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## **Economic value of gemcitabine compared to cisplatin and etoposide in non-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**

Chemotherapy using gemcitabine versus a combination of cisplatin and etoposide as a palliative strategy for patients in stages III and IV of non-small cell lung cancer (NSCLC).

### **Type of intervention**

Treatment; palliative care.

### **Economic study type**

Cost-effectiveness analysis.

### **Study population**

Patients with non-small cell lung cancer in disease stages III and IV.

### **Setting**

Community care and hospital. The economic study was carried out in Indianapolis, USA.

### **Dates to which data relate**

The data for the effectiveness analysis and resource use were derived primarily from one study (for the intervention) conducted between 1992 and 1993, and from medical records dated from 1987 to 1993 (for the comparator). The price date used was not clearly reported.

### **Source of effectiveness data**

The evidence for the outcomes related to the intervention was obtained from a single study (E018 trial), while the outcomes related to the comparator was extracted from a chart review.

### **Link between effectiveness and cost data**

The costing was retrospectively performed on the same patient sample as that used in the effectiveness study.

### **Study sample**

161 patients were included in the intervention group and 88 in the control group (after the exclusion of 14 patients who had undergone different regimens than cisplatin and etoposide).

### **Study design**

The study was a combination of two case series and was performed in multiple centres. The chart review corresponded

to patients treated at community care centres. The duration of follow up was at least 6 months.

### **Analysis of effectiveness**

The principal (intention to treat or treatment completers only) used in the analysis of the effectiveness was not explicitly specified. The primary health outcomes used were survival rate and change in performance status, measured by means of the Zubrod and the Karnofsky scales, with a change of 1 and 10 points (at midcycle), respectively, meaning improvement or worsening, relative to baseline. The groups were shown to be comparable in terms of demographic characteristics with the exception of performance status at baseline which was worse for the control group (n=46) than for the intervention group, the values being 35% and 6%, respectively, for Zubrod scale of 2 (Karnofsky 60-70). The Zubrod 1 scale (Karnofsky 80-90) value corresponded to 61% and 83% of the groups, respectively, whereas the Zubrod 0 (Karnofsky 100) values were 4% and 11%, respectively.

### **Effectiveness results**

The median survival was 8.9 months (95% CI: 0 - 20) for the gemcitabine strategy, whereas the corresponding figure for cisplatin and etoposide was 7.3 months (95% CI: 0.4 - 44.8). The 'improved', 'stable' and 'worse' status were, at a midcycle, 9%, 82%, and 9%, respectively for the gemcitabine. The corresponding values for cisplatin and etoposide were 0%, 48%, and 52%, respectively.

### **Clinical conclusions**

The study revealed that the intervention was as effective as the comparator in the palliative care and treatment of the NSCLC patients.

### **Modelling**

A Monte Carlo simulation was used to deal with the uncertainty in the cost values used.

### **Measure of benefits used in the economic analysis**

The benefit measure used was the survival rate.

### **Direct costs**

Some quantities were reported separately from the prices. The costs measured were operating costs and costs of complications. The cost analysis was performed from the perspective of a private insurance payer. The duration of costs was 6 months. The resources used were based on actual data. The unit costs were obtained mainly from third-party insurance files data and a community cancer centre. The costs of medications were calculated using the average wholesale prices. The dates during which the resources were measured range from 1992 to 1993, for the intervention, and from 1987 to 1993, for the comparator. The price date was not reported. The costs excluded and reported as common were the costs of events related to cancer and those unrelated to treatment. In addition, low cost complications were not included and nor were follow up costs.

### **Indirect Costs**

Not considered.

### **Currency**

US dollars (\$).

### **Sensitivity analysis**

A one-way simple sensitivity analysis was performed on the cost components.

### **Estimated benefits used in the economic analysis**

The median survival was 8.9 months (95% CI: 0 - 20) for the gemcitabine strategy, whereas the corresponding figure for cisplatin and etoposide was 7.3 months (95% CI: 0.4 - 44.8).

### **Cost results**

The cost savings per cycle achieved by using the intervention (with respect to the comparator), for a hypothetical cohort of 5,000 patients, 70 kg of weight and 1.8 m height, was reported to range from \$1,504 to \$7,425. The median value was \$2,154. The Monte Carlo simulation found that the intervention, relative to the comparator, resulted in savings per cycle "more than 90% of the time".

### **Synthesis of costs and benefits**

Costs and benefits were not combined since the intervention was regarded as the weakly dominant strategy. The most sensitive variables were febrile neutropenia treatment and the number of days of hospitalization required for administration of chemotherapy, on the part of the comparator. By varying the treatment costs of neutropenia, within the extremes of no occurrence of febrile neutropenia (reported as the most likely scenario) and severe febrile neutropenia, resulted in an increase of 171% in cost savings per cycle. If the percentage of patients hospitalised for drug administration was varied from 100% to 0%, the costs savings per cycle were reduced by 20%.

### **Authors' conclusions**

The authors concluded that the model showed "substantial" cost savings in using gemcitabine as opposed to a combination of cisplatin and etoposide, in patients with non-small cell lung cancer, assuming common costs of chemotherapy for both strategies. The savings achieved were for the most part related to the resources saved by the outpatient nature of the intervention. However, most of the remainder of the savings related to the side-effects (treatment of febrile neutropenia and antiemetic use).

### **CRD COMMENTARY - Selection of comparators**

A justification was given for the choice of the comparator as the "most common chemotherapy regimen used for non small cell lung cancer patients in the US". You should consider whether this is a widely used health technology in your own setting.

### **Validity of estimate of measure of benefit**

The internal validity of the estimate of measure of benefit used in the economic analysis is likely to have been weakened by the lack of a randomised design.

### **Validity of estimate of costs**

Some quantities were reported separately from the prices. Adequate details of costs estimation were given with the exception of the price date used.

### **Other Issues:**

The authors' conclusions appear to be justified particularly given the sensitivity analysis conducted and the Monte-Carlo simulation results. However, some potential biases may arise from the "hybrid" nature of the effectiveness study. Given the lack of randomisation, the results may need to be treated with some caution. The generalisability of the study results was partially addressed by comparing the clinical benefits with a phase II clinical trial carried out in the USA.

### **Implications of the study**

This study was intended as a guide for future randomised controlled trials using relevant pharmacoeconomic end points.

The authors added that "until such prospective randomised studies are completed it will not be possible to make any formal conclusions on comparative economic value".

**Source of funding**

None stated.

**Bibliographic details**

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**Other publications of related interest**

Comment in: *Lung Cancer* 1996;14(1):13-7.

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Antimetabolites, Antineoplastic /economics /therapeutic use; Antineoplastic Agents, Phytogetic /economics /therapeutic use; Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy /economics; Cisplatin /adverse effects /economics /therapeutic use; Cost Savings /statistics & numerical data; Deoxycytidine /adverse effects /analogs & derivatives /economics /therapeutic use; Direct Service Costs /statistics & numerical data; Drug Costs /statistics & numerical data; Etoposide /adverse effects /economics /therapeutic use; Female; Health Services Research /methods; Hospital Costs /statistics & numerical data; Humans; Karnofsky Performance Status; Lung Neoplasms /drug therapy /economics; Male; Middle Aged; Models, Economic; Monte Carlo Method; Oncology Service, Hospital /economics; Sensitivity and Specificity; United States

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