Zoledronic Acid Extends Survival in Lung Cancer & Multiple Myeloma Patients with High Levels of Bone Metabolism

Oncology Times
August 25, 2006
Volume 28, No. 16
Pages 37 & 40

By Mark L. Fuerst

ASCO Abstracts 7228 and 7505

ATLANTA—A bisphosphonate used in osteoporosis appears to increase survival of lung cancer and multiple myeloma patients with high levels of bone metabolism, according to data presented here at the ASCO Annual Meeting.

Zoledronic acid (zoledronate) is the most potent of all bisphosphonates. When given as a slow, 15-minute intravenous infusion once a year, it can increase bone mineral density and reduce bone turnover in postmenopausal women with low bone mineral density.

Studies show that changes in bone mineral density and bone turnover are similar to those seen with bisphosphonate pills.

Zoledronic acid is the most potent of all bisphosphonates.

A once-yearly intravenous infusion of zoledronic acid is already approved for the treatment of hypercalcemia. Many cancer patients have hypercalcemia when cancer cells overstimulate osteoclasts in the bones, which results in an increased rate of bone breakdown, which releases excess calcium into the bloodstream.

Zoledronic acid (Zometa) suppresses biochemical markers of bone resorption in patients with bone metastases and significantly reduced levels of one such marker, N-telopeptide of type I collagen (NTX), in patients with advanced multiple myeloma or with bone metastases from breast cancer; this reduction correlated with inhibition of bone disease progression.

"Zometa is the only therapy to demonstrate efficacy in reducing or delaying bone complications across a broad range of tumor types such as breast, prostate, lung, and renal cell cancers in patients with metastatic disease when administered every three to four weeks," said the author of one of the studies presented at the meeting, Pierre Major, MD, of McMaster University.

"By decreasing these events, the drug helps preserve patients' independence, and may increase survival in some lung cancer patients."

Longer Survival in Multiple Myeloma

Zoledronic acid is also indicated for the treatment of bone metastases in patients with multiple myeloma and has been demonstrated to reduce the risk of skeletal morbidity. However, it is unknown whether there is a survival benefit secondary to the reduction in skeletal complications.

"Bone metastases are a frequent complication of solid tumors. The bone provides a receptive microenvironment for cancer cells, which disrupt the normal process of bone remodeling," said James Berenson, MD, Medical and Scientific Director of the Institute for Myeloma & Bone Cancer Research in West Hollywood, CA, who also presented a study at the ASCO meeting.

"Patients may experience skeletal complications such as severe pain, impaired mobility, pathologic fractures, and spinal cord compress. Therapeutic goals are to reduce or delay these painful and debilitating complications of bone metastases."

To assess the effect of zoledronic acid on survival in patients with multiple myeloma, researchers from the University of Athens and the Institute for Myeloma & Bone Cancer Research conducted a retrospective analysis of a subset of patients in a large, randomized controlled trial.

James Berenson, MD: "This exploratory analysis suggests that zoledronic acid treatment may improve survival compared with pamidronate, and this effect was observed primarily in patients who had a high baseline BALP level, indicating more aggressive osteolytic disease."

Survival data were analyzed for 209 myeloma patients who had at least one post-baseline safety evaluation and information on baseline BALP levels. The patients were retrospectively stratified by baseline BALP levels, from low BALP (less than 146 U/L) to high BALP (146 U/L or more).

Every three to four weeks the patients were treated with 4 mg of zoledronic acid (107 patients) or 90 mg of pamidronate (102 patients). After 25 months of treatment, the overall survival rate was significantly higher in patients receiving zoledronic acid (76%) compared with those treated with pamidronate (63%).

"Among patients who had a low baseline BALP level, the survival rates were similar for both treatment groups," Dr. Berenson reported. "However, among patients with a high baseline BALP level, zoledronic acid treatment significantly improved survival—82%—at study end compared with pamidronate—55%."

This exploratory analysis "suggests that zoledronic acid treatment may improve survival compared with pamidronate, and this effect was observed primarily in patients who had a high baseline BALP level, indicating more aggressive osteolytic disease," Dr. Berenson said.