A population-based study of the use of radium 223 in metastatic castration-resistant prostate cancer: Factors associated with treatment completion

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Abstract

Introduction: Radium 223 (Ra223) given for six cycles has proven efficacy in clinical trials, but its population-level generalizability has not been well-described. The objectives of this study were to describe population-based Ra223 use in the abiraterone and enzalutamide era and identify factors associated with completion.
Methods: All Ra223 patients at the British Columbia Cancer Agency between September 2013 and February 2016 were identified. Patients who completed <5 vs. ≥5 cycles were compared on patient characteristics, lines of prior therapy, prostate-specific antigen (PSA) and alkaline phosphatase (ALP) decline >30% from baseline (R30%), and survival, to identify factors associated with therapy completion.
Results: Ninety-one patients were identified; 48 (52.7%) completed ≥5 cycles. Median overall survival (mOS) was 10.7 months, PSA and ALP R30% were 21% and 52%, respectively. Completion of <5 cycles was associated with higher baseline ALP (p=0.05) and lower baseline hemoglobin (Hb) levels (p=0.03). Patients in the ≥5 cycles group had longer mOS than those in the <5 cycles group (16.2 vs. 5.9 months; p<0.0001), as well as higher PSA R30% (33.3% vs. 7.0%; p=0.002) and ALP R30% (66.7% vs. 34.9%; p=0.03). Patients with ALP ≥220 and Hb ≤118 had 3.85 times the odds of not completing ≥5 cycles vs. ALP <220 and Hb >118.
Conclusions: Compared to clinical trials, patients in a population-based setting had more lines of therapy and shorter survival. Lower ALP and higher hemoglobin were associated with completion of ≥5 cycles, longer mOS, and greater incidence of PSA and ALP response.

Introduction

The options for therapy in metastatic castration-resistant prostate cancer (mCRPC) have greatly expanded over the past decade. Palliative radiotherapy to painful sites of bone metastases continues to be commonly used to relieve symptoms at progression of mCRPC. Targeted agents (e.g., abiraterone and enzalutamide)[1-4] and chemotherapeutics (e.g., docetaxel and cabazitaxel)[5,6] are now mainstay options. Radiopharmaceuticals have also emerged as another viable option in this patient population.

Radioisotopes, such as the beta-emitter strontium 89 (Sr89), have been used in the past to decrease the rate of progression of new site of pain either on its own, or in combination with external beam radiotherapy. Radium 223 chloride (Ra223) is a newer radiopharmaceutical agent given as a monthly intravenous injection for six cycles. It is an alpha-emitting radioisotope that mimics calcium, and is taken up into newly formed bone. Alpha particles induce double-stranded DNA breaks in adjacent cells, with a very short penetration (<10 cell diameters). As a result, Ra223 has the potential to cause a highly localized tumour cell killing immediately adjacent to areas of new bone formation, with very minimal marrow toxicity.

The definitive phase 3 trial (ALSYMPCA)[7] evaluating Ra223 or placebo in 921 mCRPC patients demonstrated an overall survival (OS) benefit of 3.5 months, with a median overall survival (mOS) of 14.9 months for Ra223 vs. 11.3 months for placebo (hazard ratio [HR] 0.70; 95% confidence interval [CI] 0.58–0.83; p<0.001). Assessments of all main secondary efficacy endpoints also showed a benefit of Ra233 as compared to placebo. Prostate-specific antigen (PSA) response rate (defined as a >30% decline from baseline) was 21% and alkaline phosphatase (ALP) response rate (defined as a decline >30%) was 52%. In addition, Ra223 was associated with low myelosuppression rates and fewer adverse events. Toxicity was minimal, as overall and serious adverse events were lower in the Ra223 group compared to the placebo group. Grade 3–4 thrombocytopenia, a particular concern with other radioisotopes, was minimal (4% with Ra223 vs. 2% with placebo), although diarrhea was more common with Ra223 (22% vs. 13%), but no difference

was seen in Grade 3 or 4 toxicity. In the ALSYMPCA trial, 72.8% of patients completed all six injections.[7]

In September 2013, Ra223 was made available for patients in British Columbia through two sequential access programs, and became publically funded in February 2015. Enzalutamide and abiraterone were also publically available during this time of Ra223 introduction, unlike during the time the ALSYMPCA trial accrued patients. We retrospectively sought to: 1) describe the use of Ra223, survival, PSA, and ALP response rate after Ra223 in a population-based setting in a contemporary era when abiraterone and enzalutamide were available; and 2) identify factors associated with successful completion of Ra223.

