Systematic review of taxane-containing versus non-taxane-containing regimens for adjuvant and neoadjuvant treatment of early breast cancer

CRD summary
This review assessed the effect of taxanes on response and survival in women with early breast cancer. Ten randomised controlled trials with 12,159 women found that adjuvant taxanes may improve survival. The effect of neoadjuvant taxanes remains uncertain. This review may need early updating as the authors identified 19 other unpublished trials available in abstract form or not yet complete.

Authors' objectives
To assess the effect of taxanes on response and survival in women with early breast cancer.

Searching
The authors searched the Cochrane Breast Cancer Review Group's specialised register (which collates information on RCTs and controlled clinical trials from MEDLINE, EMBASE, PDQ, the Cochrane Library and other online trial registers), abstracts of American Society of Clinical Oncology meetings and San Antonio Breast Cancer Symposium 2003. Only studies available in English were included. Full papers and abstracts were included.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared adjuvant or neoadjuvant chemotherapy with a regimen containing a taxane (paclitaxel and/or docetaxel) versus a regimen without taxanes were eligible for inclusion. The regimens included were heterogeneous.

Participants included in the review
Studies were eligible for inclusion if all participants were women with early breast cancer receiving chemotherapy. The authors did not define 'early' breast cancer. In the included studies, the proportion of women with positive lymph nodes ranged from 41 to 100%.

Outcomes assessed in the review
The authors did not report the outcomes that studies must include in order to be eligible for the review. They reported extracting data on overall survival, relapse-free survival, toxicity, quality of life, and for neoadjuvant studies, clinical and pathological response rates. The median length of follow-up ranged from 43 to 69 months in the included adjuvant studies. Length of follow-up was available for only one of the neoadjuvant studies (35 months).

How were decisions on the relevance of primary studies made?
Two authors screened studies independently based on a list of predefined eligibility criteria. A third author resolved any discrepancies.

Assessment of study quality
The authors reported that they assessed validity based on standardised criteria, but they did not describe these criteria. Two authors rated trial methods independently, using standardised criteria.

Data extraction
One author extracted characteristics of the trials and participants. Two authors extracted outcomes data independently. The authors extracted hazard ratios for overall or disease-free survival, or estimated these data from survival curves.

**Methods of synthesis**

How were the studies combined?
The authors provided a narrative synthesis of the studies. They reported that it was not possible to conduct a meta-analysis because limited survival data were available.

How were differences between studies investigated?
The authors provided a narrative description of differences between the studies.

**Results of the review**

Ten RCTs with 12,159 women were included in the review.

There were no statistically significant differences in complete response among women receiving taxanes in the 5 trials of neoadjuvant therapy (2948 women). The authors reported that 4 out of 5 trials suggested a non significant trend towards improved complete response with taxanes.

Taxanes were associated with a statistically significant improvement in disease-free survival in 3 of the 5 trials of adjuvant therapy (9,211 women). The authors reported that all 5 trials suggested a trend towards improved disease-free survival, regardless of oestrogen-receptor status.

Two trials found a statistically significant improvement in overall survival.

The strongest evidence was for adding four cycles of paclitaxel to four cycles of doxorubicin and cyclophosphamide, or for substituting six cycles of 5-fluorouracil, adriamycin and cytoxan with six cycles of docetaxel, doxorubicin and cyclophosphamide.

**Authors' conclusions**

The findings support the use of adjuvant taxanes in women with early breast cancer and involved lymph nodes. The evidence did not support restricting the use of taxanes to women with hormone-receptor negative status.

**CRD commentary**

The authors used pre-specified inclusion criteria, though they did not seem to pre-specify a definition of ‘early’ breast cancer. The review methods were described and included measures to avoid the introduction of bias. Studies were identified by searching the Cochrane Breast Cancer Review Group's specialised register, which searches appropriate databases, and handsearching. Studies in languages other than English were excluded and this might have introduced bias. Although the authors stated that they assessed validity and that all studies had high ratings for study quality, the criteria on which studies were assessed was unclear. Given the heterogeneity of the studies, the narrative summary appears more appropriate than a meta-analysis.

While the authors’ conclusions seem to follow from the evidence presented, this review is likely to need an early update: the authors identified 19 other unpublished trials with more than 19,000 women that met the inclusion criteria, but were only available in abstract form or had yet to be completed.

**Implications of the review for practice and research**

Practice: The authors concluded that adjuvant taxanes may be beneficial in women with early breast cancer and lymph node involvement.

Research: The authors concluded that longer follow-up of existing trials and data from new trials are needed to clarify the most appropriate use of taxanes in early breast cancer. They noted that 15 relevant trials were underway. They
suggested that future research should compare different taxanes, examine dosing and schedules, assess the benefits for subgroups, and evaluate toxicity.

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