Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Novel combination chemotherapy regimens for the treatment of patients with advanced non-small-cell lung cancer (NSCLC) were studied. The novel regimens were:

gemcitabine (1,000 mg/m²) plus cisplatin (100 mg/m²) (Gem/Cis);
vinorelbine (30 mg/m²) plus cisplatin (120 mg/m²) (Vin/Cis);
paclitaxel (135 mg/m²) plus cisplatin (75 mg/m²) (Pac/Cis);
paclitaxel (225 mg/m²) plus carboplatin (AUC 6.0 mg/mL per minute) (Pac/Carbo); and
docetaxel (75 mg/m²) plus cisplatin (75 mg/m²) (Doc/Cis).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced (Stage IIIB/IV) NSCLC. No specific inclusion or exclusion criteria were reported in the paper.

Setting
The setting was secondary care. The study was conducted in five European countries (France, Germany, Italy, Spain and the UK).

Dates to which data relate
The effectiveness data were derived from two studies published in 2000 and 2002. The resources used were mainly derived from the same literature. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies.

Outcomes assessed in the review
The outcomes assessed were the response rates, survival, the mean time to progression, and the overall efficacy of the
chemotherapy regimens.

Study designs and other criteria for inclusion in the review
The review included only two randomised clinical trials that evaluated the efficacy of the chemotherapy regimens examined in the economic analysis.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not specified.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Two primary studies were included in the review.

Methods of combining primary studies
The results of the individual studies were not combined, but this was not necessary as separate comparisons were made for each trial.

Investigation of differences between primary studies
Potential differences between the primary studies were not discussed.

Results of the review
There were no significant differences in efficacy between Gem/Cis, Vin/Cis, Pac/Cis, Pac/Carbo and Doc/Cis. The only statistically significantly different outcome found in one of the two studies was that patients treated with Gem/Cis had a longer time to disease progression (4.2 months) than patients receiving Pac/Cis (3.4 months), (p=0.001). However, as there were no significant differences for all the remaining clinical outcomes, equal efficacy was assumed.

Measure of benefits used in the economic analysis
Since the results of the review showed no statistically significant differences in effectiveness between the regimens examined, the economic analysis was based on cost-differences only (i.e. a cost-minimisation analysis).

Direct costs
It was stated that the study adopted the perspective of a national health service. The costs covered chemotherapy acquisition (novel and platinum agents), chemotherapy administration (inpatient or outpatient setting), hospitalisation for adverse events, and other medical resources (e.g. visits to health care professionals, radiotherapy, transfusions, concomitant medications). The unit costs and the quantities were not reported separately. The mean estimates for each cost element included in the analysis were provided. The quantities were estimated using data derived from the clinical trials included in the review, product information, other published literature and expert opinion. Data based on expert opinion were derived using standardised data collection questionnaires. These questionnaires provided information on treatment protocols in each of the five countries included in the analysis, such as concomitant medication, treatment of adverse events, and inpatient versus outpatient administration of the chemotherapy regimens. The unit costs were
derived from standard references for each country (e.g. reports by ministries of health, national databases of health care costs) and diagnostic-related group data. Discounting was not necessary as all the costs were incurred within 12 months. The price year was 2000.

**Statistical analysis of costs**

The costs were treated deterministically and no statistical analysis of the costs was undertaken.

**Indirect Costs**

The indirect costs were not included in the analysis.

**Currency**

The costs were expressed in Euros (Euro) for France, Germany, Italy and Spain, and in pounds sterling () for the UK. The conversion rate of 1.5909 from to Euros was based on the annual average Bank of England exchange rate for 2002.

**Sensitivity analysis**

A one-way sensitivity analysis was conducted. This investigated whether uncertainty associated with the estimation of cost elements had an impact on the results. The parameters examined were the cost of chemotherapy, the number of chemotherapy cycles, the hospitalisation unit costs, the drug administration unit costs, and the site of administration (inpatient or outpatient). The range of values used was determined by increasing or decreasing the point estimates of the examined parameters by a specific percentage. No further justification for the range of values used was provided.

**Estimated benefits used in the economic analysis**

See the "Results of the Review" section.

**Cost results**

The results were analysed separately for each of the two studies included in the review.

From the first study, the average cost per patient treated with Gem/Cis was Euro 4,072 in Spain, Euro 5,310 in Italy, Euro 5,640 in France, Euro 6,999 in Germany and 4,968 (Euro 7,904) in the UK.

The average cost per patient treated with Vin/Cis was greater than that for Gem/Cis in all five countries. It was Euro 4,899 in Spain, Euro 6,500 in Italy, Euro 7,472 in France, Euro 8,143 in Germany and 6,260 (Euro 9,959) in the UK.

The average cost-saving per patient for Gem/Cis ranged from Euro 827 in Spain to 1,292 (Euro 2,055) in the UK. Gem/Cis treatment resulted in cost-savings in all scenarios examined.

Hospitalisations provided the largest cost-savings in France, Germany and Italy. In Spain and the UK, the drug administration costs represented the greatest cost-saving in patients treated with Gem/Cis.

The results were robust to changes in the cost elements. In general, variations in the hospitalisation cost for adverse events and the site of administration (inpatient versus outpatient) had the biggest impact on the cost-differences between regimens.

