

BC Cancer Protocol Summary for Therapy for Metastatic Castration Resistant Prostate Cancer Using Radium-223

Protocol Code

GUPRAD

Tumour Group

Genitourinary

Contact Physician

Dr. Scott Tyldesley

ELIGIBILITY:

- Patients with castration resistant prostate cancer with symptomatic bone metastases.
- Patients have no known liver, lung or brain metastases and symptomatic or bulky soft tissue metastases (lymph nodes, local disease etc)
- Patients must have a good performance status (ECOG 0-2).
- Patients have recently seen or been discussed with a medical oncologist regarding other systemic therapy options.
- Patients have already received, are not eligible for, decline, or have no access to, other life-prolonging treatment options (e.g. docetaxel, abiraterone, enzalutamide).

EXCLUSIONS:

- Active inflammatory bowel disease or significant fecal incontinence.
- Creatinine clearance less than 30 mL/min.
- Chemotherapy, hemibody radiotherapy, bone targeted radioisotope or other myelosuppressive therapy within last month.
- For initial dose:
 - Hemoglobin less than 100 g/L
 - Platelets less than $100 \times 10^9/L$
 - ANC less than $1.5 \times 10^9/L$
- For subsequent doses (after initial dose):
 - Platelets less than $50 \times 10^9/L$
 - ANC less than $1.0 \times 10^9/L$
- Untreated cord compression or fracture requiring orthopedic stabilization.
- Patient currently receiving Abiraterone (Radium- 223 should not be used concurrently with Abiraterone).

TESTS:

- Baseline: CBC and differential, platelets, serum creatinine, sodium, albumin, bilirubin, alkaline phosphatase, ALT, PSA, TTT
- Before each treatment: CBC and differential, platelets, serum creatinine, bilirubin, alkaline phosphatase, ALT, PSA

PREMEDICATIONS: none.

TREATMENT:

Therapy	Dose	BC Cancer Administration Guideline
radium-223	55 kBq/kg IV bolus	infuse slowly over 1 minute

Repeat every 4 weeks x 6 cycles.

DOSE MODIFICATIONS:

There are no known dose modifications suggested for age, hematologic parameters, liver function, or renal function. Doses should be delayed until counts recover. If counts have not recovered to adequate levels:

- Hematologic:** Delay initial dose if hemoglobin less than 100 g/L (exceptions made for individual cases between 90-100), Platelets less than $100 \times 10^9/L$ or ANC is less than $1.5 \times 10^9/L$. Delay subsequent doses (after initial dose) if Platelets less than $50 \times 10^9/L$ or ANC is less than $1.0 \times 10^9/L$. If no recovery in these values within 6 weeks after the last administration of radium-223, despite receiving standard of care, further treatment with radium-223 should be discontinued.
- Hepatic:** Safety and efficacy of radium-223 have not been studied in patients with hepatic impairment. Based on subgroup analyses for the randomized trial, dose adjustment is not needed in patients with mild hepatic impairment. No dose adjustments can be recommended for patients with moderate or severe hepatic impairment due to lack of clinical data. However, since radium-223 is neither metabolized by the liver nor eliminated via the bile, hepatic impairment is not expected to affect its pharmacokinetics.
- Renal:** No dedicated study for radium-223 in patients with renal impairment has been conducted. Based on subgroup analysis in the randomized clinical trial, no dose adjustment should be needed for patients with renal impairment of mild (creatinine clearance 50 to 80 mL/min) or moderate (30 to 50 mL/min) severity. As there are limited data available on patients (N=4) with severe renal impairment (less than 30 mL/min) and no data on end-stage renal disease, no dose adjustment can be recommended for these patients. However, since excretion in urine is minimal and the major route of elimination is via the feces, renal impairment is not expected to affect the pharmacokinetics of radium-223.

PRECAUTIONS:

- Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
- Thrombocytopenia (grade 3-4):** may occur. Monitor patients for signs of bleeding, transfuse as appropriate.
- Anemia:** Anemia may occur in patients receiving radium-223, but there is no increase in the rates of grade 3-4 anemia compared to placebo. However, there are no data on delivery of radium-223 to patients with hemoglobin levels outside of

aforementioned exclusion criteria. Monitor patients for anemia, transfuse as appropriate and delay dosing if required.

4. **Extravasation:** Radium-223 should be given as a slow injection and the patient should be observed for signs of extravasation. If extravasation occurs, the infusion should be stopped. Events of extravasation should be handled on an individual basis and treatment could range from observation to surgical consult for excision and drainage.
5. **Diarrhea:** The patient should be monitored to ensure that dehydration does not occur.
6. **Vomiting:** The patient should be monitored to ensure that dehydration does not occur.
7. **Radiation safety:** Radium-223 is an alpha emitter, with a physical half life of 11 days and effective half life of 3.5 days. No meaningful dose of radiation is emitted outside of the body. Blood, urine or fecal soiling can be of risk to others if ingested. Standard body fluid precautions should be used in event of bleeding, incontinence of soiling. See patient information handouts for further details. Contact BC Cancer radiation safety officer or nuclear medicine facility in regards to specific questions.

Call Dr. Scott Tyldesley or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Bayer Inc. XOFIGO® product monograph. Mississauga, Ontario; 18 April 2016
2. Malone S, et al. Radium-223 chloride (Ra223) improves overall survival. *Radiother Oncol* 2012; 104(Suppl2):S71.
3. Nilsson S, et al. Bone-targeted radium-223 in symptomatic, hormone refractory prostate cancer: a randomised, multicentre, placebo-controlled phase II study. *Lancet Oncol* 2007; 8:587-94.
4. Parker C, et al. Alpha emitter radium 223 and survival in metastatic prostate cancer. *N Engl J Med* 2013;369; 213-23.
5. Parker C, et al. Updated survival, quality of life and safety data of radium 223 chloride in patients with castration-resistant prostate cancer with bone metastases from the phase 3 double blind randomized, multinational study (ALSYMPCA). ESMO 2012 (abstr 898PD).