Certification of Completion of the Informed Consent

IRB #

Title:

I have discussed the "Informed Consent for Participation in Research Activities" in its entirety for the above referenced research study, with the research participant listed below (or the research participant's legally authorized representative). During the review of the consent form, the possible benefits, risks and discomforts involved in his/her participation on the study, as well as potential alternatives were reviewed.

The research participant has been encouraged to ask questions, and all questions asked by the participant have been answered. The research participant affirmed that he/she has received all information that he/she desires at this time, and a copy of the signed consent form has been provided to the participant.

PRINTED NAME of Person Obtaining Informed (Consenter)	SIGNATURE	TITLE	DATE	TIME

ADULT INFORMED CONSENT

COH Protocol # 17085
TITLE: A Phase 2 Trial of Radium Ra 223 Dichloride in Combination with Androgen Deprivation Therapy and Stereotactic Body Radiation Therapy for Patients with Oligometastatic Castration-Sensitive Prostate Cancer (SHARP)

Protocol Version Date: 02/17/2022

PRINCIPAL INVESTIGATOR: Savita Dandapani, M.D.

24-HOUR TELEPHONE NUMBER: 626-256-HOPE (4673), Extension 85200
DAY TIME TELEPHONE NUMBER FROM THE HOURS OF 8:00 AM TO 5:00 PM: 626-256-HOPE (4673), Extension 82247

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or clinical trial. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

ADULT INFORMED CONSENT

COH Protocol #17085
TITLE: A Phase 2 Trial of Radium Ra 223 Dichloride in Combination with Androgen Deprivation Therapy and Stereotactic Body Radiation Therapy for Patients with Oligometastatic Castration-Sensitive Prostate Cancer (SHARP)

PRINCIPAL INVESTIGATOR: Savita Dandapani, M.D.

You are invited to take part in a clinical trial, a type of research study, because:

(1) You have hormone sensitive prostate cancer that has spread to bone and other parts of the body (metastatic), AND
(2) You refused standard of care chemotherapy for your disease, AND
(3) You are about to be given or have started standard of care Androgen Deprivation Therapy (ADT; hormone therapy) with either leuprolide OR goserelin OR degarelix OR relugolix.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

This research study is sponsored by City of Hope. Bayer is the drug company that will be providing funding and the study drug, radium Ra 223 dichloride for this study.

It is expected that about 24 people will take part in this research study.

Dr. Dorff, a Co-Investigator, is paid as an advisor for Bayer US the company that provides the drug, radium Ra 223 dichloride, you will receive and supports this research. The City of Hope Conflict of Interest and Commitment Committee and COH IRB have reviewed Dr. Dorff's financial interest in Bayer US and found that this is very unlikely to affect how you will be treated or how the study results will be determined. If you have questions about this, please ask the Principal Investigator or contact COH IRB at (626) 256-HOPE (4673) ext. 62700. You may also contact the City of Hope Conflict of Interest Manager, at (626) 256-HOPE (4673).

A. WHY IS THIS RESEARCHSTUDY BEING DONE?

This research study is a Phase 2 clinical trial. Phase 2 clinical trials test the safety and effectiveness of an investigational (experimental) intervention to learn whether the intervention works in treating a specific disease. "Investigational" means that the intervention is being studied.

ADT (hormone therapy) works by reducing levels of male hormones (e.g. testosterone) or stopping male hormone production in the body; this affects the growth of prostate cancer cells. For metastatic hormone sensitive prostate cancer, it is routine to get ADT alone or ADT with docetaxel (a type of chemotherapy) or ADT with abiraterone (another hormonal based treatment).

Radiation therapy is also an option for patients with metastatic prostate cancer. Clinical studies have shown that ADT can be effective when it is combined with radiation therapy.

This research study will look at combining ADT, Stereotactic Body Radiation Therapy (SBRT) and radium Ra 223 dichloride (Xofigo; a type of radiation therapy) as a possible future treatment for your disease.

SBRT is a type of external beam radiation therapy that delivers a very strong focused dose of radiation over a smaller number of treatments, usually 3-5 sessions. SBRT is a treatment option available for prostate cancer patients. In this study we will be treating from one to four sites of metastatic disease with SBRT. This is a treatment option but is experimental when treating multiple sites of metastatic disease and we list the side effects of SBRT below.

