PENN MEDICINE RESEARCH SUBJECT COMBINED INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:	PLATPARP: A Phase II Single-Arm Trial of Niraparib in Platinum-Sensitive Castration-Resistant Prostate Cancer with DNA Repair Defects
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Summary

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

This study is being done because your doctors are trying to develop better methods for treating prostate cancer that has spread to other organs in the body and that is worsening despite hormone therapies, such as androgen-deprivation therapy. This study is for patient who have a history of advanced prostate cancer that is growing despite standard hormonal therapies, such as androgen-deprivation therapy.

If you agree to join the study, treatment on this study consists of taking an oral pill called niraparib. Niraparib is an anticancer drug that that attempts to kill cancer cells by preventing the cells from repairing damage to their DNA, the part of the cells that contain their genetic material. You will also be asked to complete the following research procedures:

- Radiology imaging
- Multiple lab blood draws
- Multiple clinic visits/physical exams

Your participation on this study will depend on how you tolerate the treatment and how your cancer responds to the study drug.

Taking part in this study may or may not make your health better. The most common risks of participation are: feeling tired or short of breath, increased risk of bleeding, decreased ability to fight infections, constipation, nausea, vomiting, decreased appetite, pain in your belly, diarrhea, indigestion, sleeplessness, trouble sleeping, headache, feeling tired/lack of energy, pain or burning when urinating which may indicate an infection, inflammation (irritation) of the lining of the pathways that carry air to your lungs, back pain, joint pain, breathlessness or difficulty breathing, common cold, increased blood pressure, feeling lightheaded, cough, noticeably rapid, strong, or irregular heartbeat, and changes in your sense of taste.

More details on possible known risks are included in the full consent document. Please note that there are other things to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being asked to participate in this research study because you have a history of advanced prostate cancer that is growing despite standard hormonal therapies, such as androgen-deprivation therapy. Your participation is voluntary, which means you can choose whether or not you want to participate. If you choose not to participate, your clinical care will not be affected. Before agreeing to participate in this research study, it is important that you read the following explanation of the proposed procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study?

This study is being done because your doctors are trying to develop better methods for treating prostate cancer that has spread to other organs in the body and that is worsening despite hormone therapies, such as androgen-deprivation therapy. This study will evaluate the initial safety and effectiveness of an investigational drug, niraparib, given to subjects who have recently received platinum-based chemotherapy for the treatment of prostate cancer. An investigational drug is one that has not been approved by the U.S. Food and Drug Administration (FDA) for your type of cancer. The hope is that niraparib will help to prevent your cancer from continuing to grow and maintain the benefits of the chemotherapy you have received the treatment of prostate cancer.

Niraparib is an anticancer drug that attempts to kill cancer cells by preventing the cells from repairing damage to their DNA, the part of the cells that contain their genetic material.

While niraparib has not been approved for the treatment of prostate cancer, it has been studied and approved in other advanced cancers, including ovarian cancer. Niraparib is currently under investigation as a treatment for prostate cancer when given alone, and in combination with other known anticancer therapies. Various animal and human studies have shown that niraparib can shrink or slow the growth of cancer.

Who is sponsoring this study?

The Penn Medicine is the sponsor (entity responsible for the design, conduct and regulatory oversight of the study). Janssen Scientific Affairs, LLC is the manufacturer of the study drug, niraparib, and will be providing the drug free of charge to you during this research study. Dr. Vivek Narayan and the Penn Medicine will receive payments to cover some of the research costs such as the collecting and reporting of study information associated with the conduct of the study.

How long will I be in the study?

Your active treatment on this study will depend on how you tolerate the treatment and how your cancer responds to the study drug. You may also be taken off this investigational treatment if you experience intolerable or unacceptable side effects, your doctor determines that your safety is at risk or this treatment is no longer in your best interest, or the study ends. You can also choose to leave the study at any time without giving a reason. Leaving the study will not affect your future medical care.

After you complete your study treatment, you will be asked to come back to see the study doctor and team for an End of Study Visit, as well as a Follow-up Visit 30 days after completing the last dose of the study drug. We will contact you by phone 90 days (3 months) after the last dose of study drug to see how you are doing.

We will then continue to see how you are doing about every 3 months after the 90-Day Follow-up Visit.

If new information becomes available that might affect your choice to stay in the study, your study doctor will notify you as soon as possible.

What am I being asked to do?

If you meet all of the criteria for being in the study, and agree to participate by signing the informed consent form, you will be registered to participate.

