February 12, 2009

Bone Drugs May Help Fight Breast Cancer

By GINA KOLATA

A drug of a class commonly used to combat bone loss may reduce by a third the chance that some breast cancers will spread or recur, a large study has found.

While it may sound odd to treat cancer with a drug that acts on bone, evidence is accumulating that such drugs may do more than just prevent the loss of bone. Other studies are testing the drugs in patients with prostate or lung cancer.

The new study, published in Thursday's New England Journal of Medicine, involved 1,803 premenopausal women with tumors that were fueled by estrogen. As part of their treatment, all received drugs that shut down their ovaries, preventing them from making estrogen, along with drugs that stymie cancer cells from using estrogen to grow.

Half also got the bone drug zoledronic acid, or Zometa, as an intravenous infusion twice a year for three years. Those who took the drug had a 36 percent reduction in cancer recurrences and metastases, compared with women who did not get it. After nearly four years, 54 women who received zoledronic acid and 83 who did not had a recurrence of their cancer or had a new cancer in the opposite breast or a metastasis to their bones.

Some cancer researchers said they wanted to see the results from two other large studies of bone drugs and breast cancer before advocating that all women with breast cancer get such drugs. The studies, which include both premenopausal and postmenopausal women, are nearing completion, and their results should be available within the next few years. But the new study has buoyed researchers' hopes.

"This is really a landmark study," said Dr. James N. Ingle, head of the breast cancer research program at the Mayo Clinic Cancer Center. "It's a reason for real enthusiasm."

But for now, he said, "I think it is the general consensus that we are not ready to make this a standard treatment."

Others are more persuaded.

Dr. Marc E. Lippman, a breast cancer expert who is chairman of the department of medicine at the University of Miami, said many women taking hormonal therapy for breast cancer already take drugs to protect their bones. The hormonal therapy deprives the body of the bone-building effects of estrogen. So, he said, why not give these women zoledronic acid, the bone drug used in the study?

"This is something of a mitzvah," Dr. Lippman said. "The very therapy you might want to do to

counteract the toxicity" of the hormonal therapy "has an additional advantage."

"I think you have to give it," he said.

The idea of using a drug like zoledronic acid arose from research into why some cancers, like breast cancers, have a predilection to spread to bone.

One reason, Dr. Ingle said, is that cancer cells interact with a type of bone cell, osteoclasts, whose role is to break down bone. Breast cancer cells that migrate to the bones stimulate osteoclasts. Osteoclasts then produce substances that stimulate the cancer cells.

"You get this vicious cycle," he said.

Drugs used to treat osteoporosis, the bone-thinning disease that often occurs in the elderly, home in on osteoclasts and stop them from releasing substances that cause bone loss. As the osteoclasts stop working, they die.

So the idea arose: Perhaps osteoporosis drugs might prevent cancer cells from growing in bones.

Other studies of the osteoporosis drugs, known as bisphosphonates, indicated that they might also have other anticancer effects. In the laboratory, at least, they stopped cancer cells from growing new blood supplies. And bisphosphonates made cancer cells self-destruct in laboratory studies.

In addition, said Dr. Eric P. Winer, a breast cancer specialist at the Dana-Farber Cancer Institute in Boston, still other studies indicated that bisphosphonates affected how well cancer cells stuck to surrounding tissue and whether they were able to invade other tissue and proliferate.

And, said Dr. Michael Gnant of the Medical University of Vienna, the lead author of the new study, recent research indicates that particularly in the early stages of many cancers, there is a population of tumor cells that migrate to the bones and hide in bone marrow. Bisphosphonates, he said, might squelch those cells, affecting the ability of the disease to recur.

"This is a general mechanism for all cancers," Dr. Gnant said. "Not just cancers that metastasize to bone."

The idea for the cancer studies began when researchers, like Dr. Trevor J. Powles, a professor of breast oncology at Parkside Oncology in London, started asking whether bisphosphonates could treat cancer that had already spread to bone. They could, it turned out, and zoledronic acid and other bisphosphonates were subsequently approved for that use and shown to prevent further spread of cancer in bones. In fact, Zometa is approved only for bone complications of cancer, like fractures — it is not licensed as an osteoporosis drug.

Those discoveries led Dr. Powles and his colleagues and, independently, two other groups of researchers, to ask whether the drugs, in the high doses used to treat cancer, might prevent breast cancer from spreading in the first place.

The results, published a few years ago, were mixed. Dr. Powles's study found that when women took a bisphosphonate their cancer was less likely to spread to their bones and they lived longer. Another study also found that the cancer was less likely to spread. But the third study found no effect.

Dr. Gnant, in the meantime, had begun a much larger study with intravenous zoledronic acid at a much lower dose, given twice a year for three years. The concern with the drug is a rare and very serious side effect, osteonecrosis of the jaw. But in this study at least, it did not occur.

And the surprising result of his study, if it holds up, indicates that zoledronic acid could add a benefit to existing breast cancer therapy that is nearly the same magnitude as the benefit conferred by chemotherapy or hormonal therapy alone.

But Dr. Gnant urges caution.

"While everyone is very excited, we still need to be conservative about what we recommend to patients," he said. "In clinical science we do clinical trials. I am still hesitating to say, 'Well, this is good for everyone.' In the history of science we sometimes extrapolated and turned out to be absolutely wrong."

"The right way to proceed," Dr. Gnant said, "is to wait for data to come in from other studies."