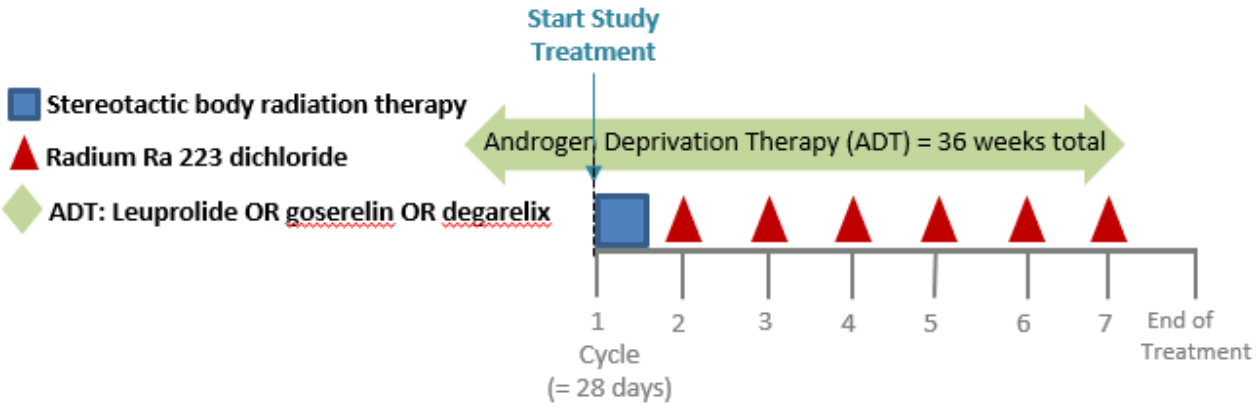
Radium Ra 223 dichloride has been approved by the U.S. Food and Drug Administration (FDA) for patients who have prostate cancer that has spread to the bone only and are no longer responding to ADT. Radium Ra 223 dichloride is not approved for your disease and is also experimental in this study.

Radium Ra 223 dichloride is made up of a radioactive material called radium 223. It goes mainly to areas of the bone that are growing quickly. In the bone, it gives off radiation that kills cancer cells. The strong radiation it gives only travels a short distance and this limits the damage to healthy cells.

This study will test the safety and effectiveness of ADT in combination with SBRT and radium Ra 223 dichloride for your disease.

B. WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:



You will start your standard of care ADT (leuprolide or goserelin or degarelix or relugolix) before you start study treatment (you may have even started your standard of care ADT prior to consenting on this study). During the study you will continue to get ADT (leuprolide or goserelin or degarelix or relugolix) for a total of 36 weeks of ADT. The length of your ADT treatment is not the same as if you were getting ADT outside of this research study.

You will get study treatment in 28 day treatment cycles. During first cycle of treatment (Cycle 1) you will be given SBRT. During Cycles 2-7 you will be given radium Ra 223 dichloride.

To protect the health of your bones while you receive these treatments, you will take a bone health agent, such as a bisphosphonate or a RANKL inhibitor, at the dose and schedule consistent with the treatment of bone metastases or prevention of osteoporosis. You will continue to take this until your testosterone levels return to the normal range or at the discretion of the principal investigator, Dr. Savita Dandapani.

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history,** which includes questions about your health, current medications, and any allergies.
- **Performance status**, which evaluates how you are able to carry on with your usual activities.
- **Vital Signs:** Weight, height, heart rate, blood pressure, respiration rate, and temperature.

- **An assessment of your tumor** by one or more of the following standard assessment tools: CT (Computerized Tomography) scan, MRI (Magnetic Resonance Imaging) or PET (Positron Emission Tomography) scans.
- **Blood tests**
  Blood will be drawn from a vein in your arm for the following tests:
  - **Organ function tests**: To check your blood counts and kidney and liver functions (about 2-3 teaspoons of blood will be drawn at each time)
  - **To check your disease**: To test your prostate-specific antigen (PSA) and testosterone levels (about 2 teaspoons of blood will be drawn at each time)
- **Urine test** to measure your kidney health
- **Tumor tissue:** If available, we will collect some stored tissue and fresh tumor biopsy (if applicable) from your standard of care procedure(s) for clinical testing to look atprostate cancer biomarkers.
- **ADT:** You will start standard of care ADT or you will already be receiving ADT.