Methods

Patient selection

Those who had received their first cycle of Ra223 at the British Columbia Cancer Agency (BCCA) between September 2013 (when Ra223 first became available) and February 2016 were included in this analysis. Eligibility for Ra223 in the province was as summarized in the online protocol at *bccancer.bc.ca* based on the ALSYMPCA trial criteria and the product monogram. All approvals for Ra223 prescriptions were centralized through the provincial Compassionate Assess Program, which involved second physician and pharmacy check of eligibility before approval for funding. The BCCA was the sole provider of all Ra223, and all provincial utilization was captured in this analysis.

Data collection and outcomes of interest

Electronic records were retrospectively reviewed and abstracted clinical and laboratory factors were collected at baseline and prior to each Ra223 treatment. The maximum number of cycles of Ra223 completed by each patient was identified. Serum ALP and PSA were collected prior to each cycle, post-therapy completion, and at time of therapy discontinuation. In those patients who discontinued Ra223 prematurely, reasons for doing so were ascertained via progress notes. Progression was defined as deterioration in clinical status, PSA progression deemed by the treating physician to warrant change of therapy, or radiological progression defined according to the modified Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v. 1.1).[8] Although anemia and thrombocytopenia could be due to progression or drug-related effect, discontinuation for these reasons was scored as a drug-related side-effect for purposes of the analysis if disease progression was not otherwise described. The study was approved by the BC Cancer Agency Research Ethics Board.

Study analysis

Overall survival and followup time were calculated using the Kaplan-Meier method. PSA and ALP response rates were calculated as best response from baseline and categorized using two response thresholds: maximum decline in PSA from baseline >30% and >50% from the baseline value separately for both PSA and ALP.

Patient characteristics were described using frequencies and proportions for categorical variables, and with measures of central tendencies for numeric variables. Cases were binarized into those that completed ≥5 cycles of Ra223 vs. those that completed <5 cycles. Abstracted clinical and biochemical factors were compared between these two groups to determine which were associated with completion of therapy. Chi square test or the Fisher's exact test, where appropriate, was used to analyze categorical variables between these two groups. Differences in medians were assessed using the two-sample median t-test.

PSA and ALP response rates were determined for the entire group and for comparison between those patients that completed ≥5 cycles versus those that completed <5 cycles of Ra223. The odds of treatment completion were compared using logistic regression for three baseline ALP and hemoglobin combinations: a) higher-risk patients with high baseline ALP (≥220 IU/L) and low hemoglobin (≤118 g/L); b) lower-risk patients with lower baseline ALP (<220 IU/L) and higher hemoglobin (>118 g/L); and c) intermediate-risk patients with baseline ALP (<220 IU/L) and hemoglobin (≤118) or baseline ALP (≥220 IU/L) and hemoglobin (>118). These cut points were selected a priori based on median values for hemoglobin in our population, and on previous reports of association with cycle completion for ALP.[9,10]

Median OS was ascertained for the entire cohort, and compared between groups completing 5 vs. <5 cycles using log rank test. Patients that were lost to followup were censored with the assumption of non-informative censoring.

Statistical analyses were performed in SAS 9.2 (SAS Institute Inc., Cary, NC, U.S.).

