Application of cost-effectiveness analysis to demonstrate the potential value of companion diagnostics in chronic myeloid leukemia

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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.

CRD summary
This study assessed the cost-effectiveness of treating chronic myeloid leukaemia, with nilotinib, dasatinib, or both, based on the results of a companion diagnostic. The authors concluded that the companion diagnostic could improve the costs and effectiveness of second-line treatment over two years. The methods were valid and the authors' conclusions appear to be appropriate, but there was a lack of clinical evidence for these conclusions.

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

Study objective
The objective was to assess the cost-effectiveness of treating chronic myeloid leukaemia, with nilotinib, dasatinib, or both, based on the results of a companion diagnostic. The population was patients, who had myeloid leukaemia in the chronic phase, who were eligible for second-line therapy with nilotinib or dasatinib, who had failed to respond to high-dose imatinib, and who did not have the T3151 gene mutation.

Interventions
The companion diagnostic was a kinase activity profiling technology that used a diagnostic microarray to predict the patient's response to each tyrosine kinase inhibitor (TKI) before initiation; patients were classified as optimal responders to dasatinib, nilotinib, both, or neither. Nonresponders were given alternative treatments. This was compared with no testing, where treatment was based on Dutch handbook recommendations, with dasatinib for the first year and nilotinib for the second year, if dasatinib failed.

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
A decision-tree model was developed to combine the data from published literature. The time horizon was two years. The authors reported that the perspective was that of the Dutch health care sector.

Effectiveness data:
The effectiveness data were from a number of sources including clinical trials, published studies, and expert clinical opinion. The main measure of effectiveness was the proportion of patients not responding to dasatinib and nilotinib. These estimates were from published clinical trials.

Monetary benefit and utility valuations:
The utility estimates were from a phase III trial assessing imatinib (Reed, et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details).

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs), which were discounted at an annual rate of 1.5%.

Cost data:
The direct costs were those of TKIs, treatment of non-responders, and diagnostic tests. The authors reported that the costs of adverse events were not included as the safety profiles of dasatinib and nilotinib did not generally differ. The costs were from Dutch health care insurance boards and authorities, and published studies. All costs were reported in 2009 Euros (EUR) and they were discounted at a rate of 4% per annum.

**Analysis of uncertainty:**
Univariate sensitivity analyses were conducted to assess the impact of variations in the model inputs on the results. The results were presented in tornado diagrams. Several scenario analyses were conducted.

**Results**
The mean cost per patient was EUR 101,500 without a companion diagnostic, compared with EUR 89,000 with a companion diagnostic. The mean QALYs gained were 1.61 without the companion diagnostic and 1.63 with the companion diagnostic.

The companion diagnostic was dominant over no companion diagnostic, as it was less costly and more effective.

The sensitivity analyses showed that the findings were sensitive to the cost of treatment, the utility for progression, and the progression-free survival.

**Authors' conclusions**
The authors concluded that the companion diagnostic could improve the effectiveness and costs of second-line treatment over two years.

**CRD commentary**

**Interventions:**
The interventions were described and appear to have been appropriate comparators. The population was well described.

**Effectiveness/benefits:**
The effectiveness estimates were from various sources. The authors reported the value used and its source, for each model parameter, but no systematic review was reported, leaving it unclear if all the best available evidence was used. The benefit measure appears to have been appropriate, as it assesses both the morbidity and mortality of the patients. No details were provided on how the utility estimates were derived and the relevant study should be consulted to assess its quality.

**Costs:**
The authors explicitly reported the perspective and it appears that all the relevant major cost categories were included. The sources for these costs were reported, as were the time horizon, discount rate, and price year.

**Analysis and results:**
All the selected evidence on costs and outcomes was synthesised in a decision-analytic model. Appropriate details of this model were given, including a diagram. The results were well reported in tables. One-way sensitivity analyses were conducted to assess which parameters had the greatest impact on the results. These go some way towards evaluating uncertainty, but probabilistic sensitivity analysis can more thoroughly investigate the overall model uncertainty. The authors reported that the main limitation to their analysis was the fact that the value of the companion diagnostic was uncertain, due to limited clinical evidence on second-line TKIs.

**Concluding remarks:**
The methods were valid and the authors' conclusions appear to be appropriate, but there was a lack of clinical evidence for these conclusions.

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