# 20-year benefit from tamoxifen therapy in ER-positive/HER2-negative breast cancer patients in the Stockholm tamoxifen randomized trials

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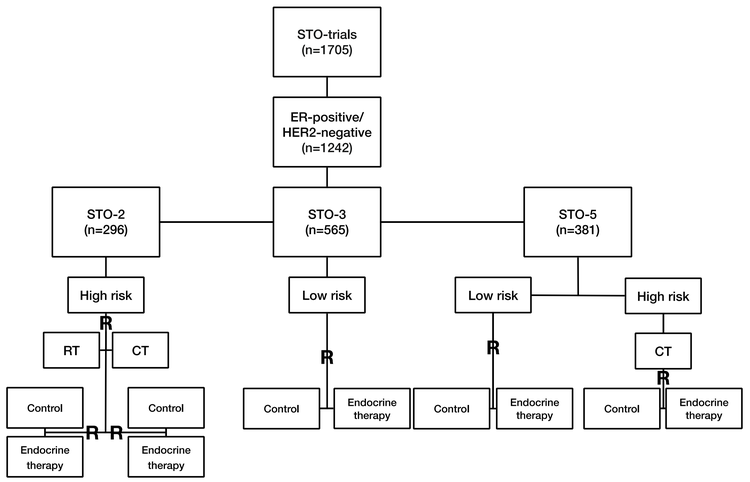
## Background

Adjuvant tamoxifen (TAM) therapy reduces the risk of recurrence and improves patient survival in ER-positive breast cancer, however not all patients benefit from TAM therapy. Given the late onset of distant recurrence and the lack of clinical studies with long-term follow-up, it is challenging to predict the true long-term benefit of TAM therapy.

## Conclusion

In this randomized trial of n=1242 patients with ER-positive/HER2-negative breast cancer, our findings indicate a long-term benefit from TAM therapy for patients with less aggressive tumor characteristics. However, larger and not smaller tumor size was associated with significant long-term TAM benefit.



