Abstract ID #19

Radium-223 Mechanism of Action

- Radium-223 is a first-in-class alpha-emitting therapeutic radioisotope that acts as a calcium mimetic, providing a targeted alpha-particle radiation dose to bone metastases.

- Acts as a calcium mimetic, leading to local bone growth and repair in and around bone metastases, delivering targeted alpha-particle radiation to the site.

- Excreted by the small intestine.

- Targeted-radium-223 exists as alpha particles with ultrashort penetration (< 100 µm; 2-10 cell diameters) causing highly localized tumor-cell killing with minimal damage to surrounding normal tissues.

METHODS AND STUDY DESIGN

- In a randomized, double-blind, placebo-controlled phase III trial, prostate cancer patients with CRPC and bone metastases were treated with radium-223 (80 kBq/kg radium-223) or placebo (50 kBq/kg radium-223) for 24 weeks.

- Patients were randomized to 1:1 to receive 6 injections of radium-223 (50 kBq/kg) every 4 weeks or matching placebo (Figure 1).

- Patients were stratified by prior docetaxel use, hazard level (ALSYMPCA trial, Z score), and current bisphosphonate use.

RESULTS

- Of the 1223 patients randomized, 614 patients received all 6 injections.

- Grade 3 or 4 neutropenia was reported in 2% of the radium-223 and placebo groups, respectively.

- Grade 3 or 4 anemia was reported in 6% and 2% of the radium-223 and placebo groups, respectively.

- Grade 3 or 4 thrombocytopenia was reported in 1.5% and 0.7% of the radium-223 and placebo groups, respectively.

- Median time to initial opioid use was significantly longer in the radium-223 group, with a risk reduction of 0.621 (HR = 0.621; 95% CI, 0.484-0.804; P = 0.00021).

- Median time to first eBRT was significantly longer in the radium-223 group, with a risk reduction of 0.670 (HR = 0.670; 95% CI, 0.525-0.854; P = 0.00117).

- Radium-223 reduced pain and opioid use in CRPC patients with bone metastases, improving overall survival.

In another phase 2 study, pain index data were available from 80 patients treated with radium-223 or placebo (Figure 1).

- Median pain index was significantly lower in the radium-223 group compared with placebo (HR = 0.621; 95% CI, 0.484-0.804; P = 0.00021).

- Median time to initial opioid use was significantly longer in the radium-223 group, with a risk reduction of 0.621 (HR = 0.621; 95% CI, 0.484-0.804; P = 0.00021).

ADVANCE EVENTS IN ALSYMPCA

- The percentage of patients experiencing AEs was lower in the radium-223 group than in the placebo group (HR = 0.621; 95% CI, 0.484-0.804; P = 0.00021).

- Radium-223 reduced pain and opioid use in CRPC patients with bone metastases, improving overall survival.


*Based on a meta-analysis of the ALSYMPCA and CRPC trial.