Summary of Changes

I. CTEP Amendment Review Letter dated 11/20/25, Comments Requiring a Response – Major Issues:

#	Page #	Comments
1	10	Due to a recent change in CTEP policy, protocols should no longer include the CAEPR for Standard of Care agents or regimens being used per FDA label. Please remove the Radium-223 CAEPR from the protocol. In place of the CAEPR, provide a list of those adverse events most likely to occur on the study and refer the reader to the package insert for the comprehensive list of adverse events. The ICD risk list should be updated using the list for your agent found here: https://dctd.cancer.gov/research/ctep-trials/trial-development/side-effects. If your agent is not on the list, please send an email to NCICTEPComments@mail.nih.gov to request they provide you with the risk list. **PI Response: The change has been made as requested.**

II. CTEP Request for Rapid Amendment (RRA), dated October 21, 2025:

#	Page #	Comments
1	All (HEADERS)	The protocol version date was changed. Added page numbers for consistency with Phase I ICF.
2	7	Removed a section break, causing pagination errors.

3	9	Updated Olaparib risk table to reflect risks from RRA due to revised CAEPR
		• Added New Risk:
		  • Rare: Damage to the liver which may cause yellowing of the eyes and skin, swelling
		• Increase in Risk Attribution
		  • Changed to Occasional from Rare: Blood clot
		• Decrease in Risk Attribution:
		  • Changed to Occasional from Common: Pain; Diarrhea; Loss of appetite
		  • Changed to Rare from Common: Rash
		  • Changed to Also Reported on Olaparib Trials But With Insufficient Evidence for Attribution from Occasional (i.e. Removed from the Risk Profile): Bloating; Sores in the mouth which may cause difficulty swallowing; Swelling of arms, legs; Infection which may cause painful and frequent urination

4	17	Deleted blank page and updated formatting for consistency.

Study Title for Participants: Comparing olaparib and radium-223 to radium-223 alone for men with advanced prostate cancer with bone metastasis

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

NCI# 10096: A Phase 2 Study of **C**ombination **O**laparib and **Rad**ium-223 in Men with Metastatic Castration-Resistant Prostate Cancer with Bone Metastases (COMRADE)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer. We are asking you to take part in this research study because you have advanced prostate cancer which has grown after standard hormone therapy.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question: Can we lower the chance of your prostate cancer growing or spreading by adding the experimental drug, olaparib, to usual treatment with radium-223? We are doing this study because we want to find out if this approach is better or worse than the usual approach for our patients with metastatic castration resistant prostate cancer. The usual approach is defined as care most people get for metastatic castration resistant prostate cancer.

What is the usual approach for my prostate cancer treatment?

The usual approach for patients who are not in a study is treatment with chemotherapy or hormone therapy. Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer.

What are my other choices if I do not take part in this study?

- You may choose to have the usual approach described above

- You may choose to take part in a different study, if one is available
- You may choose not to be treated for cancer
- You may choose to only get comfort care to help relieve symptoms and not get treatment for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will be randomly selected to either get the combination of radium-223 and olaparib or get radium-223 alone (usual care). Radium-223 is administered by vein and will be given for up to 6 doses every 4 weeks. Olaparib will be in the form of pills given orally on a daily basis. For participants receiving the combination treatment, after you complete all the radium-223 infusions, you will remain on therapy with olaparib until either your disease worsen, you experience toxicity, or you choose to no longer participate in the study. For participants receiving radium-223 alone, after you complete all the radium-223 infusions, you will continue to be monitored every month until either your disease worsen, you experience toxicity, or you choose to no longer participate in the study. After you finish the study, your doctor or the study team will be in contact with you via a phone call or review your medical record every 6 months to follow your status for 2 years after you finish the study.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the combination of radium-223 and olaparib may not be as good as the usual approach for your cancer at shrinking or stablishing your cancer.

