

Updates on radium-223 for castration-resistant prostate cancer presented at the Genitourinary Cancers Symposium, January 7-9, 2016, San Francisco, California

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Dan and associates have presented a comprehensive overview of the practical considerations for the administration of radium-223 (Xofigo) in their "How I Do It" article.¹ Several important updates on the use of radium-223 were presented at the ASCO Genitourinary Cancers Symposium, held January 7-9, 2016, San Francisco, California 2016 Genitourinary Cancers Symposium. These important updates of selected presentations will supplement the information presented in this "How I Do It" selection.

1. Phase II clinical study of radium-223 chloride in Japanese patients with symptomatic castrate resistant prostate cancer with bone metastases

Uemura and colleagues performed an open-label, single-arm, multicenter trial in Japanese men with castration-resistant prostate cancer and at least two symptomatic bone metastases and no visceral metastases.² Patients could enroll in the trial if they had previously received docetaxel, were docetaxel ineligible, or had refused docetaxel. The primary study endpoint was the change in alkaline phosphatase (ALP) levels at 12 weeks, and secondary endpoints were overall survival, time to symptomatic skeletal event, percentage of change in bone ALP/PSA/biomarkers, and safety outcomes.

A total of 49 patients received at least one injection of radium 223. At 12 weeks, the mean change in the total ALP from baseline -19.3% (95% CI: -28%- to -10%). The safety outcomes were favorable. Only one patient experienced a lymphocyte decrease grade 4 adverse event. The early, significant decrease in ALP in response to radium-223 in this study was consistent with findings in the ALSYMPCA registration trial.³

2. Open-label phase II study of concurrent radium 223 dichloride and abiraterone acetate in castration-resistant prostate cancer patients with symptomatic bone metastases

Shore reported the design of an ongoing open-label, phase 1-2 study that plans to enroll 30 patients with castration-resistant prostate cancer and bone metastases who will receive 6 doses of monthly radium-223 with concomitant 1000 mg/day abiraterone acetate plus 5 mg twice daily prednisone.⁴

The primary endpoint is efficacy, and the secondary endpoints are safety outcomes, time to progression, symptomatic skeletal events, PSA and ALP progression, and progression to further anti-neoplastic intervention. Patients will be assessed at baseline, and weeks 1, 5, 9, 13, 17, 21, and 25. The last patient visit was scheduled to occur December 2015. The study should reveal whether abiraterone acetate, one of the newer, widely accepted castration-resistant prostate cancer oral treatments will be more effective if patients receive concurrent treatment with injections of radium-223, without significantly increasing adverse effects. Preliminary retrospective analysis have demonstrated the safety of the concomitant administration of next-generation anti-androgen such as abiraterone and enzalutamide with radium-223.⁵ This larger study will further investigate the combined use of abiraterone and radium-223.

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3. First experience of radium-223 retreatment in an international, multicenter, prospective study in patients with castration-resistant prostate cancer and bone metastases

In this study by Sartor and associates 44 patients with castration-resistant prostate cancer and bone metastases who had completed 6 monthly injections of radium-223 with no evidence of progression of bone metastasis and with adequate hematologic parameters were offered a second course of therapy.⁶ The primary endpoint was safety outcomes, and the study also explored time to radiographic bone progression, time to ALP progression, and radiographic progression-free survival based on MRI and CT bone scans performed every 3 months.

A total of 29 of the 44 patients who were offered retreatment received six additional radium-223 injections. The rates of treatment-emergent adverse events in the retreated patients were similar to or lower than the rates in ALSYPMCA.³ Two retreated patients experienced grade 3 hematologic treatment-emergent adverse events. One patient had radiographic bone disease progression. The median time to ALP progression was not reached, and the median radiographic progression-free survival was 9.9 months. Radium-223 retreatment was well tolerated in this highly selected population. The patients had minimal hematologic toxicity and experienced continued control of bone disease progression.

4. Impact of symptomatic skeletal events on healthcare utilization, health-related quality of life, and pain in patients with castration-resistant prostate cancer and bone metastases.

McKay and colleagues examined electronic medical records and the clinical database in a tertiary oncology center and identified patients with castration-resistant prostate cancer and bone metastases.⁷ They reviewed medical charts to identify symptomatic skeletal events, including pathologic fracture, radiation to bone, spinal cord compression, and bone surgery. They also identified patients who visited the clinic during November 2014 to July 2015 and completed Functional Assessment of Cancer Therapy-Prostate (FACT-P) and Brief Pain Inventory-Short Form (BPI-SF) surveys. They used multivariate negative binomial regression to evaluate the impact of symptomatic skeletal events on healthcare resource utilization.

Of 832 patients, 207 patients developed at least one symptomatic skeletal event and 84% of the patients had radiation to the bone. The patients with symptomatic skeletal events had significantly more outpatient clinic visits, hospital emergency visits, and inpatient admissions, as well as lower functional well-being scores and significantly higher pain-severity scores.

Symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases had a large impact on healthcare cost and quality of life, which emphasizes the need for preventive treatments for symptomatic skeletal events in this patient population.

These ASCO GU updates on the clinical applications and ongoing investigational studies reinforce that bone metastases are common in patients with castration-resistant prostate cancer. Radium-223 can prevent or delay the progression of these symptomatic skeletal events and improve survival in these patients.

Disclosure

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