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Study Procedures:

If you are eligible to participate in this research study, the following test and procedures will occur. A chart summarizing the timing of these tests and procedures is also provided below. Some tests and procedures may be part of your standard of care.

- **SBRT***:*
  - You will sign a general informed consent to receive SBRT. The risks for SBRT will be described to you by the doctor, as well as are listed below.
  - You will start SBRT to each metastatic site seen on imaging on Cycle 1 Day 1
  - SBRT will be given over 7 to 21 days during Cycle 1.
  - Doses will begiven at least every 40 hours apart
- **Infusion of Radium Ra 223 dichloride**
  - A doctor trained to give radium Ra 223 dichloride will give you your injection
  - The doctor who administers the Radium Ra 223 dichloride will provide you with radiation precautions and instructions
  - You will be given radium Ra 223 dichloride on Day 1 of Cycles 2-7
  - The radium Ra 223 dichloride injection lasts 1-minute and it will be given straight into a vein
  - Once the injection is finished, you can leave the office and go about your daily activities
  - If you experience severe side effects, your dose of radium Ra 223 dichloride may be delayed or discontinued.

- **ADT**
    - You will continue to receive your standard of care ADT (leuprolide or goserelin or degarelix or relugolix)
    - Your ADT will last for 36 weeks total (about 9 months).
    - If you experience severe side effects, your dose of ADT may be delayed or discontinued.
- **Clinical Visits** which will involve the following**:**
    - You will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.
    - A physical exam
    - **Vital Signs:** Weight, heart rate, blood pressure, breathing rate, and temperature.
    - **Performance status evaluation**: To evaluate how you are able to perform your daily usual activities.
- **Tumor assessment:** We will assess your tumor by one or more of the following standard assessment tools: CT scan, MRI or PET scans.
- **Blood tests**
  Blood will be drawn from a vein in your arm for the following tests:
    - **Organ function tests**: To check your blood counts and kidney and liver functions (about 2-3 teaspoons of blood will be drawn at each time)
    - **To check your disease**: To test your PSA and testosterone levels (about 2 teaspoons of blood will be drawn at each time)
    - **Research tests**: To looks at the effects of radiation on immune system biomarkers we will draw about 4 teaspoons of blood at the following timepoints:
        - Before SBRT (Cycle 1)
        - After SBRT (Cycle 2)
        - After you get 36 weeks of ADT
- **Other drugs:** While you are receiving study treatment, you will be taking a bone health agent such as a bisphosphonate or RANKL inhibitor. You should not take other medications, including over-the counter-medicines, herbal medications, without first discussing them with the study doctor. The reason you should not take other medications is they may interact with your study treatment.

Research Study Calendar:

Protocol Activities	Screening	Treatment			End of treatment	Follow-up Every 3 months
		Cycle 1 Day 1	Cycle 2 Day 1	Cycle 3-7 Day 1		
Medical History	X					
Physical Exam and Vital Signs	X	X	X	X	X	X
Performance status	X	X	X	X	X	X
Blood tests	X	X	X	X	X	X
Blood tests to check your disease	X	X	X	X	X	X
Rsearch blood		X	X		X	
Research tissue (if applicable)	X					
Tumor assessment	X				X	X
ADT: Leuprolide **OR** goserelin **OR** degarelix **OR** relugolix	For 36 weeks total					
SBRT		X				
Infusion of radium Ra 223 dichloride			Day 1 of each cycle			

While on this study you will also receive a bisphosphonate or RANKL inhibitor bone health agent at the dose and schedule consistent with the treatment of bone metastases or prevention of osteoporosis. This will continue until your testosterone reaches normal levels or when your PI decides it is safe.

Planned Follow-up:
After you complete study treatment you will be followed:

- **Disease follow-up** *(only if your disease is stable)*: You will be asked to visit your doctor every 3 months to check on your disease status.

- **Follow-up for survival**(Only *if your disease worsens or ended disease follow-up*)**:**We would like to keep track of your medical condition. We would like to do this by calling you on the telephone once a year to see how you are doing or by reviewing your medical records. Keeping in touch with you and checking your condition once a year helps us look at the long-term effects of the research study.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will receive study treatment for about 8 months and you will be in follow-up for about 5 years. Your participation in this research study is expected to last about 6 years.

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different

cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away as noted below. Some may be life-threatening or fatal and are noted below as noted below.

