Consent and Authorization Document

A Phase II Study of Rucaparib Monotherapy in Nonmetastatic, Hormone-Sensitive Prostate Cancer Demonstrating "BRCAness" Genotype (ROAR)

This document may contain words and information that you do not understand. Please ask your study doctor or study staff to explain anything that is not clear to you. You are being asked to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

Once you know about the study, you will make a decision about whether to take part. If you decide to take part, you'll be asked to sign this form. Your decision to take part in this study is voluntary which means you are free to decide to join this study or not to join this study.

BACKGROUND

You are being asked to take part in this study because you have been diagnosed with prostate cancer that has a specific type of genetic mutation. The main reason for the study is to see if the drug rucaparib has an effect on your prostate-specific antigen (PSA) levels, which can be used to see how effective this treatment is on your cancer.

The standard approach to treating your disease is to either begin hormone therapy called androgen depravation therapy (ADT) or to carefully monitor and watch your disease.

Rucaparib (Rubraca®) has not been approved by the U.S Food and Drug Administration (FDA) for prostate cancer so it is being considered "investigational" for use in this study. An investigational drug is a drug that is being tested and is not approved for sale in the United States by the U.S. Food and Drug Administration (FDA).

Rucaparib has been approved by the FDA for the treatment of ovarian cancer and is available to be prescribed for patients with that disease.

The study is being conducted by Dr. Benjamin Maughan at Huntsman Cancer Institute of the University of Utah.

NUMBER OF PARTICIPANTS

Approximately 15 patients are expected to be enrolled in this study from the Huntsman Cancer Institute/University of Utah.

STUDY PROCEDURES

If you decide you will take part in the study and you sign this informed consent form, you will have some screening tests and procedures done to make sure you are eligible to enroll.

Screening Period

- Medical history will be collected as well as details about what medications and vitamins you are currently taking.
- You will have a physical exam and a measure of your vital signs.
- An evaluation of your ability to perform everyday activities will be done.
- If your doctor feels it is necessary, you will have an electrocardiogram (ECG) done. An ECG measures the electrical activity of your heart, including the rate and rhythm of your heartbeat.
- You will have a CT (Computerized Tomography) scan as well as a nuclear medicine bone scan. These are considered standard of care and would be done even if you were not participating in this study.
- You will have your blood drawn and a urine sample taken for standard lab testing to ensure you are healthy enough to take part. You will also have blood, urine and any available tissue samples taken to check different components of your cancer and blood, including genetics, which will be compared to samples that will be collected later.
- If samples are available from a tumor biopsy or cancer surgery in the past, your study doctor will request the original tumor samples (this is known as an archived tumor sample) from the medical facility where it was performed. They will be looking at genetic components to see if you qualify for this study, if this testing has not previously been done.

Treatment Period

Once it is decided that you are able to enroll into this study, you will begin study treatment. The study drug, rucaparib will be given to you in segments of time called “cycles”. For this study, a cycle will be 28 days. You will take 600 mg orally, twice a day. You should take the tablets with 8 oz. of room temperature water, with or without food. These should be taken as close to 12 hours apart as possible, preferably at the same times every day. Your doctor and study team will give you more information about your treatment plan.

You will come to the clinic on Day 1 of each cycle for various procedures. Some of the procedures are being done as part of your routine cancer care. Some are being done because you are participating in this study. You will continue on the study treatment until your disease gets worse, you have intolerable side effects, you decide to stop, or if your doctor decides it would be in your best interest to stop or the study ends.

Study Procedures during the Treatment Period:

- You will have physical exams and measures of your vital signs during your clinic visits, some of those will involve a prostate exam. You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- Evaluations of your ability to perform everyday activities will be done.

- You will have blood collected for standard lab testing for safety and to test how your cancer is responding to treatment. Researchers will also be looking at components of the samples, including genetic information, to help them learn about your cancer and how it may change after treatment.

PSA Progression Confirmation Visit

If you have confirmed PSA progression at one of your regularly scheduled visits, you may be asked to provide Informed Consent for treatment beyond PSA progression. The following tests and procedures will be done at this visit.

