A meta-analysis of paclitaxel-based chemotherapies administered once every week compared with once every 3 weeks first-line treatment of advanced non-small-cell lung cancer

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CRD summary
This review concluded that there were no significant differences between weekly paclitaxel-based chemotherapy compared with the standard once every three weeks schedule in the first-line treatment of advanced non-small-cell lung cancer. The review used appropriate methods and the authors' conclusions seem to be reliable.

Authors' objectives
To compare once weekly paclitaxel-based chemotherapy with standard paclitaxel-based chemotherapy once every three weeks in the first-line treatment of advanced non-small-cell lung cancer.

Searching
PubMed, EMBASE, Cochrane Central Register of Controlled Trials (Issue 3), and Chinese Biomedical database were searched up to July 2010 with no language restrictions. Search terms were reported. Conference proceedings of the American Society of Clinical Oncology and the European Society of Medical Oncology were searched from 1995 up to 2010. Reference lists from studies, published systematic reviews and practice guidelines were searched.

Study selection
Randomised controlled trials (RCTs) that compared a once weekly paclitaxel-based chemotherapy schedule with the standard paclitaxel-based chemotherapy schedule given once every three weeks were eligible for inclusion. Eligible patients had pathologically proven untreated non-small-cell lung cancer (stage III to IV) and had to be aged 18 years or older. Ongoing trials, interim analyses, non-randomised studies, and trials with 10 or fewer patients per trial arm were excluded. The primary outcome was overall survival. Secondary outcomes were progression-free survival, overall response rate, and adverse events.

Chemotherapy regimens in the included trials were: paclitaxel and carboplatin; paclitaxel and gemcitabine; and paclitaxel, carboplatin and cetuximab. The median patient age was over 60 years in all trials. The proportion of men ranged from 52% to 90%. From 84% to 100% of patients had performance stages of 0 to 1; 55% to 89.3% had stage IV cancer.

Two reviewers independently selected the studies; disagreements were resolved by consensus with a third reviewer.

Assessment of study quality
Trial quality was assessed with the Jadad scale, which covered: randomisation; allocation concealment; patient and clinician blinding; reporting of drop-outs and withdrawals; and use of intention-to-treat analysis.

Two reviewers independently assessed quality; disagreements were resolved by consensus with a third reviewer.

Data extraction
Median overall and progression-free survival times and hazard ratios were extracted. Relative risks were calculated for response rate and odds ratios (OR) for adverse events, with 95% confidence intervals.

Two reviewers independently assessed extracted the data; disagreements were resolved by consensus with a third reviewer.

Methods of synthesis
Results were combined using random-effects meta-analysis. Heterogeneity was assessed using $I^2$. Sensitivity analyses were performed to explore sources of heterogeneity, assessing cancer stage, trial duration, trial quality, and the source of the data of the once weekly paclitaxel treatment.

Publication bias was assessed using funnel plots, Begg’s and Egger’s tests.
Results of the review

Five trials (942 patients) were included in the review; one was a phase III trial, the remaining four were phase II trials. All scored trials 3 out of 5 for quality and reported randomisation, allocation concealment, and drop-outs.

There were no statistically significant differences between once weekly and once every three weeks paclitaxel-based chemotherapy for overall survival (five trials), progression-free survival (four trials), or overall response rate (five trials). No differences were observed for carboplatin/paclitaxel trials.

Median survival was 9.8 months for once-weekly chemotherapy and 10.7 months for chemotherapy once every three weeks. Median progression-free survival was 5.2 months for once-weekly chemotherapy and 4.7 months for chemotherapy once every three weeks.

The most commonly reported grade 3 and 4 adverse events were haematological toxicity (anaemia, leukocytopenia, thrombocytopenia or granulocytopenia), fever, and peripheral neuropathy. There was a lower incidence of neutropenia (OR 0.47, 95% CI 0.27 to 0.83), febrile neutropenia (OR 0.46, 95% CI 0.21 to 0.98) and peripheral neuropathy (OR 0.50, 95% CI 0.33 to 0.76) and a higher incidence of anaemia (OR 2.08, 95% CI 1.20 to 3.58) for once-weekly chemotherapy compared with once every three weeks chemotherapy. There was no difference in treatment-related deaths.

No evidence of publication bias was found (funnel plots and test results not shown), although this was a cautious interpretation as there were only five trials in the analysis.

Authors’ conclusions

There were no significant differences between weekly paclitaxel-based chemotherapy compared with the standard once every three weeks schedule in the first-line treatment of advanced non-small-cell lung cancer.

CRD commentary

The review had clear and reproducible inclusion criteria. A number of databases were searched with no language restrictions, as well as relevant conference abstracts, so the risk of language and publication bias was reduced. Review processes were performed in duplicate to reduce reviewer error and bias.

The quality of the evidence was assessed, but the tool used was brief and only reported on selected items. The methods of meta-analysis appeared to be appropriate.

The review used appropriate methods and the authors’ conclusions seem to be reliable.

Implications of the review for practice and research

Practice: The authors stated that once-weekly paclitaxel may be a better choice for patients who could not tolerate the standard regimen, such as the elderly or those with poor conditions.

Research: The authors did not state any recommendations for research.

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