<u>Screening Procedures</u>

These procedures are done to evaluate your cancer, overall health, and eligibility to participate. If you have had some of these tests/procedures recently, they may not need to be repeated. These tests and procedures need to be done within 28 days before you receive your first dose of study drug, unless otherwise indicated. One of the reasons screening procedures are conducted is to make sure it is safe for you to be on this study.

These tests/procedures will be performed during the screening visit. Before these tests/procedures can be performed, you will first be asked to sign this consent form.

- Review of your medical history including any other medical problems you may have, and other treatments you have received for your cancer and how you responded to them.
    - You should let your study doctor know about any medications you have taken recently or are currently taking. This includes prescription and over-the-counter drugs, illegal drugs, vitamins and health food supplements. You should also let your doctor know about any changes in your medication throughout your participation in this study. Many commonly used medications may interact with the study drug and cause them to be less effective or more toxic.
- Physical examination including an assessment of your vital signs (heart rate, temperature, blood pressure), height, and weight
- Assessment of your ability to perform daily life activities (i.e. walking, house work, etc.)
- Electrocardiogram (ECG/EKG)- non-invasive test that monitors the electrical activity and health of your heart.
- Safety blood tests - about 4 tablespoons of blood will be drawn to check for the following:
    - Blood cell counts (number of each type of blood cell)
    - Blood chemistry levels (to test your kidney and liver function and the minerals in your blood)

  - Prostate specific antigen (PSA) and total testosterone
- Tumor imaging of the chest, abdomen, and pelvis. This can include computed tomography (CT) or magnetic resonance imaging (MRI) scans. These scans may require contrasts and dyes. In addition, a bone scan may be performed to assess any of the prostate cancer in the bones (if applicable). These tests should be done within 28 days of starting the study. Therefore, if you have had them performed recently, they may not need to be repeated.
  - CT - a computerized x-ray that gives your doctor clearer pictures of the inside of your body.
  - MRI - a test that uses magnetic pulses to take computerized pictures of the inside of your body.
  - Bone Scan- this scan of your bones requires injection of a small amount of radioactive material into the vein in your arm.
- If available, a sample of your archived tumor tissue (taken and stored from a prior biopsy and/or surgery) will be collected and used for future research testing. You will likely not directly benefit from future research with your information and samples. Research with your identifiable information and samples may help others by improving our understanding of health and disease, improving health care and making safer or more effective medical therapies, and developing new scientific knowledge.

Procedures associated with the administration of the study drug(s)
When all of the above tests/procedures have been completed, and you have been found eligible to enter this study, and you agree to participate, you will be scheduled to receive study drug.

All subjects enrolled in this study will receive the study drug. Treatment will occur in cycles. Each cycle is about 28 days long. The treatment will consist of an oral pill medication, two pills taken once daily. You may continue on this study drug as long as your disease is responding to treatment and your doctor believes that you are benefiting from this study drug.

Study Tests/Procedures
These exams, tests, and procedures are being done to evaluate your health and response to the study drug. At each of these study visits you will be asked how you are feeling, if you have had any side effects, if you have had any medical procedures, and about any medications you are taking. It is important you check with your study doctor before starting any new medications. Taking other drugs (including alcohol, over-the-counter medications, herbal preparations, illegal drugs, or nutritional supplements) may cause additional side effects or even life-threatening reactions when combined with the drugs being used in this study. If you experience side effects, changes in your health and/or changes in medications, please contact your study doctor or a study team member.

You will have the following tests, procedures, and assessments done at the time points listed in the study calendar below.

Study Calendar					
Procedures	**Cycle 1, Day 1**	**Cycle 1, Day 15**	**Cycle 2 and Beyond**	**End of Study Visit**	**30 Day Post-Treatment Visit**
Physical Examination (including an assessment of your vital signs)	X	X	Every 4 weeks	X	X
Blood pressure and heart rate	Your blood pressure and heart rate will be taken every week for the first two months, then once per month after that.				
Review of current medications you are taking and any side effect symptoms you may have experienced	X	X	Every 4 weeks	X	X
Assessment of your ability to perform daily activities	X	X	Every 4 weeks	X	X
Safety Blood Tests (about 2 tablespoons of blood to check your blood cell counts and organ function)	X	X	Every 4 weeks	X	X
Additional Safety Blood Tests: Blood Counts	One safety blood test to measure your blood counts will be performed weekly for the first month, then monthly after that, including within 30 days of the last dose of study drug.				
Research Blood Tests (about 2 tablespoons of blood)	X		Cycles 2 and 4 only	X	
PSA Blood Test	X		Every 4 weeks	X	
Niraparib Administration	X	X	X		
Tumor Imaging			Every 12 weeks starting at Cycle 4	X[a]	

a. Tumor Imaging (CT, MRI, and Bone Scan) will be performed at the End of Study visit if treatment was discontinued for a reason other than disease progression and if not performed within the preceding 8 weeks.

