Cost effectiveness of bortezomib in the 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 use of bortezomib for the treatment of advanced multiple myeloma (MM) in adult patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of average adult patients with advanced myeloma.

Setting
The setting appears to have been secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from a clinical study published in 2003 (Richardson et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details) and a Delphi panel of six experts in MM. The resource use data were derived from the same study, as well as the Delphi panel and published literature (2000 - 2002). The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a single study and estimates based on a Delphi panel.

Study sample
The data for the bortezomib therapy arm of the model were derived from a Phase II pivotal study (Richardson et al. 2003). The study sample was not reported. Patients in the bortezomib group had received at least two lines of previous therapy (range: 2 - 15 lines; median 6). Their median age was 59 years, 60% were males, and the mean duration of diagnosis was 48 months.

Study design
This was a single-arm, multi-centre, Phase II pivotal study. Further details of the study design were given elsewhere (Richardson et al. 2003).

Analysis of effectiveness
The basis for the analysis of the clinical study (intention to treat or treatment completers only) was not stated. The primary health outcome was median overall survival. The baseline demographic characteristics derived from the clinical study for the bortezomib group were comparable with those provided by the expert panel for the BSC and thalidomide group.

**Effectiveness results**

The median overall survival for the bortezomib group was 16 months (62% of the patients were estimated to survive for one year).

The probabilities associated with major chronic events were as follows:

- developing anaemia requiring red blood cell transfusion, 0.079;
- developing anaemia requiring erythropoietin, 0.405; and
- developing thrombocytopenia requiring platelet transfusions, 0.138.

**Clinical conclusions**

No clinical conclusions were stated as these results were used in a decision model.

**Modelling**

A decision analysis model was constructed in order to evaluate the cost-effectiveness of bortezomib relative to currently available therapeutic options (BSC and thalidomide). A second decision analysis stratified bortezomib patients based on prior thalidomide therapy. The duration of survival associated with the different treatments was used as the model time horizon. The aim of the model was to evaluate the median overall survival and medical costs associated with different treatments for an average relapsed, refractory patient with MM.

**Methods used to derive estimates of effectiveness**

A panel of six US experts in MM was surveyed using a modified Delphi technique to obtain demographic, clinical and medical resource-use estimates. Relevant published data were abstracted and presented to the experts, who reviewed and applied it to the hypothetical BSC and thalidomide groups.

**Estimates of effectiveness and key assumptions**

The median overall survival for the BSC group was 2.5 months (7% of the patients were estimated to survive for one year).

The probabilities associated with major chronic events were as follows:

- developing anaemia requiring red blood cell transfusion, 0.54;
- developing anaemia requiring erythropoietin, 0.60; and
- developing thrombocytopenia requiring platelet transfusions, 0.156).

The median overall survival for bortezomib patients was 15.7 months (60% estimated to survive for one year) for those who had used thalidomide before and 26 months (83% estimated to survive for one year) for those who had not used thalidomide before. Among the thalidomide patients, median survival was estimated at 8.6 months and 46% were estimated to survive for one year.

**Measure of benefits used in the economic analysis**
The benefit measure used was the life-years (LYs) gained. This summary measure of benefit was directly obtained from the effectiveness analysis. The benefits were not discounted.

**Direct costs**
Only medical costs were evaluated. The main resource use categories associated with each therapy were the cost of the medication, disease management (i.e. concomitant medications, office or clinic visits, diagnostic tests) and the treatment of adverse events. All the costs related to disease management and chronic events were assumed to incur for the duration of the patient's survival. Resource use was estimated from Richardson et al 2003, other recent published literature and estimates from the Delphi panel. National sources were used for the cost data, such as the Red Book and the Hospital Outpatient Prospective Payment System. The costs were not discounted.

**Statistical analysis of costs**
The costs were treated deterministically. No statistical analysis of the costs was reported in the paper.

**Indirect Costs**
The indirect costs were not considered in the economic study. A rationale for their exclusion was not provided.

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors explored the uncertainty around a number of key parameters to assess the robustness of the models. Such parameters included the price of bortezomib and thalidomide vials, the proportion of patients using bisphosphonates, the frequency of chronic events, the frequency of skeletal complications and median survival. Sensitivity analyses were performed by changing their values by plus or minus 25%. The type of analysis used was not stated, but it can be inferred that they were all one-way sensitivity analyses.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' and the 'Estimates of Effectiveness and Key Assumptions' sections.