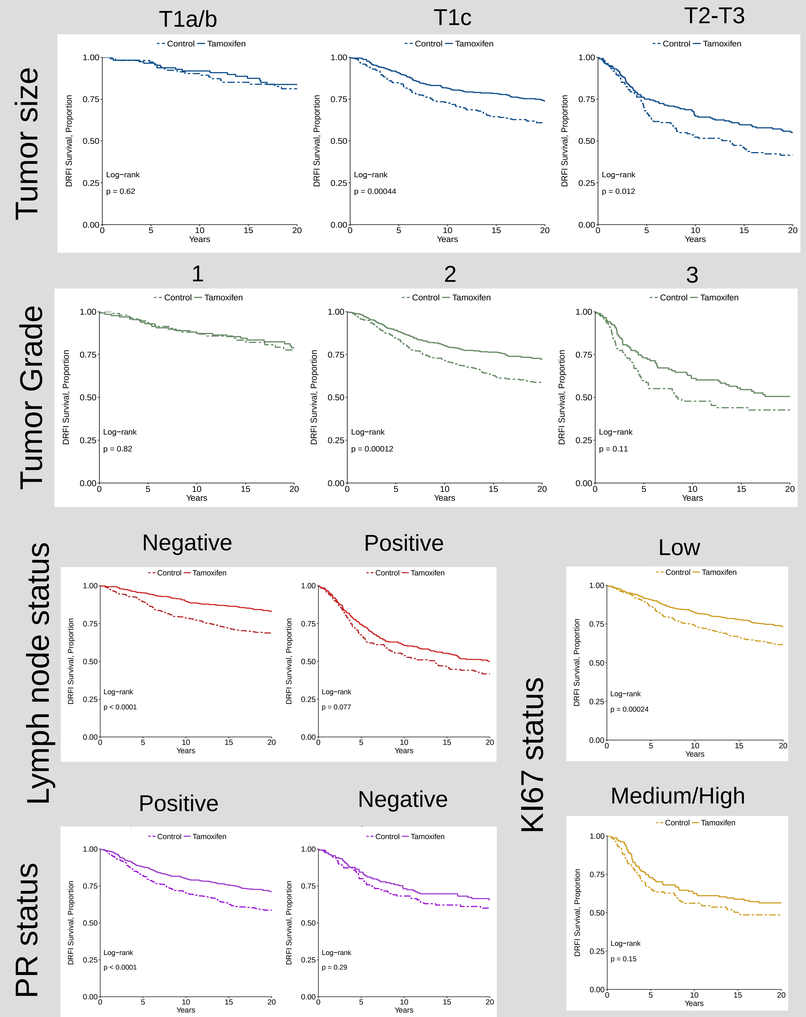

## Figure 1. Consort diagram for the STO-trials

Secondary analysis of patients from the Stockholm tamoxifen (STO)-trials, conducted from 1976 to 1997, randomizing patients to endocrine therapy or no endocrine therapy (control). Patients in the STO-trials have detailed and complete long-term follow-up.

## Author disclosures

All authors declare there are no conflicts of interest.

## Figure 2. Kaplan-Meier analysis of long-term tamoxifen therapy benefit




## Research questions

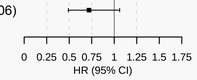
Are the clinically used tumor characteristics, i.e. tumor size, tumor grade, lymph node status, progesterone receptor (PR), and Ki-67, independent 20-year predictors of tamoxifen therapy benefit?

## Figure 3: Multivariable Cox analysis of long-term tamoxifen therapy benefit

A significant long-term TAM benefit was seen for patients with larger tumor size. Furthermore, significant long-term TAM benefit was seen in patients with grade 2 tumors, lymph node-negative tumors, PR-positive tumors and Ki-67-low disease.

**Adjusted estimates for patient and tumor characteristics**

| Clinically used markers | | | Patients No. | Distant recurrences 20 year No. | Risk of distant recurrence HR (95% CI) |
|---|---|---|---|---|---|
| Tumor size | T1a/b | Tamoxifen | 114 | 16 | 0.81 (0.39−1.68) |
| | | Control | 106 | 18 | 1.0 ref. |
| | T1c | Tamoxifen | 381 | 94 | 0.56 (0.42−0.75) |
| | | Control | 267 | 99 | 1.0 ref. |
| | T2−T3 | Tamoxifen | 200 | 84 | 0.67 (0.49−0.92) |
| | | Control | 161 | 90 | 1.0 ref. |
| Tumor grade | Grade 1 | Tamoxifen | 130 | 24 | 0.85 (0.43−1.71) |
| | | Control | 95 | 19 | 1.0 ref. |
| | Grade 2 | Tamoxifen | 445 | 116 | 0.55 (0.42−0.71) |
| | | Control | 350 | 137 | 1.0 ref. |
| | Grade 3 | Tamoxifen | 120 | 64 | 0.91 (0.61−1.38) |
| | | Control | 90 | 89 | 1.0 ref. |
| Lymph node status | Negative | Tamoxifen | 431 | 66 | 0.45 (0.33−0.62) |
| | | Control | 349 | 102 | 1.0 ref. |
| | Positive | Tamoxifen | 272 | 132 | 0.85 (0.64−1.11) |
| | | Control | 190 | 107 | 1.0 ref. |
| PR status | Positive | Tamoxifen | 545 | 146 | 0.59 (0.47−0.75) |
| | | Control | 407 | 160 | 1.0 ref. |
| | Negative | Tamoxifen | 155 | 51 | 0.68 (0.45−1.03) |
| | | Control | 128 | 48 | 1.0 ref. |
| Ki−67 status | Low | Tamoxifen | 524 | 130 | 0.55 (0.43−0.71) |
| | | Control | 393 | 141 | 1.0 ref. |
| | Medium/High | Tamoxifen | 154 | 64 | 0.72 (0.49−1.06) |
| | | Control | 133 | 66 | 1.0 ref. |




HR = hazard ratio, CI = confidence interval, PR-positivity was defined as ≥10%, and Ki-67 threshold for medium/ high expression was 15% or greater. Modeled by multivariable Cox proportional hazard analysis adjusting for age at primary diagnosis, calendar period of diagnosis, tumor size, tumor grade, progesterone receptor (PR) status, Ki-67 status, lymph node status, type of surgery, chemotherapy, and radiotherapy.

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