Weekly docetaxel as second line chemotherapy for advanced non-small-cell lung cancer: meta-analysis of randomized trials


CRD summary
The authors concluded that weekly and 3-weekly docetaxel for advanced non-small-cell lung cancer have similar effects on overall survival and overall response rate, but weekly docetaxel is associated with a significantly lower risk of neutropenia. Incomplete reporting of review methods and the lack of a validity assessment mean that the reliability of the results is uncertain.

Authors' objectives
To determine whether docetaxel given weekly compared with 3-weekly improved survival in patients with non-small-cell lung cancer (NSCLC) pre-treated for advanced disease.

Searching
Electronic searches of MEDLINE up to March 2006 and the websites of the following societies were conducted: American Society of Clinical Oncology, European Society for Medical Oncology, Federation of European Cancer Societies and International Association for the Study of Lung Cancer. The keywords used were listed in the review. The bibliographies of identified studies and reviews were handsearched. The proceedings of the major meetings of the societies listed above were also screened. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Phase II and phase III randomised controlled trials were eligible for inclusion.

Specific interventions included in the review
Studies in which docetaxel was given weekly (intervention) compared with 3-weekly (control) were eligible for inclusion. Weekly treatment doses ranged from 33 to 40 mg/m2, and 3-weekly treatment doses ranged from 66 to 75 mg/m2.

Participants included in the review
Patients who had previously undergone chemotherapy for advanced NSCLC were eligible for inclusion. No further details of the participants in the included studies were given in the review.

Outcomes assessed in the review
The primary outcome was overall survival defined as the time from randomisation till death. The secondary outcomes were overall response rate (determined according to World Health Organization criteria) and grade 3 to 4 neutropenia (determined according to NCI-NCIC criteria version 2). All of the included studies reported results for each of these outcomes.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the data extraction.

Assessment of study quality
The authors did not state that validity was assessed.
Data extraction
Two reviewers independently extracted the data. It was not stated how any disagreements were resolved or given in the review. Events were extracted to estimate disease-free survival and overall survival, assuming an exponential distribution of survival, based on the median overall survival. A relative risk ratio (RR) and 95% confidence interval (CI) were derived. Where significant differences in outcomes were found, absolute benefit and numbers-needed-to-treat were calculated.

Methods of synthesis
How were the studies combined?
The studies were combined using fixed-effect and random-effects models, based on the Mantel-Haenszel method of inverse variance.

How were differences between studies investigated?
The Q statistic was used to test for heterogeneity between studies. A subgroup analysis based only on phase III trials was conducted.

Results of the review
Six trials (1,018 participants) were included in the overall analysis, of which three (682 participants) were phase III trials.

Main analysis (6 trials, 1,018 patients).
There was no difference in overall survival (RR 1.06, 95% CI: 0.81, 1.38, p=0.666) or overall response rate (RR 1.00, 95% CI: 0.64, 1.58, p=0.979) between participants treated with weekly compared with 3-weekly docetaxel. Participants treated with weekly docetaxel were significantly less likely to have neutropenia (RR 0.26, 95% CI 0.19, 0.35, p<0.001). There was no evidence of heterogeneity between the studies (p=0.37). This advantage was equivalent to 19% absolute benefit, with 5 patients needing to be treated for one to benefit.

Phase III trial subgroup analysis (3 trials, 682 patients).
There was no difference in overall survival or overall response rate between participants treated with weekly compared with 3-weekly docetaxel. Participants treated with weekly docetaxel were significantly less likely to have neutropenia (RR 0.22, 95% CI 0.19, 0.42, p<0.001). There was no evidence of heterogeneity between the studies (p=0.40). This advantage was equivalent to 12% absolute benefit, with 9 patients needing to be treated for one to benefit.

Authors’ conclusions
Weekly and 3-weekly docetaxel have similar effects on survival, but weekly treatment has a significant benefit on the risk of neutropenia.

CRD commentary
The inclusion criteria for the intervention, participant, outcome and study design were stated. Many sources were searched and no language restrictions were applied, but no attempt appears to have been made to search for unpublished data. Methods were used to minimise reviewer errors and bias when extracting the data, but it is not clear whether similar steps were taken when selecting the studies. No validity assessment was performed, which makes it difficult for the reader to assess the reliability of the findings. The lack of any details about the participants in the included studies makes it hard to assess the generalisability of the findings of the review. The use of meta-analytical methods was an appropriate way to combine the statistically homogeneous studies, as was the subgroup analysis. The authors' conclusions appear to reflect the presented data, but incomplete reporting of review methods and the lack of a validity assessment of the included studies mean that the reliability of the results is uncertain.
Implications of the review for practice and research
Practice: The authors stated that patients pre-treated for advanced NSCLC should be given weekly rather than 3-weekly docetaxel therapy.

Research: The authors stated that quality-of-life analyses should be conducted using meta-analyses of individual patient data.

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