End of Study Visit
Upon treatment discontinuation, all subjects will return to the clinic for an End of Study Visit. These tests/procedures will be performed during the End of Study Visit:

- Review of your medical history and review of current medications you are taking and any side effects symptoms you may have experienced
- Physical examination including an assessment of your vital signs (heart rate, temperature, blood pressure), and weight
- Assessment of your ability to perform daily life activities (i.e. walking, house work, etc.)
- PSA blood test
- Safety blood tests - about 2 tablespoons of blood will be drawn to check for the following:
  - Blood cell counts (number of each type of blood cell)
  - Blood chemistry levels (to test your kidney and liver function and the minerals in your blood)
- Research Blood Tests - about 2 tablespoons of blood will be drawn for research blood tests. One sample of this blood may be used to perform testing of your blood DNA for hereditary genes that may increase risk of cancer.
- Tumor imaging of the chest, abdomen, and pelvis and bone scan may be performed (if treatment was discontinued for a reason other than disease progression determined by imaging tests and if not already performed within the preceding 8 weeks).

In addition, you will have a follow-up visit to assess for side effects and safety 30 days following your completion of the study drug and a phone call from study staff to see how you are doing at 90 days after you last dose of study drug.

Post-Study Procedures
After you complete your study treatment, we would like to continue to follow you to see how you are doing. This may occur every 3 months following completion of your participation in the study. We may do this by looking into your medical records or calling you by phone every 3 months to gather information related to your overall health and any additional cancer treatments/procedures you may have undergone.

What are the possible risks or discomforts?

Niraparib has been studied in more than 1379 subjects in clinical trials run by TESARO, a pharmaceutical company. Niraparib capsule is marketed as ZEJULA® and is approved to treat adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in the United States and in Europe. Niraparib is currently being studied as a single medication and in combination with other drugs in variety of cancer clinical studies.

All drugs can cause side effects. The possible side effects related to niraparib treatment are not all known. Some side effects may be serious and may require treatment or additional testing and may be life threatening. If you have any side effects during your participation in this study, you should let your study doctor know right away.
This section describes how frequently side effects occurred in subjects who were treated with niraparib as a single drug therapy.

Very Common ≥10% occurrence (happens in greater than 10 out of 100 subjects)

- Decrease in red blood cells that carry oxygen; this may make you feel tired or short of breath (anemia)
- Decrease in a type of blood cell called platelets that help stop bleeding; this may increase your risk of bleeding (thrombocytopenia)
- Decrease in all types of white blood cells which fight infection (leukopenia)

- Decrease in a type of white blood cell called neutrophils that fight infection (neutropenia)
- Difficulty with emptying the bowels, often because of hard stools (constipation)
- Feeling sick to your stomach (nausea)
- Vomiting
- Reduced desire to eat (decreased appetite)
- Pain in your belly (abdominal pain)
- Frequent watery stools (diarrhea)
- Indigestion (dyspepsia)
- Sleeplessness, trouble sleeping (insomnia)
- Headache
- Feeling tired, lack of energy (asthenia/fatigue)
- Pain or burning when urinating which may indicate an infection (Urinary tract infection)
- Inflammation of the lining of the airways or passageways that carry air to your lungs (bronchitis)
- Back pain
- Joint pain (arthralgia)
- Breathlessness or difficulty breathing (dyspnea)
- Common cold (nasopharyngitis)
- Increased blood pressure (hypertension)
- Feeling lightheaded or like you are about to faint (dizziness)
- Cough
- Noticeably rapid, strong, or irregular heartbeat (palpitations)
- Altered sense of taste; this means that foods might taste differently than you are used to (dysgeusia)

<u>Common < 10%, but ≥ 1% occurrence (happens in less than 10, but more than 1 out of every 100 subjects)</u>

