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The importance of denosumab in the treatment of giant cell bone cancer

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Abstract

Denosumab is a monoclonal antibody that is used in targeted therapies. This drug targets the RANKL protein to prevent bone destruction and eliminate potential giant cells. Denosumab is used to prevent the complications of bone in patients who have spread to the bone due to cancer. The use of denosumab in giant cell bone cancer allows the postponement of surgery, the need for surgery in most patients, or the reduction of the surgical area. However, it is important to determine the indications, drug dose and duration for which this treatment should be used or not.

Introduction

Bisphosphonates (Bf) are a group of drugs that have been used for about thirty years to prevent bone resorption. Denosumab (Dmab), a newly synthesized molecule used for similar purposes, is a completely human monoclonal antibody that inhibits the effect of RANK on osteoclasts by binding receptor receptor activator nuclear factor kappa B ligand (RANKL). FDA-approved is the first RANK-Ligand inhibitor. Since 2010, FDA has recommended the use of multiple myeloma in breast, prostate and lung cancer. Ease of application, not binding to bone mineral, reversible effect and not eliminating from kidney are the important advantages of this drug. Side effects are hypocalcemia and osteonecrosis in the jaw bones [1-3].

Dmab has been shown to be effective in the treatment of malignant or non-malignant osteolysis [2-7]. In a phase III study by Simith *et al.* Dmab was compared with patients with non-metastatic prostate cancer and a placebo group. According to placebo, Dmab reported that it prolongs bone formation time and significantly decreases bone turnover markers [5]. Zheng *et al.* evaluated the effect of Dmab and zoledronic acid (ZA) on delaying skeletal-related events (SRE) and improving overall survival for the treatment of bone metastasis in patients with advanced solid tumors. This meta-analysis included three randomized controlled trials of a total of 5,544 patients. Dmab was found to be superior to ZA in the first study-SRE delay time ($p < 0.0001$). However, there was no significant difference in overall survival improvement between Dmab and ZA ($p = 0.71$). As a result, Dmab was found to be superior to ZA in delaying SREs for patients with bone metastasis, whereas overall survival was reported to be the same in both groups [8]. In a meta-analysis study by Peddi *et al.* it was reported that subcutaneous Dmab administration significantly reduced the incidence of skeletal complications and delayed these complications and was superior to ZA in decreasing bone turnover markers and delaying complications. Again, in this study, the risk of hypocalcemia was found to be twice as high in the Dmab group [4].

Studies have shown that the protein known as RANKL plays an important role in bone resorption. It has been shown that serum RANKL is increased in malignant cases such as breast cancer, clear cell renal tumors, multiple myeloma, lymphoma and prostate cancer. It has also been shown to be directly related to RANKL in giant cell bone cancer. Although it is a rare, histologically benign tumor of the bone, it has been reported that RANKL is elevated in the locally aggressive giant cell tumor. In these patients, the use of a RANKL inhibitor, Dmab, has been confirmed in studies that have delayed surgical intervention, no surgery is needed in most patients, or the area to be operated will be reduced. However, in these studies, the long-term and actual administration data of Dmab therapy as well as the combination strategy with surgery have not been well investigated [3,7,8,9]. Chawla and colleagues in their phase 2 study group of patients with giant cell bone cancer divided into 3 groups (group I, which can be recovered by surgery, group 2, surgery was associated with severe morbidity, group III, the previous denosumab participated in the study of the giant cell bone patients with cancer). In the first two groups, 120 mg denosumab was given subcutaneously at 8 and 15 days intervals. The third group continued the denosumab dosage given in the previous study. At the end of a mean follow-up period of 13 months, 96%, 74% and 62% of the patients did not progress to disease. Overall, 72% of all patients responded objectively to denosumab. As side effects, osteonecrosis was observed in 1% of the jaw and hypocalcemia was observed in 5% [10].

As a result, Denosumab is a monoclonal antibody that is used in targeted therapies. This drug targets the RANKL protein to prevent bone destruction and eliminate potential giant cells. Denosumab is used to prevent the complications of bone in patients who have spread to the bone due to cancer. The use of denosumab in giant cell bone cancer allows the postponement of surgery, the need for surgery in most patients, or the reduction of the surgical area. However, it is important to determine the indications, drug dose and duration for which this treatment should be used or not. Studies on long-term results are needed.

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