Possible risks and discomforts you could experience during this study include:

Risks associated with Radium Ra 223 dichloride:

COMMON, SOME MAY BE SERIOUS **In 100 people receiving Radium Ra 223 dichloride, more than 10 and up to 100 may have:**
• Nausea • Diarrhea • Vomiting • Swelling of the arms or legs (peripheral edema) • Low blood cell counts

RARE, AND SERIOUS **In 100 people receiving Radium Ra 223 dichloride, 3 or fewer may have:**
• Bone marrow failure (possible fatigue, increased risk of bleeding, and/or increased risk of infection)* • Kidney failure* • Infusion reaction (possible chills and/or hives) • The study drug may cause you to develop another type of cancer.

* This may be life threatening.

You should:

- Make sure you that you keep your study appointments
- Tell your study doctor about any symptoms or signs of low blood cell counts,
- Report symptoms or signs of shortness of breath, tiredness, bleeding (such as bruising), or infection (such as fever)
- Stay well hydrated and report any signs of dehydration (such as dry mouth and increased thirst), or urinary or kidney problems (such as burning when urinating)

Bathroom hygiene is important. Your body removes radioactivity mostly through feces and urine. So, while you are being treated with Radium Ra 223 dichloride—until at least 1 week after the last infusion—you should:

- Wash your hands well every time you go to the bathroom
- Flush the toilet several times after each use
- Make sure that if bodily waste is spilled, it is removed completely and quickly. If bodily waste gets on clothing, wash it right away by itself. Afterward, you should wash your hands very well. Anyone who helps you should wash their hands well, too
- Wear one-use gloves or gowns any time you clean up bodily waste. Dispose of gloves and gowns as directed by your healthcare provider
- Keep your bathroom area clean

Risks for HIV Positive Patients:

We do not know if treatment with radium Ra 223 dichloride is safe for Human Immunodeficiency Virus (HIV) positive patients. If you have HIV you may be at increased risk of infection because radium Ra 223 dichloride can lower your white blood cells. White blood cells make up your immune system and help fight infections. It is important that you keep your study appointments so that we can keep track your white blood cell counts. If your white blood cell counts drop, your treatment with radium Ra 223 dichloride may be interrupted or stopped permanently.

We do not know if treatment with radium Ra 223 dichloride would affect the natural course of your underlying immune deficiency.

Reproductive Risks:

We do not know whether the radium Ra 223 dichloride might hurt an unborn child. Let your doctor know immediately if you find out that you are going to be the father of a child.

If you are sexually active and capable of bearing or fathering a child, both you and your partner must agree to use medically effective forms of birth control while you are on this study.

You must use birth control while on this study or practice complete abstinence while you are being given study treatment and at least 6 months after you discontinue study treatment.

Acceptable medically effective forms of birth control are:

- Abstinence,
- Surgical sterilization (tubal ligation or hysterectomy for women, or vasectomy for men),
- Double-barrier methods (i.e. condoms, diaphragm, cervical cap, or sponge used with spermicidal gel or foam),
- Intrauterine device (IUD) (i.e. Progestin, Copper),
- Hormonal Contraceptives (Birth control patches, implants, pills, rings, or injections)

Possible Risks Associated with SBRT Radiation Therapy

The tables below show the most common and the most serious side effects of radiation that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, more than 20 and up to 100 may have one or more of the following:
• Reddening, tanning, or peeling of the skin • Mild pain • Hair loss • Tiredness • Diarrhea, nausea, decreased appetite • Anemia, which may require transfusion • Infection, especially when white blood cell count is low, which may require additional medication • Frequent urination • Fatigue

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, from 4 to 20 may have one or more of the following:
• Thickening and numbness of the skin • Sores or ulcers on the skin or near the cancer location • Permanent hair loss • Bleeding from the skin • Sores in mouth which may cause difficulty swallowing • Cough • Shortness of breath • Pain in your ribs • Belly pain • Sexual dysfunction which may include the inability to develop or maintain a penile erection during sexual intercourse and/or pain during intercourse •

You may also experience the additional risks specific to the area of the body where you receive the radiation.

