Consent and Authorization Document

A Phase 2 study of Radium-223 and Radiotherapy in Hormone-Naïve Men with Oligometastatic Prostate Cancer to bone (RROPE)

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 spread to your bones. In this study you will be given an investigational drug called Radium Ra-223 dichloride (also known as Xofigo) as well as radiation treatment to your bones. The purpose of this research is to see if using these two treatments combined will help to delay the need to start androgen deprivation therapy, which is a type of hormone therapy. These androgen deprivation therapies can decrease your quality of life, so the researchers are hoping to find that delaying the start of them will improve your quality of life versus starting right away on hormone therapy.

Radium Ra-223 has not been approved by the U.S Food and Drug Administration (FDA) for your type of 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). The combination of Ra-223 and radiation is also considered investigational in this study.

Radium Ra-223 is approved by the FDA for the treatment of metastatic castration-resistant prostate cancer and is available to be prescribed for patients with that type of prostate cancer.

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

NUMBER OF PARTICIPANTS

Approximately 20 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
- You will answer some questions about your quality of life
- An evaluation of your ability to perform everyday activities (performance status) will be done
- You will have a CT (Computerized Tomography) scan, PET/CT scan, or MRI. This is considered standard of care and would be done even if you were not participating in this study.
- You will have a bone scan. This is considered standard of care and would be done even if you were not participating in this study.
- You will have an ECG (electrocardiogram) if your doctor thinks it is necessary.
- You will have your blood drawn for standard lab testing to ensure you are healthy enough to take part. You will also have your testosterone and PSA (prostate-specific antigen) levels checked.
- Optional tissue analysis - The researchers want to use some of your previously collected tumor tissue to look at components of your tumor and how that may relate to how your cancer reacts to the treatments. See the end of this form for more information and to make your choice about participation.

Treatment Period

Once it is decided that you are able to enroll into this study, you will begin study treatment. The study drug, Ra-223 will be given to you in segments of time called “cycles”. For this study, a cycle will be 28 days. You will be given Ra-223 on day 1 of each cycle, for a maximum of 6 cycles. It will be given to you as an intravenous (IV) infusion. The first cycle will be given to you, and then prior to cycle 2, the external beam radiation will be given.

The external beam radiation will be targeted to the bone tumors that were seen on your imaging tests. You will receive anywhere from 1 to 6 external beam radiation treatments. The number of external beam treatments will depend on where your bone tumors are located and your doctor’s recommendation.

This radiation from the radium-223 is expected to last for 2-6 weeks. Once your external beam radiation is completed, cycle 2 will be given and will continue as described above. Your doctor will give you more information about your treatment and radiation 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 for a maximum of 6 cycles unless your disease gets worse, you have intolerable side effects, you decide to stop, your doctor decides it would be in your best interest to stop or the study ends.

During the first few days after your Radium-223 treatments, Radium will be present in your stools, with a small amount also in your blood and urine. It is very important that you take the following precautions for one week after each Radium-223 treatment cycle. After this time you do not need to take any special precautions:

- A normal toilet should be used in preference to a urinal. The sitting position should be used instead of the standing position. Flush the toilet twice after use.
- Use disposable gloves when wiping up blood, urine, stools or vomit, or when handling stained clothes.
- Wipe up any spilled urine or stool with a tissue and flush it away.
- If you are sick, wipe up spilled vomit with a tissue and flush it away.
- Ensure that you always thoroughly wash your hands after using the toilet or after wiping up spilled fluids.
- Machine-wash (without pre-washing by hand) any linen or clothes that become stained with urine, blood or stools, separately from other clothes.
- If you are sexually active, the use of a condom is recommended during intercourse for the first week after each injection because there may be some radioactivity in the body fluids.
- If sampling of your blood, urine or stools is necessary during the first week following Radium treatment, please tell the people treating you that you have been treated with radioactive Radium-223. If possible show them your appointment card with our contact details on it.
- If you need medical care such as an operation or hospital admission during the first week following the treatment, please also inform your care providers that you have recently been treated with Radium-223

Study Procedures during the Treatment Period:

- You will have physical exams and measures of your vital signs during your clinic visits. 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 (performance status) will be done.
- You will answer some questions about your quality of life
- You will have bone scans. This will be done between cycles 3 and 4 and then at any other time that your doctor might think is necessary. This is considered standard of care and would be done even if you were not participating in this study.

- You will have your blood drawn for standard lab testing to ensure your safety and to check on your health. You will also have your testosterone and PSA (prostate-specific antigen) levels checked.