There is also a risk that you could have side effects from the combination of radium-223 and olaparib. These side effects may be worse and may be different than what you experience with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Low number of red blood cells (anemia) that may require a blood transfusion
- Decreased number of white blood cells (leukopenia, lymphopenia) which help your immune system and may increase risk of infection
- Low number of platelets (thrombocytopenia) which may cause bleeding or bruising and may require a transfusion
- Diarrhea or nausea
- Tiredness

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that radium-223 has been shown to improve survival in patients with prostate cancer with bone metastases. However, it is not possible to know at this time if the combination of radium-223 and olaparib is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (IRB), FDA, or study sponsor. The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare olaparib given with radium-223 compared to radium-223 (the usual care) by itself for men with metastatic castration resistant prostate cancer. The combination of radium-223 and olaparib is experimental. Either approach could shrink your cancer but could also cause side effects. There will be about 133 participants taking part in this phase of the study.

What are the study groups?

This study has two study groups.

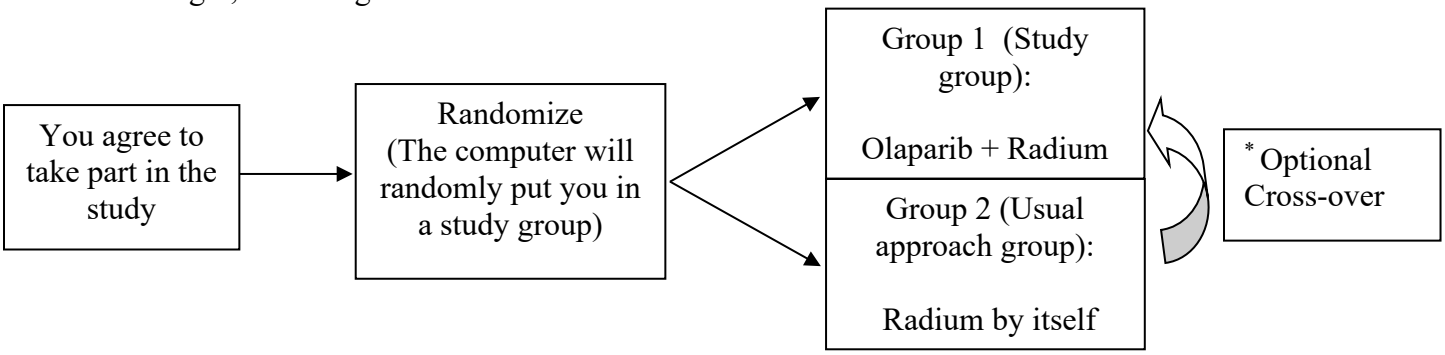
Group 1 will receive the combination study drugs (olaparib and radium-223).

The Olaparib will be taken by mouth twice a day. The radium-223 will be given by vein every 28-days for up to 6 doses. Persons in group 1 will receive a Patient Study Drug Diary, which will give you the detailed

instructions on how to take olaparib. You must maintain the diary to record the time that you take the study drug and must return the diary with the used pill bottles.

Group 2 will receive a single drug (radium-223). The radium-223 will be given by vein every 28-days for up to 6 doses.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other. Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



Note: The participants in Group 2 can choose to cross-over to Group 1 to receive the combination of olaparib and radium-223 when the cancer gets worse. If you have already received all six doses of radium-223 you will receive single agent olaparib at the time of cross-over.

Participants in groups 1 and 2 must continue with regular androgen deprivation therapy to maintain castrated level of testosterone.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Before you begin the study:

- Archival sample is needed from your diagnosis biopsy if it is available. Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer. This sample is a required part of the study. Biomarkers in the tumor will be looked at to see if they are related to your response to the study drugs. You and your study doctor will not get the results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.
- One research tumor biopsy within 2 weeks before you start the study drug(s). The research biopsy is done in a similar way to biopsies done for diagnosis. During a biopsy, a doctor will remove a small piece of tumor from your body. Biomarkers in the tumor will be looked at to see if they are related to

your response to the study drugs. Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. You will sign a separate consent for any biopsy procedure.

