Cost-effectiveness of dasatinib and nilotinib for imatinib-resistant or -intolerant chronic phase 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
The study assessed the cost-effectiveness of dasatinib and nilotinib for chronic phase chronic myeloid leukaemia compared with both high-dose imatinib in patients resistant to normal-dose imatinib and interferon-alpha for patients intolerant to imatinib. The cost-effectiveness of dasatinib and nilotinib was uncertain in people intolerant to imatinib. The two drugs provided poor value for money in patients resistant to imatinib. The analysis was based on robust methodology that ensures the validity of the authors’ conclusions.

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

Study objective
The study assessed the cost-effectiveness of dasatinib and nilotinib for people with chronic phase chronic myeloid leukaemia in comparison with high-dose imatinib in patients who were resistant to normal-dose imatinib and in comparison with interferon-alpha for patients intolerant of imatinib.

Interventions
Two comparisons were made depending on the patient population. Dasatinib (100mg once per day) and nilotinib (400mg twice per day) were compared against high-dose imatinib (400mg twice per day) for patients resistant to normal-dose imatinib. Dasatinib and nilotinib were compared against interferon-alpha for patients intolerant to imatinib.

Location/setting
UK/outpatient.

Methods
Analytical approach:
The analysis used an area under the curve partitioned survival Markov-type model to investigate disease progression in chronic myeloid leukaemia and the cost-effectiveness of the alternative strategies. The time horizon was 44 years (lifetime).

The authors stated that the analysis was carried out from the perspective of the UK National Health Service (NHS).

Effectiveness data:
Clinical data were derived from a systematic review of the published literature. Some data on disease progression and treatment duration were obtained from drug company submissions to NICE (National Institute for Clinical Excellence). The proportion of patients who achieved a major cytogenetic response was a key input and was used to estimate overall survival. Survival curves were used to extrapolate short-term data on progression-free survival over the model time horizon. Some assumptions were made, often based on experts’ opinions.

Monetary benefit and utility valuations:
Utility estimates were from six published studies that used the EQ5D (EuroQol) questionnaire.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were used as the summary benefit measures. An annual discount
rate of 3.5% was applied to QALYs.

Cost data:
Costs included were drug acquisition, drug administration for interferon-alpha (district nurse visits), consultant visits, bone marrow tests, X-rays, computed tomography (CT) scans, blood transfusions, third-line treatment and in-patient terminal care. Costs of drugs were from the British National Formulary. Other costs were based on NHS reference costs and national tariffs. Patterns of resource consumption were based on the opinions of a sample of UK clinicians and dosages reported in the clinical trials. Costs were in UK pounds (£) and were discounted at an annual rate of 3.5%. The price year was 2010.

Analysis of uncertainty:
One-way sensitivity analyses were carried out for all model inputs. Ranges of values were obtained from published studies. A probabilistic sensitivity analysis was performed for all inputs. The sensitivity analysis focused in particular on progression-free survival and overall survival.

Results
In the imatinib-resistant population, for dasatinib versus high-dose imatinib the incremental cost per QALY was £91,499. Nilotinib dominated high-dose imatinib. The incremental cost per QALY gained with dasatinib versus nilotinib was £277,700. These results were generally stable in the sensitivity analyses.

In the imatinib-intolerant population, the incremental cost per QALY gained with nilotinib versus interferon-alpha was £104,698 and with dasatinib versus nilotinib was £58,000. Deterministic sensitivity analyses showed that the incremental cost per QALY gained remained above £54,000 with dasatinib over interferon-alpha and above £48,000 with nilotinib over interferon-alpha. Probabilistic sensitivity analysis confirmed that interferon-alpha was likely to be the preferred strategy at all but the highest levels of willingness-to-pay thresholds.

Undiscounted mean life years and discounted QALYs were reported for both populations.

Authors' conclusions
The authors concluded that the cost-effectiveness of dasatinib and nilotinib was uncertain in people intolerant to imatinib and provided poor value for money in patients resistant to imatinib from the UK NHS perspective.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as some of the available treatments for the two patient populations were considered on the basis of experts’ opinions.

Effectiveness/benefits:
Clinical inputs were retrieved through a systematic review of the literature. Most data were from single arm observational studies due to a lack of head-to-head clinical trials. Only short-term estimates were available and assumptions had to be made on long-term values. A high level of uncertainty surrounded the available data.

Key characteristics of the patient population and other methodological details of studies used to derive selected inputs were reported in an appendix.

QALYs and life-years were appropriate benefit measures with which to capture the impact of the disease on patients’ health. The assumptions used to calculate survival were stated explicitly. Utility weights were taken from published studies that used EQ5D; these were not available for all treatments and equivalence of some data were assumed, which made most utility estimates uncertain.

Costs:
The included cost categories were consistent with the perspective of the study. Unit costs and resource quantities were presented separately, which enhanced generalisability. Data sources were reported and represented NHS tariffs. Resource quantities reflected typical management of the two groups of patients in the authors’ setting. The price year was reported and would enable reflation exercises for other time periods. The impact of variations in key cost inputs
was tested in sensitivity analyses.

Analysis and results:
The authors described the decision model and justified their exclusion of costs and disutility associated with adverse events. Valid approaches were used to deal with the issue of uncertainty. Methods and main results were presented clearly and discussed. The study results were presented extensively. The incremental approach used to synthesise costs and benefits of the alternative strategies was appropriate. The authors stated that study findings could be transferred only to settings with similar costs. It was acknowledged that this analysis was exploratory and further studies should be performed once data from clinical trials were available.

Concluding remarks:
The analysis was based on robust and transparent methods that should ensure the validity of the authors’ conclusions. The authors conclusions reflect the uncertainty of the evidence base.

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