Possible Side Effects of Radiation Therapy to the Lung, Neck or Chest

COMMON, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the lung, neck or chest, more than 20 and up to 100 may have one or more of the following:

- A common effect of this treatment in previous studies was scaring of the lung tissue that can lead to cough, thick mucous (phlegm), difficulty breathing, and other symptoms of pneumonia. There can also be permanent scaring of a portion of the lung or ribs. Efforts will be made to reduce this risk and limit its effect. However, it is possible you will have shortness of breath at rest or during exercise, may need to receive oxygen, and/or may have chest wall pain. A few patients may need oxygen therapy permanently. In rare cases this can be life threatening
- Tiredness, which is temporary
- The skin in the treatment area may become reddened and/or dry, and chest hair in the treatment area may fall out and may not grow back

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the lung, neck or chest, from 4 to 20 may have one or more of the following:

- Cough
- Difficulty breathing
- Chest radiotherapy can cause changes in normal lungs. These changes can be as unimportant as small amounts of "scarring" seen on x-rays that does not cause symptoms. Sometimes chest radiotherapy can cause lung damage that leads to symptoms such as chest pain, shortness of breath, cough, or fever. Rarely, these symptoms can be severe or life threatening. Treatment for this lung damage involves pain medicines, anti-inflammatory medicines (corticosteroids), and rarely, oxygen therapy, which may be permanent. You should tell your doctors immediately if you have any of these symptoms
- Irritation of the esophagus, which may result in heartburn or pain on swallowing
- Fever
- Chest wall discomfort or pain
- Rib fracture, which may cause pain
- Bone fracture

RARE, AND SERIOUS

In 100 people receiving radiation therapy to the lung, neck or chest, 3 or fewer may have one or more of the following:

- Irritation of the lining around the heart, which can cause chest pain, shortness of breath, and irregular or rapid heartbeat; rarely, this can require surgery to correct.
- Irritation and/or damage to the muscle of the heart; rarely, this can cause a heart attack, heart failure, and/or death
- Irritation and/or damage to the spinal cord (the major nerve within the spine), which can lead to weakness, tingling or numbness of the lower body and legs; very rarely, this can lead to inability to move or control the lower half of the body.
- Damage or scarring of nerves in the chest, which may result in a hoarse voice or a tingling “pins and needles” sensation, or pain in the chest and rib area, depending on the nerve affected
- Damage or scarring of nerves at the top of the lungs, which may result in a tingling “pins and needles” sensation or pain or weakness of the muscles of the arm and hand, since these nerves provide sensation and muscle control for the arm and hand
- Narrowing of the esophagus (tube to the stomach), which can result in swallowing difficulty
- Thinning of the wall of the esophagus; rarely, this can cause a hole in the esophagus and/or a hole in your lung which could result in difficulty with eating and breathing
- Irritation of the large blood vessels surrounding the heart; rarely, this can cause bleeding (coughing up blood) and/or death
- Irritation of the voice box which can cause hoarseness and/or pain
- Damage to the blood vessels in the neck

Possible Side Effects of Radiation Therapy to the Liver or Abdomen (Belly)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the liver or abdomen (belly), more than 20 and up to 100 may have one or more of the following:

- Fatigue (which generally goes away after the radiation therapy is completed)
- Skin irritation, redness, sunburn or ulcer in the skin of upper abdomen and chest wall, itchiness, discomfort
- Temporary changes in blood work (decrease in blood counts, increase in liver enzymes), without symptoms

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the liver or abdomen (belly), from 4 to 20 may have one or more of the following:

- Nausea, vomiting (during therapy) (more common if stomach or gastrointestinal track receives radiation)
- Gastric, esophagus, small bowel or large bowel irritation/ulceration, bleeding, obstruction, connection with other tissues, or changes in bowel habits (may require medications or surgery)
- Chest wall pain requiring medications, rib fracture
- Temporary bleeding due to low platelet count

RARE, AND SERIOUS

In 100 people receiving radiation therapy to the liver or abdomen (belly), 3 or fewer may have one or more of the following:

- Liver toxicity, classic radiation toxicity that can cause swelling of your abdomen (belly) and pain in the liver and spleen (right and left upper abdomen) within 3 months of completing therapy.
- Non-typical liver toxicity includes elevation of liver enzymes and/or any decline in liver function within 12 weeks from start of therapy. This can cause similar symptoms to those above, plus fatigue, confusion, itchiness and/or change in skin color. This can lead to liver toxicity that can lead to death. There is an increased risk of liver toxicity in patients with large tumors and in patients with pre-existing liver disease
- Permanent low platelets which may lead to bleeding
- Kidney injury which may lead to a need for medication