- An abnormally rapid heart rate (tachycardia)
- Infection related to a decrease in white blood cells called neutrophils that fight infection (neutropenic infection)
- Reduced potassium in blood (hypokalemia)
- Dry mouth
- Feeling anxious (anxiety)
- Mood change to feeling sad/discouraged, listless (depression)
- Nose bleed (epistaxis)
- Rash
- Muscle pain (myalgia)
- An accumulation of fluid that causes swelling in lower extremities such as lower legs, hands and feet (peripheral edema)
- Swelling or irritation of the mouth (mucositis/stomatitis)
- Increased liver enzymes in the blood; aspartate transaminase (“AST”), alanine aminotransferase (“ALT”), gamma glutamyl transferase increased (“GGT”), or alkaline phosphatase (ALP); this may be a sign of damage to liver cells
- Increase level of creatinine in your blood; this may be a sign of kidney damage (blood creatinine increase)
- Decrease in weight
- Inflammation of the white area of the eye (conjunctivitis)
- Photosensitivity - An immune system reaction that is triggered by sunlight. People develop itchy eruptions or areas of redness and inflammation on patches of sun-exposed skin. These reactions typically resolve without treatment.

Uncommon ≥ 0.1% and < 1% (happens in less than 1 out of 100 but more than 1 out of 1000 patients)

- Development of fever in a patient with a decrease in a type of white blood cell called neutrophils that fight infection (febrile neutropenia)
- Development of low counts for all three types of blood cells: red blood cells, white blood cells, and platelets (pancytopenia)

Rare ≥1/10,000 and <1/1,000 (happens in less than 1 out of 1000 patients but more than 1 out of 10,000 patients)

- Posterior reversible encephalopathy syndrome (PRES) is a syndrome characterized by headache, confusion, seizures and visual loss. On magnetic resonance imaging (MRI) of the brain, areas of edema (swelling) are seen. The symptoms tend to resolve after a period of time, although visual changes sometimes remain.
- Neutropenic sepsis – a potentially life-threatening condition affecting multiple organ systems, caused by the body's response to an infection related to a decrease in a type of white blood cell called neutrophils.
- Hypertensive crisis - Extremely high blood pressure — a top number (systolic pressure) of 180 millimeters of mercury (mm Hg) or higher or a bottom number (diastolic pressure) of 120 mm Hg or higher. Blood pressure this high can damage blood vessels, lead to a stroke or other complication

Adverse Events with unknown frequency:

The following adverse reactions have been identified during post-approval use of niraparib in an ovarian cancer population. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate how often these events occur (frequency) or establish if they were caused directly by taking niraparib. These events are:

Immune System Disorders:

- hypersensitivity (including anaphylaxis) – Hypersensitivity is when your body has an exaggerated immune response to a drug or another substance. Anaphylaxis is a serious, life-threatening allergic reaction. It typically causes more than one of the following: an itchy rash, throat or tongue swelling, shortness of breath, vomiting, lightheadedness, and low blood pressure.

Psychiatric Disorders:

- confused state/ disorientation - Serious disturbance in mental abilities that results in confused thinking and reduced awareness of surroundings
- hallucination - A perception of having seen, heard, touched, tasted, or smelled something that wasn't actually there
- cognitive impairment (memory impairment, concentration impairment) – Difficulty remembering, learning new things, concentrating, or making decisions

Respiratory, Thoracic, and Mediastinal Disorders:

- non-infectious pneumonitis – Inflammation of the lung tissue

Potential for a new blood cancer myelodysplastic syndrome and acute myeloid leukemia (MDS / AML); a new primary cancer; pneumonitis (inflammation of the lungs); or embolic and thrombotic events (blood clots)

Niraparib belongs to a group of drugs called PARP inhibitors. This group of drugs are suspected of causing new blood cancers known as myelodysplastic syndrome (MDS and acute myeloid leukemia (AML). Because niraparib is a PARP inhibitor there is a potential risk of developing a new blood cancer leading to leukemia.

If you have had MDS or leukemia before entering this study, you are at increased risk for developing leukemia again and must tell your Study Doctor before starting this study.

The occurrence of MDS/AML in subjects participating in niraparib clinical trials is rare. In a randomized trial comparing niraparib to placebo (i.e. sugar pill) of recurrent ovarian cancer subjects, the incidences of MDS/AML in subjects who took niraparib were similar to those in subjects who took placebo.

PARP inhibitors may also cause a new primary cancer (that is, a cancer other than the one for which you were treated).

Inflammation of the lungs has been noted very rarely with use of niraparib. This condition may cause symptoms such as coughing, difficulty breathing, shortness of breath, and chest pain. Please report any of these symptoms as soon as possible to the study staff.

Blood clotting in the veins (venous thrombosis) has been noted in ovarian cancer subjects with and without use of niraparib. This may cause symptoms such as swelling, pain, warmth and redness in your legs or elsewhere. Clotting in the lungs may cause trouble breathing, cough and rapid heart rate. Please report any of these symptoms as soon as possible to study staff.

