Cost-effectiveness analysis of amifostine (Ethyol) in patients with non-small cell lung cancer

Touche D R, Stevenson J G, Jensen G

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
The study examined amifostine (single dose of 1,000 mg), a cytoprotective free radical scavenger given to protect patients with non-small-cell lung cancer (NSCLC) from toxicity associated with some chemotherapy agents (cisplatin, carboplatin and paclitaxel).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with advanced (Stage III or IV) NSCLC who underwent chemotherapy with cisplatin, carboplatin or paclitaxel.

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

Dates to which data relate
The effectiveness data were derived from a series of patients followed from 1995 to 1997 and from a study published in 1996. No dates for resource use were reported. The price year was 2000.

Source of effectiveness data
The clinical data used in the decision model were:

- the probability of minor and major toxicity with the chemotherapy regimens,
- the reduction in major toxicity (anaemia, neutropenia, thrombocytopenia) attributable to amifostine, and
- information on blood products received by the patients.

Modelling
A Markov model was developed to predict the impact of protection from chemotherapy-related toxicity on the costs of care in patients with NSCLC. Six monthly cycles were considered, thus the time horizon was 6 months (initial treatment period). A clear description of the health states and transition patterns was given, together with the input values. The structure of the model was depicted.
Sources searched to identify primary studies
The probability of toxicity with chemotherapy regimens was derived from 58 patients with NSCLC treated at the Detroit Medical Center's Karmanos Cancer Institute between 1995 and 1997. The reduction in toxicity attributable to amifostine was derived from a published clinical trial. Information on blood products received by the patients came from an institutional laboratory database.

Methods used to judge relevance and validity, and for extracting data
The effectiveness (reduction in major toxicity) of amifostine was estimated from a review of the literature, which resulted in the identification of five clinical trials. However, data were retrieved only from the largest of these studies (242 patients with ovarian cancer).

Measure of benefits used in the economic analysis
The summary benefit measure used was the reduction in the number of serious haematologic toxicities. This was derived from the published clinical trial. Serious toxicities included febrile neutropenia, thrombocytopenia requiring platelet infusions, and anaemia requiring packed red blood cell infusions.

Direct costs
The analysis of the costs was restricted to the viewpoint of the health payer. It included the direct costs of amifostine, blood products, chemotherapy and the treatment of febrile neutropenia, anaemia and thrombocytopenia. The unit costs and the quantities of resources used were presented separately for most items. Amifostine costs were based on average wholesale prices using doses reported in clinical trials. The cost of blood products was determined from an institution-specific pricing table supplied by the Red Cross to the Detroit Medical Center's Karmanos Cancer Institute. Other costs were derived from an institutional cost accounting system. Discounting was not performed because of the short time horizon of the analysis. The costs were inflated to 2000 prices using the Consumer Price Index for medical care.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
Productivity costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
One- and two-way sensitivity analyses were carried out to assess the robustness of basecase cost-effectiveness ratios to variations in the model inputs. A Monte Carlo simulation was also performed by assigning probabilistic distributions to the model inputs. Mean and median values and 95% confidence intervals (CIs) were generated.

Estimated benefits used in the economic analysis
In a hypothetical cohort of 100 patients, serious adverse events occurred in 7 patients in the amifostine group and 15 patients in the non-amifostine group.

The probabilistic sensitivity analysis showed that the mean incidence of serious adverse events was 13.9 (median 13, 95% CI: 4 to 31) with amifostine and 28.3 (median 28, 95% CI: 12 to 49) without amifostine.
**Cost results**
The average cost per patient was $4,421 with amifostine and $2,709 without amifostine. The difference was $1,711.

The probabilistic sensitivity analysis showed that the mean cost of therapy was $4,717 (median 4,698, 95% CI: 3,820 to 5,746) with amifostine and $3,280 (median 3,209, 95% CI: 2,608 to 4,308) without amifostine.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio was calculated in order to combine the costs and benefits of the two strategies.

The incremental cost per adverse event avoided with amifostine was $21,388.

The deterministic sensitivity analysis showed that amifostine remained the most expensive strategy under all scenarios. The total cost of therapy equalled $2,628 for both options only when the cost of amifostine was $96.73 per dose ($775 in the base-case).

The probabilistic sensitivity analysis showed that the mean incremental cost-effectiveness ratio with amifostine over no therapy was $14,371 (median 11,072, 95% CI: 1,628 to 47,184).

**Authors' conclusions**
The use of amifostine to prevent toxicity in non-small-cell lung cancer (NSCLC) patients undergoing chemotherapy was effective but led to a substantial increase in health care costs.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator (i.e. no amifostine) was appropriate as it represented the current pattern of treatment for patients undergoing chemotherapy. The dosage of amifostine was given. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The clinical data came from different sources. A review of the literature was undertaken to identify data on amifostine effectiveness, although it was derived from a single study where amifostine was given to patients with ovarian cancer. This raises some questions on the applicability of these data to a sample of patients with NSCLC. However, an extensive sensitivity analysis on toxicity reduction with amifostine was conducted, in which the relative risk was varied from 0 to 1. Other data came from hospital databases, which appears to have been appropriate.

**Validity of estimate of measure of benefit**
The summary benefit measure was specific to the interventions considered in the analysis and would be difficult to compare with the benefits of other health care interventions. It represents the direct effect of amifostine therapy. However, it would have been interesting had the impact of toxicity reduction on patient quality of life been estimated.

**Validity of estimate of costs**
The analysis of the costs was limited to the direct medical costs, which was consistent with the perspective of the analysis. A breakdown of the cost items was not reported for all costs, as some were presented as macro-categories. The sources of data were reported for all costs. Statistical analyses of the costs were not performed in the base-case analysis, but probabilistic distributions were given to costs in the sensitivity analysis. The impact of cost variations was also investigated. The price year was reported, which will assist reflation exercises in other time periods.

**Other issues**
The authors stated that similar results were found in a study that evaluated the cost-effectiveness of amifostine in ovarian cancer patients. The issue of the generalisability of the study results to other settings was implicitly addressed in...
the extensive sensitivity analyses. The authors noted that a limitation of the analysis was the exclusion of the costs and benefits of amifostine associated with peripheral neuropathies and nephrotoxicity, owing to the lack of prospective data. The benefits of amifostine were not evaluated in patients receiving radiotherapy concurrently.

**Implications of the study**
The study results suggest that amifostine is an effective therapy in reducing chemotherapy-related toxicity, but this benefit comes at high cost. There is also a need to evaluate the impact on patient quality of life of reducing chemotherapy-related toxicities, in order to fully understand the benefits of amifostine. The authors state that further studies should be carried out to evaluate the economic and clinical impact of amifostine in NSCLC patients.

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**Bibliographic details**

**Other publications of related interest**
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**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Amifostine /adverse effects /economics /therapeutic use; Carboplatin /adverse effects /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy /prevention & control; Cisplatin /adverse effects /therapeutic use; Cost-Benefit Analysis; Drug Therapy, Combination; Health Care Costs; Markov Chains; Monte Carlo Method; Paclitaxel /adverse effects /therapeutic use; Treatment Outcome

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