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EMCC 2011 Update: Radium-223 plus Chemo Shows Clear OS Benefit

By Anna Azvolinsky, PhD | September 29, 2011

Radium-223, an alpha particle given intravenously, has been shown to improve overall survival in men with castrate-resistant prostate cancer (CRPC), with a 30% risk reduction of death (HR = 0.695, *P* = .00185).

The positive results from the phase III, randomized ALSYMPCA (ALpharadin in SYMPtomatic prostate CAncer) study were reported at a late-breaking session on Saturday, September 24, 2011 at the European Multidisciplinary Cancer Congress in Stockholm, Sweden. Chris Parker of the Royal Marsden Hospital in Sutton, UK presented data showing that the radium-223 combined with best standard of care arm showed a 14 month medial overall survival, compared to 11.2 months for the placebo plus best standard of care arm.

The difference in the overall survival primary endpoint was great enough during a preplanned interim analysis that the trial was stopped early by an independent committee on June 3, 2011. From a total of 809 patients enrolled in the trial, 314 events had occurred at the time of the interim analysis.

The experimental arm was also associated with a delay in the time to first skeletal-related events and in the time to prostate-specific antigen (PSA) progression. The median time to first skeletal-related events was 13.6 months for the radium-223 arm compared to 8.4 months for the control (HR= 0.610, *P* = .00046).

Patients with symptomatic prostate cancer and at least two bone metastases but no visceral metastases were randomized two to one to the experimental and control arms. All patients were either pretreated with the current standard of care, docetaxel(Drug information on docetaxel), or were unfit for docetaxel treatment. The mean age of the patients was 70. Many of the patients had very advanced prostate cancer, with 40% of patients having 20 or more bone metastases.

Six intravenous radium-223 injections were given every 4 weeks. Treatment with radium-223 was completed in minutes and patients are able to return home right after injection. Additionally, because radium-223 consists of alpha particles that have a very short path length, relatively few precautions were needed when handling the agent.

The particles have a high affinity for bone and are able to kill prostate cancer cells without penetrating far into the bone marrow, one of the reasons for the low toxicity and high tolerability of the treatment. Adverse events included hematological, gastrointestinal (diarrhea, constipation, nausea, vomiting) and bone pain and were generally mild. Bone pain and anemia were the highest grade 3 and 4 events experienced by patients (approximately 20% and 12% of all patients, respectively). 13% of patients in the experimental arm compared to 20% of patients in the control arm discontinued treatment due to adverse events.

According to Dr. Parker, radium-223 may provide a new standard of care for CRPC patients with bone metastases. He noted that adding radium-223 to combination chemotherapy regiments may provide the opportunity to improve patient outcomes.

The improvement in overall survival results are very encouraging as prostate cancer is still the second-most diagnosed cancer among men worldwide, and is the sixth highest cause of death from cancer worldwide among men.

It is generally difficult to show an overall survival benefit for an advanced stage and pre-treated cancer population. Prior to 2010, docetaxel was the only radiotherapy that had shown a survival benefit. Radium-223 is the only bone-targeting agent that has shown a survival benefit in advanced stage prostate cancer; it is also being explored as a potential adjuvant treatment for low-volume, microscopic prostate cancer.