Meta-analysis of trials comparing anastrozole and tamoxifen for adjuvant treatment of postmenopausal women with early breast cancer

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CRD summary

This review found that anastrozole was more effective than tamoxifen in adjuvant hormonal treatment of early breast cancer in postmenopausal women, and that aromatase inhibitors should be the initial hormone therapy for its treatment. However, the review did not provide direct evidence for any treatment approach, and this, along with review methodological limitations, imply cautious interpretation of the results.

Authors' objectives

To assess the impact of upfront, switching and sequencing schedules of anastrozole adjuvant treatment in early breast cancer.

Searching

The following sources were searched, with no date restrictions, for trials published in English: PubMed, the Cochrane Library and ClinicalTrials.gov. Search terms were reported.

Study selection

To be eligible, studies needed to be randomised controlled trials (RCTs) that compared anastrozole with another agent in the adjuvant treatment of early breast cancer. There were no dose or schedule restrictions, but dose escalation trials and single arm trials were excluded.

In the included multi-centre trials, percentages of oestrogen receptor-positive patients ranged from 83.7 to 99%, where known. Two trials involved switching to anastrozole or continuing with tamoxifen, after two to three years of tamoxifen. One trial sequenced patients prospectively to anastrozole or tamoxifen after two years of tamoxifen treatment. One trial gave upfront treatment with anastrozole or tamoxifen alone or in combination for five years.

One reviewer selected studies for the review.

Assessment of study quality

Quality was assessed based on method of randomisation and allocation concealment, comparability of baseline treatment groups, reasons for drop-outs, and if there was any evidence of differential drop-outs between treatment arms.

It appeared that quality assessment was conducted by one reviewer.

Data extraction

Trial definitions of event free survival, disease free survival and recurrence free survival were extracted, along with their relevant hazard ratios (HR) and associated confidence intervals (CIs). Where multiple publications related to the same trial, end-point data from the report with the longest follow-up were extracted.

One reviewer extracted data for the review.

Methods of synthesis

Log hazard ratios were weighted by the inverse variance method and combined in meta-analyses. Both fixed-effect and random-effects models were used; fixed-effect model results were reported when both results were nearly identical, in addition to a non-significant heterogeneity test (assessed using the Q statistic). The primary analysis used event free survival rates from all trials except one, where recurrence free survival rates were used due to lack of reporting of event

free survival. Sensitivity analysis excluding this trial was conducted, as were sensitivity analyses including only oestrogen receptor-positive patient groups.

Publication bias was not assessed.

Results of the review

Four RCTs were included in the review (n=13,332 women; sample sizes ranging from 448 to 9,366 women). Results of quality assessment were not presented. Median follow-up ranged from 31 to 68 months.

All trials reported a significant improvement in event free survival with anastrozole compared with tamoxifen; the pooled result reflected this (HR 0.77, 95% CI 0.70 to 0.85).

Excluding the "Arimidex, Tamoxifen Alone or in Combination" (ATAC) upfront trial gave a hazard ratio for event free survival of 0.64 (95% CI 0.52 to 0.79).

The analysis of oestrogen receptor-positive patients gave a combined hazard ratio for event free survival (recurrence free survival for the ATAC trial) of 0.73 (95% CI 0.65 to 0.81).

No statistically significant heterogeneity was noted for any of the analyses conducted.

Authors' conclusions

Anastrozole appeared to be more effective than tamoxifen in the adjuvant hormonal treatment of early breast cancer. Until further clinical evidence becomes available, aromatase inhibitors should be the initial hormone therapy in postmenopausal early breast cancer patients.

CRD commentary

This review was based on defined inclusion criteria for participants, interventions and study design. Criteria on outcomes did not appear to have been pre-specified. Searching encompassed a range of sources, but only English language, published material. The review appeared to have been conducted by one reviewer, which could have allowed the introduction of bias and error into the processes of study selection, data extraction and quality assessment.

Quality was assessed, but results were not presented in full, so the impact on results was unclear. Pooling all the trials may not have been appropriate given the clinical heterogeneity observed. However, sensitivity analyses were conducted to address this issue. Although the finding of overall superiority of anastrozole appeared sound, the review did not provide direct evidence of the superiority of upfront, switching or sequencing approaches to treatment. This, along with limitations identified in the review process, imply caution in interpretation of the results.

Implications of the review for practice and research

Practice: The authors stated that, until further clinical evidence becomes available, aromatase inhibitors should be the initial hormone therapy in postmenopausal early breast cancer patients. Switching should only be considered for patients who are currently receiving tamoxifen.

Research: The authors stated that trials are needed that compare upfront, switching, sequencing and extended hormonal treatment for early breast cancer. The introduction of tamoxifen or another oestrogen antagonist after the completion of aromatase inhibitor therapy may also be a research topic of interest.

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