Results

Ninety-one patients were included in this study and their baseline characteristics are described in Table 1. Relative to patients enrolled on the ALSYMPCA trial, the patients treated in this population-based cohort appeared to be older (median of 73.9 years in this cohort vs. 71 years in ALSYMPCA), had worse Eastern Cooperative Oncology Group (ECOG) performance status (i.e., ECOG performance status ≥2 29.7% vs. 13% in ALSYMPCA), and had more lines of therapy for CRPC (including abiraterone, enzalutamide, docetaxel, carbazitaxel, mitoxanthrone, or an experimental therapy). In the present series, the 71% of the patients had two or

Table 1. Baseline characteristics of mCRPC patients receiving Ra223

Baseline clinical characteristics	All patients[a]	<5 cycles[b]	≥5 cycles[c]	P comparing >5 vs. <5 cycles	Patients on ALSYMPCA receiving Ra223[d]
Age, median (range)	73.9 (50.0–94.0)	71.5 (57.0–91.3)	72.5 (50.0–94.0)	0.17	71 (49–90)
Ra223 cycles, median (range)	5 (1–6)	3 (1-4)	6 (5-6)	<0.0001	6
ECOG performance status >2, n (%)	27 (29.7)	16 (37.2)	11 (22.9)	0.14	77 (13)
Patients with >6 bone metastases, n (%)	80 (87.9)	40 (93.0)	40 (83.3)	0.16	511 (84)
Patients with nodal metastases, n (%)	30 (33.0)	14 (32.6)	16 (33.3)	0.94	N/A
Laboratory values					
Hemoglobin, median (range) (g/L)	118 (92–167)	114 (95–167)	120 (92–143)	0.03	122 (85–157)
ALP, median (range) (IU/L)	148 (27–3440)	210 (68–3440)	131.5 (27–713)	0.05	211 (32–6431)
Albumin, median (range) (g/L)	39 (27–99)	38 (27–99)	39 (30–44)	0.19	40 (24–53)
Lactate dehydrogenase, median (range) (IU/L)	296 (68–958)	295 (68–958)	304 (136–567)	0.29	315 (76–2171)
PSA (ug/L), median (range)	112.2 (0.4–2800)	137.28 (0.96–2800)	102.1 (0.4–1662.2)	0.76	146 (3.8–6026)
Prior systemic treatments for CRPC, median (range)	2 (0–5)	2 (0–5)	2 (0–5)	0.21	NR
Median number of systemic treatments (range)	2 (0–5)	2 (0–5)	2 (0–5)	0.21	NR
Previous docetaxel, n (%)	47 (57.7)	25 (58.1)	22 (45.8)	0.24	352 (57.3)
Previous abiraterone, n (%)	60 (65.9)	31 (72.1)	29 (60.4)	0.24	0
Previous enzalutamide, n (%)	77 (84.6)	36 (83.7)	41 (85.4)	0.82	0
Previous cabazitaxel, n (%)	4 (4.4)	1 (2.3)	3 (6.3)	0.62	NR
Previous clinical trial, n (%)	23(25.3)	12 (27.9)	11 (22.9)	0.58	N/A

[a]All patients: 91, patients with albumin level recorded: 46; [b]all patients: 43, patients with albumin level recorded: 19; [c]all patients: 48, patients with albumin level recorded: 27; [d]patients on ALSYMPCA receiving Ra223: 614. ALP: alkaline phosphatase; ECOG: Eastern Cooperative Oncology Group; mCRPC: metastatic castration-resistant prostate cancer; PSA:prostate-specific antigen.

more, and some (3%) up to five, prior lines of such therapy; whereas in the ALSYMPCA study, 57% of patients had prior docetaxel and none had prior abiraterone or enzalutamide.

Median followup time was 10.3 months and all cases started their first cycle of Ra223 at least six months before analysis. The mOS was 10.7 months (95% CI 9.2–12.7) (Fig. 1). PSA response rate for a >30% decline from baseline was 21%, and PSA response rate for a >50% decline from baseline was 11%. ALP response rate for >30% decline was 52%, and ALP response >50% was 29%.

Patients completing ≥5 cycles had longer mOS than those completing <5 cycles (16.2 vs. 5.9 months; p<0.0001) (Fig. 2). Notably, only 48 patients (52.7%) completed ≥5 cycles of Ra223 in this study (72.8% in ALSYMPCA).

