Double-Blind, Placebo-Controlled Trial of Radium-223 Adjuvant to External Beam Radiotherapy Demonstrates Significant Decline in Bone-Alkaline Phosphatase and PSA in Patients with Hormone Refractory Prostate Cancer (HRPC)

Background

The alpha emitter radium-223 (Alpharadin™; t½ = 11.4 days) is a bone-seeking radionuclide currently explored as a novel treatment of bone metastases. Radium-223 has shown minimal toxicity in a phase I study (1). The present trial was initiated to study therapeutic efficacy in HRPC-patients with painful skeletal metastases using biomarkers and clinical endpoints as outcome measures. Safety and changes in biomarkers are reported based on analyses at 12 months after start of treatment.

Methods and Trial Design

Methods: After receiving palliative external beam radiotherapy HRPC-patients were randomised to 4 i.v. injections of radium-223 (50 MBq/kg b.w.) or saline, repeated at four-week intervals. Bone-isoenzyme ALP (primary endpoint) and PSA were analyzed (radium-223 versus saline) following the 12-month visit when the data was unblinded.

Main Eligibility Criteria

• Confirmed hormone refractory prostate cancer with painful skeletal metastases.
• Referred to palliative external radiotherapy for skeletal metastases.
• No other currently active malignancy or known metastases to other organ than skeleton.

Results

• Fewer placebo treated patients received 4 injections.
• Five patients received less than 2 injections (1 Alpharadin, 4 Placebo).

Hematological Toxicity

- No grade 4 hematological events in Alpharadin treated patients.
- No grade 3 hematological events in Alpharadin treated patients.
- Five patients received less than 2 injections (1 Alpharadin, 4 Placebo).

Conclusions

Radium-223 treatment demonstrated strong and consistent effects in this double-blind placebo-controlled trial in 64 patients. Statistically significant effects were shown on a range of markers of bone turn-over as well as a favorable PSA response. The beneficial effects had duration of approximately 3 months after end of treatment. The favorable side effect profile may allow longer duration of treatment.

References