Denosumab Superior to Zoledronic Acid in Preventing Skeletal-Related Events In Patients With Bone Metastases

M. H. Wright

Denosumab has been shown to be superior to zoledronic acid (ZA) in preventing initial and subsequent skeletal-related events (SREs) in patients with several types of primary cancer with bone metastases, and across various other baseline variables. [1]

Patients with bone metastases are at risk for SREs, including pathologic fracture, spinal cord compression, and radiation or surgery to the bone.[1,3] Lipton et al. state, “SREs are associated with not only substantial morbidity, but also greater mortality, increased pain, decreased quality of life, and increased treatment costs.”[1]

In 2012, analyses of three phase lll trials by Lipton et al. found that in patients with breast, prostate, or other solid tumors, denosumab was superior to zoledronic acid in preventing SREs regardless of age, history of SREs, and baseline pain status.[2] More recently, researchers extended the analyses by looking at other baseline characteristics which are typically important to clinicians in assessing risk of developing SREs; subgroups included Eastern Cooperative Oncology Group performance status (ECOG PS), location and number of bone metastases, presence or absence of visceral metastases, and urinary N-telopeptide level (uNtx), a marker of bone turnover.[1]

In the extended analyses, denosumab was superior to ZA in protecting against first SREs in all four subgroups, with hazard ratio (HR) ranges as follows: ECOG PS, 0.79–0.84; bone metastasis location, 0.78–0.83; bone metastasis number, 0.78–0.84; visceral metastasis presence/absence, 0.80–0.82; and uNTx level, 0.73–0.86. Similarly, denosumab was superior to ZA in protecting against first and subsequent SREs across all four subgroups and in all three tumor types.[1]

Denosumab is a human monoclonal antibody that binds with the receptor activator of the NF-kB (RANK) ligand (RANKL), interfering with RANK/RANKL- mediated bone destruction.[3] Thus, according to Lipton et al., the findings confirm “the importance of the RANK/RANKL pathway in SRE pathophysiology in patients with bone metastases from solid tumours.”[1]

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2. Lipton A, Fizazi K, Stopeck AT, et al. Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: a combined analysis of 3 pivotal, randomised, phase 3 trials. *Eur J Cancer*. 2012;48(16):3082-3092. doi:10.1016/j.ejca.2012.08.002

3. Body J-J. Denosumab for the management of bone disease in patients with solid tumors. *Expert Rev Anticancer Ther*. 2012;12(3):307-322. doi:10.1586/era.11.204