Alpharadin inhibits osteoclast differentiation in vitro and progression of established breast cancer bone metastases in vivo

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INTRODUCTION

• Alpharadin (Algeta ASA, Oslo, Norway) is an alpha-emitting radium-223 isotope currently being tested in a randomized Phase III clinical trial for the treatment of castration-resistant prostate cancer with bone metastases.
• Alpharadin is a calcium mimetic radium-223 that localizes to bone and offers a bone-targeted therapy for skeletal metastases.
• Alpharadin demonstrated promising preliminary Phase II clinical data in predominately osteoblastic bone metastases in prostate cancer and on treatment of established breast cancer bone metastases in vivo.

MATERIALS AND METHODS

• The in vitro effects of Alpharadin (50-1000 Bq/mL, n=3/group) on osteoclasts were studied using human osteoclast precursor cells cultured on bone tissue slices.
• Alpharadin was added to the osteoclast differentiation assay day 3 and to the activity assay day 7.
• Secreted tartrate-resistant acid phosphatase isoenform 5b (TRACP 5b) was measured at day 7 as a marker of osteoclast differentiation and activity of human osteoclasts in vitro.
• This study aimed to clarify the effects of Alpharadin on differentiation and activity of human osteoclasts in vitro and on treatment of established breast cancer bone metastases in vivo.

CONCLUSIONS

• Alpharadin is an alpha-emitting radium-223 isotope currently being tested in a randomized Phase III clinical trial for the treatment of castration-resistant prostate cancer with bone metastases.
• Alpharadin showed therapeutic efficacy in an established osteolytic breast cancer bone metastases preclinical model.
• Alpharadin increased the level of tumor cell necrosis, and inhibited the differentiation of osteoclasts in vitro and the number and activity of osteoclasts at sites of osteolytic bone resorption in vivo.
• These preclinical findings support the clinical development of Alpharadin in additional cancer indications, such as osteolytic breast metastases in breast cancer.

ACKNOWLEDGMENTS

We thank Professor Theresa Guiney for generously providing the MDA-MB-231(SA) cell line and Giol Selberg at Algeta ASA for help in the Alpharadin in prenats. We thank Tui Svanberg, Johanna Bartanen, and Anneli Lauterinen for their skilful technical assistance. Rachel Fairbank, BA, at Complete Health/NM provided editorial assistance in the development of this paper.

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Poster presented at the 102nd Annual Meeting of the American Association for Cancer Research, April 2-6, 2011, Orlando, Florida, USA

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