Unforeseen risks

When study drugs are taken alone or in combination with other medications, there may be other side effects that are unknown. All drugs have a possible risk of an allergic reaction, which if not treated right away, could become life-threatening.

There is a risk that you may have other side effects or discomforts after taking niraparib that are not included here. It is important to tell your Study Doctor and study staff about any symptoms you have during the time you participate in this study.

Additionally, there may be some side effects of niraparib that are not yet known, and every risk or side effect cannot be predicted. You may have unexpected side effects or be at risk for symptoms, illnesses, and/or complications that could not be predicted. Tell your Study Doctor or study staff right away if you have any problems.

Sometimes during a study, Janssen Scientific Affairs, LLC may learn new information about the study drug and the risks. It is possible that this new information might make you change your mind about being in the study. If new information is discovered, your study doctor will tell you about it right away.

What additional precautions do I need to take during the study?

Safe Handling of Drug

Caregivers should wear gloves if they need to touch the niraparib capsules. You should notify any caregivers of this information, to ensure the appropriate precautions are taken.

Birth control and pregnancy during the study

You cannot participate in this study if you are planning to father a child. Taking the Study Drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby), or nursing

infant. Furthermore, it is not known whether niraparib has side effects that might affect sperm for a period of time.

To participate in the study, male study participants must adhere to contraception requirements.

If you are sexually active with a woman who can become pregnant, you and your partner must use a highly effective method of birth control while you are participating in this study and for at least 90 days after your last dose of Study Drug. You must not donate sperm for at least 90 days after your last dose of Study Drug.

Birth control methods could include:

- combined (estrogen and progestogen containing) hormonal birth control; birth control pill or patch, device inserted into vagina
- progestogen-only hormonal birth control by injection
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS)
- tubes tied
- vasectomy for partner
- condom with spermicide for partner
- sexual abstinence, if this is the preferred and usual lifestyle

If you agree to participate in this study, you are expected to inform your female sexual partner(s) that you are participating in a clinical research study of an investigational drug and that the effects of the drug on sperm, an unborn baby and on a pregnant woman are unknown. You are also expected to provide your female sexual partner(s) with contact information for the Study Doctor for any additional questions.

If your female partner becomes pregnant while you are participating in this study or within 90 days after your last dose of Study Drug, tell your Study Doctor or study nurse right away as the Study Doctor is required to follow up and document the course and the outcome of all pregnancies. The Study Doctor may seek the pregnant woman's permission to review her medical records and the infant's medical records up to delivery, if applicable. The Study Doctor will share the information about your pregnant partner and the baby with Janssen Scientific Affairs, LLC to help understand the effects, if any, that the Study Drug may have on the pregnancy and maybe the child.

Payment for all aspects of obstetrical care, child, or related care will be the responsibility of you and or the pregnant woman. Neither the Penn Medicine nor Janssen Scientific Affairs, LLC will provide payment for any aspects of obstetrical care, child, or related care.

Other Study Related Risks

Risks of Blood Draws

Blood samples will be taken for tests throughout this study. The amount of blood to be taken by these blood draws is very small, and may be associated with discomfort and/or bruising at the site where the needle is inserted; and less commonly, fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding, and infection.

Risks of Electrocardiogram

The electrocardiogram (ECG or EKG) is a noninvasive test used to measure the electrical activity of the heart. By positioning leads (electrical sensing devices) on the body in set locations, information about many heart conditions can be learned by looking for patterns on the ECG. You may develop a slight rash or skin irritation in the locations where these leads (electrodes) were placed on your skin. There are no other known risks associated with an ECG.

Risks of Imaging Tests

During your participation in this study, you may undergo routine imaging tests to assess your disease. These can include CT. MRI, and bone scans. Each of these procedures has risks associated with it, and you should talk to your study doctor or the person doing these procedures about the risks before they start.

- Radiation Exposure
  This research study involves exposure to radiation from the CT and bone scans. Therefore, you will receive a radiation dose. Some of these procedures may not be necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer many years after the radiation exposure. At the doses you will receive, it is very likely that you will see no effects at all.

