

# Utilization of Denosumab on Survival in Breast Cancer Patients with Bone Metastasis: A short literature review.

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## Introduction

Breast cancer most commonly spreads to the bones. The majority of bone metastases are osteolytic, but some are osteoblastic and mixed (1). Osteoclast cell activity plays a significant role in maintaining normal bone health. Osteoclasts are activated in many ways. When they are activated, the bone matrix is destabilized, leading to rapid bone loss and creating an agreeable bone environment for cancer growth. Two major groups of bone-modifying agents (BMAs) are bisphosphonates and denosumab. Both modulate osteoclastic activity by inhibiting osteoclast-mediated bone turnover, leading to the interruption of the cancer effects on bones (2).

Denosumab is a monoclonal antibody medication used in the treatment of osteoporosis, bone metastases, and other bone-related conditions. It works by inhibiting a protein called RANKL (receptor activator of nuclear factor kappa-B ligand), which plays a key role in the formation, function, and survival of osteoclasts, the cells responsible for breaking down bone tissue. By blocking RANKL, denosumab reduces bone resorption, leading to an increase in bone mineral density and strength. It is typically administered as a subcutaneous injection of 120 mg every month for breast cancer patients with bone metastasis (3).

The primary indication of denosumab is not for improving overall survival but rather for the treatment of osteoporosis and bone-related conditions, including bone metastases. However, in the context of breast cancer treatment, particularly in cases where denosumab is used to prevent skeletal-related events (SREs) in patients with bone metastases, there have been studies examining its impact on survival (4).

Some clinical trials have shown that denosumab can delay the onset of SREs, such as fractures or spinal cord compression, in patients with advanced cancer disease and bone metastases compared to bisphosphonates, which were previously the standard treatment. By reducing these complications, denosumab indirectly can contribute to a better quality of life and potentially longer survival in cancer patients (5).

In a recent large meta-analysis, BMA's have been shown to reduce skeletal-related events (SREs) by 16%-17 % and decreased median time to SREs compared to placebo, but there was no effect on overall survival (6). However, it's important to note that the effect of denosumab on overall

survival in cancer patients is still an area of ongoing research and debate. While some studies have suggested a potential survival benefit, others have not shown a significant difference in survival outcomes between denosumab and bisphosphonates or placebo. Ultimately, decisions regarding the use of denosumab in cancer patients should be made based on individual patient factors, including the extent of bone involvement, overall treatment goals, and potential risks and benefits. Patients with cancer should discuss with their healthcare providers to determine the most appropriate treatment approach for their specific situation (4, 6).

As with any medication, denosumab may have side effects, including but not limited to hypocalcemia (low calcium levels), infections, skin reactions at the injection site, and osteonecrosis of the jaw (a rare condition characterized by the death of jawbone tissue). Therefore, it's essential for patients to be closely monitored by the oncologists while on denosumab therapy (5, 6).

Future research is needed to identify key molecular and genomic pathways that might be potential therapeutic targets (7).

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