Economic analysis of amifostine as adjunctive support for patients with advanced head and neck cancer: preliminary results from a randomized phase II clinical trial from Germany

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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
The use of amifostine (500 mg) was examined. Amifostine is a new agent used to ameliorate the haematological and oral toxicities associated with carboplatin administered in standard radiochemotherapy treatments given to patients with cancer.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with stage III or IV squamous cell carcinoma of the head and neck region (Union Internationale Contre le Cancer classification), who were aged between 16 and 80 years, and showed no evidence of systemic infection, liver impairment or renal dysfunction.

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

Dates to which data relate
The dates during which the effectiveness evidence and resource use data were gathered were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations to determine the sample size were not performed. In addition, the method used to select the sample was not reported. Overall, 28 patients participated in the study. There were 14 patients in the RCT group and 14 in the RCT+A group. The mean age in both groups was 60 years. There were 10 men in the RCT group and 13 men in the RCT+A group. No patients were excluded from the study.
Study design
This was a phase II randomised clinical trial, which was carried out in a single centre (the Ear, Nose, and Throat Diseases and Plastic Surgery Clinic, Klinikum Suhl, Suhl, Germany). No details relating to randomisation were provided. The average length of follow-up was 5.5 months (range: 2 - 8). No patient was lost to follow-up.

Analysis of effectiveness
All patients included in the study were accounted for in the analysis, thus the analysis was conducted on an intention to treat basis. The primary health outcomes were:

- overall toxicity episodes, such as mucositis, dysphagia, loss of taste, xerostomia, dermatitis, anaemia, and leukopenia;
- amifostine tolerance, measured in terms of hypotension, the requirement for discontinuation, somnolence, and nausea or vomiting.

The study groups appear to have been comparable at baseline in terms of their age, gender, disease sites and stage, dose of radiotherapy received, and response to the therapy, although statistical tests were performed.

Effectiveness results
Grade 3 or 4 mucositis did not occur in the RCT+A group, but occurred in 85.7% of the patients in the RCT group, (p<0.05).

Dysphagia occurred in 7% of the patients in the RCT+A group and 100% of the patients in the RCT group, (p<0.05).

No statistically significant difference was found between the study groups in terms of loss of taste, xerostomia, dermatitis, anaemia, and leukopenia (results not reported).

Amifostine episodes of hypotension were 24% with a blood-pressure drop of 10 mmHg, 8% with a drop between 11 and 15 mmHg, and 8% with a drop between 16 and 20 mmHg. No patient required discontinuation of therapy due to hypotension.

Amifostine somnolence occurred in 12% of the patients. No episodes of nausea or vomiting were reported.

Clinical conclusions
The analysis of effectiveness showed that amifostine was well tolerated and reduced the incidence of toxicity episodes.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore carried out.

Direct costs
Discounting was irrelevant since the costs were incurred over less than 2 years. The unit costs and the quantities of resources were reported separately. The cost/resource boundary adopted was that of the third-party payer. The health costs included in the analysis were for:

- hospitalisation (due to anaemia, leukocytopenia, thrombocytopenia, dysphagia, or dermatitis),
- infection (granulocyte colony stimulating factor and granulocyte macrophage colony stimulating factor),
- haematological products (erythropoietin, platelet, and erythrocytes),
alimentation efforts (beriglobin, percutaneous enteral gastrostomy, enteral nutrition, and megace), and amifostine and ondansetron.

The resources associated with radiochemotherapy were not included as they were similar among the groups. The costs were estimated using actual data derived from average wholesale prices in Germany, such as the Red List for drugs and billing records from specific German hospital for the other resources. The quantities were estimated from the clinical trial. The dates during which the quantities were collected were not reported. The price year was not reported.

**Statistical analysis of costs**
Statistical analyses of the costs were carried out to test for statistical significance of the results.

**Indirect Costs**
The indirect costs were not included.

**Currency**
German marks (DM) converted into US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were carried out.

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

**Cost results**
The infection costs were $1,413.52 in the RCT group and $240.66 in the RCT+A group, (p<0.01).

The haematological costs were $1,275.40 in the RCT group and $286.39 in the RCT+A group, (p=0.06).

The alimentation costs were $1,063.15 in the RCT group and $340.70 in the RCT+A group, (p<0.01).

The hospitalisation costs were $2,428.55 in the RCT group and $285.72 in the RCT+A group, (p<0.01).

Amifostine cost $2,700.00 and ondansetron cost $546.28. These costs were only incurred in the RCT+A group.

The total costs were $6,180.62 in the RCT group and $4,399.75 in the RCT+A group, (p=0.016).

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
The use of amifostine, with the intention of reducing haematological and oral toxicities associated with radiochemotherapy treatments in patients with cancer, proved to be effective and resulted in cost-savings from the perspective of the third-party payer.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. The radiation and carboplatin alone strategy (RCT) was
selected, as it represented the standard intervention for the treatment of patients with neck and head cancer. You should assess whether it represents a widely used intervention in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness measures were derived from a phase II randomised controlled trial, which was carried out in a single centre. The study groups appear to have been comparable at baseline, and the study sample appears to have been representative of the study population. All patients included in the study were accounted for in the analysis. However, details of randomisation and the method used to select the sample were not given. Another threat to the internal validity of the analysis was the small sample size and the lack of power calculations, with some outcome measures showing a lack of statistically significant differences.

Validity of estimate of measure of benefit
No benefit measure was used in the economic analysis as the health outcomes were left disaggregated. Quantity and quality of life considerations would have been useful, since both are likely to be affected by the interventions considered.

Validity of estimate of costs
The analysis of the costs was carried out from the perspective of the German third-party payer. It appears that all the relevant categories of costs have been included in the analysis. The costs of radiochemotherapy were not considered as they were similar in the study groups. Consequently, their exclusion is unlikely to have affected the study conclusions. The unit costs and the quantities were reported separately, thus increasing transparency and enhancing generalisability. However, no price year was given, and thus reflation exercises to other countries could be difficult. Both the cost and quantity were estimated using actual data, which reflected prices specific to the German setting. However, the authors noted that the cost estimates used in the analysis were likely to be lower than actual patient charges "because (1) only supportive care resources are evaluated, and (2) estimated costs used in our study are lower than current charges in most hospitals".

Other issues
The authors made few comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. Thus, the external validity of the study may be somewhat limited. The authors acknowledged that patterns of therapeutic and supportive care may vary across countries. The study enrolled patients with stage III or IV squamous cell carcinoma of the head and neck region, and this was reflected in the study conclusions. The authors appear to have presented the effectiveness results selectively since the clinical results were published in a different paper (see Other Publications of Related Interest). The authors reported some limitations of their analysis. In particular, these were the small sample size and the fact that a phase II trial was conducted.

Implications of the study
The authors point out that the study provides preliminary insights concerning the usefulness of amifostine for patients with neck and head cancer. "Additional evaluations of economic and clinical benefits of amifostine in a subsequent phase III clinical trial as well as in different countries are needed".

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Other publications of related interest

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