Radiation Oncology Consultants

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ROC September 2013 Newsletter

Radium 223 Xofigo Improves Survival for Metastatic Hormone Resistant Prostate Cancer Patients

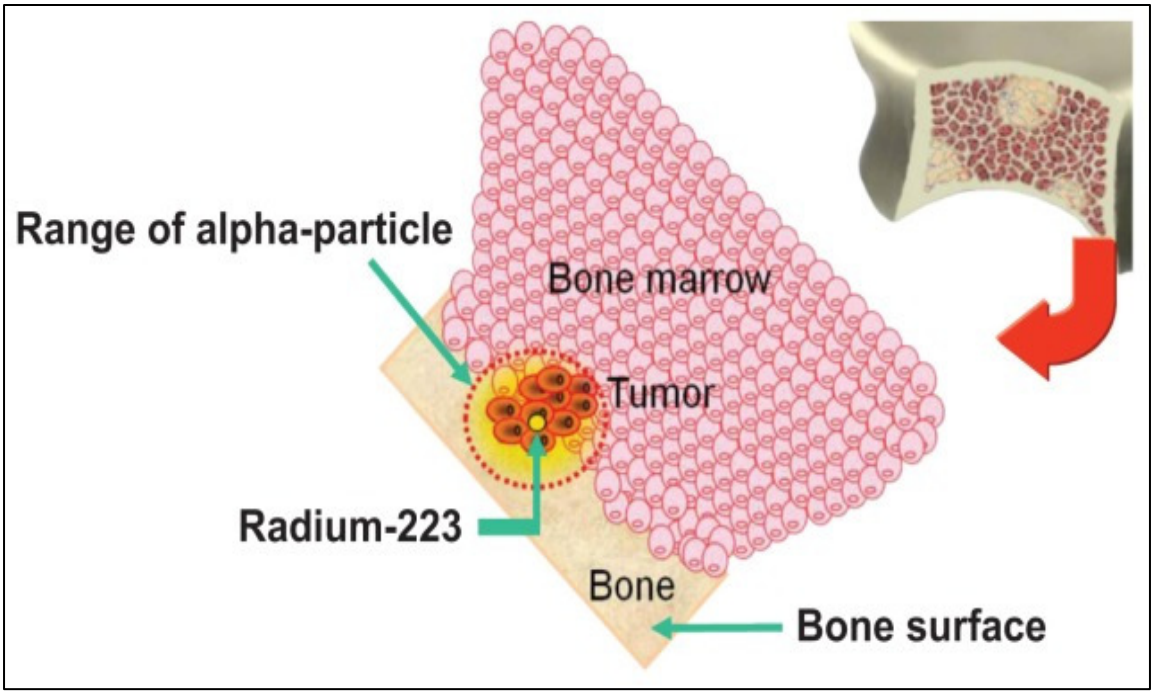
The physicians of ROC are pleased to offer Radium 223 (Xofigo, Bayer Health Care) as a treatment for patients with metastatic hormone resistant prostate cancer. On 5/15/2013, Radium 223 was approved for treatment of patients with castrate resistant prostate cancer for symptomatic bone metastases and no known visceral disease. Approval was based on a double-blind, randomized, placebo-controlled trial called the ALSYMPCA (Alpharadin in Symptomatic Prostate Cancer) Trial (1). Patients had painful castrate-resistant prostate cancer and no visceral disease. All patients had prior treatment with docetaxel or deemed unable to tolerate docetaxel treatment. 921 patients were entered into the study and a 2:1 radomization was used. Patients were given an injection of Radium 223 every four weeks for six cycles plus best standard of care (n=614) or placebo plus best standard of care(n=307). Standard of care included local radiotherapy, corticosteroids, anti-androgens, estrogens, estramustine or ketoconazole. All patients continued anti-androgen therapy.

At a prespecified interim analysis, median overall survival, which was the primary endpoint of this trial, was significantly prolonged with this drug in the Radium 223 group (14.9 vs. 11.3 months, p<0.001). This improvement in overall survival is supported by a delay in time to the first symptomatic skeletal event. A skeletal event was defined as the need for external beam radiation therapy to relieve skeletal pain, new pathologic fracture, new spinal cord compression, or tumor-related orthopedic surgical intervention. Other secondary events that were improved are represented in the table below compared to placebo:

Secondary Endpoint	**Result with Radium 223 versus placebo**
Time to first skeletal event	15.6 months vs 9.8 months p<0.001
Time to PSA progression	P<0.001
Total Alkaline Phosphatase Response	43% vs 3% p<0.001
Time to increase in Alkaline Phosphatase	Median 7.4 months vs 3.8 months
Total Alkaline Phosphatase normalization	34% versus 1% p<0.001

Fewer adverse events were reported in patients who received Radium 223 than in the placebo group. Quality of life scores improved in Radium 223 group (25%) compared to the placebo group (16%, p=0.02). Thrombocyoptenia (12%vs 6%), neutropenia (5% vs 1%), and diarrhea (25% vs 15%) were the major side effects that occurred greater in the Radium 223 group versus the placebo group. Thus, Radium 223 use in patients with bone only castrate resistant prosate cancer, improves overall survival, quality of life, and biochemical disease markers without increase in adverse events.

MECHANISM OF ACTION: The active component of radium-223 is the alpha particle Radium-223 dichloride. This compound mimics calcium and forms complexes at areas of increased bone turnover. The alpha particles lead to a high frequency of double-strand DNA breaks in adjacent cells. The range of the alpha particles is 100 micrometers which is less than 10 cell diameters. This limits damage to surrounding normal tissue including the adjacent bone marrow.



DELIVERY: The patient is given a dose of Radium 223 intravenously at four week intervals for six 1 minute injections. The volume of drug given is calculated based on the patient's weight and the radioactivity concentration of the product.

DISTRIBUTION: The majority of the Radium-223 is delivered to the bone within 4 hours of injection. The major route of excretion is through the bowels with only a very small amount excreted through the bladder and therefore the most common side effects seen were GI including nausea, vomiting and diarrhea. Also seen were peripheral edema and changes in blood counts.

If you are interested in learning more about this drug or if you would like to have your patients receive consultation regarding treatment with Radium 223, please contact one of our physicians. www.chicagocancer.org

INDICATION	
Patients with Hormone Resistant Prostate Cancer and Symptomatic Metastatic Bony Disease – Overall Suvival Benefit 15 vs 11 months	
DETAILS OF PATIENT ENROLLMENT	
Median Age	71 years old
Performance Status	ECOG 0 or 1
Received Prior Docetaxel	58%
Received Prior Bisphosphonates	41%
Six or more Bone Scan Lesions	85%
Used Narcotic Analgesics	54%
Used Non-Narcotic Analgesics	44%
EXCLUSION	
Chrons' Disease, Ulcerative Colitis, Prior Hemibody Radiation Therapy, or Untreated imminent spinal cord compression	

During treatment 83% of patients in the Radium 223 group and 82% of the placebo group received gonadotropin-releasing hormone agonists. Also, 21% of the Radium 223 group and 34% of the placebo group received antiandrogens. Use of systemic steroids (41%) and bisphosphonates (40%) was also balanced between the groups.

Patients with prior bone fractures or impending fractures received orthopedic stabilization prior to starting treatment with Radium 223.

1) Parker C, et al., (2013) Alpha emitter Radium-223 and survival in metastatic prostate cancer. N Engl J Med 2013; 369:213-223.