Economics evaluation of three two-drug chemotherapy regimens in advanced non-small-cell lung cancer


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
Three two-drug chemotherapy regimens for patients with advanced non-small-cell lung cancer (NSCLC) were examined:

- cisplatin-paclitaxel (CIS-PAC) consisted of 175 mg/m² PAC on day 1 followed by 80 mg/m² CIS on day 1;
- cisplatin-gemcitabine (CIS-GEM) consisted of 1,250 mg/m² GEM on days 1 and day 8 and 80 mg/m² CIS on day 1 after GEM;
- gemcitabine-paclitaxel (GEM-PAC) consisted of 175 mg/m² PAC on day 1 followed by 1,250 mg/m² GEM on days 1 and 8.

PAC was administered as a 3-hour intravenous (IV) infusion after pre-medication to avoid hypersensitivity reactions. GEM was administered as a 30- to 60-minute IV infusion. CIS was administered as an IV infusion. The treatment cycles were repeated every 3 weeks and all patients received at least 2 cycles. Treatment was interrupted in the event of disease progression or intolerable toxicity. Responding patients received a maximum of 6 cycles.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with cytologically or histologically confirmed Stage IIIB or Stage IV NSCLC. The inclusion criteria were age between 18 and 76 years, World Health Organization performance status of 0 ; 2, measurable disease, and adequate haematological, renal and hepatic function.

Setting
The setting was a hospital. The economic study was carried out in the Netherlands.

Dates to which data relate
The effectiveness and resource use data were derived from a sample of patients recruited between August 1998 and July 2000. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a single study.
Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Limited information on the study sample was provided. Overall, 480 patients were enrolled in the study. There were 159 patients in the CIS-PAC group, 160 patients in the CIS-GEM group, and 161 patients in the GEM-PAC group.

Study design
This was a prospective, randomised clinical trial that was carried out at 28 centres across Europe. The patients appear to have been followed until death. Information on randomisation and follow-up was not reported.

Analysis of effectiveness
The analysis of the clinical study appears to have been conducted on an intention to treat basis. The primary outcome measure used in the current analysis was the average survival time. Because of censoring, mean survival time could not be estimated directly from the observed survival data. Thus, it was assessed using the Kaplan-Meier approach and the restricted means analysis (restricted period of 3.0 years), which was extensively described. Details of the baseline comparability of the study groups were not reported.

Effectiveness results
The mean survival time was 0.94 years (95% confidence interval, CI: 0.82 to 1.07) in the CIS-PAC group, 0.98 years (95% CI: 0.86 to 1.11) in the CIS-GEM group, and 0.80 (95% CI: 0.69 to 0.92) in the GEM-PAC group.

Clinical conclusions
The effectiveness analysis showed that average survival was comparable for patients in the three groups.

Measure of benefits used in the economic analysis
The summary benefit measure was the average survival. This was estimated directly from the effectiveness analysis. Discounting was not applied.

Direct costs
The cost analysis took the perspective of the Dutch health insurance system. Accordingly, only the direct medical costs were included in the analysis. The items considered were study drugs, hospital stay, day hospital, outpatient specialist consultation, transfusions of red blood cells and platelets, pre-medication before PAC, anti-emetics, radiotherapy, chemotherapy and surgery. The unit costs and the quantities of resources used were presented separately for all items. Resource use was derived directly from the clinical trial using appropriate case report forms. When a precise estimate of resource consumption could not be derived from the clinical trial (i.e. the cost of a day in the hospital), the authors made some assumption on the most appropriate quantities of resources. The costs came from national reimbursement tariffs and prices. Details of the cost calculation were reported. Discounting was not relevant since the costs were incurred during a short timeframe, owing to the poor survival of patients considered in the analysis. The price year was 2002.

Statistical analysis of costs
Statistical analyses of the costs were carried out to deal with data censoring, as in the effectiveness analysis.

Indirect Costs
The indirect costs were not included in the economic analysis.
Currency
Euros (EUR).

Sensitivity analysis
The issue of uncertainty in clinical and economic data was addressed not only by performing univariate sensitivity analyses on the cost of a day in the hospital, but also by the use of non-parametric bootstrap techniques. These generated distributions of cost-effectiveness ratios and cost-effectiveness acceptability curves. In each case, 5,000 bootstrap re-samples were generated using the bias-corrected accelerated method.