- Research blood test (1 ½ teaspoon) along with the first research biopsy.
- Questionnaires to record your family history will be given at baseline. If you choose to take part in this study, you will be asked to fill out a form with questions about your family cancer history. Researchers will use this information to learn more about cancer risk development. The form takes about 5-10 minutes to complete.
- Questionnaire to record your function and pain level will be given at baseline. If you choose to take part in this study, you will be asked to fill out two forms with questions about your function and pain. Research will use this information to learn more about how cancer and cancer treatment affects people. The forms will take about 10-15 minutes to complete. The forms will ask questions like "do you a lack of energy" or "do you have pain." You don't have to answer any question that makes you feel uncomfortable.

During the study:

- Additional research blood tests (approximately 1 tablespoon) for immune profiling on Day 1 of cycle 1, 4, 7 and every 3 cycles thereafter (a cycle is every 28 days), and one additional blood test when off the treatment. Note: If the end of treatment collection of blood for immune profiling is within 2 weeks of prior collection, research samples for immune profiling do not need to be collected.
- Research blood tests (approximately 1 tablespoon) for looking at changes in circulating DNA on Days 1 of cycles 1, 2, 4, and every 3 cycles thereafter, and one additional blood test at the end of the study. Note: If the end of treatment collection of blood for immune profiling is within 2 weeks of prior collection, research samples for immune profiling do not need to be collected.
- The first 52 patients on the study will undergo an additional research blood test (approximately 1 tablespoon) for additional immune profiling on Day 1 of cycle 1, 4, 7 and every 3 cycles thereafter (a cycle is every 28 days), and one additional blood test when off the treatment. Note: If the end of treatment collection of blood for immune profiling is within 2 weeks of prior collection, research samples for immune profiling do not need to be collected.
- Questionnaires to record your function and pain will be given every 12 weeks and when off study. If you choose to take part in this study, you will be asked to fill out two forms with questions about your function and pain. Research will use this information to learn more about how cancer and cancer treatment affects people. The forms will take about 10-15 minutes to complete. The forms will ask questions like "do you a lack of energy" or "do you have pain." You don't have to answer any question that makes you feel uncomfortable.
- We will ask for an optional tumor biopsy when your cancer gets worse or when the off study. This will be discussed in the section on optional studies.

A study calendar that shows when and how often the exams, tests and procedures will be done is attached to the end of this consent form.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the research tumor biopsies or research blood tests.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that the study treatment may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissues for genetic changes in genes necessary for DNA repair. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

The study drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may make it hard for you to have children.

- Some side effects may be serious and may even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of standard drug used to treat this type of cancer (radium-223) plus a study drug (olaparib) compared to the standard drug alone (radium-223). This combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and the most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Olaparib

If you choose to take part in this study, there is a risk that the olaparib (AZD2281) **IN COMBINATION WITH RADIUM-223** may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The olaparib (AZD2281) used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.

- Your study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

COMMON, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Nausea, vomiting • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), from 4 to 20 may have:
• Pain • Constipation, diarrhea, heartburn • Cold symptoms such as stuffy nose, sneezing, sore throat • Infection, especially when white blood cell count is low • Loss of appetite • Dizziness, headache • Changes in taste • Cough, shortness of breath • Blood clot

RARE, AND SERIOUS In 100 people receiving olaparib (AZD2281), 3 or fewer may have:
• Damage to the liver which may cause yellowing of the eyes and skin, swelling • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Bruising, bleeding • Cancer of bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Damage to the lungs which may cause shortness of breath • Rash

Possible Side Effects of Radium-223

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.

- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The radium-223 dichloride (BAY 88-223) used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:
- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:
- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Usual Treatment Risks
The usual treatment for your cancer has side effects. This study consent form does not talk about all the risks of your usual treatment. Some important side effects of Radium-223 dichloride are:

- Swelling of arms, legs
- Low blood counts which may result in infection, bleeding, blood transfusions
- Nausea, vomiting, diarrhea, dehydration
- Kidney damage which may cause swelling
- Swelling and redness at the site of the medication injection
- A new cancer (including leukemia) resulting from treatment

Your doctor and your care team will talk to you in more detail about all the side effects, how common and serious they are, and how to manage them.
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.

