Chemotherapy for relapsed small cell lung cancer: a clinical practice guideline
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CRD summary
This review examined the effects of chemotherapy on survival and quality of life in relapsed small cell lung cancer, concluding that the evidence is limited and insufficient to recommend a specific chemotherapy regimen in this group of patients. Because important methodological details were not reported, the conclusions should be interpreted with caution, as they may not be reliable.

Authors' objectives
To determine if chemotherapy improves survival and quality of life in patients with relapsed small cell lung cancer, which chemotherapy regimen is most effective in treatment of relapsed small cell lung cancer and which patients are most likely to benefit from additional chemotherapy.

Searching
MEDLINE (1985 to October 2005), CANCERLIT (1985 to March 2002) and the Cochrane Library (2005, Issue 4) were searched for relevant studies published in English. Search terms were reported. In addition, conference proceedings, evidence-based practice guidelines and the reference lists of retrieved studies were searched for further relevant evidence.

Study selection
Studies were eligible for inclusion if they were phase II or III randomised controlled trials (RCTs) comparing chemotherapy against no chemotherapy or comparing different chemotherapy regimens as second-line treatment for small cell lung cancer. Included trials had to report survival or response rate data.

Among included trials, treatments varied by type, dose and duration. Partial and complete response rates, as well as stable disease, were reported.

The authors did not state how many reviewers screened the studies for inclusion.

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

Data extraction
Complete and partial response rates, with related p values, and where reported, survival hazard ratios (HRs) were presented in tables. In addition, the proportion of patients with stable disease was also reported for each trial.

The authors did not state how data were extracted for the review or how many reviewers performed the extraction.

Methods of synthesis
Studies were combined in a narrative synthesis, grouped by intervention/comparison.

Results of the review
Six RCTs were included in the review (n=930).

One phase III RCT (n=141) compared chemotherapy to best supportive care. This reported that oral topotecan plus best supportive care increased median survival compared to best supportive care alone (26 versus14 weeks, HR 0.64, 95% CI: 0.45, 0.90, p=0.0104), though the response rate in the chemotherapy group was only 7%.

Three RCTs (n=379) compared different second-line chemotherapy regimens. One phase II RCT found no significant differences in response rate or survival between carboplatin with cisplatin and etoposide versus cisplatin and etoposide.
only. A second phase II RCT reported no significant differences on either outcome between combination chemotherapy (cyclophosphamide, doxorubicin and vincristine) and treatment with single agent topotecan. Neither were significant differences reported for a phase III RCT comparing BTOC (bis-chloro-ethynitrosourea, thiotepa, vincristine, and cyclophosphamide) with combination etoposide/cisplatin.

Survival and response rates were not significantly different between oral and intravenous administration of topotecan, in either of the two RCTs (n=410) evaluating this comparison.

Toxicity and quality of life data for individual studies were reported in the review.

Authors’ conclusions
The evidence for the clinical benefit of second-line therapy in the treatment of patients with relapsed small cell lung cancer is limited and there is insufficient evidence to recommend a specific chemotherapy regimen.

CRD commentary
This review was based on a research question well-defined in terms of participants, interventions, outcomes and study designs of interest. Several sources were searched to identify relevant literature, although the search was limited to English language publications, meaning relevant non-English language literature may have been missed, potentially introducing bias. The use of a narrative synthesis was appropriate, given the clear clinical and methodological heterogeneity between studies. However, despite identifying a limited number of relatively small studies, the authors did not report any attempts to differentiate between studies in terms of their validity; neither did they report any attempts to minimise the potential for errors or bias during the review process. Because these data are not reported, the conclusions should be interpreted with caution, as they may not be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that clinical trials are needed to establish the optimal second-line chemotherapy regimen for small cell lung cancer patients who fail to respond to or relapse shortly after first-line therapy.

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