Taxanes as primary chemotherapy for early breast cancer: meta-analysis of randomized trials

CRD summary
This review concluded that the combination of taxanes and anthracyclines as neoadjuvant chemotherapy for early breast cancer improved the chance of achieving higher breast-conserving surgery rates and pathologic complete response rates. This main conclusion followed from the evidence presented, but did not clearly acknowledge limitations of the evidence discussed by the review authors, so it may not be entirely reliable.

Authors' objectives
To establish how much the combination of anthracyclines and taxanes improves patient outcomes compared with standard treatment.

Searching
MEDLINE and the websites of the American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), Federation of European Cancer Societies (FECS) and San Antonio Breast Cancer Symposium (SABCS) were searched for relevant evidence published in any language up to 30 November 2007. Search terms were reported. Reference lists of retrieved articles and presentations at major meetings were also searched.

Study selection
Randomised controlled trials (RCTs) that compared primary/neoadjuvant anthracycline-based chemotherapy alone against the same regimen plus taxanes in patients with previously untreated resectable early breast cancer were eligible for inclusion in the review.

Primary outcomes were the rate of pathologic complete response and the rate of breast-conserving surgery.

Among included trials, non-taxane intervention arms included the following chemotherapy regimens: 5-fluorouracil-epirubicin-cyclophosphamide, 5-fluorouracil-doxorubicin-cyclophosphamide, cyclophosphamide-vincristine-doxorubicin-prednisone, and doxorubicin-cyclophosphamide. Comparison arms included sequential docetaxel and concomitant or sequential paclitaxel. Most of the included patients had stage II or stage III disease.

The authors did not state how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted to permit the calculation of relative risks (RRs) and related 95% confidence intervals (CIs). Data were extracted on an intention-to-treat basis. Outcomes were also calculated as absolute risk differences and numbers needed to treat to benefit a single patient.

Four reviewers independently extracted the data from included studies; there were no disagreements between reviewers.

Methods of synthesis
Relative risks and 95% confidence intervals were pooled using a fixed-effect or random-effect model. Statistical heterogeneity was assessed using the Q statistic.

As well as overall pooled values, separate subgroup meta-analyses were undertaken for concomitant and sequential taxane regimens.
Results of the review

Seven RCTs (n=2,455 patients; range 30 to 1,605) were included in the review.

Overall there was no statistically significant benefit of receiving taxanes in terms of pathologic complete response (seven RCTs; p=0.11), although the benefit was statistically significant for the subgroup of trials evaluating sequential taxane therapy (RR 1.73, 95% CI 1.12 to 2.68; two RCTs; n=1,709 patients).

There was a statistically significant benefit of receiving taxanes overall in terms of breast-conserving surgery (RR 1.11, 95% CI 1.02 to 1.21; six RCTs; n=2,425 patients). The benefit remained statistically significant for the subgroup of trials evaluating concomitant taxane therapy (RR 1.22, 95% CI 1.02 to 1.47; four RCTs; n=716 patients), but not those evaluating sequential therapy (two RCTs; p=0.95).

Statistically significant benefits of taxane therapy overall were observed for the secondary outcomes of clinical response (RR 1.59, 95% CI 1.44 to 1.74; six RCTs, n=2,405 patients) and lymph node-negative status (RR 1.13, 95% CI 1.02 to 1.21; four RCTs; n=2,272 patients), but not for partial response (six RCTs; p=0.92) or disease-free survival (five RCTs; p=0.12).

Absolute risk differences and numbers needed to treat to benefit a single patient were also reported for these outcomes.

Authors' conclusions

The combination of taxanes and anthracyclines as neoadjuvant chemotherapy for early breast cancer improved the chance of achieving higher breast-conserving surgery rates and pathologic complete response rates.

CRD commentary

The review question was clearly defined in terms of the participants, interventions, comparators and outcomes of interest. Attempts were made to identify relevant published and unpublished evidence, without language restrictions. Although attempts were made to minimise the potential for errors and bias in the extraction of data from included trials, it was unclear whether such attempts were made elsewhere in the review process.

Although the authors discussed aspects of trial quality, the validity of individual trials was not assessed or incorporated into the synthesis. Included trials were synthesised using established methods.

The authors' main conclusion followed from the evidence presented, but did not clearly acknowledge the limitations of the evidence discussed elsewhere in the review. Therefore, the main conclusions may not be entirely reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors suggested that further research may be needed to identify which breast cancer patients truly benefit from the addition of taxane therapy.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.