next scheduled time.

You will then have visits with the study team every 4 weeks. At each visit, you will be asked about any updates to your medical history, review your medications, undergo a physical exam, have blood tests (2 tablespoons of blood), be asked about any side effects or new symptoms that you are having.

You will have a CT scan and bone scan every 6 months while you are enrolled in the study, as well as a CT and bone scan at the end of the study (if it has been at least 3 months since your last CT and bone scan).

The procedures and visits in this clinical trial are different from the standard treatments. If you choose to join the study, there are more frequent clinic visits (every month instead of every 3-6 months), more frequent blood tests (weekly for 2 months, then every month instead of every 3-6 months), and receiving olaparib instead of standard treatments. The standard treatments are surveillance (continuing to monitor PSA and look for areas of cancer) or medicines to lower testosterone.

The results from all study tests (blood tests, CT and bone scans, genetic tests) will be given to you and be available to your physicians. Genetic counseling (discussing of what the tests may mean for your health and the health of any family members who may also have the same genetic changes) will be available to you regarding any findings on genetic tests.

Request to collect and store biospecimens for future research

As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could involve other diseases and involve research tools such as gene sequencing or creation of cell lines. These samples may also be distributed to other researchers, but they will not contain any information that could be used to identify you. You may limit the future use of any banked samples by contacting the study doctor.

The research may involve research tools such as gene sequencing or the creation of cell lines.

- Gene sequencing of your DNA provides researchers with the code to your genetic material.

- Cell lines are living tissue samples that can be grown in a laboratory. A cell line can provide an unlimited supply of cells in the future without requiring more samples from you. Each cell contains your complete DNA.

The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading *What happens to Data and Biospecimens that are collected in the study?*

Will you allow us to store the biospecimens we collect in the study for use in future research?

YES □ _____ **NO** □ _____
Signature of Participant Signature of Participant

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or health-related employment discrimination based on genetic information.

The law provides that health insurance companies and group health plans
- may not ask for genetic information from this research and
- may not use genetic information when making decision about eligibility or premiums

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law does not apply to other types of insurance (such as life, disability or long-term care).

Despite the GINA protections and the best efforts of the research team to protect your information, you may still be at risk if information about you were to become known to people outside of this study.

How long will you be in the study?
We anticipate that most participants will be on the study for about 6 months. Some participants may be a part of the study for a shorter time period and some may be for a longer time period.

4. What are the risks or discomforts of the study?

It is important that you tell the study staff about any other medicines, vitamins, nutritional or herbal supplements you are taking before and during the study as you may not be able to take some of these with your study medication because they may affect each other. This may include other anti-cancer therapies and certain vaccines. Your study doctor will provide you with a list of medications that you must avoid while you are taking your study drug, so it is important to consult your study doctor before taking anything new.

Side effects can be mild, moderate or severe (these are explained below).
- Mild: You are aware of the side effect but it doesn't really bother you
- Moderate: You need to take some sort of action (like painkillers for a headache)
- Severe: The side effect stops you doing what you normally would be doing

Treatment with olaparib has been associated with the following laboratory findings and/or clinical symptoms, generally of mild or moderate severity and generally not requiring treatment to be stopped.

You may experience none, some or all of the side effects listed below.

Very common (affects more than 1 in 10 patients) side effects that may occur are:
- Feeling sick (nausea)
- Tiredness/weakness
- Loss of appetite

- Headache
- Dizziness

Common (affects up to 1 in 10 patients) side effects that may occur are:

- Cough
- Being sick/throwing up (vomiting)
- Abdominal discomfort

The following side effects are commonly shown in blood tests:

- Decrease in the number of white blood cells that support the immune system (lymphopenia), which can be associated with increased susceptibility to infection
- Decrease in the number of red blood cells (anaemia) which can be associated with symptoms of shortness of breath, fatigue, pale skin, or fast heart beat.

Uncommon (affects up to 1 in 100 patients) side effects that may occur are:

- Diarrhoea. If it gets severe, tell your doctor straight away.
- Physical weakness or lack of energy (asthenia)
- Neutropenia and lymphopenia: Decrease in the number of two certain types of white blood cells (neutrophils and lymphocytes), which can lead to a reduced ability to fight certain infections. Although this does not mean you will get an infection, it is important that if you become unwell or have a fever, you contact your Study Doctor immediately, even if this is after-hours or at the weekend. If you have a fever or infection, you may be admitted to a hospital for treatment.
- Decrease in the number of platelets in blood (thrombocytopenia), which can be associated with symptoms of bruising or bleeding for longer if injured
- Shortness of breath (dyspnoea)
- Fever and neutropenia
- Myelodysplastic syndrome is 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 is 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. This can be fatal.

