Bisphosphonates: Expanded Roles in the Treatment of Patients With Cancer

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Bisphosphonates are a class of drugs originally developed for and used in the treatment and prevention of osteoporosis; they now are known to be instrumental in the treatment of bone metastases and hypercalcemia of malignancy. Several oral agents have been used for osteoporosis, and, although side effects are associated with oral bisphosphonates, their advantages in the treatment of this often debilitating illness have been a therapeutic boon to patients with osteoporosis. In particular, since the advent of new warnings about the use of hormone replacement therapy in menopausal women, bisphosphonates may carry an even more important role in the prevention of osteoporosis-related fractures.

Although bisphosphonates first were used in osteoporosis, these agents are effective in treating bone metastases, reducing skeletal-related events, and decreasing risk of spinal cord compromise (Ali et al., 2001; Van Poznak, 2002). Many patients with cancer develop metastases to bone, which affects quality of life and contributes to the morbidity of the disease. Bisphosphonates are useful in the treatment and prevention of fractures related to metastatic disease and are the treatment of choice for hypercalcemia of malignancy; researchers currently are looking at these agents in the treatment of cancer as well.

Bisphosphonates are important inhibitors of osteoclastic bone resorption seen in patients with bone metastases associated with malignancy. Bisphosphonates are used in the treatment of patients with bone metastases and have been shown to reduce skeletal-related events and symptoms, contributing to improved patient outcomes and quality of life. These agents first were approved in the treatment of patients with osteoporosis and have been used for the past two decades in this role. Because bisphosphonates inhibit osteoclast-mediated bone resorption, the bone remodeling cycle slows down and an increase in bone mineral density occurs. These agents are useful in treatment for both hypercalcemia and pain, although they have not definitively shown improvement in survival time. Considerable interest exists in the use of bisphosphonates for prevention of bone metastases and their potential antitumor activity. These drugs are well tolerated and have minimal side effects, but they are not inexpensive. This article discusses the role of bisphosphonates in patients with cancer and future directions for further research.

Key Words: neoplasm metastases, bone; hypercalcemia; osteoporosis

Bisphosphonates in the Treatment of Osteoporosis

Osteoporosis is characterized by low bone mass and deterioration of bone, leading to bone weakness and an increased susceptibility to fractures. Bone density correlates with bone strength and is a major determinant of fracture risk. Osteoporosis is responsible for 1.5 million low-trauma fractures per year, and the incidence is much higher in women than in men. One of every two women and one in eight men older than 50 will have an osteoporosis-related fracture in their lifetimes. Risk factors for osteoporosis include Caucasian race, low weight or history of weight loss, and history of previous fracture or family history of fracture (Messinger-Rapport & Thacker, 2002).

The World Health Organization has defined low bone mass, osteopenia, as bone mineral density (BMD) 1.0–2.5 standard deviations below the mean for a young adult woman. Osteoporosis is defined as BMD equal to or greater than 2.5 standard deviations below the young adult mean (Miller & Lane, 2001).

The indications for bone mass measurement are to diagnose osteopenia or osteoporosis, predict fracture risk, and monitor the response of BMD to therapy. The dual-energy x-ray absorptiometer is the examination most commonly used because it depicts early bone loss (see Figure 1).