A pharmacoeconomic evaluation of cisplatin in combination with either etoposide or etoposide phosphate in small cell lung cancer

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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

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with previously untreated limited or extensive small cell lung cancer. The mean age of patients in the study was 64 years and 79 men and 42 women were included. 41 patients (34%) had limited SCLC with the remainder having extensive SCLC. In addition all patients had to meet the following criteria: Eastern Oncology Group Performance of 0 to 12, minimum of 12 weeks life expectancy, WBC count more than 4,000L, platelet count more than 100,000L, serum bilirubin levels <= 20 mg, serum creatinine concentration <= 1.5 mg, and no prior history of malignancies other than squamous or basal cell carcinoma of the skin or in situ carcinoma of the uterine cervix.

Setting
The clinical study was conducted at 23 institutions in the United States providing outpatient chemotherapy. The economic analysis was conducted in East Brunswick, New Jersey, USA.

Dates to which data relate
Data for the effectiveness study were collected between May 1992 and September 1993. Resource and cost data were derived from publications between 1992 and 1996. The price date was not clearly stated.

Source of effectiveness data
The estimates of effectiveness data were based on a single clinical study.

Link between effectiveness and cost data
Costing was not undertaken on the same patient sample as in the clinical analysis. Costs were determined retrospectively.

Study sample
121 patients from 23 institutions were randomly selected for the study. Power calculations were not used to determine
sample size. There were 61 patients in the etoposide phosphate group and 60 patients in the etoposide group. One of the patients in the former group received no treatment (2% of the group; less than 1% overall).

**Study design**
The study was a randomised controlled multicentre trial conducted using patients from 23 institutions. Randomisation was performed using a computer generated randomisation list and patients were stratified according to disease severity but not by geographic location. There was no loss to follow up, although the duration of follow up was not clearly stated.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat. The primary health outcomes used in the analysis were the response rates of symptoms to treatment, length of time to disease progression and length of survival time. At analysis both groups were shown to be comparable in age, sex and prognostic features.

**Effectiveness results**
There were no significant differences in response rates between the two groups with 37 patients (61%) (95% CI: 43% - 73%) having a complete or partial response to treatment in the etoposide phosphate group and 35 patients (58%) (95% CI: 45% - 71%) in the etoposide group, (P=0.85). There were also no differences in response rates for the sub groups of patients with limited or extensive disease or between complete response rates. No significant differences were found between time to progression in the two groups, 6.9 months for the etoposide phosphate group and 7.0 for the etoposide groups (relative risk 0.90; 95% CI: 0.59 - 1.37), (P=0.50) There were also no significant differences in survival times between the two groups, at 11.4 months and 10.4 months respectively. (relative risk 0.98; 95% CI: 0.59 - 1.61), (P=0.78). In addition there were no significant differences in adverse events between the two groups.

**Clinical conclusions**
Although the use of etoposide phosphate with cisplatin is equal in efficacy to etoposide and cisplatin, etoposide phosphate is a preferable regimen, due to its greater ease of preparation.

**Modelling**
A cost reduction model based on the treatment courses, as defined by a panel of experts, was used in estimating costs.

**Measure of benefits used in the economic analysis**
Since the effectiveness analysis showed no difference in effectiveness or clinical benefit between the intervention and the comparator, the economic analysis was based on the difference in costs only.

**Direct costs**
Although some quantities of resource use were reported separately from costs, the analysis included costs for skilled labour, facility, direct equipment, and supplies as well as general and administrative expenses. The resources used were matched with current procedure terminology (CPT) level of costs. Out-patient direct costs were collected from a representative oncology group from 90 hospitals in Washington State. In-patient costs were identified from the Health Care Financing Administration form 2552-92, Medicare cost reports, the Medicare Resource Based Relative Value Scale, the Physicians’ Guide and physician salary survey data. Drug costs were estimated using fee schedules and expected payment rates, pharmaceutical price lists and the 1996 Red Book. An expert group was used to identify resources used in the management of adverse events and to scrutinise the cost figures used in the analysis, thereby designing a model of resource use and costs from which total costs were estimated. Direct costs were estimated for staging, diagnostics, laboratory tests, drugs, concomitant medications, concomitant procedures, transfusions, drug related hospitalisations and infusions. Costs were not discounted and the price years used were not stated. Costs were estimated from the perspectives of the payer (reimbursement rates) and provider (true costs).
Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis of cost parameters was conducted using a multivariate Monte Carlo simulation analysis.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
From the perspective of the provider (true costs) the average total costs per patient treated with etoposide and etoposide phosphate were $26,764.48 and $26,026.70 respectively. From the perspective of the payer (reimbursement rates) the average 'cost' of treatment per patient was $34,270.65 for etoposide and $34,320.70 for etoposide phosphate. Sensitivity analysis demonstrated that the model was robust to changes in the costs of the treatments. In a cost reduction scenario, the outpatient facility was assumed to treat an additional 16 new patients per year and fixed costs would be spread over a greater number of patients. The average cost of etoposide phosphate patients would now be $23,867.45 and $31,473.36 from the provider's and payer's perspectives.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The authors concluded that, from the perspective of the provider, costs were lower using etoposide phosphate and, from the perspective of the payer, costs were approximately equivalent. If the time savings from the shorter preparation time for etoposide phosphate are used to treat additional patients then the costs differentials between the two groups increase with the average costs in the etoposide phosphate group being $2,897.03 and $2,797.29 lower than in the etoposide group. They further recommended that a prospective economic trial to compare the costs of the two treatment options should be conducted.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. Etoposide is a common chemotherapeutic agent for the treatment of cancer and etoposide phosphate is a pro-drug of etoposide that is easier to prepare.

Validity of estimate of measure of benefit
The estimates of clinical outcomes were based on the results of a randomised controlled trial that demonstrated that the benefits from the two chemotherapeutic agents were equivalent. These results were consistent with others reported in the literature.

Validity of estimate of costs
Adequate details were provided of the sources of estimates of costs and resource use although the price years used were not stated and costs were not taken from the same patient sample as in the clinical analysis, since the economic study was conducted retrospectively. In addition, some elements of costs were taken from a sample of 90 hospitals in Washington State and these may not be representative of other parts of the United States or other countries.

Other issues
The analysis should also consider the use of alternative chemotherapy agents in terms of both effectiveness and costs. In addition the quality of life for terminally ill patients who have to undergo regular cycles of chemotherapy should also be taken into consideration in an economic analysis. The possible effects of uncertainties in the data were analysed in a
sensitivity analysis that served to support the authors' conclusions.

**Implications of the study**
Prospective economic evaluations are desirable to compare etoposide phosphate with etoposide in the treatment of SCLC. This study provides valuable information on the magnitude of resources involved in a decision of treatment modality in the health area in question. Further studies may also consider other commonly used therapeutic agents in the treatment of SCLC.

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**Other publications of related interest**

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