Cost effectiveness of lenalidomide in the treatment of transfusion-dependent myelodysplastic syndromes in the United States


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.

CRD summary
The objective of the study was to determine the cost-effectiveness of lenalidomide versus best supportive care for the treatment of transfusion-dependent low- or intermediate-1-risk myelodysplastic syndromes associated with a chromosome 5q deletion with or without additional cytogenetic abnormalities. The authors concluded that oral lenalidomide represented the optimal treatment from the perspective of a health care payer in the USA. On the whole, the quality of the study was satisfactory and the results were well reported and solid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective of the study was to determine the cost-effectiveness of lenalidomide versus best supportive care (BSC) for the treatment of transfusion-dependent low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a chromosome 5q deletion with or without additional cytogenetic abnormalities.

Interventions
Lenalidomide added to BSC without erythropoetin (EPO) was compared with BSC with EPO. Oral lenalidomide was given at a dose of 10 mg, either daily or for 21 days every 4 weeks (dosage was reduced to 5 mg daily in the majority of patients during the course of treatment). The standard weekly maintenance dose for the comparator group was 35,000 IU EPO and 375 μg granulocyte-colony stimulating factor.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A decision modelling analysis was undertaken to simulate the clinical and economic outcomes associated with the two strategies under examination. The time horizon of the analysis was 1 year. The perspective was reported to have been that of a US health care payer.

Effectiveness data:
The clinical data appear to have been derived from the published literature, based on a selection of known studies, since details of a review of the literature were not reported. Key data on lenalidomide were derived from a pivotal multi-centre phase II clinical trial, while key clinical data on BSC with EPO came from an observational cohort study. The main clinical effectiveness estimates were the rate and duration of transfusion independence.

Monetary benefit and utility valuations:
Face-to-face interviews with a group of 8 MDS patients in the US were carried out to elicit utility weights based on the time trade-off method.

Measure of benefit:
The summary benefit measures were transfusion-free years (TFYs) and quality-adjusted life-years (QALYs).
Cost data:
The cost categories included in the analysis were drugs, transfusions, laboratory tests, office visits, and other health care resources such as drug monitoring. Dose adjustments due to complications were also incorporated in the model. The costs were based on discounted average wholesale prices and Medicare fee schedules. Key resource use data were derived from the pivotal clinical trial (lenalidomide) and the observational study (BSC) used in the effectiveness analysis, augmented with clinical recommendations and expert opinions. The price year was 2005 and all prices were adjusted to US dollars ($). The time horizon of the analysis was 1 year.

Analysis of uncertainty:
The issue of uncertainty was addressed by a one-way sensitivity analysis on key model inputs and by a multi-way probabilistic sensitivity analysis using Monte Carlo simulations.

Results
Over a 1-year time-period, the TFYs were 0.61 and 0.08 with lenalidomide and BSC, respectively, and the QALYs were 0.78 and 0.53.

The total annual costs were $63,385 with lenalidomide and $54,940 with BSC.

The incremental cost per TFY gained with lenalidomide plus BSC over BSC with EPO was $16,066, while the incremental cost per QALY gained was $35,050.

The deterministic sensitivity analysis showed that the cost per QALY with lenalidomide ranged from $30,310 to $40,417 depending on the model assumptions. Even considering real-world drug wastage, the cost per QALY reached a maximum of $51,130. The probabilistic sensitivity analysis confirmed the cost-effectiveness of lenalidomide.

Authors' conclusions
The authors concluded that lenalidomide was a cost-effective alternative to BSC with EPO in patients with transfusion-dependent low- or intermediate-1-risk MDS associated with a chromosome 5q deletion with or without additional cytogenetic abnormalities. The findings from an ongoing randomised, phase III, placebo-controlled trial would provide important data for validation of the current results.

CRD commentary
Interventions:
Both treatments were adequately described, lenalidomide being compared with current standard practice in the authors’ setting. Dosages for both treatments were also presented.

Effectiveness/benefits:
The two published studies used to derive clinical data appear to have been identified selectively rather than through a review of the literature. However, one of the two studies was the pivotal randomised trial for lenalidomide, which seems the most adequate source of clinical and safety data. Key details of the two studies were provided and adjustments were appropriately carried out to deal with the heterogeneity in patient population. The choice of the two benefit measures was appropriate to reflect the impact of the two treatments on patient health. The utility weights were derived from a small sample of patients, whose representativeness might be limited.

Costs:
The analysis of the costs appears to have been consistent with the authors' stated perspective. The unit costs and their sources were extensively reported. However, resource use data were not given for all items, which might limit the possibility of replicating the analysis in other settings. Statistical analyses of the costs were not performed and the issue of variability in individual cost items was not addressed, although they were varied in the probabilistic analysis. The price year was reported, which assists reflation exercises in other time periods.

Analysis and results:
The costs and benefits were appropriately synthesised in incremental cost-effectiveness and cost-utility ratios. The description of the results from both the base-case analysis and sensitivity analysis was satisfactory. The issue of...
uncertainty was well addressed, although it was mainly restricted to key model inputs. The issue of generalisability was discussed and the authors pointed out that caution is required when extrapolating these findings given the limited availability of clinical data. However, the use of wide ranges of values in the sensitivity analysis enhances the external validity of the study results. Overall, there was little information on the decision model and no graphical depiction. A longer follow-up period would have been more appropriate to capture the full impact of the treatment, as the authors acknowledged. However, the choice of a 1-year follow up was justified by the data availability from a phase II trial, the fast track designation status of lenalidomide, and the lack of data to inform longer-term extrapolation of the trial results.

Concluding remark:
: The methodology of the study appears to have been sound and clearly reported. The selection of the key model inputs was justified and appropriate, despite the poor reporting of the decision model. The conclusions reached by the authors were robust.

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Other publications of related interest


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