Patients in the group that did not complete five cycles of Ra223 had a lower baseline hemoglobin (114 vs. 120;

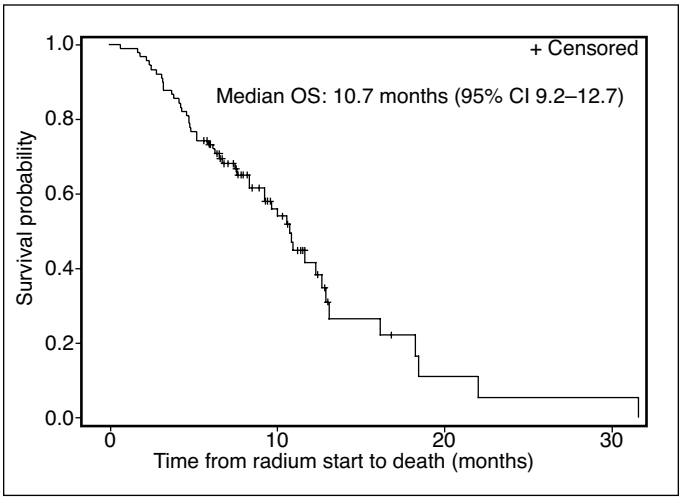

Fig. 1. Median overall survival (OS) for all patients on Ra223. CI: confidence interval.

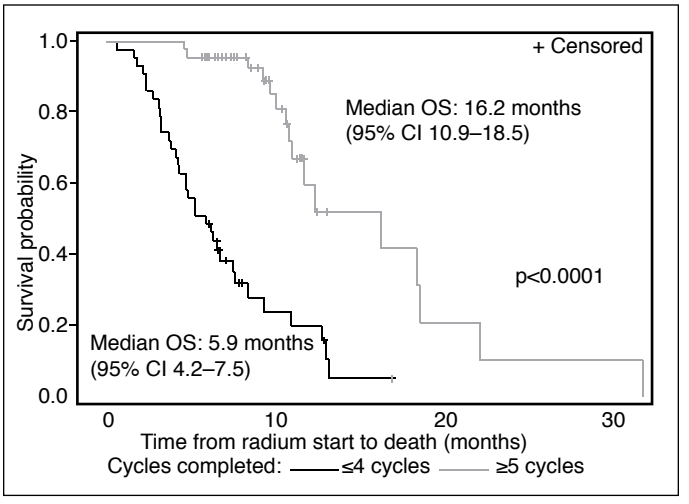

Fig. 2. Median overall survival (OS) compared between patients completing >5 vs. <5 cycles of Ra223. CI: confidence interval.

p=0.03) and a higher baseline ALP (p=0.05) level (Table 1). Logistic regression results indicate that patients in the higher-risk baseline ALP and hemoglobin group (high baseline ALP [≥220 IU/L] and low hemoglobin [≤118 g/L]) had significantly higher odds of not completing therapy compared to patients in the lower-risk group (lower baseline ALP [<220 IU/L] and higher hemoglobin [>118 g/L]) and intermediate-risk group (baseline ALP [<220 IU/L] and hemoglobin [≤118] or baseline ALP [≥220 IU/L] and hemoglobin [>118]) (OR 3.85; p=0.02 and OR 3.82; p=0.02, respectively). There was no difference in the proportion of cases with an ECOG performance status greater than 2, an elevated lactate dehydrogenase (LDH), or extent of metastatic disease. The median number of previous systemic treatments was not significantly different between those completing ≥5 cycles (median 2, range 0–5) vs. those completing <5 cycles (median 2, range 0–5) (p=0.21).

Table 2 describes PSA and ALP response rates for patients completing ≥5 vs. <5 cycles. PSA response rate >30% decline was greater in the group completing ≥5 cycles (33.3% vs. 7.0%; p=0.002). PSA response rate >50% decline was also higher in this group (16.7% vs. 4.7%; p=0.10), although not statistically significant (Fig. 3).

A lower proportion of patients in the group completing ≥5 cycles had an ALP response >30% (66.7% vs. 34.9%; p=0.03). This held true for ALP response rate >50% as well (37.5% vs. 18.6%; p=0.046) (Fig. 4).