- You will have a physical exam that includes a prostate exam and measures of your vital sign. You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- An evaluation of your ability to perform everyday activities will be done.
- You will have your blood drawn for safety testing. You will also have blood and urine samples taken to check different components, including genetics.
- You will have a CT (Computerized Tomography) scan as well as a nuclear medicine bone scan. These are considered standard of care and would be done even if you were not participating in this study.
- Optional tissue collection –,If you have disease progression, you may be asked to have an optional biopsy for additional tissue collection. Researchers will be looking at components of the samples, including genetic information, to help them learn about your cancer and how it may change after treatment. This additional biopsy is optional. Please see the end of this form to make your choice about participation.

End of Treatment

- You will have a physical exam that includes a prostate exam and measures of your vital signs. You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- An evaluation of your ability to perform everyday activities will be done.
- You will have blood collected for standard lab testing for safety.
- You will have your blood drawn for safety testing. You will also have blood and urine samples taken to check different components, including genetics.

Follow-up

Once you complete your end of treatment visit, you will continue to be followed about every 3 months for 2 years. These visits may be conducted via phone call. At these visits, you may have PSA testing completed.

RISKS

Rucaparib

You may have side effects from taking rucaparib or from the procedures used in this study. Side effects may vary from person to person, and can range from mild to very serious. If you have any side effects as a result of taking part in this study, tell your study doctor right away, even if you don't think they are due to the study drug.

Rucaparib (marketed name: Rubraca) is an experimental drug that may have side effects that cannot be predicted at this time. Rare or unknown side effects could possibly occur, including life-threatening events or death. If you experience certain side effects, the study doctor may decide to stop or lower your dose of study drug until you recover from the side effects.

The following is a list of reported side effects as well as other notable side effects as reported by physicians about their patients who are taking rucaparib alone:

Very common (Occurring in ≥ 10% of patients)

- Nausea
- Feeling tired (known as fatigue or lethargy)
- Low blood counts (red blood cells, white blood cells, and platelets). Sometimes fever occurs with low blood counts. These low blood count effects may be more likely to occur after multiple cycles of treatment.
    - A low red blood cells count may make you feel tired or dizzy. If you feel dizzy while taking rucaparib, you should avoid potentially hazardous tasks such as driving or operating machinery.
    - A low white blood cell count puts you at higher risk for bacterial or viral infections. Having a high temperature or fever while your white blood cell count is low is a medical emergency and you must proceed to the nearest emergency room as soon as possible.
    - A low platelet count affects the ability of your blood to clot and could lead to bleeding events. Symptoms include but are not limited to easy bruising, prolonged bleeding from cuts, blood in stools or urine, or nose bleeding.
- A low phosphate level in your blood. Usually there are no symptoms but if the levels are critically low, you may notice trouble breathing, confusion, muscle weakness, and/or irritability.
- Increase in cholesterol. If your cholesterol increases significantly, your doctor may prescribe a medicine to lower your cholesterol level.
- Changes in kidney and liver function blood tests. These changes will be evaluated by your study doctor along with any other side effects that you are experiencing as well as other test results.
- Changes in your sense of taste.
- Stomach-related effects such as constipation, vomiting, diarrhea, decreased appetite, stomach pain (epigastric pain), and indigestion.

- Difficulty breathing (dyspnea)
- Dizziness
- Photosensitivity reaction
    - It is possible that rucaparib may make your skin and eyes more sensitive to sunlight. You should take all of the usual sun protection precautions when going outside. It is advised that you avoid excessive sun exposure, wear protective clothing (including wearing a hat and sunglasses), and use sunscreens regularly (sun protection factor 50 or greater).
- Difficulty sleeping

<u>Common (Occurring in ≥1 to <10% of patients)</u>

- Upper Airway Infection (like the common cold)
    - You may experience infections involving the nose, pharynx, larynx, and sinuses. Symptoms include a blocked (congested) nose, a runny nose, and sneezing. You may also have clear discharge (mucus) from the nose. You may feel generally unwell and may also be associated with fever. Treatment is usually supportive but if symptoms persist please inform your doctor.

