■ Online Exclusive Article

Analysis of Denosumab on Skeletal-Related Events in Patients With Advanced Breast Cancer

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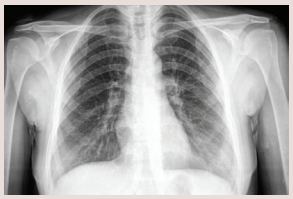

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Background: Bisphosphonates, which are also known as osteoclast modifiers, are the standard of care in the treatment of skeletal-related events (SREs) in patients with breast cancer with metastatic bone disease. SREs are frequently a complication of advanced breast cancer, and they greatly increase morbidity and mortality in these patients. Unfortunately, even while undergoing bisphosphonate therapy, many patients experience SREs. In 2010, a fully human monoclonal antibody, denosumab (Xgeva®), was approved by the U.S. Food and Drug Administration as another option to treat SREs.

Objectives: This article analyzes four primary human research studies looking at the effectiveness and safety of denosumab as compared to bisphosphonates in the prevention of SREs in this vulnerable population.

Methods: Articles published from 2006–2012 were located and reviewed through online database searches (CINAHL®, MEDLINE®, PubMed Plus) using the key words *denosumab, skeletal-related event, breast cancer, metastases, and bisphosphonates.*

Findings: Studies reviewed showed comparative adverse events and safety profile between denosumab and bisphosphonates. However, denosumab was shown to have increased effectiveness in the prevention of SREs. This knowledge can influence the preventive measures taken by physicians and advanced practice nurses to improve the prevention of SREs in patients with metastatic breast cancer. It can also increase staff nurse knowledge and implementation of evidence-based practice.

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Key words: denosumab; skeletal-related event; breast cancer; metastases; bisphosphonates

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According to American Cancer Society ([ACS], 2015a) estimates, 231,840 new cases of invasive breast cancer are expected to be diagnosed among women in the United States during 2015, and more than 40,000 women will die from breast cancer in the same year. Breast cancer is the second leading cause of cancer death in women in the United States (ACS, 2015b). About 20% of patients diagnosed with breast cancer develop metastatic disease (Eckhardt, Francis, Parker, & Anderson, 2012), and, of those patients with metastatic breast cancer, as many as 80% will have metastatic disease present in the bone (Kennedy & Patel, 2011).

The formation of bone metastases indicates an increase of osteoclast activity, leading to bone destruction and potential skeletal complications (e.g., severe pain, hypercalcemia, skeletal-related events [SREs]) (Stopeck et al., 2010). SRE is an umbrella term used to refer to a pathologic fracture, spinal cord compression, the use of radiation therapy to improve pain or prevent fracture, and/or the use of surgery to treat or prevent fracture (Kennedy & Patel, 2011). SREs greatly increase morbidity and mortality in patients with advanced breast cancer (Kennedy & Patel, 2011). In addition, SREs can decrease patients' functionality and ability to maintain independence in activities of daily living. They may also contribute to pain, requiring additional medications used to control SRE-related symptoms. The purpose of this article is to analyze published primary sources that have evaluated denosumab (Xgeva®) and bisphosphonates, also known as osteoclast modifiers, in the prevention of SREs, specifically in the population of patients diagnosed with metastatic breast cancer.

Skeletal-Related Events

SREs may cause paresthesias, incontinence, paralysis, pain, and functional dependence, and they may lead to the inability to