The following side effects are uncommonly shown in blood tests:

- Increase in the size of red blood cells (not associated with any symptoms)
- Increase in blood creatinine. This test is used to check how your kidneys are working.

Rare (affects less than 1 in 100 patients) side effects that may occur are:

- Erythema nodosum is a type of skin inflammation that is located in a part of the fatty layer of skin and results in reddish, painful, tender lumps most commonly located in the front of the legs below the knees.
- Increase in the size of red blood cells (not associated with any symptoms)
- Pain in the stomach area under the ribs (upper abdominal pain)
- Dyspepsia- indigestion and heartburn
- Soreness or sores of the mouth and lips
- Angioedema which is swelling with a red colored rash beneath the surface of the skin. It may occur in a specific area on or near the feet, hands, eyes, or lips. In more severe cases, the swelling can spread to other parts of the body.

- Hypersensitivity reaction
- Neutropenic sepsis (infection throughout the body)
- Allergic reactions
- Dysgeusia: taste changes which may affect the way food normally tastes.
- Itchy rash on swollen, reddened skin (dermatitis)
- Rash

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.

Other potential risks
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 some reports have been fatal. It is not known if olaparib caused the pneumonitis in these patients as they 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.

Myelodysplastic syndrome and acute myeloid leukaemia or other cancers: These side effects have been reported in a small number of patients treated with olaparib in previous studies and the majority of cases have been fatal. It is not known if olaparib caused myelodysplastic syndrome and/or acute myeloid leukaemia or other cancers in these patients as they had other possible causes, in particular they had received extensive previous chemotherapy. Your Study Doctor will monitor your blood cell levels during the study and may decide you need to have further tests, which may include a bone marrow sample or a blood sample.

- Myelodysplastic syndrome is 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 leukaemia
- Acute myeloid leukaemia is 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.

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.

There may be risks involved in taking this drug that have not yet been discovered. There is always a risk involved in taking an experimental drug but every precaution will be taken. If you suffer any side effects or injuries, or your condition gets worse, tell your study doctor immediately so you can receive appropriate care.

<u>Other Risks in the Study</u>:
Your cancer may continue to grow if you elect to participate in this trial. You may develop symptoms from cancer or the cancer may spread during this clinical trial.

Genetic information is unique to you and your family, even without your name or other identifiers. Johns Hopkins follows procedures to prevent people who work with your DNA information from being

able to discover it belongs to you. However, new techniques are constantly being developed that may in the future make it easier to re-identify genetic data, so we cannot promise that your genetic information will never be linked to you.

There may be side effects and discomforts that are not yet known.

5. Are there risks related to pregnancy?

Olaparib may cause harm to a fetus. Participants with partners capable of becoming pregnant who subsequently become pregnant may risk problems in the fetus. While taking the study drug, and for 3 months after stopping the study drug, you must use a condom when having sexual intercourse with a female partner, even if they are pregnant. Your female partner must also use a suitable method of contraception. You must not donate sperm while taking the study drug and for 3 months after the last dose of study drug.

Tell your study doctor immediately if your partner becomes pregnant while taking you are on the study drug regimen or within 3 months for after your last dose of study drug. Please discuss with your doctor suitable methods of birth control.

This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to being in the study?

You may or may not directly benefit from being in this study. If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. Other treatments include ongoing surveillance with blood work, CT scans, and bone scans; or androgen deprivation therapy.

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

You will not be paid to join this study.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study or stop taking the study drug, we will ask you to come in for a final visit about 1 month after your last dose of study drug. You will have a physical exam, blood tests, review of your medications, CT, and bone scan.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team who may be a part of Johns Hopkins Health System, Johns Hopkins University or the Johns Hopkins Applied Physics Laboratory will know your identity and that you are in the research study. Other people at Johns Hopkins, including your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study, AstraZeneca and its related companies which are located around the world and companies who work for AstraZeneca which also may be located around the world.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your

information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Catherine Handy Marshall at 410-955-8893. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of

this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

If you think you are injured or ill because of this study, call Dr. Catherine Handy Marshall at 410-955-8893 during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call the medical oncology clinic at 410-955-8893 during regular office hours and at 410-955-4331 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

16. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time
Signature of Participant	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).