

## Long-term tamoxifen use increases risk of aggressive secondary tumours

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While long-term tamoxifen use among breast cancer survivors decreases their risk of developing oestrogen receptor-positive (ER-positive) second breast cancer, such use is associated with a more than 4-fold increased risk of developing oestrogen receptor-negative (ER-negative) contralateral breast cancer.

The findings are published in the online August 25 issue of the journal Cancer Research.

Hormonal therapy with drugs like tamoxifen is one of the most common treatments for breast cancer because it has been shown to reduce the risk of dying from the disease but, as this study suggests, it does have risks.

Comparing breast-cancer patients who received t tamoxifen to those who did not, the researchers found that while the drug was associated with a 60% reduction in oestrogen receptor-positive (ER-positive) second breast cancer, it also appeared to increase the risk of ER-negative second cancer by 440%.

"This is of concern, given the poorer prognosis of ER-negative tumours, which are also more difficult to treat," Christopher Li, MD, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington.

These findings confirm preliminary research by Li and colleagues, published in 2001, which was the first to suggest a link between long-term tamoxifen use and an increased risk of ER-negative second cancers.

"The earlier study had a number of limitations. For example, we did not have information on the duration of tamoxifen therapy the women received," said Dr. Li. "The current study is larger, is based on much more detailed data, and is the first study specifically designed to determine whether tamoxifen use among breast cancer survivors influences their risk of different types of second breast cancers."

The present study assessed history of tamoxifen use among 1,103 breast cancer survivors from the Seattle-Puget Sound region who were initially diagnosed with ER-positive breast cancer between the ages of 40 and 79.

Of these, 369 of the women went on to develop a second breast cancer. Nearly all of the women in the study who took adjuvant hormonal therapy used tamoxifen specifically. Detailed information about tamoxifen use was ascertained from telephone interviews and medical record reviews.

While the study confirmed a strong association between long-term tamoxifen therapy and an increased risk of ER-negative second cancer, it does not suggest that breast cancer survivors should stop taking hormone therapy to prevent a second cancer, Dr. Li said.

"It is clear that oestrogen-blocking drugs like tamoxifen have important clinical benefits and have led to major improvements in breast cancer survival rates," said Dr. Li. "However, these therapies have risks, and an increased risk of ER-negative second cancer may be one of them. Still, the benefits of this

therapy are well established and doctors should continue to recommend hormonal therapy for breast cancer patients who can benefit from it."

Dr Alison Ross, senior science information officer at Cancer Research UK, said: "Women should be reassured that, based on extensive scientific evidence, the benefits of taking hormone-blocking drugs, such as tamoxifen, after their first diagnosis of breast cancer far outweigh any potential risks.

"More research will be needed to confirm the possible link between its long-term use and the relatively rare occurrence of an aggressive form of the disease in the other breast."

**Source:** Fred Hutchinson Cancer Research Center

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