Rare Side Effect Is Seen in Long-Term Use of a Breast Cancer Drug

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A new report suggests that a drug widely used to prevent the recurrence of breast cancer may have a rare but dangerous side effect: increasing the odds that long-term users may develop an uncommon but aggressive new tumor.

But medical experts were quick to question the significance and methodology of the study, saying clinical trials had repeatedly found that the drug, tamoxifen, reduced the recurrence and spread of common breast cancers and that its benefits exceeded any possible risks.

Even the author of the report, which is based on an observational study and not the kind of randomized, controlled clinical trial considered the gold standard in medicine, said the findings should not affect practice because the drug's benefits were well established.

"All treatments have risks associated with them," said Dr. Christopher I. Li, an associate member of the Fred Hutchinson Cancer Research Center in Seattle and the first author of the study, which appeared Tuesday in Cancer Research. "Here we're adding another potential risk to the risk side of the equation for tamoxifen. But the broader context is that tamoxifen lowers a patient's risk of dying of the disease."

Tamoxifen, which blocks the effects of estrogen, significantly reduces the recurrence and spread of estrogen-sensitive cancers, which are the most prevalent.

The new study, which assessed the likelihood of developing a new cancer in the second breast, found that women who took tamoxifen for five years or more were 60 percent less likely than nonusers to develop a new estrogen-sensitive tumor in the second breast, and 40 percent less likely to develop a new tumor of any kind in the second breast.

But the study also found that the long-term tamoxifen users were possibly four times as likely as nonusers to develop a new tumor that was not estrogen-sensitive. Those tumors are harder to treat, but also relatively rare; only 1 in 7 of the women studied who developed a cancer in the second breast had the kind of tumor that falls into this category.

The finding of a four-fold increase was questionable both because the number of women who developed the unusual tumor was small, and because women who took tamoxifen for one to four years were not affected, statisticians said.

Dan Berry, a biostatistician with the M. D. Anderson Cancer Center in Houston, said the findings might well be "a statistical fluke."

"This is what we call a case control study, and we all know the problems associated with these studies," Dr. Berry said. "Case control studies showed conclusively that

hormone replacement therapy protected women from cardiovascular disease, which turned out to be not only wrong but in the wrong direction."

The study assessed the history of tamoxifen use among more than 1,000 breast cancer survivors from the Seattle-Puget Sound region who learned they had an estrogen-sensitive breast cancer when they were 40 to 79 years old. It compared the histories of 358 women who developed a new cancer in the second breast with 674 women who did not develop a second cancer. Most of the women who took hormonal therapy used tamoxifen.

Several breast cancer experts said they were concerned that breast cancer patients who heard about the new study might stop taking their tamoxifen, even though the main reason to take the drug is to prevent the cancer they already have from recurring and spreading, which can lead to death.

"You have to keep in mind, this drug isn't being given to women to prevent cancer in the other breast — it's to prevent cancer from spreading to the bones and the liver and the lungs," said Dr. Eric Winer, director of the breast oncology center at the Dana-Farber Cancer Institute in Boston. "We know from other studies that in this setting, tamoxifen is able to lower the chance the cancer will spread to other parts of the body and improve overall survival."