Bone drug suppresses wandering tumor cells in breast cancer patients

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The bone-strengthening drug zoledronic acid (Zometa) can help fight metastatic breast cancer when given before surgery, suggests research at Washington University School of Medicine in St. Louis.

When the drug was given along with chemotherapy for three months before breast cancer surgery, it reduced the number of women who had tumor cells in their bone marrow at the time of surgery.

The study was published in the May issue of *The* Lancet Oncology.

Every day, tumors shed thousands of cells, which spread throughout the body and are referred to as disseminated tumor cells (DTCs). Breast cancer DTCs often lodge in bone marrow where bone growth factors help them survive.

Chemotherapy can increase bone turnover and bone growth factors, potentially exacerbating the problem of DTCs in the bone, which can resurface later to cause metastatic disease in cancer patients.

"Bone marrow seems to be a DTC sanctuary, allowing them to adapt and disseminate to different organs, where they're a leading cause of death," says study leader Rebecca Aft, MD, PhD, associate professor of surgery and a breast cancer specialist at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. "We believe that zoledronic acid inhibits the release of growth factors that help support the growth of DTCs."

Zoledronic acid is generally prescribed to reduce and delay bone complications due to multiple myeloma and bone metastases from solid tumors. Two recent studies showed that zoledronic acid improves disease-free survival when used along with estrogen-lowering therapy before breast cancer surgery. Estrogen-lowering therapy, like chemotherapy, potentially increases bone loss.

In this randomized phase II clinical trial, researchers split 109 women with newly diagnosed stage II or stage III breast cancer into two groups. The control group received chemotherapy alone, while the other received a combination treatment of chemotherapy and zoledronic acid.

After three months of therapy, patients with DTCs in their bone marrow decreased from 43 percent to 30 percent in the combination group, compared with a decrease from 48 percent to 47 percent in the control group. This result approached statistical significance.

The researchers also found that of those patients who had no DTCs in their bone marrow at the start of the study, 87 percent remained negative after three months of combination treatment compared to 60 percent of those who received chemotherapy alone, a result that was statistically significant.

Zoledronic acid treatment with chemotherapy had additional benefits. Women in the combination group experienced significant gains in bone density after 12 months. This is helpful for breast cancer patients, who often develop osteoporosis as a side effect of chemotherapy and other breast cancer treatments.

The study also suggested that zoledronic acid may help fight certain types of breast tumors directly. Aft speculates that the drug may stop the tumor from making its own blood supply, modify the immune system in a way that makes it harder for tumor cells to survive or even cause the cancer cells to commit suicide.

"Although it's common practice to administer zoledronic acid during chemotherapy given after breast cancer surgery, it isn't common when chemotherapy is given before surgery," Aft says. "Because chemotherapy increases bone loss, we

would argue that women should receive zoledronic acid at the time of chemotherapy in the presurgical setting. Our single-institutional study also suggests that similar protocols using zoledronic acid for high-risk breast cancer patients should continue to be tested in larger, multi-institutional studies."

Provided by Washington University School of Medicine