Possible Side Effects of Radiation Therapy to the Spine

COMMON, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the spine, more than 20 and up to 100 may have one or more of the following:

- Inflammation of the lining of the mouth and esophagus (passageway from mouth to stomach), one or more of the following which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur (your body does not have as much water and fluids as it should)
- Inflammation of the back of the throat, which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur
- Inflammation of the part of the airway that includes the vocal cords, which can result in hoarseness or loss of voice

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the spine, from 4 to 20 may have one or more of the following:
• Inflammation of the lungs due to radiation treatment, which can result in cough, phlegm (thick mucous), difficulty breathing, and/or pneumonia • Fracture or compression of the treated bones of the spine, which can result in pain and which may need nonsurgical or surgical treatment • Discomfort or anxiety due to 60-90 minutes lying in a specific position, possibly within a frame device, for the planning session and 60 minutes for treatment; your doctor may give you medicine to decrease the discomfort and/or anxiety

RARE, AND SERIOUS In In 100 people receiving radiation therapy to the spine, 3 or fewer may have one or more of the following:
• Esophageal fistula (abnormal opening in the passageway from mouth to belly) • Scarring of the small or large bowel, which can result in a blockage in the bowel that would require treatment • Temporary or permanent damage to the spinal cord, which can result in: • Skin sensations, such as burning, prickling, itching, or tingling • Muscle weakness causing inability to walk (paralysis)

Possible Side Effects of Radiation Therapy to the Bone

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the bone, more than 20 and up to 100 may have:
• Skin irritation

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the bone, from 4 to 20 may have:
• Pain • Fracture

RARE, AND SERIOUS In 100 people receiving radiation therapy to the bone, 3 or fewer may have one or more of the following:
• Weakening of your bone(s) potentially resulting in a fracture • Hair loss • Reddening, rash, or peeling of the skin

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not father a baby while in this study. Radiation used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

Risks Associated with Blood Draw

Risks of blood draws include mild pain or discomfort, bruising and swelling around the puncture site, dizziness or fainting, or infection (rare).

Other Risks

Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

There is a risk of bone fracture in patients receiving a combination of Ra-223, abiraterone, and prednisone. However, in this study, you will not be receiving abiraterone or prednisone, and we are investigating in this study if the combination of Ra-223, ADT, and SBRT has more risk for bone fracture.

Incidental Findings

It is possible the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

Risks associated with Breach of Confidentiality

There is a small risk that people who are not connected with this study will learn your identity or your personal information.

Risks from Research Studies

The research samples will be stored with a coded number that does not contain personal identifying information. These research tests are being done in a research lab, rather than the clinical lab. The results of the tests will not become part of the medical record. Therefore, the risks of these research studies to you are small.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

Any information learned from this study in which you might be identified will be confidential and disclosed only with your permission. Every effort will be made to keep any information collected about you confidential. However, it is impossible to guarantee that information about you will not be mistakenly released. If, despite our best efforts, identifying information about you is released, it could negatively impact you or your family members. This risk is small.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- City of Hope, the sponsor of this study
- Bayer, the drug company that is providing radium Ra 223 dichloride and funding this study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- Regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study as required by law.

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.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCHSTUDY?

There is no guarantee that you will receive any benefits from this study. The possible benefit of the study drugs for your diagnosis is not known. If you decide to participate in this study, your health will be monitored very closely. By being in this study, you will give doctors more information about how

well the study drugs works. It may help doctors understand your condition better and may help future patients with this medical condition.

H. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options that may include the following:

- Have the usual approach for your cancer, which is to take ADT alone, ADT with docetaxel (chemotherapy) or abiraterone (another hormone based treatment) or combine ADT with another type of radiation therapy.
- Take part in another research study, if one is available.
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

You will not be paid for being in this study.

Possible Commercial Products

We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries.

J. WHAT ARE THE COSTS?

Radium Ra 223 dichloride will be provided free of charge by Bayer. It is possible that the study drug may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

Standard of care procedures provided to you will be the responsibility of you and/or your insurance carrier. You will be responsible for all copayments, deductibles, and other costs of treatment and diagnostic procedures as set forth by your insurance carrier. You and/or your insurance carrier will be billed for the costs of treatment and diagnostic procedures in the same way as if you were not in a research study.

