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Late treatment with letrozole can reduce breast cancer recurrence risk

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Treatment with the aromatase inhibitor letrozole (Femara) can reduce the risk of breast cancer recurrence even when initiated one to seven years after a course of tamoxifen therapy. The results of a study involving women originally in the placebo arm of an international trial of letrozole will appear in the *Journal of Clinical Oncology* and are receiving early online release.

Among those who chose to begin letrozole treatment after the initial trial was halted, the risk that their cancer would recur was cut in half compared with those who never received letrozole. In addition, the risk of metastasis was 60 percent lower with letrozole, and the chance that a new tumor would develop in the unaffected breast dropped more than 80 percent.

“It appears that estrogen-sensitive tumors remain hormone dependent and that patients’ survival can be improved with careful use of aromatase inhibitors, even many years after completing tamoxifen treatment,” says Paul E. Goss, MD, PhD, director of Breast Cancer Research at Massachusetts General Hospital Cancer Center, who led both the current study and the earlier investigation, called the MA.17 trial. “These results can be put into practice right away to improve the outlook for women treated for receptor-positive breast cancer.”

Letrozole is one of a class of drugs called aromatase inhibitors that suppress the production of estrogen, which stimulates the growth of breast tumors expressing the estrogen receptor. The most widely used

estrogen-blocking drug is tamoxifen, but the benefits of tamoxifen treatment drop significantly after five years, while the drugs' side effects continue.

The original MA.17 trial, conducted through the National Cancer Institute of Canada, was designed to test whether letrozole could reduce tumor recurrence and increase survival in breast cancer patients who had completed five years of tamoxifen treatment. The study was halted in October 2003 – a year earlier than planned – when interim data analysis showed that tumors of women taking letrozole were significantly less likely to recur. The final analysis of MA.17 data, published in the September 7, 2005 Journal of the National Cancer Institute, confirmed that women taking letrozole had significantly better disease-free survival than those taking a placebo.

Since women who received letrozole in the MA.17 trial began taking the drug within a few months of stopping tamoxifen treatment, letrozole's current approval restricts the initiation of therapy to the first three months after tamoxifen discontinuation. However, participants in the placebo arm of the MA.17 trial were offered the opportunity to begin letrozole treatment when that trial was halted, which gave investigators the opportunity to determine whether those women could also benefit from the drug.

The current study analyzes data on more than 1,500 women from the placebo group who chose to take letrozole and about 800 who chose no further treatment. Almost three years after the MA.17 trial was halted and letrozole offered, those who began letrozole therapy had only a 2 percent risk of tumor recurrence, compared with almost 5 percent in those choosing no treatment. The risk of death from breast cancer during that period was cut in half in those receiving letrozole. Treatment also reduced the risk of metastasis by 61 percent and appeared to prevent development of a new tumor in the opposite breast by 82 percent.

The research team notes that this study is limited by the fact that participants choose whether to take the drug themselves and were not randomly assigned. While a randomized clinical trial would more conclusively determine the benefit of letrozole treatment for those who have been off tamoxifen for several months or years – or even those who never took the drug – the results of this study can help guide physicians and patients in deciding whether letrozole therapy would be appropriate.

“Every patient who has previously taken tamoxifen should discuss these new results with her oncologist. The risk that hormone-dependent breast cancer will recur continues indefinitely, and our results imply that aromatase inhibition is effective whenever initiated,” says Goss, a professor of Medicine at Harvard Medical School

Source: Massachusetts General Hospital