

# Toxicity of aromatase inhibitors may explain lack of overall survival improvement

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The toxicities associated with aromatase inhibitors (AIs) may explain the lack of overall survival improvement compared with tamoxifen, according to a study published August 22 in the *Journal of The National Cancer Institute*.

AIs are a class of drugs used to treat [breast cancer](#) in postmenopausal women. The drugs are normally taken as an alternative to tamoxifen or after initial treatment with tamoxifen. In general, they are associated with a reduction in [breast cancer recurrence](#) but not in improved survival. Furthermore, the drugs are associated with a number of concerning adverse toxic effects compared with tamoxifen.

To examine whether the relative toxicity of AIs versus tamoxifen may explain the lack of overall [survival benefit](#) in postmenopausal [breast cancer patients](#), Eitan Amir, MB ChB, of the Division of Medical Oncology and Hematology at Princess Margaret Hospital in Toronto, Ontario and colleagues conducted a systematic review to identify all randomized trials which compared AIs and tamoxifen in postmenopausal women. They then performed a meta-analysis of the data from the selected [randomized trials](#). Their meta-analysis used data from seven trials enrolling 30,023 patients.

The researchers found that compared to tamoxifen, longer use of AIs was associated with increased heart disease and [bone fractures](#), but lower rates of blood clots and cancer of the womb. There were no differences in the risk of stroke or other types of cancer. Furthermore, use of AIs

for 2-3 years after initial treatment with tamoxifen was associated with a lower risk of death unrelated to breast cancer compared to the use of either AIs or tamoxifen alone. The authors therefore concluded that the toxicity of AIs when used for longer periods of treatment may explain the lack of overall survival benefit while still having a positive effect on breast cancer recurrence.

The researchers write, "The cumulative toxicity of aromatase inhibitors when used as up-front treatment may explain the lack of overall survival benefit despite improvements in disease-free survival. Switching from tamoxifen to aromatase inhibitors reduces this toxicity and is likely the best balance between efficacy and toxicity."

In an accompanying editorial, Nancy E. Davidson, M.D., Shannon Puhalla, M.D., and Rachel C. Jankowitz, M.D., of the UPMC Cancer Center at Magee-Womens Hospital, write that, "survival benefits with adjuvant tamoxifen were not truly evident until after 5 years of follow-up. Thus, it is conceivable that a late survival advantage with [aromatase inhibitors](#) over tamoxifen may also emerge over time."

The editorialists conclude that doctors should, "choose initial endocrine therapy for the individual patient with careful attention to the risk of breast cancer recurrence, the risk of toxicity, and comorbidities."

Provided by Journal of the National Cancer Institute

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