Estimated benefits used in the economic analysis
See the Effectiveness Results section.

Cost results
The average total costs per patient were EUR 16,662 (95% CI: 15,251 to 18,072) in the CIS-PAC group, EUR 13,944 (95% CI: 12,829 to 15,060) in the CIS-GEM group, and EUR 17,377 (95% CI: 16,088 to 18,667) in the GEM-PAC group.

The cost-differences were mainly explained by differences in the administration of therapy.

Synthesis of costs and benefits
An incremental analysis was carried out to combine the costs and survival of CIS-GEM or GEM-PAC versus CIS-PAC. However, incremental cost-effectiveness ratios (ICERs) were not actually calculated as the results of the analysis were reported using point distributions on the cost-effectiveness plane. In effect, differences in terms of survival were not noted between the treatment groups.

In the comparison between CIS-GEM and CIS-PAC, less than 1% of the ICERs indicated that CIS-GEM increased costs in comparison with CIS-PAC, while in 72% of replications CIS-GEM improved survival and reduced costs at the same time. In the remaining 27% of replications CIS-GEM reduced costs but also reduced survival.

In the comparison between GEM-PAC and CIS-PAC, 82% of the ICER replicates suggested that GEM-PAC reduced survival while increasing costs. In 12% of cases GEM-PAC reduced costs but also survival, while in 6% of replications GEM-PAC improved both survival and costs.

The sensitivity analysis showed that alternative estimates of the calculation of the cost of a day in the hospital did not alter the conclusions of the analysis.

Authors’ conclusions
The two cisplatin-based strategies for patients with advanced non-small-cell lung cancer (NSCLC) in the Netherlands were almost equivalent in terms of survival, although there was a modest trend towards better survival with cisplatin-gemcitabine (CIS-GEM). CIS-Gem was less costly than the standard therapy consisting of cisplatin-paclitaxel (CIS-PAC), with a possible cost-saving of about EUR 2,000 per patient. On the other hand, gemcitabine-paclitaxel (GEM-PAC) was almost dominated by the standard therapy, which was less costly and similarly effective.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, thus the rationale for the therapies examined in the study was clear. The dosages were clearly reported. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from a clinical trial, which was appropriate for the study question. The randomised and multi-centre design, as well as the use of intention to treat, should ensure the internal validity of the analysis. However, since the clinical trial had been published in a separate study, few details of the design and other features of the study were reported in the present paper. Thus, it is difficult to make an objective assessment of the robustness of the analysis.

Validity of estimate of measure of benefit
The summary benefit measure was appropriate as survival is the most relevant dimension of health for patients undergoing palliative care for advanced NSCLC. Survival was based on estimates observed in the clinical trial, and the approach used to deal with censoring was explicitly described and discussed. Survival has the advantage of being comparable with the benefits of other health care interventions.

Validity of estimate of costs
The cost analysis was carried out in accordance with the perspective adopted in the study. The indirect costs were not considered, but their impact was probably not substantial due to the poor survival of the patients included in the study. However, the inclusion of patient expenses would have been interesting. Extensive details on the unit costs and quantities of resources used were provided, which enhances the possibility of replicating the analysis in other settings. The authors highlighted the problems associated with the estimation of some costs, the values of which were not readily available in the Dutch health insurance system. However, the use of alternative cost calculations did not change the conclusions of the main analysis. The price year was reported, which will enable reflation exercises in different time periods. The authors noted that the evaluation of the costs was incomplete, although it was not possible to quantify the underestimation of the total costs.

Other issues
The authors stated that few economic evaluations of poly-chemotherapy for advanced NSCLC had been published. The results of another study were reported, and these would appear to confirm those observed in the current economic evaluation. The authors addressed the issue of the generalisability of their findings to other settings, stating that caution would be required when extrapolating the current results given potential differences in treatment patterns across countries. The study referred to patients with advanced NSCLC and this was reflected in the authors’ conclusions. The authors noted some limitations of their analysis, generally those commonly observed in economic studies carried out alongside clinical trials.

Implications of the study
The study results would appear to support the use of CIS-GEM for the treatment of patients with advanced NSCLC.

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None stated.

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Other publications of related interest

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