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# Good News on Evista Comes Too Late for Some

*By ACSH Staff — April 28, 2006*

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The National Cancer Institute-sponsored STAR (Study of Tamoxifen and Raloxifene) trial [2] brings good news for women, especially those at higher than average risk of breast cancer. Lilly's estrogen modulator, raloxifene (Evista), prevented breast cancer just as efficiently as the only drug approved by the Food and Drug Administration (FDA) for this purpose, tamoxifen. Both drugs reduced the risk of invasive breast cancer in postmenopausal women by about half (though tamoxifen -- which has been used to treat breast cancer for over twenty-five years and to prevent it since 1998 -- also lowered the risk of non-invasive ductal lesions, while raloxifene did not). Moreover, Evista was safer than tamoxifen, with fewer clots, uterine cancer and cataracts.

Evista was approved in 1998 to prevent and treat osteoporosis, the bone-thinning disorder that mainly affects older women and can cause debilitating fractures. The study of raloxifene's effect on bone mineral content was called the MORE trial (Multiple Outcomes of Raloxifene Evaluation). Lilly conducted that study to support its application to the FDA for Evista's osteoporosis indication -- but one of the secondary results of MORE was showing that the drug reduced the rate of breast cancer by about three-quarters. It reduced the rate even more in women with tumors that had estrogen receptors, who were the majority. In those estrogen receptor positive women, the group taking Evista saw a 90% reduction in new breast cancers.

So why did high-risk women have to wait so long for these results? The efficacy of Evista as a cancer preventive agent seemed sufficiently documented after the MORE trial was published, seven years back, to have allowed doctors and patients to have the FDA's blessing for such use. While the newer data is welcome, in this case the price paid to get it was withholding a safe and effective drug from those who could most benefit from it. While there's no such thing as a completely safe drug, the FDA focuses on risks to an excessive degree. What about the risk to patients who are forbidden to have a nuanced discussion with their caregivers about drugs like Evista due to excessive concern about risk emanating from the FDA?

Since doctors can prescribe any approved drug approved for other uses, a practice termed "off-label use," doctors who wanted to prescribe Evista to patients for prevention of breast cancer could do so. But such prescribing puts the doctor at some risk of liability, and many patients are put off when the doctor discusses off-label use.

Yet, the use of Evista to prevent breast cancer in high-risk women has even today not been approved by the FDA. Fortunately, the new results (which have not yet been published formally and will be discussed in detail at cancer meetings in June) will support Lilly's application for this use from the FDA, and it's likely that the agency will grant approval within a short time. Any extra ammunition in the fight against breast cancer is welcome, as this disease is the most common

cause of cancer in women (lung cancer is the most common cause of cancer *death* in women, as it is in men).

The STAR results raise questions along with answers: are trials underway to evaluate the efficacy of Evista as a therapy for secondary treatment of diagnosed breast cancer? How would Evista stack up against the newer aromatase inhibitors against breast cancer -- both as a preventive and as treatment? Is there any added value in comparing one type of drug against another for the same use, instead of against a placebo -- and if so, is it worth the extra time and expense? What about chemoprevention for younger women at high risk -- chemoprevention that does not involve shutting down estrogen production and producing a chemical menopause, as all the current drugs do? Will Evista now largely replace tamoxifen in the treatment of previously-diagnosed breast cancer?

Will we have to wait another seven years for these answers?

Beginning this year, the FDA has instituted several reforms in its drug evaluation process, collectively called "the Critical Path Initiative." This new approach includes methods to streamline evaluation and approval of new cancer therapies and preventatives. I wonder if this new philosophy would have accelerated the process of getting Evista information out to doctors and patients years ago and perhaps have saved some women from needless illness and death. Let us hope that it will do so in the future.

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