

5 years of tamoxifen improves 15-year survival by about a third in women with most common type of breast cancer

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In women with hormone-sensitive breast cancer (ie, oestrogen-receptor (ER) positive breast cancer), further benefits of adjuvant tamoxifen continue to accrue for at least 10 years after women stop taking the drug, according to an **Article** published **Online First** in *The Lancet*. The findings suggest that full compliance with 5 years of daily tamoxifen therapy would reduce the long-term chances of dying from breast cancer by at least a third.

Various treatments can be given after apparently successful breast cancer surgery to prevent any microscopic residual fragments eventually causing incurable breast cancer recurrence and death, and many randomised trials of them have been conducted. Every 5 years for the past 25 years the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) has brought together all the evidence in the world from all of these trials.

The EBCTCG now report meta-analyses of individual patient data for over 20 000 women with early breast cancer in 20 randomised trials of about 5 years of tamoxifen versus no tamoxifen, with about 80% compliance with the randomly allocated treatment. Most of the trials of 5 years of tamoxifen began in the 1980s. Long-term follow-up now reveals large additional effects on breast cancer mortality more than 10 years after treatment began.

The researchers found that in ER-positive disease 5 years of daily tamoxifen safely reduced the long-term (15-year) risks of breast cancer recurrence and death. It was effective whether or not chemotherapy had been given. Importantly, even in weakly ER positive disease, tamoxifen substantially reduced the likelihood of the cancer recurring.*

Remarkably, the risk of dying from breast cancer was reduced by about a third throughout the 15 years after beginning treatment—there was a highly significant reduction in breast cancer mortality not only during years 0-4 and 5-9 but also during years 10-14.

Aromatase inhibitors (AIs), a newer class of drugs, offer an alternative to tamoxifen for some patients, but AIs are effective only in post-menopausal women.**Worldwide, half of all new patients with breast cancer (0.7 million out of 1.4 million a year) are younger than 55 years. The authors point out that, especially for pre-menopausal or peri-menopausal women who have had a breast cancer removed that is ER-positive, 5 years of tamoxifen remains a major hormonal treatment option. Moreover, they note, the rare life-threatening side-effects of tamoxifen (uterine cancer and venous thromboembolic events such as blood clots) are mainly experienced by women over 55 years of age, so there is little risk from giving tamoxifen to younger women.

Christina Davies, a lead EBCTCG investigator, concludes: "Breast cancer is a nasty disease because it can come back years later. This study now shows that tamoxifen produces really long-term protection. For ER-positive disease, tamoxifen reduces 15-year breast cancer mortality by at least a third, whether or not chemotherapy has been given. Tamoxifen was developed 50 years ago and is long out of patent, but even if costs are ignored it remains a major first-line treatment option, especially for women whose ovaries are still functioning."***

In a linked [Comment](#), Dr Stephen K Chia, British Columbia Cancer Agency, University of British Columbia, Vancouver, Canada, and Dr Antonio C Wolff, The John Hopkins Kimmel Comprehensive Cancer Centre, Baltimore, MD, USA , say: “We can confidently and clearly state that tamoxifen is an important treatment option for early-stage ER-positive breast cancer, whether or not chemotherapy is also given... Breast cancer is the most common female cancer worldwide. ER-positive phenotype is the most common, and half of the 1·4 million diagnoses worldwide every year occur in premenopausal or perimenopausal women for whom aromatase inhibitors are ineffective. Therefore, access to accurate ER testing, and to tamoxifen (a relatively inexpensive drug) or other endocrine therapies is a public health imperative for all women with breast cancer.”

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For full **Article** and **Comment**, see: <http://press.thelancet.com/tamoxifen.pdf>

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Notes to Editors: *A simple test on surgically removed breast cancers finds some to be ER-negative, but most are ER-positive (in countries such as the US or UK, about 4 out of 5 breast cancers are ER-positive). Tamoxifen acts on the ER protein in breast cancer cells, but it can do this only if those cells contain some ER protein.

**ER-positive breast cancer is the most common of the two main types of breast cancer and its growth is stimulated by the body's own oestrogen, which binds to the oestrogen receptor (ER) protein in the cancer cells. This circulating oestrogen comes mainly from the ovaries in premenopausal women, but it comes mainly from other parts of the body in postmenopausal women. Tamoxifen prevents oestrogen binding to the ER protein. Aromatase inhibitors are drugs that prevent oestrogen synthesis only in places other than the ovaries, so they are useful only in postmenopausal women.

***Quote direct from authors, and cannot be found in text of **Article**.