Treatments for newly diagnosed multiple myeloma: analysis of survival data and cost-effectiveness evaluation

Trippoli S, Messori A, Becagli P, Alterini R, Tendi E

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
Therapeutic options to induce remission in newly diagnosed cases of symptomatic multiple myeloma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with newly diagnosed symptomatic multiple myeloma.

Setting
Hospital. The study was carried out in Florence, Italy.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1993 and 1996. Cost data were collected from studies published between 1 January 1995 to 15 March 1998. The price year was not reported.

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

Modelling
Mean lifetime survival (MLS) for each treatment group was calculated using the Gompertz model.

Outcomes assessed in the review
The review assessed undiscounted and discounted mean lifetime survival per patient (in years).

Study designs and other criteria for inclusion in the review
Primary studies included both controlled and uncontrolled clinical trials. Only large-scale clinical trials (with at least 100 patients per treatment modality) were eligible. Only trials published in English were considered. Only studies which enrolled cases of newly diagnosed symptomatic multiple myeloma were included. Studies in which interferon was given exclusively during either the induction phase or the maintenance phase were excluded. Patient groups for which no separate survival data were presented were excluded. Studies which enrolled pretreated patients were not considered.
Only control groups in which patients received the conventional induction treatment based on melphalan and prednisone were included.

**Sources searched to identify primary studies**
The authors searched the IOWA-IDIS compact-disk database (from January 1985 to March 1998), MEDLINE (from 1 January 1985 to 15 March 1998), reviews, textbooks and experts in this particular field of study. The authors also reviewed all references listed in these trials.

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

**Methods used to judge relevance and validity, and for extracting data**
Individual data.

**Number of primary studies included**
5 primary studies were included in the review.

**Methods of combining primary studies**
Meta-analysis. To obtain pooled estimates, trial-specific values were weighted according to sample size.

**Investigation of differences between primary studies**
Statistical comparisons of MLS across trials were carried out using the method of Simes (reference given in the paper).

**Results of the review**
Each patient treated with melphalan required an average of 12 days of outpatient therapy.

Patients treated with melphalan had a 20% frequency of serious infections.

Undiscounted mean lifetime survival per patient was 3.47 years with melphalan compared to 3.74 years with melphalan and interferon (p>0.05). Undiscounted mean lifetime survival per patient was 7.28 years with ABMT.

Discounted mean lifetime survival per patient was 2.92 years with melphalan compared to 3.04 years with melphalan and interferon. Discounted mean lifetime survival per patient was 5.15 years with ABMT.

When comparing ABMT with melphalan at conventional dosage, the relative risk reduction of death using ABMT was statistically significant (relative risk reduction of 54%, 95% CI: 47%-59%, p<0.05).

**Measure of benefits used in the economic analysis**
Undiscounted and discounted mean lifetime survival per patient (in years) was used as the primary measure of benefits. Benefits were discounted at an annual rate of 5%. MLS for each treatment group was calculated using the Gompertz model.

**Direct costs**
Direct costs were discounted at an annual rate of 5% where appropriate. Quantities and costs were not reported separately. Direct costs reflected the cost for autologous transplantation, the cost of induction therapy (including drug acquisition costs, hospitalisations, physician time for control of medication, costs incurred by patients experiencing
melphalan-related toxicity, etc.), and the cost of maintenance therapy. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Cost estimates for ABMT were derived from information published in the literature over the period 1 January 1995 to 15 March 1998. Cost estimates of conventional induction therapy with melphalan were derived from 4 of the foregoing clinical trials together with information obtained from Azienda Ospedaliera Careggi, Florence, Italy. The price year was not reported.

### Statistical analysis of costs
Not reported.

### Indirect Costs
Not included.

### Currency
US dollars ($).

### Sensitivity analysis
Sensitivity analysis was conducted on the following parameters: survival data for transplanted patients, frequency of cure for patients receiving transplantation, and the cost of ABMT.

### Estimated benefits used in the economic analysis
No significant difference in survival was found between melphalan combined with interferon and melphalan without interferon. When comparing ABMT and conventional treatment with melphalan, the incremental effectiveness was $5.15-2.92=2.23$ discounted years gained per patient.

### Cost results
When comparing ABMT and conventional treatment with melphalan, the incremental costs amounted to $60,000-$2,667=$57,333 per patient.

### Synthesis of costs and benefits
When comparing ABMT and conventional treatment with melphalan, the incremental cost-effectiveness was $25,710 per discounted life year gained. Sensitivity analyses did not change these results.

### Authors' conclusions
The use of interferon as first-line adjunctive therapy for myeloma patients yields no significant survival advantage. ABMT seems to produce a better survival than conventional chemotherapy with melphalan and prednisone and its cost-effectiveness profile is advantageous.

### CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. You, as a user of this database, should verify whether these health technologies are relevant to your setting.

### Validity of estimate of measure of benefit
A relevant measure of benefit was used. The authors adopted a systematic and thorough search of the literature and used appropriate methods for combining results. Selection criteria for inclusion of patients varied across primary trials but the authors excluded subgroups of patients who received forms of conventional chemotherapy other than standard-
dose melphalan. The analysis did not examine the effectiveness of the treatment with high-dose melphalan according to the schedule proposed by Cunningham et al (1994). Effectiveness data were collected retrospectively from both controlled and uncontrolled clinical trials.

Validity of estimate of costs
Only direct costs were considered. Indirect costs, such as productivity lost because of illness or death were not considered. Long-term follow-up costs were assumed to be identical, irrespective of treatment option. The information on costs used in the comparisons was affected by a considerable degree of variability across different institutions and different countries. The sensitivity analysis was only performed on the cost of ABMT. It may be argued that this represents a limitation of the economic analysis.

Other issues
Adequate comparisons with other studies were not made, but the generalisability of the results to other settings or countries was discussed. The role of allogeneic transplantation was not specifically addressed by this study. Moreover, the study only considered three therapeutic options for treating myeloma patients. There are, however, other first-line treatments that have been proposed in recent years. The authors do not appear to have presented their results selectively. The study enrolled newly diagnosed cases of symptomatic multiple myeloma and this was reflected in the authors’ conclusions.

Implications of the study
Further research is needed on other therapeutic options for treating myeloma patients that were not considered in this study.

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