- CT Scans
  A CT scan is an imaging method that uses x-rays to create cross-sectional pictures of the body. You will be asked to lie on a narrow table that slides into the center of the CT scanner. Depending on the study being done, you may need to lie on your stomach, back, or side. Once you are inside the scanner, the machine's x-ray beam rotates around you. It is important to remain still during the exam, because movement causes blurred images. You may be told to hold your breath for short periods of time. The scans take about 15 minutes or less to complete.
    - It is important to inform your study doctor if you have had an allergic reaction to IV contrast material in the past, or if you have an allergy to iodine. Most CT contrast reactions (approximately 95%) are mild to moderate in degree and most resolve themselves without treatment. However, life-threatening reactions and fatalities, mostly of cardiovascular origin, have occurred. People with heart disease, kidney disease or allergies are more likely to have a more severe reaction to contrast agents. If you have a history of kidney disease, allergies or heart disease, please inform the study staff. Likely contrast reactions include feelings of overall warmth (especially in the bladder area after injection), a metallic taste during the injection, and warmth, burning sensation, or momentary pain during the contrast injection at the injection site. Less likely contrast reactions include nausea, vomiting, headache, hives, and itching. Rare but serious contrast reactions include faster than normal heart rate (tachycardia), high blood pressure (hypertension), low blood pressure (hypotension), heart attack, kidney failure, fluid in the lungs (pulmonary edema), serious allergic reaction, and death. There is also a risk that multiple needle sticks will be necessary to ensure proper intravenous line placement. There may be a small amount of pain or bruising with the placement of the intravenous catheter (IV) and a small risk of infection at the injection site.

- MRI
  The known risks associated with an MRI are minimal. The procedure uses radio waves and a magnetic field to take pictures, typically following the intravenous administration of a contrast dye. The greatest risk of having an MRI is the chance of metal objects flying

through the air toward the magnet and hitting you. To reduce this risk, all people involved with the study are instructed to remove all metal from their clothing and all metal objects from their pocket. You must tell your study doctor if you have any metal plates, implants, or clips in your body. No metal objects are allowed to be brought into the magnet room at any time. Metal objects inside your body can affect the test results and could lead to injury. Because the magnetic field of the MRI scanner attracts metal, these studies will not be performed on anyone with a pacemaker or any non-removable metallic foreign objects in their body. If you have any such object on your body, you will not receive the scan. You may feel claustrophobic (fear of being closed in) or anxious, and may need a mild sedative in order to undergo the MRI. You may experience some discomfort and fatigue from lying in a confined space. There are no known effects from exposure to the magnetic fields. Multiple needle-sticks may be necessary if a vein cannot be properly accessed and this will be carried out upon your permission. It is possible that during the course of the research study, the research staff may notice an unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the Principal Investigator will inform you if necessary. These possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician.

- Bone Scans
  A bone scan creates images of your bones using a computer to take pictures. An injection of a solution will be given so that images of your bones can be viewed by the machine. The injection may cause you to have a rash or other signs of allergy, pass-out or have pain, swelling, bruising, a small blood clot or infection at the injection site.

Risks of Using Up Stored Tumor Tissue Samples
If it is available, stored tumor tissue will be collected at the beginning of the study. It is possible that this entire stored sample will be used for the purposes of this research study and therefore may not be available for future clinical assessments as part of your routine care.

Risks of Genetic Research
This research includes genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you (such as new information about how the drug works or newly discovered side effects). If we discover new information about the study that could affect your decision to stay in the study, you will be notified in a timely manner. You will be able to ask questions about this new information and can discuss it with your family, friends, or doctor.

What are the possible benefits of the study?

Taking part in this study may or may not make your health better. However, while you may not benefit personally, the knowledge learned from your participation in this research study may benefit other people in the future. It is possible that your disease and/or health may worsen as a result of participating in this study.

What other choices do I have if I do not participate?

Your participation in this study is entirely voluntary. Other possible options include:

- Getting treatment or care for your cancer without being in a study.
- Taking part in another study.
- Not receiving treatment at this time.
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

Will I be paid for being in this study?

You will not be paid for taking part in this study.

Will I have to pay for anything?

Janssen Scientific Affairs, LLC will supply the study drug, niraparib, at no charge while you take part in this study.

You will be responsible for any deductibles or applicable co-pays for the standard tests, exams or procedures that would be done for your routine clinical care, such as office visits, scans and blood work. You and/or your insurance provider will be responsible for standard tests, exams or procedures that would be done even if you were not in this study. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance. There will be no charge to you for those laboratory tests and other procedures that are being done specifically for the purposes of this research study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Website at: http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Website.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured from being in the study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. If you think you have been injured as a result of taking part in this Study, you should contact the Principal Investigator or Emergency contact listed on page one of this form as soon as possible. You may also contact your own doctor, or seek treatment outside of the Penn Medicine. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the Penn Medicine. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

The Penn Medicine will also offer you the care needed to treat side effects and/or injuries that occur while you are taking part in this research.

