Effectiveness of switching from adjuvant tamoxifen to anastrozole in postmenopausal women with hormone-sensitive early-stage breast cancer: a meta-analysis

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CRD summary

This review concluded that participants who changed to anastrozole after 2 to 3 years' treatment with tamoxifen had significantly fewer disease recurrences than those remaining on tamoxifen for 5 years. Survival was also significantly improved. Poor reporting of review methodology and the lack of knowledge about the quality of the trials mean that the authors' conclusions should be interpreted with caution.

Authors' objectives

To evaluate whether changing the treatment of postmenopausal women with hormone-sensitive early-stage breast cancer to anastrozole after treatment with tamoxifen for 2 to 3 years would be more effective than continuation on tamoxifen for 5 years.

Searching

PubMed and ClinicalTrials.gov were searched from January 2004 to end of March 2005; the search terms were reported.

Study selection

Randomised controlled trials (RCTs) of postmenopausal women with histologically confirmed hormone-positive early-stage breast cancer that compared switching from tamoxifen to anastrozole to continuing with tamoxifen, and reported overall, disease-free, event-free or distant recurrence-free survival, were eligible for inclusion. Studies assessing a steroidal aromatase inhibitor were excluded. The proportion of participants differed between the trials in terms of node involvement, grading, undergoing previous chemotherapy and type of surgery, and had a median follow-up of 30 months (range: 0 to 89.5)

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality

The authors did not report a validity assessment.

Data extraction

Individual patient data (IPD) were used, stratified by trial in order not to break randomisation. Data from the individual trials were used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs) for survival outcomes.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis

IPD were analysed using a stratified Cox-proportional hazards model. Pooled HRs and 95% CIs were calculated. Each trial was stratified and covariates were age, tumour size, nodal status, grade, surgery and chemotherapy. The results were displayed using forest plots and Kaplan-Meier curves were generated for each outcome. Heterogeneity was assessed using summary statistics from IPD. Two reviewers independently analysed the data.

Results of the review

Three RCTs (n=4,006) were included in the review.

Participants treated with anastrozole had fewer disease recurrences (5% versus 8%) and deaths (3% versus 5%) than those who continued to be treated with tamoxifen. This resulted in significant improvements for participants changing to anastrozole compared with those remaining on tamoxifen for disease-free survival (HR 0.59, 95% CI: 0.48, 0.74,

p<0.0001), event-free survival (HR 0.55, 95% CI: 0.42, 0.71, p<0.0001), distant recurrence-free survival (HR 0.61, 95% CI: 0.45, 0.83, p=0.002) and overall survival (HR 0.71, 95% CI: 0.52, 0.98, p=0.04).

Subgroup analyses showed that the benefits of treatment with anastrozole remained, regardless of nodal or receptor status, previous chemotherapy or tumour size.

There was no evidence of statistical heterogeneity between the studies (data not reported in the review).

Authors' conclusions

Participants who changed to anastrozole after 2 to 3 years' treatment with tamoxifen had significantly fewer disease recurrences than those remaining on tamoxifen for 5 years. Disease-free, event-free and overall survival were also significantly improved for those who changed to anastrozole.

CRD commentary

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. The search was limited, with no attempt to locate unpublished data or any contact with trialists or experts in the field to identify other studies, thereby introducing the potential for publication bias. There is also the potential for language bias since it is unclear if language restrictions were applied. The methods used to select the studies and extract the data were not reported, so it is not possible to determine if appropriate steps were taken to reduce reviewer error or bias. In addition, since trial quality was not assessed and study details were not provided, it is not possible for the reader to evaluate the studies. The authors did not report cross-checking of data to ensure accuracy, or describe how they dealt with missing data; it is therefore not possible to assess the reliability of the findings. The authors reported no evidence of statistical heterogeneity, but did not report the specific methods used. There was evidence of clinical heterogeneity across trials and some potential causes were investigated. In view of the lack of reporting of review methodology and the lack of knowledge about the quality of the trials from which the data were derived, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors stated that clinicians should consider changing treatment to anastrozole for postmenopausal women who have been treated with adjuvant tamoxifen for 2 to 3 years.

Research: The authors stated that further well-designed clinical trials are required to inform treatment strategies, including whether aromatase inhibitors should be offered as initial adjuvant treatment or after 2 or more years' treatment with tamoxifen.

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