From the second study, the average cost per patient treated with Gem/Cis was Euro 5082 in Spain, Euro 5,972 in Italy, Euro 6,551 in France, Euro 8,250 in Germany and 6,061 (Euro 9,642) in the UK.

The average cost per patient treated with Pac/Cis was Euro 6,746 in Spain, Euro 8,082 in Italy, Euro 8,694 in France, Euro 11,052 in Germany and 7,077 (Euro 11,259) in the UK.

The average cost per patient treated with Pac/Carbo was Euro 9,750 in Spain, Euro 8,640 in Italy, Euro 11,893 in
France, Euro 12,265 in Germany and 8,488 (Euro 13,504) in the UK.

The average cost per patient treated with Doc/Cis was Euro 6,512 in Spain, Euro 8,121 in Italy, Euro 7,135 in France, Euro 8,329 in Germany and 6,319 (Euro 10,053) in the UK.

Gem/Cis was associated with lower total costs over the course of therapy than the two Pac-containing regimens in all five countries.

The difference between Gem/Cis and Pac/Cis ranged from Euro 1,664 to Euro 2,802 in France, Germany, Italy and Spain, and was equal to 1,016 (Euro 1,616) in the UK.

The differences were even greater between Gem/Cis and Pac/Carbo, ranging from Euro 2,668 to Euro 5,342 in France, Germany, Italy and Spain, and equalling 2,427 (Euro 3,861) in the UK.

Gem/Cis and Doc/Cis were associated with similar total costs in Germany, France and the UK. However, in Italy and Spain, Gem/Cis was associated with lower total costs than Doc/Cis.

The results were generally found to be robust in the sensitivity analysis. Gem/Cis was less costly overall than either of the Pac-containing regimens in all scenarios, except when chemotherapy was administered entirely on an inpatient basis in Italy and the UK. The site of administration (inpatient versus outpatient) had the greatest impact on the cost disparity between regimens. In some cases it changed the cost-differences in favour of the other comparators instead of Gem/Cis.

Synthesis of costs and benefits
Not applicable. The interventions examined were shown to be equivalent in terms of their effectiveness. Therefore, the economic analysis was based on a comparison of costs only (i.e. a cost-minimisation analysis).

Authors' conclusions
The combination of gemcitabine and cisplatin (Gem/Cis) provided cost-savings over other commonly used doublet combinations (e.g. paclitaxel/cisplatin, paclitaxel/carboplatin and docetaxel/cisplatin) in the treatment of advanced non-small-cell lung cancer (NSCLC), in Europe.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was implicitly justified. All the comparators were combinations of platinum-containing agents (the most commonly used regimens for the treatment of NSCLC) with novel chemotherapy agents that had shown promising activity in the treatment of NSCLC, particularly when combined with a platinum compound. However, it was stated that the regimens examined did not necessarily reflect routine treatment practices. You should consider whether any of the health technologies evaluated represent widely used practice in your own setting.

Validity of estimate of measure of effectiveness
It was not stated that a systematic review of the literature had been undertaken. The effectiveness results were derived from two randomised clinical trials. It was not reported whether further trials evaluating the health technologies in question were identified in the published literature. It was not necessary to combine the results since separate comparisons were made for each trial.

Validity of estimate of measure of benefit
The analysis of benefits was based upon the therapeutic equivalence of treatment alternatives. Therefore, the economic analysis included only costs.

Validity of estimate of costs
The study adopted the perspective of a national health service. All the categories of costs relevant to this perspective were included in the analysis. The costs and the quantities were not analysed separately, which hinders the generalisability of the results. The cost estimates were derived from published literature and expert opinion. A sensitivity analysis of the quantities and unit costs that were anticipated to have a strong impact on the results was undertaken. The ranges used were not explicitly justified, but they seem to have been appropriate. The authors performed appropriate currency conversions. Discounting was not necessary since the costs were incurred within 12 months. The date to which the prices referred was reported, which improves the reproducibility of the results.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of the generalisability of the results to other countries and also to other settings (routine practice versus conditions of clinical trials on which the study results were based) was addressed. The authors reported further limitations of their study. For example, the resource use data were not, in all instances, collected prospectively alongside clinical trials. Also, the analysis was based on estimated rather than actual costs. Moreover, owing to the delay between the time of conduct of the clinical trials and the date of publication, routine clinical practice might have changed and thus may not be reflected in the resource use estimated in the economic analysis. A final reported limitation of the study was that it did not consider the impact of adverse effects and/or quality of life of the patients. Nevertheless, the results of the study were adequately reported and the authors' conclusions reflected the scope of the analysis.

Implications of the study
The authors expressed the opinion that the value for money provided by the Gem/Cis combination, for the treatment of patients with advanced NSCLC, was an economic incentive for the use of this regimen as a first-line treatment option for fund holders with a limited budget. Moreover, it was stated that since Pac/Carbo was the most costly regimen in the analysis and did not produce improved efficacy over Pac/Cis, the use of this regimen in the treatment of advanced NSCLC should not be recommended on purely pharmacoeconomic grounds.

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None stated.

Bibliographic details

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Other publications of related interest


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