Additional Drug Risks

The study drug could interact with other drugs. Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Reproductive Risks

You should not father a baby while in this study. The drugs used in this study could be very damaging to an unborn baby. You must also agree to use adequate contraception and not to donate sperms prior to the study, for the duration of study participation, and for 6 months after completion of study drug administration. You

should notify your health care team immediately if you think your partner has become pregnant while participating in this study.

Other Risks

Radium-223, an alpha particle-emitting pharmaceutical, is a radioactive therapeutic agent. Though the external radiation exposure associated with radium-223 is low, care must be used to keep body fluids from coming in contact with family members or caregivers. Wash soiled clothing right away and use gloves when touching body fluids for at least 5 days after each treatment. Use the same toilet each time you use the bathroom in your home. Sit down on the toilet to urinate to keep urine from splashing or spraying. Flush the toilet a few times after each use. You should notify your health care team with questions you may have related to radiation exposure with this drug.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the drug ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- Research biopsies
- Research blood testing
- Collection of archival tissue specimens

You or your insurance provider will not have to pay for the olaparib while you take part in this study. Olaparib will be supplied by the National Cancer Institute at no charge while you take part in this study. Radium-223 is a standard treatment for patients with advanced prostate cancer will be covered by you or your insurance company. The cost of getting the study drug(s) ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that olaparib may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any drug company supporting the study now or in the future.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other participants to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number)*.

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in the optional studies is your choice. You can still take part in the main study even if you say "no" to the optional studies. There is no penalty for saying "no." You and your insurance company will not be billed for optional studies. If you sign up for, but cannot complete the optional studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the optional studies.

1. Optional Sample Collection for Laboratory Studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect tissue for research of your cancer at the time you come off the study. The research biopsy is done in a similar way to biopsies done for diagnosis. During a biopsy, a doctor will remove a small piece of tumor from your body. Biomarkers in the tumor will be looked at to see if they are related to your response to the study drugs. Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. You will sign a separate consent for any biopsy procedure.

Unknown future studies

If you choose to take part in this optional study, any remaining tissue after known studies are performed will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

Right now, we don't know what research may be done in the future using your tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

If you agree to take part in the Sample Collection for Laboratory Studies, here is what will happen next:

- A sample of tissue will be collected from the optional extra biopsy to be performed at the time you end the study. Your sample and some related health information will be sent to a researcher for use in the study described above. Any remaining tissue will be stored in the biobank.
- Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
- Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
- Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- For a biopsy, risks include a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur.
- There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.

2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show if you would or would not like to take part in each optional study.

Collection of optional biopsy at study discontinuation for known future studies:

I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

Collection of optional biopsy at study discontinuation for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Study Calendar

Study Evaluation Cycle = 28 days	**Baseline**	**Cycle 1-6**	**Cycles 7+**		
		Day 1	**Day 1**	**Every 12 weeks**	**Study End**
Physical Exam/Vital Signs/Performance Status	X	X	X		
Discussion of Side Effects And Medications	X	X	X	X	X
Routine Blood Tests	X	X	X		
Testosterone	X				
Electrocardiogram	X				
CT and MRI Imaging	X			X	
Research Blood Tests	X	X		X	X
Research Biopsy	X				X*
Questionnaires		X		X	
Radium-223		X			

*Olaparib will be given to participants in group 1. The participants in Group 2 can choose to cross-over to Group 1 to receive the combination of olaparib and radium-223 when the cancer gets worse. If you have already received all six doses of radium-223 you will receive single agent olaparib at the time of cross-over.

*An optional research tumor biopsy will be performed at study discontinuation.

*Long term follow-up after you complete the study will happen every 6 months for 2 years.