<u>Uncommon (Occurring in ≥0.1 to < 1% of patients)</u>

- Myelodysplastic syndrome (MDS)[a] and acute myeloid leukemia (AML)[a]
    - Effects possibly related to rucaparib, but whose casual link has not yet been formally established, have been reported in a very small number of patients treated with rucaparib during the safety period (while on treatment with rucaparib and 28 days after last dose). MDS is a pre-cancerous condition where the bone marrow is not as good at producing blood cells (red and/or white blood cells and/or platelets). People with MDS need transfusions (red blood cells and/or platelets) and/or other treatments. In some cases, MDS can progress to AML, which is a cancer of the bone marrow where more abnormal and immature white blood cells (also called blasts) are made than normal white blood cells. People with AML need treatment with chemotherapy and/or a bone marrow transplant. Patients may develop AML without first being diagnosed with MDS.
    - Events of MDS and AML have also been reported with PARP inhibitors similar to rucaparib. At this time it is not known whether rucaparib or other PARP inhibitors cause MDS or AML, or if these developed as a result of previous chemotherapy these patients received. Your study doctor will closely monitor your blood cell levels during treatment. If he/she has any concerns about your blood counts you may be asked to have a biopsy of your bone marrow.

Allergic Reactions

As with any drug, it is possible that you could have allergic reactions to study drug, such as itching, skin rash, facial swelling, and/or a severe or sudden drop in blood pressure. A sudden drop in blood pressure could lead to shock with loss of consciousness and/or possible seizures, including the possibility of death. If you have any of the above symptoms, seek medical attention right away.

REPRODUCTIVE RISKS

It is unknown if rucaparib has an effect on semen. Because of this, you must practice abstinence or use a condom to avoid passing rucaparib to your partner with all sexual activity. You should not father a baby or donate sperm while you are in this study and for at least 6 months after you are off treatment. If your partner is of childbearing potential, you must use (or have her use) an effective contraceptive while on the study and for 6 months after the last dose. Examples of medically acceptable birth control include medically prescribed IUDs, oral pill, skin patch, vaginal ring or injectable hormonal contraceptives. Please ask the study team for more information about these options.

If you think that you have fathered a baby while receiving treatment or within 6 months of completing treatment in this study, you should inform your doctor immediately.

Other Risks and Inconveniences including Genetic Risks

There are also non-physical risks associated with taking part in this study, such as the risks associated with a breach of privacy or confidentiality. For example, if your identity as a participant in genetic research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The risks of such improper disclosure are very small because Huntsman Cancer Institute has adopted strict privacy and confidentiality procedures for this research.

Blood draws or IV: Risks associated with drawing blood or putting a needle in your vein might include pain from the puncture, bruising, bleeding, infection, or fainting. Every effort will be made to minimize discomfort.

Risk of Biopsy: Tumor biopsies may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

UNFORESEEABLE RISKS

Problems or side effects that are not known could also occur. Most side effects are expected to go away after treatment is stopped or interrupted; however in some cases the side effects may be serious, long-lasting, permanent or lead eventually to death.

What are the Uses for my Samples Collected During the Study

Your participation in genetic testing is a mandatory part of this study. It will be performed in order to learn more about factors which may predict response to the study treatments.

Segments of the DNA called genes are responsible for passing particular traits such as eye color from parents to children.

In the United States, the **Genetic Information Nondiscrimination Act of 2008 (GINA)** prohibits discrimination in health coverage and employment based on genetic information. GINA, together with the Health Insurance Portability and Accountability Act (HIPAA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or the individual's family members, or using it for decisions regarding coverage, rates, or preexisting conditions. The law also prohibits most employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. Utah State Law also offers protection against discrimination in health coverage and employment.

You will not receive any of your genetic information that comes from the testing in this study, nor will it become a part of your medical record. The results will be kept on password-protected computers and results will be accessible only to the investigator and other authorized people.

BENEFITS
There may not be any benefit to you from your being in the study. The information gained in this study will aid in the understanding of cancer and help in the development of new approaches to its treatment in the future.

