25-year survival and benefit from tamoxifen therapy by the clinically used breast cancer markers in lymph node-negative and ER-positive / HER2-negative breast cancer

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Background
The clinically used breast cancer markers are known to predict short-term survival, but whether these markers predict long-term (25-year) survival is unclear.

Conclusion
In this randomized trial of n=565 postmenopausal lymph node-negative patients with estrogen receptor (ER)-positive / HER2-negative breast cancer, our findings indicate that for this selected subgroup tumor size followed by grade are significant long-term prognosticators. Further, a significant long-term benefit from tamoxifen therapy was seen in patients with larger tumor size, lower tumor grade and PR-positive tumors.

Research questions
Are the clinically used markers, i.e. tumor size, grade, progesterone receptor (PR), and Ki-67, independent 25-year prognosticators and predictors of tamoxifen therapy benefit?

Table 1: DRFI by treatment stratified by tumor size, tumor grade, PR status, and Ki-67 status
A statistically significant reduced long-term risk was seen for tamoxifen (TAM) treated patients with larger tumor size and lower tumor grade, as compared to untreated patients. Furthermore, treated patients with PR-positive disease had a reduced long-term risk as compared to untreated patients, in contrast to PR-negative patients with no significant long-term benefit of tamoxifen treatment. Finally, treated patients with both Ki-67-medium/ high and Ki-67-low disease had a reduced long-term risk.

Figure 2. Kaplan-Meier analysis of DRFI by Tumor size, grade, PR, and Ki-67 status.
A statistically significant reduced long-term distant recurrence-free interval (DRFI) was seen for patients with (A) smaller tumor size and (B) lower tumor grade as compared to patients with larger (T2) tumor size and grade 3 tumors, respectively. A statistically significant difference in long-term DRFI was seen not seen by (C) PR and (D) Ki-67 status.

Figure 1. Consort diagram for the STO-3 trial
Secondary analysis of the Stockholm Tamoxifen (STO-3) trial conducted from 1976-1990, randomizing postmenopausal lymph node-negative breast cancer patients to adjuvant tamoxifen therapy.

Author disclosures
All authors declare there are no conflicts of interest.