The reasons for premature discontinuation are outlined in Table 3. Of note, 27.9% of patients prematurely discontinued Ra223 potentially due to drug-related side effects and 57.4% of patients prematurely discontinuing due to disease progression. The side effect profile was consistent with that seen in the ALSYMPCA trial, particularly since determination of whether the discontinuations in the current study related to low platelet and hemoglobin levels were due to disease progression or true drug-related side effect was difficult to determine.

Discussion

This retrospective study was performed to determine whether the findings in the ALSYMPCA trial were generalizable to a population level in the contemporary era of having abiraterone and enzalutamide available, and to identify factors associated with completion of therapy. Such data could help inform practitioners about the probability of treatment completion and to identify which patients may need to be monitored more closely.

Compared to the ALSYMPCA study, patients in the present series were more heavily pre-treated, particularly with abiraterone and or enzalutamide, had a shorter median survival (11.7 months compared to 14.9 months), but had similar PSA (R30% of 21% compared to 16%) and ALP (R30% 52% compared to 47%) response rates.

The results of this study demonstrate that therapy completion of five or more cycles was associated with a longer mOS and more frequent PSA and ALP responses. Patients that did not complete five or more cycles of Ra223 generally had higher ALP and lower hemoglobin levels at baseline. Elevated alkaline phosphatase and low hemoglobin levels are recognized poor prognostic factors for survival.[7,10] It might be expected that poor prognosis patients would be less likely to respond or complete therapy; however other poor prognostic factors, like LDH and performance status, were not different between the two patient groups.

Patients in the higher-risk risk baseline ALP and hemoglobin group, who had a combination of an ALP ≥220 (the usual upper limit of normal) and a hemoglobin of ≤118, had significantly 3.85 (3.82) times higher odds of not completing ≥5 cycles, compared to patients in the lower (intermediate) group. Thus, the higher ALP and lower hemoglobin may be specifically reflecting a higher burden of bone metastases and propensity to bone marrow toxicity, as almost 30% of patients discontinued because of toxic effects. Marrow toxicity in particular is often hard to clearly delineate as disease progression or drug effect, as both can lead to decreasing blood counts, but in either case, may make further doses ill-advised. Of the 12 patients that were scored as having stopped radium due to marrow toxicity, nine (75%) had coincident rise in PSA at the time of discontinuation, suggesting the underlying cause of decline in hematological

Table 2. PSA and ALP response rates

Response rates	All patients (n=91)	Completion of <5 Ra223 cycles (n=43)	Completion of >5 Ra223 cycles (n=48)	p
PSA response >30%, n (%)	19 (20.9)	3 (7.0)	16 (33.3)	0.002
PSA response >50%, n (%)	10 (11.0)	2 (4.7)	8 (16.7)	0.10
ALP response >30%, n (%)	47 (51.7)	15 (34.9)	32 (66.7)	0.03
ALP response >50%, n (%)	26 (28.6)	8 (18.6)	18 (37.5)	0.046

ALP: alkaline phosphatase; PSA: prostate-specific antigen.

Table 3. Reasons for premature discontinuation of Ra223 (n=54)

Reasons for Ra223 discontinuation	n (%)
Gastrointestinal side effects	3 (5.6)
Anemia	9 (16.7)
Thrombocytopenia	3 (5.6)
Disease progression*	31 (57.4)
Other**	8 (14.8)

*Disease progression included clinical biochemical, or radiological progression. Clinical progression included skeletal related events (i.e., pathological fractures, spinal cord compression, necessity for radiation therapy or surgery to the bone), and bone pain, or fatigue deemed due to cancer progression. **Other included the following: exacerbation of osteomyelitis, cardiac-related death, switch to clinical trial, hypercalcemia, renal function decline, exacerbation of multiple prior comorbidities, worsening of known aortic stenosis, and lack of Ra223.