**Cost results**
For the base-case analysis, the total cost of bortezomib therapy for MM was $65,220 per patient, compared with $14,423 for BSC therapy.

The total cost of thalidomide therapy for MM was $37,265 per patient.

The main contributor to the total costs was the treatment cost of adverse events, followed by the cost of medication.

The authors provided a breakdown of the calculation of the costs for each therapy. They also provided a detailed breakdown of the costs of adverse events for each therapy.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were estimated as the additional cost incurred per LY gained with bortezomib when compared with the alternative therapies.

From a health care payer perspective, the base-case scenario of the full-cohort model showed an ICER of $45,356 per additional LY for treatment with bortezomib compared with BSC.
The incremental cost of bortezomib among patients with previous thalidomide treatment, relative to BSC, was $49,797 for an additional LY.

For bortezomib patients without previous thalidomide use, the ICER decreased to $21,483 per additional LY when compared with thalidomide.

The authors reported that the sensitivity analyses showed that changes in the ICERs did not alter the direction of the results. Thus, the results can be considered robust.

**Authors’ conclusions**

Bortezomib was found to be cost-effective relative to best supportive care (BSC) and thalidomide for the treatment of relapsed, refractory myeloma. In the full cohort model, the incremental cost-effectiveness ratio (ICER) of bortezomib compared with BSC was $45,356 per life-year (LY) gained. The cost-effectiveness of bortezomib is greater when compared with active treatment with thalidomide: the ICER of treatment with bortezomib amongst those without previous thalidomide use, relative to those treated with thalidomide, was $21,483 per LY gained.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparator was clear. Until recently, thalidomide represented the only new treatment approach for relapsed myeloma. A description of what the authors meant by “best supportive care” is needed. You should decide whether this represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of effectiveness was based on data derived from a clinical trial and estimates from a Delphi panel. Further details on the trial design and the type of analysis are needed. The description of the clinical trial as a single-arm phase 2 pivotal study was not clear. The authors did not report evidence that the study sample in the clinical trial was representative of the study population.

**Validity of estimate of measure of benefit**

The main benefit measure used in the economic analysis was the LYs gained. The authors noted that a major aim of treatment was to improve quality of life, so a quality-adjusted life-year outcome measure might have been more appropriate. The authors recognised the difference in severity between patients in the published thalidomide studies and the cohort of the bortezomib pivotal trial. This factor accounts for the difference in median survival between groups, and it is a major limitation of the study.

**Validity of estimate of costs**

Patients treated with bortezomib were assumed to have received at least three cycles and a maximum of eight, following the clinical study, whereas the mean duration of thalidomide therapy was 6 months for responders and 2 months for nonresponders. This assumption was not justified. The probability of responding to treatment should also be incorporated into the modelling of the bortezomib group.

**Other issues**

Further details on the methods used to combine data from the clinical trial and estimates from the Delphi panel should have been provided. A statistical analysis of both the costs and effectiveness per treatment group should also have been performed. The authors reported a detailed discussion of the limitations of their analysis.

One of the authors is a consultant to, and is on the speakers' bureau for Millennium Pharmaceuticals Inc and Celgene Corporation. Another author is also a consultant to Millennium Pharmaceuticals.
Implications of the study
Although clinical outcomes and patient preferences must ultimately guide the final therapy selection, bortezomib is the most cost-effective option among the currently available therapies for the treatment of advanced MM. The authors made no comment regarding the need for further research.

Source of funding
Supported by Millennium Pharmaceuticals Inc.

Bibliographic details
Mehta J, Duff S B, Gupta S. Cost effectiveness of bortezomib in the treatment of advanced multiple myeloma. Managed Care Interface 2004; 17(9): 52-61

PubMedID
15521286

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Boronic Acids /adverse effects /economics /therapeutic use; Bortezomib; Cost-Benefit Analysis; Delphi Technique; Economics, Pharmaceutical; Female; Humans; Male; Middle Aged; Multiple Myeloma /drug therapy; Pyrazines /adverse effects /economics /therapeutic use; Thalidomide /administration & dosage; Treatment Outcome

AccessionNumber
22005000084

Date bibliographic record published
30/04/2006

Date abstract record published
30/04/2006