

Does tamoxifen prevent breast cancer?

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■ EVIDENCE-BASED ANSWER

Tamoxifen prevents breast cancer in women older than 60 years and in younger women with equally high risk because of breast disease and reproductive and family history, but there is no current evidence for or against long-term survival or overall health benefits.^{1,2} (Grade of recommendation A: randomized controlled trials [RCTs]) a 49% reduction in 5-year incidence of invasive and noninvasive breast cancer but increased risk for endometrial cancer, pulmonary emboli, deep vein thrombosis, and cataracts. The long-term benefits and overall health effects of tamoxifen for primary prevention of breast cancer remain unclear; the ongoing International Breast Cancer Intervention Study trial is designed to address this question.

■ EVIDENCE SUMMARY

There have been 3 RCTs of tamoxifen for primary prevention of cancer. The best, by Fisher and colleagues,² reported a 49% ($P < .001$) reduction in incidence of invasive breast cancer and 50% in noninvasive breast cancer ($P < .002$) among women with a 5-year risk of breast cancer $\geq 1.66\%$ based on the Gail Risk Index (<http://bcra.nci.nih.gov/brc/>). Estrogen receptor (ER)-negative breast cancers were unaffected. See the for summary of risks and benefits.

Veronesi and coworkers³ reported no overall benefit from treatment with tamoxifen in low-risk hysterectomized women, but the trial was underpowered, had a high dropout rate in the first year, and allowed hormone replacement therapy (HRT).

Powles and colleagues⁴ reported no benefit from tamoxifen in young women with at least one first-degree relative with breast cancer. HRT was allowed, and the study had 90% power to detect a reduction of 50% in breast cancer incidence. Authors estimated that 36% of participants and 60% of women who developed breast cancer had a greater than 80% chance of having a breast cancer predisposition gene. Breast cancers in women with the Breast Cancer 1 gene (BRCA1) are more likely to be ER negative.

The optimal duration of treatment for primary prevention has not been determined. Fisher and coworkers⁵ reported that women given tamoxifen for only 5 years for ER-positive breast cancer with negative nodes had improved disease-free survival compared with women randomized to continue tamoxifen more than 5 years (92% vs 86% respectively, $P = .003$).

■ RECOMMENDATIONS FROM OTHERS

Canadian Task Force on Preventive Health Care and the Canadian Breast Cancer Initiatives Steering

Committee on Clinical Practice Guidelines: Evidence supports counseling women at high risk (Ž 1.66% over 5 years) on the potential benefits and harms. There is fair evidence to recommend against the use of tamoxifen to reduce the risk of breast cancer in women at low or normal risk of disease (Grade D recommendation)."⁴

CLINICAL COMMENTARY

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Counseling patients is difficult because of conflicting data. Based on the US trial, I explain that, at best, using tamoxifen to treat 1000 high-risk women for 5 years would prevent 17 cases of invasive breast cancer and 7 cases on noninvasive breast cancer while contributing to at least 9 adverse events, including 7 uterine cancers and 2 pulmonary emboli.² I find that each patient weighs the risks and benefits differently. Keep in mind, with an average wholesale price of \$3.75 per day, 5 years of tamoxifen therapy costs approximately \$402,000 to prevent 1 case of invasive breast cancer. Other treatment options include raloxifene and bilateral prophylactic mastectomy.

R E F E R E N C E S

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3. Veronesi U, Maisonneuve P, Costa A , et al. *Lancet* 1998;352:93–97.
4. Powles T, Eeles R, Ashley S , et al. *Lancet* 1998;352:98–101.
5. Fisher B, Dignam J, Bryant J , et al. *JNCI* 1996;88:1529–42.