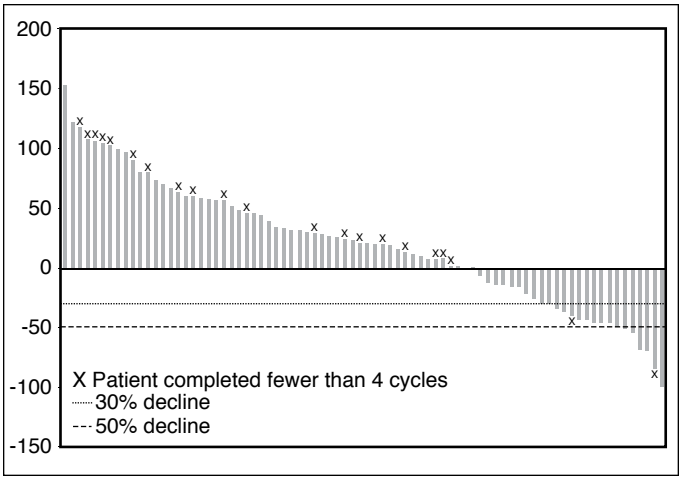

Fig. 3. Waterfall plot of maximum prostate-specific antigen (PSA) decline up to Cycle 4.

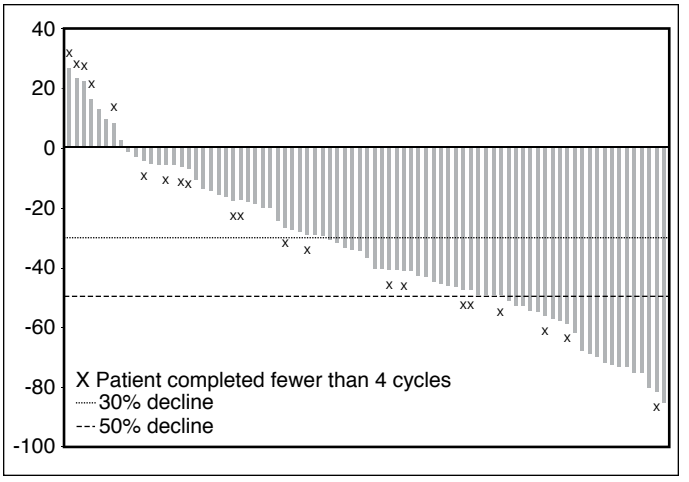

Fig. 4. Waterfall plot of maximum alkaline phosphatase (ALP) decline up to Cycle 4.

function may have been related to disease progression rather than drug toxicity.

Other studies have had similar findings to ours. Recent work by McKay and colleagues[9] has suggested that receipt of less than five cycles of Ra223 was also associated with poor prognosis features and baseline marrow compromise: baseline hemoglobin levels ≥ lower limit of normal (LLN), prior sipuleucel-T therapy, and ANC ≥ LLN in multivariable analysis. Saad and colleagues[10] investigated efficacy data on mCRPC patients receiving Ra223 in an international, early access, open-label, single-arm phase 3b trial. They determined that mOS was longer for patients with a baseline hemoglobin level ≥100 mg/L, baseline ALP levels < upper limit of normal, ECOG status of 0, and for those with no reported baseline pain. Several of these and/or other factors have been studied with various agents in mCRPC and have similarly shown to be effective prognostic markers.[11-15]

Obtaining results from real-world settings is an informative aspect of retrospective data and strength of this study. Another important strength is that these results reflect patients treated across several oncology centres, which increases the generalizability of results. The study is limited by its retrospective nature, small patient numbers, and limited followup. Although we are unable to identify a control group for robust statistical comparison, our group has previously investigated the outcomes of a similar group of patients (those with symptomatic bone metastases requiring palliative radiotherapy to bone [PRTB]), and the survival of such patients after first course of PRTB was 8.5 months.[16] In addition, for a sense of context of the proportion of patients receiving Ra223 relative to those that need it, we were able to assess the number of symptomatic patients receiving PRTB in a one-year period for the Vancouver Cancer Centre catchment area from the previous study.[16] In the three years preceding the availability of Ra223, 40–56 patients received PRTB prior to eventual death from prostate cancer per year; whereas, in the first full year of Ra223 availability in the Vancouver Cancer Centre catchment area in the current study, 15 patients received Ra223, suggesting a radium utilization rate of approximately one-third relative to symptomatic patients referred for and receiving PRTB.

