The role of single-agent docetaxel (Taxotere) as a second-line treatment for advanced non-small-cell lung cancer


CRD summary
This review found that second-line treatment with 75 mg/m2 docetaxel every three weeks may increase survival and quality of life among adults with good performance status and advanced or metastatic non-small-cell lung cancer who are resistant to platinum-based therapy. While these conclusions are appropriate, they are largely based on data from two randomised controlled trials.

Authors' objectives
To assess whether there is a role for single-agent docetaxel as a second-line therapy in adults with advanced or metastatic non-small-cell lung cancer which has become resistant to platinum-based combination chemotherapy.

Searching
MEDLINE (1985 to September 2000), Cancerlit (1985 to September 2000), the Cochrane Library (Issue 3, 2000), PDQ, the proceedings of annual meetings of the American Society of Clinical Oncology (1993 to 2000), and the reference lists of identified trials and review articles were searched; the search terms were reported. Both full reports and abstracts were included in the review. Papers published in languages other than English were not included unless an abstract in English was available.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and phase II (i.e. uncontrolled) trials were considered for inclusion.

Specific interventions included in the review
Studies were eligible for inclusion if they compared single-agent docetaxel as second-line therapy versus either best supportive care or another chemotherapy regimen. Studies in which docetaxel followed a first-line therapy that was not platinum-based were excluded. The main interventions included in the review were: 100 mg/m2 docetaxel versus 75 mg/m2 docetaxel versus best supportive care; and 100 mg/m2 docetaxel versus 75 mg/m2 docetaxel versus vinorelbine or ifosfamide. Docetaxel was administered over a 3-week period. Other regimens used docetaxel 60 mg/m2 every 3 weeks, 43 mg/m2 per week, or 35 mg/m2 per week.

Participants included in the review
Studies were considered for the review if they included adults with advanced or metastatic non-small-cell lung cancer that was resistant to platinum-based combination chemotherapy. Trials that enrolled both chemotherapy naive patients and those pre-treated with platinum-based therapy were eligible if the results were reported separately for the two groups. The authors did not describe the participants' demographic characteristics such as age or gender, but disease stage and ECOG (Eastern Cooperative Oncology Group) performance were reported.

Outcomes assessed in the review
The authors did not specify any outcomes that the studies had to include for consideration in the review. The primary outcome of the review was survival. The secondary outcomes were toxicity, quality of life and response rates.

How were decisions on the relevance of primary studies made?
Five members of the Practice Guidelines Initiative's Lung Cancer Disease Site Group and a methodologist selected and reviewed studies. Apart from this, the authors did not provide details of how the studies were selected for the review.
Assessment of study quality
The authors did not state that they assessed validity. This review was developed using the Practice Guidelines Development Cycle (see Other Publications of Related Interest).

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on publication details, treatment regimens, sample size, disease stage, ECOG performance status, inclusion and exclusion criteria, response rates, survival outcomes and toxicity.

Methods of synthesis
How were the studies combined?
The authors summarised the findings narratively. They did not pool the results of the RCTs since each one used a different control condition.

How were differences between studies investigated?
The authors reported differences between the studies narratively and in tables.

Results of the review
The review comprised 13 studies: 2 RCTs (577 participants) and 11 phase II (uncontrolled) trials (538 participants).

One randomised trial found that, compared with best supportive care, 75 mg/m2 docetaxel was associated with improved median survival (7.5 versus 4.6 months, log rank P=0.010), 1-year overall survival (37% versus 12%, chi-squared P=0.003), overall survival (log rank P=0.01) and quality of life. Similar survival benefits were not found with 100 mg/m2 docetaxel.

Another RCT found a benefit in terms of 1-year survival with 75 mg/m2 docetaxel compared with second-line single-agent therapy with vinorelbine or ifosfamide (32% versus 19%, chi-squared P== 0.025). Docetaxel at doses of 100 and 75 mg/m2 were both associated with enhanced progression-free survival and quality of life in comparison with vinorelbine or ifosfamide. The major adverse effect was neutropenia. Neutropenia was less evident with docetaxel doses of 75 mg/m2 than with doses of 100 mg/m2. There was no significant neurotoxicity.

The data from the uncontrolled trials indicated response rates of 15 to 25%, which were substantially higher than those reported in the RCTs. The 1-year survival rates reported in these studies ranged from 23 to 46%.

Authors’ conclusions
Based on data from 2 RCTs, the authors concluded that 75mg/m2 docetaxel has a moderate survival benefit when used as a single-agent second-line therapy for people with advanced or metastatic non-small-cell lung cancer that is resistant to platinum-based regimens.

CRD commentary
This review included a defined research question and specific inclusion and exclusion criteria. The search strategy appears to have been appropriate, although the authors could have considered extending their search by using different databases and by approaching industrial sources and experts in the field for unpublished studies. Language bias might have been introduced as studies reported in languages other than English were excluded. The authors did not report how they assessed studies for relevance or validity; this makes it difficult to consider the overall quality of the review and the studies on which it is based. They mentioned that five reviewers were involved in selecting evidence for the review, but it is unclear whether these reviewers assessed the same evidence multiple times.

Given the small number of randomised trials and the different comparators in these trials, it would appear appropriate not to pool the data.
The data presented support the authors' conclusions, but the generalisability of these conclusions may be limited as they are based largely on only 2 RCTs.

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

Practice: The authors stated that second-line treatment with 75 mg/m² docetaxel every 3 weeks may increase survival and quality of life among adults with good performance status and advanced or metastatic non-small-cell lung cancer who are resistant to platinum-based therapy. The benefits, limitations and toxicities of the treatment should be discussed fully with the patients. Research: The authors stated that the possibility of re-treating selected patients with their previous chemotherapy before proceeding to docetaxel should be further investigated. They did not identify any ongoing trials on this topic (as at January 2001).

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**Bibliographic details**


**Original Paper URL**

https://www.cancercare.on.ca/toolbox/qualityguidelines/diseasesite/lung-ebs/

**Other publications of related interest**


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the reliability of the review and the conclusions drawn.