Single-agent chemotherapy versus combination chemotherapy in advanced non-small cell lung cancer: a quality and meta-analysis study

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Authors' objectives
To compare single-agent with combination chemotherapy in advanced non-small cell lung cancer (NSCLC) and to examine the quality of the studies.

Searching
MEDLINE was searched for English and foreign language papers (no years or search terms given), and bibliographies of identified review articles and abstracts were examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing single-agent with combination chemotherapy were included.

Specific interventions included in the review
Single agent and combination chemotherapy in NSCLC. Single agents included are: cyclophosphamide, vindesine, etoposide, cisplatin and vinorelbine. Combination regimens included are: cyclophosphamide+adriamycin+lomustine, cisplatin+vindesine, lomustine+cyclophosphamide+methotrexate+vindesine, cisplatin+etoposide; cisplatin+carboplatin and vinorelbine+cisplatin.

Participants included in the review
Patients with advanced NSCLC at stage IIIa, IIIb or stage IV of Mountain's (1986) classification were included.

Outcomes assessed in the review
Survival at one year was assessed.

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

Assessment of study quality
The methodological quality of the studies was assessed using a detailed checklist, which considered the design, conduct and analysis of the trial, among other aspects. This was not used to weight the studies in the meta-analysis, but to calculate a quality score for individual trials and a median quality score for all trials. Independent scoring by two reviewers (non-blinded).

Data extraction
The number of deaths at one year was extracted from each arm of each trial based on the survival rate. Where rates for three arms were reported, the arm which reported better median survival for both types of treatment was chosen. Where one-year survival rate was not reported, the number of deaths was extracted by proportional arithmetic calculation based on the survival curve.

Methods of synthesis
How were the studies combined?
A meta-analysis was undertaken using a modified Mantel-Haenzel method to produce a pooled odds ratio (OR).
How were differences between studies investigated?
Heterogeneity was not tested statistically. A subgroup analysis was carried out to examine the effect of excluding one study.

Results of the review
Nine studies involving a total of 1,493 patients were included.

The pooled OR of 0.8 (95% confidence interval, CI: 0.6, 1.0) showed a trend in favour of combination therapy, albeit of marginal significance. The subgroup analysis excluded one set of results which showed a particularly high benefit of combination chemotherapy. The analysis excluding this trial showed no significant effect in favour of combination therapy. The quality of individual studies was assessed and shown overall to be low.

Authors’ conclusions
Given the methodological problems with the trials and the need to consider issues such as quality of life of the patient, costs and toxicity, the issue of single agent versus combination chemotherapy remains open.

CRD commentary
The authors seem to have slightly overstated in the results section the trend in favour of combination therapy: the CI includes 1.00, and the subgroup analysis indicates the result is strongly influenced by one trial. Overall the quality of this review is poor, and in the absence of more detailed examination of heterogeneity the conclusions may not be robust.

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