ALTERNATIVE PROCEDURES
You do not have to be in this study to get help for the type of cancer you have. The study doctor will talk to you about other things you can do for this type of cancer, including the important risks and benefits.

Some other things you might do are:
- Use other approved chemotherapy regimens.
- Use other investigational treatments.
- Get supportive care.
- Choose to have no further treatment.

PERSON TO CONTACT
If you have questions, complaints or concerns about this study, you can contact Dr. Benjamin Maughan at 801-585-0255. If you think you may have been injured from being in this study, please call Dr. Maughan at 801-585-0255. The University Hospital Operator can be reached at this number: 801-581-2121 available 24-hours a day. Please ask for the oncologist on call.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

Taking part in this research study is voluntary. You may decide not to take part or you may leave the study at any time. Refusal to take part or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled.

Tell the study doctor if you are thinking about stopping or decide to stop, as it may be necessary to do certain tests in order to ensure your safety. If you choose not to return for an assessment, we may ask for medical records from your current general practitioner in order to continue to monitor your health.

If you decide not to continue in the study at any time, your study doctor will arrange for you to receive alternative treatment and any necessary assessments or procedures according to standard of care.

RIGHT OF INVESTIGATOR TO WITHDRAW

Your study doctor may decide to take you off this study at any time without your consent for any of the following reasons:

- if your disease becomes worse and is not responding to the study drug,
- if he or she believes it is in your best interest,
- if you do not follow the study rules,
- if you miss study visits and/or procedures,
- if you have serious side effects,
- if you become pregnant,
- you do not later consent to any future changes that may be made in the study plan; or any other reason.

There is also the possibility that the investigator, may close the study before your participation is complete and without prior warning. If any of these events were to happen, your study doctor would assist with arrangements for your continued care as appropriate.

COSTS AND COMPENSATION TO PARTICIPANTS

Some of the procedures and treatments you'll have while you are on the study are considered "standard of care" for your type of illness. Even though you will be a part of the study, these types of procedures and treatments will be billed to you and/or your insurance company just like regular medical care. Some procedures and treatments you'll have while you are on the study are considered "study related" and are not billed to you and your insurance company. You should ask your study coordinator and treating physician for details about the specific procedures you or your insurance company will be financially responsible for.

Clovis, the manufacturer of rucaparib, will be supplying the study drug to you free of charge in this study.

You may be eligible for assistance with costs associated with travel for purposes of research participation. Please speak with your study coordinator or physician for details. If eligible, you may be asked to provide receipts in order to receive reimbursement. It will be necessary for us to collect your Social Security Number for your reimbursement. You will need to provide this information on a Federal W-9 Form that is filed with our accounts payable department. No other information (e.g. the name of this study) will be provided to that office. This amount will not be reported to the Internal Revenue Service (IRS).

NEW INFORMATION

You will be given any new information about the study drugs that may affect your willingness to start or continue in the study as it becomes available. You will not receive any results from the genetic testing performed in this study. The results will also not be included as part of your medical records.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like your name, address, telephone number, and email address.
- Related medical information about you like family medical history, allergies, current and past medications or therapies, information from physical examinations such as blood pressure readings, heart rate, temperature, and lab results.
- All tests and procedures that will be done in the study.

How we will protect and share your information:

We will do everything we can to keep you information private, but we cannot guarantee this. The research records will be kept in a secured manner and computer records will be password protected. We may need to disclose information about you as required by law.
Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital.
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.

In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:

- Members of the research team and University of Utah Health Sciences Center
- The University of Utah Institutional Review Board (IRB), who reviews research involving people to make sure the study protects your rights;
- Clovis, the manufacturer of rucaparib, and their affiliates
- Government agencies responsible to confirm research accuracy such as the United States Food and Drug Administration (FDA), and the National Cancer Institute (NCI) which is a part of the National Institute of Health (NIH)
- Governmental agencies in other countries where the study drug may be considered for approval.

