

## ALSYMPCA trial - Alpharadin (Radium 223)

### Bone-targeted radium-223 in symptomatic, hormone-refractory prostate cancer: a randomised, multicentre, placebo-controlled phase II study

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#### Summary

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#### Background

The alpha-emitter radium-223 (<sup>223</sup>Ra) is a bone-seeking radionuclide studied as a new treatment for patients with bone metastases from hormone-refractory prostate cancer. We aimed to study mature outcomes from a randomised, multicentre, phase II study of <sup>223</sup>Ra.

#### Methods

Patients with hormone-refractory prostate cancer and bone pain needing external-beam radiotherapy were assigned to four intravenous injections of <sup>223</sup>Ra (50 kBq/kg, 33 patients) or placebo (31 patients), given every 4 weeks. Primary endpoints were change in bone-alkaline phosphatase (ALP) concentration and time to skeletal-related events (SREs). Secondary endpoints included toxic effects, time to prostate-specific-antigen (PSA) progression, and overall survival. All tests were done at a 5% significance level, based on intention to treat.

#### Findings

Median relative change in bone-ALP during treatment was -65.6% (95% CI -69.5 to -57.7) and 9.3% (3.8-60.9) in the <sup>223</sup>Ra group and placebo groups, respectively ( $p < 0.0001$ , Wilcoxon ranked-sums test). Hazard ratio for time to first SRE, adjusted for baseline covariates, was 1.75 (0.96-3.19,  $p = 0.065$ , Cox regression). Haematological toxic effects did not differ significantly between two groups. No patient discontinued <sup>223</sup>Ra because of treatment

toxicity. Median time to PSA progression was 26 weeks (16–39) versus 8 weeks (4–12;  $p=0.048$ ) for 223Ra versus placebo, respectively. Median overall survival was 65.3 weeks (48.7– $\infty$ ) for 223Ra and 46.4 weeks (32.1–77.4) for placebo ( $p=0.066$ , log rank). The hazard ratio for overall survival, adjusted for baseline covariates was 2.12 (1.13–3.98,  $p=0.020$ , Cox regression).

### Interpretation

223Ra was well tolerated with minimum myelotoxicity, and had a significant effect on bone-ALP concentrations. Larger clinical trials are warranted to study 223Ra on the prevention of SREs and on overall survival in patients with hormone-refractory prostate cancer. Bone-targeting properties of 223Ra could also potentially be used for treating skeletal metastasis from other primary cancers.

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