Economic analysis of decitabine versus best supportive care in the treatment of intermediate- and high-risk myelodysplastic syndromes from a US payer perspective


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
This study examined the cost-effectiveness of decitabine, compared with best supportive care, for patients suffering from myelodysplastic syndrome, who had an intermediate or high risk of progressing to acute myeloid leukaemia. The authors concluded that decitabine was likely to be cost-effective from the perspective of the US health care payer. The methods were robust and various areas of uncertainty were considered. The authors’ conclusions appear to be valid, but the findings were highly sensitive to changes in some model parameters.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of decitabine, compared with best supportive care, for patients suffering from myelodysplastic syndrome, who had an intermediate or high risk of progressing to acute myeloid leukaemia (AML).

Interventions
Decitabine was given to out-patients, at a dose of 20mg per m$^2$ over one hour, every day for five consecutive days in a four-week cycle. This was given in addition to best supportive care and compared with best supportive care alone, which consisted of red blood cell transfusions, deferoxamine, erythropoiesis-stimulating agents, platelet transfusions, and colony-stimulating factors.

Location/setting
USA/out-patient.

Methods
Analytical approach:
The analysis was based on a Markov model, with a maximum follow-up of five years. The authors stated that the perspective of the health care payer or managed care was adopted.

Effectiveness data:
The clinical data for the model were from a selection of relevant studies. The treatment effect, which was the key input for the clinical analysis, was measured by survival and AML-free survival. These data, as well as the patient population details, were from a decitabine clinical trial (Kantarjian, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). This was a phase III randomised clinical trial, of 170 patients with intermediate- or high-risk myelodysplastic syndrome, that directly compared decitabine with best supportive care. Survival functions were used to project the trial data to the long-term.

Monetary benefit and utility valuations:
Most of the utility values were from a study that used the time trade-off instrument with patients with myelodysplastic syndrome. The AML-related utility values were from published quality-of-life measures for older adults, assessed using the European Organisation for Research and Treatment of Cancer's core 30-item questionnaire. These values were converted to European Quality of life (EQ-5D) utility scores using a published algorithm.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%. Survival and AML-free survival data were reported.

Cost data:
The economic analysis included the costs of drugs (acquisition and administration), transfusions, hospitalisations, physician visits, laboratory test or bone marrow aspiration, treatment of adverse events, and treatment of AML (with or without chemotherapy). The drug costs were based on average wholesale prices. Best supportive care costs were from the Healthcare Cost and Utilization Project database, while the costs of AML treatment were from Medicare reimbursement rates. Most of the resource use data were from the phase III clinical trial of decitabine. Published studies were used where data were not available from the trial. The costs were in US dollars ($) and a 3% annual discount rate was applied. The price year was 2009.

Analysis of uncertainty:
The uncertainty was investigated by means of deterministic and probabilistic sensitivity analyses, using published or assumed ranges of values. One-way sensitivity analyses were performed on the estimates of costs, risk of death, discount rate, time horizon, utility values, patients receiving chemotherapy, and other clinical inputs from the decitabine trial. Typical probability distributions were assigned to the model inputs in the probabilistic analysis. Subgroups of patients were analysed.

Results
Over five years, decitabine added 0.052 QALYs at an additional cost of $274 over best supportive care. The resulting incremental cost per QALY gained with decitabine was $5,277.

The model findings were very sensitive to variations in the discount rate and time horizon. For example, with no discounting decitabine was dominant, while with a one-year time horizon the incremental cost per QALY of decitabine rose to more than $800,000. The proportion of patients receiving chemotherapy was influential. In general, decitabine ranged from being dominant (less expensive and more effective) to having a very high (unfavourable) cost-utility ratio.

Using resource use data from a hospital database, instead of from the decitabine clinical trial, made decitabine dominant. The probabilistic analysis showed that decitabine had a higher probability than best supportive care of being cost-effective at all willingness-to-pay thresholds. In general, decitabine was more cost-effective in patients with more severe disease.

Authors' conclusions
The authors concluded that decitabine was likely to be cost-effective from the perspective of the US health care payer.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Decitabine was the proposed treatment, while best supportive care was the most common treatment for myelodysplastic syndrome, in the USA. The authors stated that other novel myelodysplastic syndrome treatments were not considered because of the heterogeneity of published data, in terms of patient population and clinical trial design, which did not allow a valid comparison with decitabine.

Effectiveness/benefits:
All clinical data were based on the decitabine trial, a phase III trial, with a head-to-head comparison of the study drug and best supportive care. The analysis was based on an intention-to-treat approach. Power calculations were not reported, but are likely to have been conducted. The design of the trial was good, but the trial was not fully described. Standard survival functions were used to extrapolate the long-term outcomes. Extensive sensitivity analysis of the clinical inputs was conducted. QALYs were appropriate as the benefit measure, because the disease affects both survival and quality of life. They also allow comparisons to be made with other disease treatments. The instruments used to obtain the utility weights were reported and were valid. They were appropriately derived from patients with myelodysplastic syndrome. Disease-specific outcomes were also reported.
Costs:
The economic analysis was appropriately carried out as the cost categories were relevant to the perspective of the health care payer and the cost sources were appropriate. Some unit costs were presented, while costs were reported as category totals, due to the use of Medicare data. The resource use data were directly from the decitabine clinical trial and reflected the trial-specific pattern of health care resources. An alternative analysis was conducted, using data from a claims database. The price year and discounting were reported. Alternative estimates of costs were assessed in the sensitivity analysis.

Analysis and results:
An appropriate incremental approach was used to synthesise the projected costs and benefits, and the findings were clearly presented. A clear description of both the simulation model and the transition patterns across health states was given. Appropriate sensitivity analyses were carried out to investigate the uncertainty underlying several inputs for the model. The analysis appears to have been specific to the US context and will not be easy to transfer to other settings.

Concluding remarks:
The methods were robust and various areas of uncertainty were considered. The authors' conclusions appear to be valid, but the findings were highly sensitive to changes in some model parameters.

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