

Denosumab Superior to Zoledronic Acid in Preventing Skeletal-Related Events

New study shows benefit of zoledronic acid in patients with bone metastases across multiple baseline characteristics

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June 14, 2017 – Among patients with bone metastases from advanced cancer, denosumab demonstrated superiority versus zoledronic acid (ZA) in preventing skeletal-related events (SREs) in patients across multiple baseline characteristics, according to a recent post hoc analysis of phase III trials.

Allan Lipton, MD, with Pennsylvania State University Hershey Medical Center, in Hershey, Pennsylvania, and colleagues reported their findings in the January 2016 issue of the *European Journal of Cancer*.

Denosumab is a human monoclonal antibody that acts as an inhibitor of RANK ligand (RANKL), which regulates osteoclast bone resorption.

In previous phase III trial analyses, denosumab has shown superiority to ZA in the risk reduction of first and subsequent on-study SREs in patients with bone metastases from prostate cancer, breast cancer, other solid tumors and multiple myeloma.

The current study was a post hoc analysis of 3 identical phase III trials evaluating denosumab in patients with breast cancer, prostate cancer, or other solid tumors who had radiographic evidence of at least one bone metastasis. Patients in the phase III trials were randomized to receive denosumab 120 mg subcutaneous or ZA 4 mg IV every 4 weeks, with the primary endpoint being time to first on-study SRE.

This analysis stratified patients across a group of prespecified baseline subgroups – location of bone metastases, status of visceral metastases, urinary N-telopeptide (uNTx) level, and Eastern Cooperative Oncology Group performance status (ECOG PS), to evaluate the efficacy of denosumab versus ZA to reduce SRE risk.

Treatment with denosumab significantly reduced the risk of first and subsequent SREs, and increased median time to first on-study SRE compared with ZA across all baseline subgroups ($P < 0.05$), with the exception of patients with appendicular bone metastases at baseline ($P = 0.072$). The results were found to be consistent across solid tumor types (breast, prostate, and other solid tumors).

The authors concluded that denosumab may be superior to ZA in preventing SREs in patients with metastatic bone disease “regardless of the baseline characteristics of ECOG PS, number of bone metastases, presence or absence of visceral metastases, and uNTx level.”

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Lipton A, Fizazi K, Stopeck AT, et al. Effect of denosumab versus zoledronic acid in preventing skeletal-related events in patients with bone metastases by baseline characteristics. *Eur J Cancer*. 2016;53:75-83.