We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for any injury that is not included in what Sponsor has agreed to cover. You may also be responsible for some of these costs. There are no plans for the Penn Medicine or Janssen Scientific Affairs, LLC to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

You may receive bills for side effects/injuries that occur during your participation in this study, even if they may be covered by Sponsor. If you have questions about these bills and whether or not they are covered by the research study, please bring copies of these bills to a member of the study team and they will be able to answer your questions.

When is the Study over? Can I leave the Study before it ends?

Your active treatment on this study will depend on how you tolerate the treatment and how your cancer responds to the study drug. You may be taken off treatment if you experience intolerable or unacceptable side effects, your doctor determines that your safety is at risk or this treatment is no longer in your best interest, or the study ends.

You may stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. You can also choose to leave the study at any time without giving a reason. It is important to tell the doctor if you are thinking about stopping so any risks for the treatments that you received can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you. Leaving the study will not affect your future medical care.

The doctor may stop you from taking part in this study at any time if he/she believes that it is in your best interest, if you do not follow the study rules, or if the study is stopped. If new information becomes available that might affect your choice to stay in the study, your study doctor will notify you as soon as possible.

This study may also be stopped at any time by your study doctor, Janssen Scientific Affairs, LLC (the drug manufacturer), or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator or the drug manufacturer feels that it is in your best interest to discontinue the study. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision
- You have not followed study instructions, or your female partner has become pregnant
- The drug manufacturer, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study due to new information regarding side effects.

- It is determined that you are no longer benefiting from the study drug
- For any other reason that is not known at this time

If you are removed from the research study, your study doctor will explain to you why you were removed. The study doctor and study team will help arrange for your continued care.

How will my personal information be protected during the study?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. This study is being overseen by the Food and Drug Administration (FDA); therefore, they may review your research records. Janssen Scientific Affairs, LLC may also receive information (personal health information is not actively requested, however, may be seen during a for-cause audit as an example). Please refer to the information below which explains more specifically how your personal information will be protected. If you do not want to allow these uses, you should not participate in this study. Information identifying you will be kept confidential as described below.

While collected as part of this study by your study doctor and study team, identifying information (including, but not limited to, your name, address, telephone number, medical record number, or any number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside of Penn Medicine. Personal health information that could be used to identify you will not routinely be sent to Janssen Scientific Affairs, LLC., and/or their designated representatives.

You will be assigned a unique subject identification number upon enrollment to the study. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the Penn Medicine study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

Will information about this study be available to the public?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What may happen to my information and samples collected on this study?

Collection of Identifiable Specimens

Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Whole genome sequencing may be conducted on your samples. Whole genome sequencing involves analyzing your entire personal genetic code.

Future Use of Data and/or Specimens

Your identifiable information and samples will be stored for future research purposes. Future researchers may receive information that could identify you. This can be done without again

seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected on this study.

Your identification number will be retained with your samples. Your information and samples may be stored and used for future research purposes for an indefinite amount of time.

There are no plans to tell you about any of the specific research that will be done. These tests may help doctors better understand your disease, how the drug is working in your body, and which patients may benefit most from this study drug in the future.

We may share your identifiable information and samples with other researchers within Penn or other research institutions, as well as pharmaceutical, device or biotechnology companies. We will not follow up with you to tell you about the specific research that will be done. We will not give you any results from these studies.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by only using your unique registration number to label your information and samples.

If you have questions about the storage of your information and samples, or have changed your mind, you can contact the Principal Investigator at the number listed on the first page.

If you change your mind, any remaining samples will be destroyed. However, your samples will not be removed from analyses which have begun.

Electronic Medical Record and Release of Study Related Information

What is an Electronic Medical Record?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.
A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the Penn Medicine and are participating in a Penn Medicine research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within Penn Medicine and are participating in a Penn Medicine research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, basic information about you will be obtained that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have).

What may be placed in the EMR?
Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a subject, have access to research related information within the EMR?
Please note the following about diagnostic test and/or imaging results:

- Results that may be placed in the medical record: Results from testing conducted in a laboratory or center that is part of Penn Medicine (i.e., the results would have been placed in the medical record, regardless of research participation). Results placed in the medical record are part of the designated record set and you have a right to review these results per HIPAA regulations.