However, neither you nor your insurance carrier will be responsible for the research procedures related to this study.

Financial counselors are available Monday through Friday, 8:00 a.m. to 5:00 p.m. For additional questions, please call City of Hope Financial Support Services: 626-256-HOPE (4673), extension: 80258.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:
www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the study doctor as soon as possible.

It is a City of Hope policy that in the event of physical injury to a research participant, resulting from research procedures, appropriate medical treatment will be available at City of Hope to the injured research participant. No funds have been set aside to compensate you in the event of injury.

There are no plans for any of the sponsors of this study to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments.

M. CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons:

- You do not follow the study doctor's instructions
- At the discretion of the study doctor or the sponsor
- Your disease gets worse or
- The sponsor closes the study.

If this happens, the study doctor will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Savita Dandapani or a colleague, Dr. _____, responsible for your care or treatment, has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Savita Dandapani at (626) 256-HOPE (4673) ext. 82247 or Dr. _____ at (626) 256-HOPE (4673) ext. _____.

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

O. OPTIONAL TUMOR TISSUE RESEARCH ANALYSIS

As mentioned above, if available, some your tumor tissue will be sent for clinical testing as part of your standard of care. We would like to perform research analysis on the clinical results from these tests to find other prostate cancer biomarkers. You do not have to participate in optional research analysis if you do not want to. You can still be in the main study if you do not want us to perform research analysis on your clinical tests. At the end of this section, there is a place to record your decision about taking part in optional tumor tissue research analysis.

You may not benefit from optional tumor tissue research analysis. This research may help other cancer patients in the future.

You will not be billed for optional tumor tissue research analysis.

Neither you nor your study doctor will be notified of the research results or given reports or other information about any research that is done using your samples.

If you have any questions, please talk to your study doctor or nurse, or call our research review board at the IRB's phone number included in this consent.

Please circle your answer: I agree to have optional tumor tissue research analysis be performed on my clinical tests:

YES NO

This is the end of the optional tumor tissue research analysis.

P. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

_____	_____	_____
Research Participant's/Legally Authorized Representative's Signature (date and time must be in research participant's/LAR's handwriting)	Date	Time

_____
Print Research Participant's Name/Legally Authorized Representative's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____	_____	_____
Signature of Individual Obtaining Consent	Date	Time

_____
Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name

COH# 17085: A Phase 2 Trial of Radium Ra 223 Dichloride in Combination with Androgen Deprivation Therapy and Stereotactic Body Radiation Therapy for Patients with Oligometastatic Castration-Sensitive Prostate Cancer

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

I. **Purpose of this Authorization**: The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the *Study Consent Form*.

II. **The Information About You that is Covered By this Authorization**: PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI**: Your PHI will be used and shared with others for the purpose of doing this research as described in the *Study Consent Form*. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of Hope physicians and the health care team; and the Health Information Management Services Department (i.e., Medical Records Department). This also

includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board ("IRB"), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections ("OHRP"), and with any person or agency as required by law. In addition, certain other regulatory agencies, including, the Food and Drug Administration ("FDA"); the National Cancer Institute ("NCI") will have access to your PHI.

Use and disclosure of your PHI may also continue for as long as Bayer(the company that provides radium Ra 223 dichloride and funding this study) needs to maintain the PHI for purposes of obtaining approval of radium Ra 223 dichloride from the FDA or for other FDA reporting.

Your information will also be shared, with City of Hope**,** the "Research Sponsor" and Bayer, the drug company, its employees, agents or contractors who are involved in the administration of the Study.

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is included in this authorization. City of Hope's Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

IV. **Expiration of this Authorization**: This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.

V. **Further Sharing of Your PHI**: Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside our control may not be governed by federal or state privacy laws and it is possible

that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

VI. **<u>Your Rights Under this Authorization</u>**: You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, *Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research*. Fill this form out and return it as the form instructs. Your cancellation begins when the Health Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

VII. **<u>Signing this Authorization is Your Choice</u>:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

_____ _____ _____

Research Participant's Legally Authorized Representative's Signature
(date and time must be in research participant's/LAR's handwriting)

Date Time

_____

Print Research Participant's Name/Legally Authorized Representative's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

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_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name