Clodronate appeared safe, modestly affected breast cancer disease events

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A recently presented study revealed that the bisphosphonate clodronate had a low incidence of adverse events and toxicity among patients with breast cancer and may modestly reduce the incidence of distant metastases in postmenopausal women.

The results of B-34, a prospective, randomized, double-blind, phase 3 clinical trial, presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 6-10, 2011, are similar to those of trials on other bisphosphonates in this group of patients, according to Alexander H.G. Paterson, M.D., professor in the departments of medicine and oncology at the University of Calgary in Canada.

He and his colleagues enrolled 3,323 patients with stage I, II or III breast cancer between Jan. 22, 2001, and March 31, 2004. Paterson presented data on the 3,311 patients (99.6 percent) with follow-up information. Slightly more than 75 percent of the patients had pathologically negative axillary nodes, 64 percent were 50 years or older at entry and 22 percent had estrogen receptor (ER)-negative or progesterone receptor (PgR)-negative breast cancer.

Researchers randomly assigned patients to receive three years of clodronate or an oral placebo three times a day. In addition, the patients also underwent surgery (lumpectomies or mastectomies) and received radiation therapy and chemotherapy or hormonal therapy. Median follow-up for patients who were still alive was 7.6 years.

Five hundred ninety-eight patients experienced disease events, defined as any cancer (either recurrent breast cancer or a new primary) or death (cancer related or otherwise): 286 in the clodronate group and 312 in the placebo group. The relative reduction of events in the clodronate group was about 9 percent compared with the placebo group.

"This reduction was smaller than had been hoped for and was not statistically significant," Paterson said.

Researchers observed a 16 percent relative reduction in mortality in the clodronate group. They also observed relative reductions of 23 percent and 26 percent in the clodronate group for the occurrence of skeletal and nonskeletal metastases, respectively.

"Although clodronate appeared more favorable for all endpoints, only the comparisons of the distant metastasis-free interval and nonskeletal metastasis-free interval were statistically significant and favorable for the clodronate patients," Paterson said.

Results also demonstrated that clodronate might perform better for patients aged 50 years or older when diagnosed with breast cancer and for women with ER/PgR-positive nodes. Clodronate was generally tolerable, and the toxicities observed were mainly due to concomitant systemic chemotherapy, according to the researchers. This was the largest study to assess clodronate in a placebo-controlled trial, Paterson said.

"At this point, clinical indications are not absolute, but a tolerable agent that has a known beneficial effect on osteopenia with a small reduction in distant disease recurrence may be of interest to some patients and clinicians," he said. "The current trials of targeted RANK-ligand inhibitors against placebo are of great interest."