A meta-analysis of platinum plus gemcitabine or vinorelbine in the treatment of advanced non-small-cell lung cancer

CRD summary
This review compared gemcitabine plus platinum with vinorelbine plus platinum regimens in first-line treatment of advanced non-small cell lung cancer and concluded that they appeared to be similarly efficacious; choice of which to use depended on patient tolerance to certain toxicities. Due to the limited information on toxicity comparisons, it is difficult to establish the reliability of these conclusions.

Authors' objectives
To compare the effects of gemcitabine plus platinum regimens with vinorelbine plus platinum regimens in first-line treatment of advanced non-small-cell lung cancer (NSCLC).

Searching
PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE and PDQ databases were searched up to July 2008 for relevant studies published in any language. Search terms were reported. American Society of Clinical Oncology annual meeting abstracts were searched from 1996 to 2008. Reference lists of relevant publications were examined to identify further relevant evidence.

Study selection
Randomised controlled trials (RCTs) that compared gemcitabine plus platinum chemotherapy with vinorelbine plus platinum chemotherapy in first-line treatment of advanced NSCLC were eligible for inclusion. To be included, patients had to have pathologically confirmed stage III to IV NSCLC. The authors did not state how many reviewers selected studies for inclusion.

Most patients in the included RCTs were male. Mean age ranged from 55 to 90 years. Patients received either gemcitabine or vinorelbine in combination with either cisplatin or carboplatin; doses and cycle lengths varied.

Assessment of study quality
Two reviewers independently assessed included studies using Jadad criteria (randomisation, allocation concealment, blinding and follow-up). Disagreements were resolved by discussion. The maximum possible score was 5 points.

Data extraction
Two reviewers independently extracted data from included studies. Disagreements were resolved by discussion. Data were extracted on relative risks (RRs) for overall response to treatment and for one-year survival. Odds ratios (ORs) were calculated for grade 3 and 4 toxicity outcomes.

Methods of synthesis
Heterogeneity of included studies was assessed using $\chi^2$ and $I^2$ tests. In the presence of statistical heterogeneity (p<0.1), studies were combined using a random-effects model (DerSimonian and Laird), otherwise a fixed-effect model was used. A subgroup analysis was conducted of studies that evaluated gemcitabine or vinorelbine in combination with cisplatin.

Results of the review
A total of nine RCTs (n=2,186 participants) were included in the review. All received a quality score of 2 out of a possible 5 points.

No statistically significant difference was found between gemcitabine and vinorelbine regimens in terms of overall response (34% versus 37%, RR 0.91, 95% CI 0.81 to 1.03) and one-year survival (39.4% versus 36.8%, RR 1.06, 95% CI: 0.96 to 1.18). Subgroup analyses of gemcitabine or vinorelbine in combination with cisplatin found no statistically
significant difference between these outcomes (RR 0.93, 95% CI 0.82 to 1.05 for overall response and RR 1.06, 95% CI 0.95 to 1.19 for one-year survival).

Regarding toxicity (reported in all nine trials), vinorelbine plus platinum was associated with more grade 3 and 4 neutropenia (OR 0.37, 95% CI 0.26 to 0.52), nephrotoxicity (OR 0.38, 95% CI 0.25 to 0.57), constipation (OR 0.50, 95% CI 0.27 to 0.92) and phlebitis (OR 0.13, 95% CI 0.05 to 0.32). Gemcitabine plus platinum was associated with more grade 3 and 4 thrombocytopenia (OR 11.37, 95% CI 4.56 to 28.38). There was no significant difference in rates of anaemia, nausea or vomiting between the two groups.

There was no significant statistical heterogeneity for any efficacy outcomes; seven of the 13 toxicity estimates were statistically heterogeneous.

Authors' conclusions
Gemcitabine plus platinum and vinorelbine plus platinum regimens appear to be similarly efficacious. The choice of which regimen to use depends on the toxicity of the drugs and patients' tolerance.

CRD commentary
This review was based on a question that was clearly defined in terms of the participants, interventions, comparators and study designs of interest. Multiple sources were searched to identify relevant evidence, regardless of language. The authors clearly made efforts to minimise potential for errors and bias in the data extraction and validity assessment processes; it was unclear whether such efforts were made during initial selection of studies for inclusion. Heterogeneity was investigated and studies were combined using appropriate statistical methods. The highly significant statistical heterogeneity observed for some adverse event outcomes may have indicated a level of underlying clinical heterogeneity that would make pooling inappropriate, but details of these comparisons were insufficient to determine whether this was the case. To avoid bias when attempting to establish equivalency between regimens, outcomes of interest and range of values considered clinically equivalent should be stated a priori. Since this information was not reported, it is difficult to establish the reliability of the authors' conclusions.

Implications of the review for practice and research
Practice: The authors stated that gemcitabine plus platinum regimens may be the better choice for patients in whom thrombocytopenia needed to be taken care of, especially for elderly patients. They stated that vinorelbine plus platinum regimens might be more suitable for patients who were likely to bleed or who were supersensitive to thrombopoietin or interleukin-11.

The authors did not state any implications for research.

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