- Results that may not be placed in the medical record: Results from biospecimen testing conducted in a laboratory that is not part of Penn Medicine and/or results from testing conducted in a non-certified laboratory (i.e., the results would not have been placed in the medical record as part of clinical care)

Will I receive the results of research testing?
Clinically relevant research results will be disclosed to you; this will be done in the context of discussion with your study doctor and/or clinical treatment team. Results from clinical testing done as part of this research will be placed in your medical record. Results placed in the medical record and will be available to you per HIPAA regulations, as noted above.

What information about me may be collected, used or shared with others?
The following personal health information will be collected and used for the purposes of this study.

- Name, address, telephone number, sex, date of birth
- The history and diagnosis of your disease, including genetic test results
- Specific information about the therapy you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your care
- Medical data including laboratory test results, health status, EKGs, CTs, MRIs, bone scans, pathology results, etc.
- Information on side effects (adverse events) you may experience, and how these were treated
- Long-term information about your general health status and the status of your disease. This may include information from other health care providers.
- Data that may be related to tissue samples that may be collected from you
- Numbers or codes that will identify you, such as your medical record number
- Information related to study visits and other tests/procedures performed while you are participating on this study.

While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, medical record number, or any

number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside of the Penn Medicine. Personal health information that could be used to identify you will not be sent to Janssen Scientific Affairs, LLC and/or their designated representatives.

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the Penn Medicine study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

Why is my personal health information being used?
Your personal contact information is important for the research team to contact you during the study. For this study we may need to contact you via email, text message or phone calls to provide you information about scheduling, appointments, notes or to send you information about your participation in the study. Email communications are often not secure and may be seen by others as a result. By signing below, you accept this risk. If you wish for us to use a different means to communicate with you during the course of this study, please discuss this with the research team and alternative methods can be arranged.

Your personal health information and results of tests and procedures are being collected as part of this research study, and will be used to conduct and oversee this research study, and to help guide your medical care.

Where might my information be stored?
Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS) and EMR. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases.

Who can see or use my information?

Which Penn Medicine personnel may use or disclose my personal health information?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of Penn Medicine and support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide care as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at the Penn Medicine who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of Penn Medicine, might receive my personal health information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. This study data may be processed and transmitted using

secure computer systems. In all disclosures outside of Penn Medicine you will not be identified by name, medical record number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. In records and information disclosed outside of the Penn Medicine, you will be assigned a unique code number.

Your original medical records also may be reviewed by the sponsor of this study or its designated representatives, the Institutional Review Board overseeing this study, and any of the regulatory or safety oversight organizations outlined below. They may review these records for the purpose of checking data collected for the study, to make sure the study is being done properly, and to analyze the results of the study.

Individuals or organizations responsible for administering the study

- Janssen Scientific Affairs, LLC.

Regulatory and safety oversight organizations

- The U.S. Food and Drug Administration (FDA)
- Other regulatory agencies and/or their designated representatives, including international agencies
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law

Once your personal health information is disclosed to others outside of Penn Medicine, it may no longer be covered by United States federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine be able to use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records even after you finish taking part in this study or after your death. We will keep all of the information forever in case we need to look at it again. We will protect this information and keep it confidential.

Your information may be held in a research database. However, Penn Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- Penn Medicine's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

The data from this study may be published or used for teaching purposes, however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to participate in this research study.

Can I change my mind?
You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission,

your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected. However, even if you do withdraw your permission to use the data about you, we are required by the FDA and other national regulatory authorities to record anything that relates to the safety of the investigational drug under study.

Subjects who withdrawal their consent early will be asked by the study team to look into their survival status via publically available means.

Will I be able to access my research records?
You have the right to see and get a copy of your medical records kept by the Penn Medicine However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed. When the study is over, you may write to the study doctor to ask to see or copy all of your medical information that was collected during the study. You also have the right to say how your medical information may be used, and to have any incorrect data about yourself updated or corrected.

By signing this document, you are permitting Penn Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the by calling (215) 898-2614.

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). You may also visit the NCI website at http://cancer.gov/. For NCI's clinical trials information, go to http://cancer.gov/clinicaltrials/. For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

Making Your Decision

Archived Tumor Collection

I agree to the collection of my archived tumor tissue, if it is available. Please circle Yes or No and initial on the line.

Yes No Initials: _____

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability, and report any changes in your health that may occur during the study.

Your signature also means that you are permitting the Penn Medicine Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the Penn Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this clinical trial.

A copy of this consent form will be given to you.

Name of Subject (Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

Name of Legally Authorized subject representative (print)	Signature of Legally Authorized subject representative	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.

_____