Conclusion

This data reflects a population-based experience with Ra223 in mCRPC. It demonstrates less cycle completion, shorter survival, and more lines of prior therapy relative to the randomized trial data, and that higher ALP and lower hemoglobin levels were factors associated lower rate of treatment completion.

Competing interests: Dr. Parimi has received speaker honoraria from and participated in clinical trials supported by Astellas and Janssen. Dr. Alexander has received speaker honoraria from Bayer. Dr. McKenzie has been an advisor for and participated in clinical trials supported by Janssen; and has received honoraria from Amgen and Bayer. Dr. Bachand has received speaker honoraria from Bayer. Dr. Chi has received grant and honoraria from Astellas, Bayer, Essa, Janssen, and Sanofi; and has participated in clinical trials supported by Astellas, Bayer, Eli Lilly, Janssen, Merck, and Novartis. Dr. Tyldesley has received speaker honoraria from Bayer. The remaining authors report no competing personal or financial interests.

This paper has been peer-reviewed.

References

1. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med* 2014;371:424-33. https://doi.org/10.1056/NEJMoa1405095
2. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med* 2013;368:138-48. https://doi.org/10.1056/NEJMoa1209096
3. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med* 2012;367:1187-97. https://doi.org/10.1056/NEJMoa1207506
4. De Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011;364:1995-2005. https://doi.org/10.1056/NEJMoa1014618

5. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med* 2004;351:1502-12. https://doi.org/10.1056/NEJMoa040720
6. De Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: A randomized, open-label trial. *Lancet* 2010;376:1147-54. https://doi.org/10.1016/S0140-6736(10)61389-X
7. Parker C, Nilsson S, Heinrich D, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med* 2013;369:213-23. https://doi.org/10.1056/NEJMoa1213755
8. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* 2009;45:228-47. https://doi.org/10.1016/j.ejca.2008.10.026
9. McKay RR, Jacobus S, Fiorillo M, et al. Radium-223 utilization in clinical practice and variables associated with completion of therapy. *Clin Genitourin Cancer* 2017;15:e289-e98. https://doi.org/10.1016/j.clgc.2016.08.015
10. Saad F, Carles J, Gillessen S, et al. Radium-223 and concomitant therapies in patients with metastatic castration-resistant prostate cancer: An international, early access, open-label, single-arm phase 3b trial. *Lancet Oncol* 2016;17:1306-16. https://doi.org/10.1016/S1470-2045(16)30173-5
11. Armstrong AJ, Garrett-Mayer E, de Wit R, et al. Prediction of survival following first-line chemotherapy in men with castration-resistant metastatic prostate cancer. *Clin Cancer Res* 2010;16:203-11. https://doi.org/10.1158/1078-0432.CCR-09-2514
12. Fizazi K, Massard C, Smith M, et al. Bone-related parameters are the main prognostic factors for overall survival in men with bone metastases from castration-resistant prostate cancer. *Eur Urol* 2015;68:42-50. https://doi.org/10.1016/j.eururo.2014.10.001
13. Azad AA, Eigl BJ, Leibowitz-Amit R, et al. Outcomes with abiraterone acetate in metastatic castration-resistant prostate cancer patients who have poor performance status. *Eur Urol* 2014;1-7.
14. Etchebehere EC, Milton DR, Araujo JC, et al. Factors affecting 223Ra therapy:Clinical experience after 532 cycles from a single institution. *Eur J Nucl Med Mol Imaging* 2016;43:8-20. https://doi.org/10.1007/s00259-015-3185-4
15. Chi KN, Kheoh T, Ryan CJ, et al. A prognostic index model for predicting overall survival in patients with metastatic castration-resistant prostate cancer treated with abiraterone acetate after docetaxel. *Ann Oncol* 2016;27:454-60. https://doi.org/10.1093/annonc/mdv594
16. Cho J, Pickles T, Bachand F, et al. Palliative radiotherapy for bone metastases in patients dying of prostate cancer: The British Columbia experience. CARO 2016. *Radioth Oncol* 2016:120: S89-90. https://doi.org/10.1016/S0167-8140(16)33645-3

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