End of Treatment

- You will have physical exams 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.
- You will answer some questions about your quality of life
- An evaluation of your ability to perform everyday activities (performance status) will be done
- You will have a CT (Computerized Tomography) scan, PET/CT scan, or MRI. This is considered standard of care and would be done even if you were not participating in this study.
- You will have a bone scan. This is considered standard of care and would be done even if you were not participating in this study.
- You will have your blood drawn for standard lab testing to check on your health and cancer. You will also have your testosterone and PSA (prostate-specific antigen) levels checked.

Follow-up

Follow-up visits will occur every 3 months for an approximate duration of two years from the time you enrolled in the study and will include the following assessments and procedures:

- You will have physical exams and measures of your vital signs during your clinic visits. 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.
- You will answer some questions about your quality of life
- You will have bone scans. This is considered standard of care and would be done even if you were not participating in this study.
- You will have your blood drawn to test your testosterone and PSA (prostate-specific antigen) levels.

RISKS

Radium Ra-223

Blood and Lymphatic System Problems (Occurred in ≥ 1 out of 10 patients)

- Anemia (not enough red blood cells)
- Leukopenia (not enough white blood cells)
- Thrombocytopenia (not enough platelets)
- Lymphocytopenia (not enough lymphocytes- a special kind of immune system cell)
- Neutropenia (not enough of a type of white blood cell called neutrophils)
- Bone Marrow suppression

Gastrointestinal Problems (Occurred in 1 out of approximately 37 patients)

- Nausea
- Diarrhea

- Vomiting
- Dehydration

Injection Site Conditions (Occurred in 1 out of 100 patients)

- Fluid build-up, redness and pain

Other (Occurred in ≥ 1 out of 50 patients)

- Swelling and water retention in your legs
- Kidney failure and/or harm

The radiation dose resulting from therapeutic exposure to Radium-223 dichloride may result in secondary cancers.

Radiation
Common, some may be serious
In 100 people receiving radiation therapy, more than 20 may have:

- Tiredness
- Swelling, redness, and/or sores in the area of radiation

Occasional, some may be serious
In 100 people receiving radiation therapy, from 4 to 20 may have:

- Nausea, vomiting
- Pain
- Internal bleeding
- Diarrhea, passing gas, blockage of the stomach
- Broken bone
- Bruising, bleeding

Rare, and serious
In 100 people receiving radiation therapy, 3 or fewer may have:

- Liver damage which may cause yellowing of eyes and skin, swelling

You may experience a risk or side effect that we are not aware of yet. There may be side effects of taking Radium Ra-223 and having radiation treatments around the same time that we are not aware of.

REPRODUCTIVE RISKS

Because study drugs may affect an unborn baby, you should not father a baby while taking part in this study. You and your sexual partner should use an effective method of birth control while taking part in this investigational treatment. Examples of medically acceptable birth control include medically prescribed IUDs, and double barrier methods, e.g., condom in combination with spermicide. Check with your study doctor about what kind of birth control methods to use. You should continue using birth control for 6 months after receiving the last dose of study drugs. If you think that you have fathered a baby while receiving treatments in this study, you should inform your doctor immediately.

Other Risks and Inconveniences
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 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.

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. You will be given any new information when it becomes available that may affect your willingness to start or continue in the study.

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. Jonathan Tward at 801-585-0255. If you think you may have been injured from being in this study, please call Dr. Tward 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,

- 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.

Radium Ra-223 will be provided to you free of charge by Bayer, the drug maker.

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.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and other 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;
- Bayer, the drug supplier of Ra-223, and its authorized agents
- 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 RESEARCH (Making your choice about having optional procedures)

We would like to use some of your previously collected tumor tissue for optional research. You do not need to participate in the optional research. If you choose not to participate, it will not affect your ability to participate in the main study nor exclude you from it.

Tumor Tissue

There may be extra tissue from your prostate biopsy that was performed when you were diagnosed with prostate cancer, or if you had surgery, and this extra tissue is being stored. We would like to use some of that extra stored tissue for the optional research. Please **initial** and **date** the corresponding line below to let us know if you would like to participate.

_____ I **do** want my stored tissue to be used for optional research.

_____ I **do not** want my stored tissue to be used for optional research.

CONSENT

I have been given adequate time to read and consider the information in this consent form prior to signing (or it has been read to me). All my questions about the study and my participation in it have been answered and I will be given a copy of this signed and dated consent form for my records and continued reference.

My signature below indicates that I voluntarily agree to take part in this research study. By signing this consent form, I do not release the study doctor or his study staff, the institution or the sponsor from their professional and legal duties.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

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.**