If we share your identifying information with groups outside of the University of Utah Health Sciences Center, the groups may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

What if I decide not to take part after I sign the Consent and Authorization Form?
You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

Optional Biopsy for Research

Researchers would like for you to have an optional tumor biopsy to collect tissue if you experience disease progression while on study treatment. You do not have to participate in this optional study component. If you choose to participate in the optional tumor biopsy and tissue collection, you will have a tumor biopsy taken at the time of disease progression. This tumor tissue will be used for research related to this study only. If you choose not to participate in the biopsy sample part of the study, your decision will not exclude you from the main study. Please **initial** and **date** the corresponding line below to let us know if you would like to participate:

_____ I **do** want to participate in the optional tumor tissue collection.

_____ I **do not** want to participate in the optional tumor tissue collection.

FUTURE USE OF SAMPLES

If you agree, the study team would like to save any leftover samples to bank it for future unspecified cancer related research (tissue banking). This testing may include genetic testing. The tissue bank will be managed here at HCI by the Biorepository and Molecular Pathology (BMP) department and will be kept by them. Participation in tissue banking is completely optional. Your samples will be stored with the following information: type of specimen, diagnosis, sex, age, treatment, and treatment response. Only the study doctor and the study staff, including those who manage the tissue bank at the BMP, will have access to those identifiers. Any lab that does testing outside of HCI will not receive these identifiers. You do not have the option to have your samples de-identified. If this is not acceptable to you, you should not participate in the optional specimen banking portion of the study. All information obtained from your samples will be kept confidential as stated in the AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION section of this form.

At any time, you may ask that your samples not be used for future research and that they be destroyed by contacting the study doctor and/or study team. If you ask for this, study tests will be done, but samples will not be used for future research testing. However, any information collected from your samples before your request to destroy them will be kept by HCI.

If you decide to stop taking part in the study, but do not request that your samples be destroyed, HCI and its authorized representatives may continue to use your samples for future research and genetic testing.

Because the results from future research will not directly affect your health care, we will not share the results from future studies with you or your doctors.

Samples obtained from you in this research may help in the development of a commercial product by the investigator or the benefactor or its research partners. There are no plans to provide financial compensation to you should this occur.

Banking for Future Use

Researchers would like to save any of your left over samples for future unspecified cancer research as described above. If you choose not to participate in the tissue banking part of the study, your decision will not exclude you from the main study. Please **initial** and **date** the corresponding line below to let us know if you would like to participate:

initial_____ /date_____ I **do** want to participate in the optional tissue banking.

initial_____ /date_____ I **do not** want to participate in the optional tissue banking.

CONSENT

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____
Participant's Name

_____ _____ _____
Participant's Signature Date Time

_____
Name of Person Obtaining Authorization and Consent

_____ _____ _____
Signature of Person Obtaining Authorization and Consent Date Time

LANGUAGE INTERPRETER STATEMENT (if applicable):

I confirm that I was present as an interpreter for the duration of the consent process for this research study. I confirm that I am qualified/have the necessary skills to provide interpretation between [insert target language] _____ and English. By signing this form, I confirm that I provided a full and complete interpretation of the exchange between the research staff member named above and the patient named above, to the best of my ability.

Name of Interpreter_____ Employer/Vendor (if applicable) _____

_____ _____ _____
Signature of Interpreter Date/Time Target Language

Information requested for federal grant reporting purposes *(optional)*

Sex/Gender

- ❑ **Male**
- ❑ **Female**

Ethnicity

Do you consider yourself to be Hispanic or Latino? (see definition below)

Hispanic or Latino. A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race.

Select one:

- ❑ **Hispanic or Latino**
- ❑ **Not Hispanic or Latino**

Race

What race do you consider yourself to be? SELECT ONE OR MORE OF THE FOLLOWING:

- ❑ **American Indian or Alaska Native.** A person having origins in any of the original peoples of North America (including, Central or South America) who maintains cultural identification through tribal affiliation or community recognition.
- ❑ **Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
- ❑ **Black or African American.** A person having origins in any of the black racial groups of Africa.
- ❑ **Native Hawaiian or other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
- ❑ **White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
- ❑ **Unknown.**

❑ **Check here if you do not wish to provide some or all of the above information.**

Initial and Date