Cost-effectiveness of high-dose chemotherapy in first-line treatment of advanced multiple myeloma

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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 health intervention examined in the study was high-dose chemotherapy (HDC) supported by autologous stem cell transplantation as a first-line treatment for advanced multiple myeloma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced multiple myeloma.

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

Dates to which data relate
Data on effectiveness were derived from a study published in 1996. Neither dates for resource use nor the price year were reported.

Source of effectiveness data
Effectiveness data were derived from a systematic review of the literature.

Outcomes assessed in the review
The outcomes estimated in the systematic review of the literature were life-years gained (LYG) and event-free survival (EFS).

Study designs and other criteria for inclusion in the review
Randomised control trials (RCTs) were considered by the authors to be the gold standard evidence, although case-series data were also examined to assess long term benefits when RCT data were not available.

Sources searched to identify primary studies
The MEDLINE, EMBASE, and BIDS Science Citation Index databases were searched from January 1983 to March 2000. Information was also obtained from internet web sites, personal contacts, and a review of health technology
assessment sites.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
The systematic review identified several uncontrolled studies, but only one randomised controlled study, which was used as the source of effectiveness data.

Methods of combining primary studies
Primary studies were not combined as only one study was used as the source of effectiveness evidence.

Investigation of differences between primary studies
Not stated.

Results of the review
The intention to treat analysis of the primary study showed that the incremental survival with HDC over conventional chemotherapy was an expected mean of 0.7 LYG for all patients and 0.8 LYG when restricted to patients younger than 60 years of age. The improvement in EFS was 0.7 event-free LYG for all patients. The authors stated that these findings were biased in favour of conventional chemotherapy.

Measure of benefits used in the economic analysis
LYG and EFS were used as benefit measures in the economic analysis. Data on survival were derived from the literature review, as reported above. Marginal benefits were estimated from published Kaplan-Meier graphs, using the area under the cure (AUC) approach to assess the mean difference between the survival of the two arms. Using the mean difference, instead of the median, allows the experience of the whole cohort to be considered.

Direct costs
Discounting was not performed although the time horizon of the study was 5 years. Unit costs and quantities of resources were not reported separately. The health service costs included in the economic evaluation of HDC were mobilisation, stem cell harvest, high-dose chemotherapy including three-week inpatient stay in a haematology ward, outpatient follow-up, and additional drug use. The cost of standard chemotherapy was based on 6-9 courses of chemotherapy plus additional day-case cost per course. The cost/resource boundary adopted was that of the UK payer. Long-term follow-up costs were assumed to be identical for the two treatments. The estimation of costs and quantities was based on actual data derived from the Central Sheffield University Hospital NHS Trust. No price year was reported.

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

Indirect Costs
Indirect costs were not included in the analysis.
Currency
UK pounds sterling (£).

Sensitivity analysis
Sensitivity analyses were conducted to assess the impact of variations in both cost and LYG data on the estimated cost-effectiveness ratios. Incremental benefits were reduced to half the baseline figures and incremental costs were varied between 10,000 and 20,000. The type of analysis appears to have been univariate. As the trial data on effectiveness were limited to a time horizon of 5 years, the authors used two approaches to estimate the long-term cost-effectiveness ratio of the interventions: first, data from a non-randomised study were used; second, extrapolation analysis (Weibull curve) using published survival data was conducted.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results above.

Cost results
Total costs were 1,980 per patient with conventional chemotherapy and 12,460 per patient with HDC. Thus the incremental cost of HDC over conventional chemotherapy was 10,480.

Synthesis of costs and benefits
An incremental analysis was conducted to combine the costs and benefits of the interventions. The incremental cost per LYG was 14,970 for all patients. The results of the sensitivity analyses showed that, for the cost-effectiveness ratio to increase beyond a threshold of 20,000 the marginal costs would have to be greater than 14,000, assuming the same baseline benefit level, or the marginal benefits would have to decrease to 0.5 LYG, assuming the same baseline costs. The incremental cost-effectiveness ratio of HDC over conventional chemotherapy decreased sensibly when simulated long-term data were used.

Authors’ conclusions
The authors concluded that HDC proved to be a cost-effective intervention in comparison with conventional chemotherapy. HDC improved survival and its cost-effectiveness ratio was well below the standard threshold of 20,000 used in the UK.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Conventional chemotherapy was selected as it represented the standard treatment for patients with multiple myeloma. You, as a user of this database, should decide whether it is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on the results of a systematic review of the literature. Search methods and inclusion criteria were reported. Only one relevant study was found and used as source of clinical evidence, this may highlight the lack of research in this particular area. The authors performed a sensitivity analysis to investigate the robustness of the effectiveness estimate used in the analysis, and found the results to be fairly robust to sensible changes.

Validity of estimate of measure of benefit
Life-years gained were used as benefit measure in the economic evaluation and were derived from a systematic review of published studies. The use of life-years gained increases the comparability of the results of this study with the
benefits of other oncology interventions implemented in the health care system. The authors commented that there were not reliable published data on quality of life with which to perform a cost-utility analysis.

**Validity of estimate of costs**
The analysis of costs was carried out from the perspective of the UK payer and it appears that all relevant categories of costs were included in the analysis. Unit costs were not reported separately from quantities of resources and the price year was not mentioned, thus making reflation exercises in other settings difficult. The source of cost data was clearly reported and a detailed breakdown of costs was given. Although costs were treated deterministically in the base case, sensitivity analyses were conducted to assess the impact of variations in the baseline costs. Discounting was not mentioned, although the time horizon of the study was 5 years. The authors commented that the inclusion of long-term cost data could affect the estimated costs.

**Other issues**
The authors made several comparisons of their findings with those from other studies. The authors acknowledged the wide regional variations in cost data and performed several sensitivity analyses to address the issue of the generalisability of the study results to other settings. The study referred to a population of patients with advanced multiple myeloma and this was reflected in the conclusions of the analysis.

**Implications of the study**
The authors highlighted that the cost-effectiveness of HDC was quite robust to variations in incremental costs and benefits and stated that future research on HDC would be helpful.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
11442497

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antineoplastic Agents /administration & dosage /economics; Combined Modality Therapy; Cost-Benefit Analysis; Disease-Free Survival; Drug Administration Schedule; Drug Costs; Evidence-Based Medicine; Great Britain; Hematopoietic Stem Cell Transplantation; Humans; Multiple Myeloma /drug therapy /economics /surgery; Quality of Life; State Medicine /economics

**AccessionNumber**
22001001519

**Date bibliographic record published**
31/05/2003

**Date abstract record published**
31/05/2003