Cost-effectiveness considerations in the treatment of essential thrombocythemia
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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 initial treatment of thrombocythaemia with anagrelide, hydroxyurea or interferon (IFN)-alpha was examined. If initial treatment with anagrelide or IFN-alpha failed, hydroxyurea would be used, followed by IFN-alpha or anagrelide. In the case of initial treatment with hydroxyurea, IFN-alpha would be used.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of a hypothetical 40-year-old man with essential thrombocythaemia.

Setting
The setting was secondary care. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data were gathered from studies published between 1992 and 2000. The dates to which the resource use data related were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review of the literature.

Modelling
A Markov model was used to compare the costs and effectiveness of the three treatment alternatives. The model consisted of seven health states. These were uncomplicated essential thrombocythaemia, thrombotic complication, gastrointestinal complication, cardiac complication, cerebrovascular complication, leukaemia and death. The cycle duration was 3 months. The time horizon was lifetime.

Outcomes assessed in the review
The outcomes assessed in the review and used as model inputs were:

the drug efficacy,

the probabilities of complications of essential thrombocythaemia,
the lifetime probability of leukaemia as a complication of hydroxyurea, and

the probabilities of dying of essential thrombocythaemia or treatment complications.

Drug efficacy was considered to be the probability of not experiencing a major complication or death during each 3-month time period. This took the effect and tolerance of the drugs into consideration.

Study designs and other criteria for inclusion in the review
The clinical outcomes were derived from non-randomised clinical trials.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
About 13 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The drug efficacy, based on a target of 400,000 platelets, was 0.8 for both anagrelide and hydroxyurea and 0.75 for IFN-alpha.

The probability of cardiac complications was 0.043, while the probability of dying from a cardiac complication was 0.3.

The probability of cerebrovascular complications was 0.036, while the probability of dying from a cerebrovascular complication was 0.15.

The probability of gastrointestinal complications was 0.0021, while the probability of dying from a gastrointestinal complication was 0.05.

The probability of thrombotic complications was 0.05, while the probability of dying from a thrombolic complication was 0.05.

The lifetime probability of leukaemia as a complication of hydroxyurea was 0.10, while the probability of dying from leukaemia was 0.85.

Methods used to derive estimates of effectiveness
The authors made one assumption on the impact of effective treatment on the probabilities of complications.

Estimates of effectiveness and key assumptions
It was assumed that if the drug treatment was effective, the probability of essential thrombocythaemia was reduced by 86%.

Measure of benefits used in the economic analysis
The authors used life expectancy as the benefit measure. The health benefits were discounted at a rate of 3%.

Direct costs
A societal perspective was adopted in the analysis. However, only the direct costs were included. These were for medications, the treatment of complications and hospitalisation. The resources were derived from information abstracted from observational studies. The dates to which the resource data related were not reported. The unit costs and the quantities were not reported separately. The costs were discounted at 3%. The price year was not reported.

Statistical analysis of costs
No statistical analysis of the costs was performed.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A Monte Carlo (probabilistic) sensitivity analysis was performed on drug efficacy (+/- 5%), costs (+/- 10%) and lifetime leukaemia risk from hydroxyurea (a decrease from 0.10 to 0.05). The results were expressed using an acceptability curve (willingness to pay).

Estimated benefits used in the economic analysis
Patients treated with hydroxyurea could expect to have 20.492 years of life expectancy, compared with 21.229 years for patients treated with anagrelide and 21.183 for those treated with IFN-alpha.

The marginal estimated benefits of anagrelide compared with hydroxyurea were 0.737 years.

Cost results
The total direct costs were $79,981 with hydroxyurea, $132,876 with anagrelide and $148,306 with IFN-alpha.

The marginal cost of anagrelide versus hydroxyurea was $52,894.

The marginal cost of IFN-alpha versus anagrelide was $15,430.

Synthesis of costs and benefits
The incremental cost-effectiveness ratio of anagrelide versus hydroxyurea was $72,000/life-year saved.
IFN-alpha was found to be both more costly and less effective than anagrelide.

The sensitivity analysis showed that, if the lifetime leukaemia risk was reduced from the baseline assumption of 0.10 to 0.05, the incremental cost-effectiveness ratio of anagrelide versus hydroxyurea increased to $156,969/life-year saved.

At a leukaemia risk of 0.10, using a threshold willingness to pay of $75,000, anagrelide was optimal in 66% of 1,000 trials.

At a leukaemia risk of 0.10, if the willingness to pay was set at $50,000, hydroxyurea was optimal in all trials.

Authors' conclusions
Anagrelide could be considered a therapeutic alternative that is clinically effective at an acceptable cost.

CRD COMMENTARY - Selection of comparators
The comparators used were justified on the grounds that they were the common treatment alternatives for thrombocythaemia in the authors' setting. You should consider whether these technologies are widely used practices in your own setting.

Validity of estimate of measure of effectiveness
The principal input parameters for the model were derived from published studies. However, it was unclear whether the review was conducted systematically to identify relevant research and minimise biases. The authors did not report, in the text, the methods used to derive the estimates of effectiveness. The estimates were investigated in a sensitivity analysis, using what appear to have been appropriate ranges.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The decision analysis model used to derive the measure of health benefit (life expectancy) appears to have been appropriate. However, it was unclear whether the natural mortality for a 40-year-old man was considered in the model. The health benefits were discounted at the same rate as that used for the costs.

Validity of estimate of costs
The authors reported that they adopted a societal perspective, although they did not include the indirect costs. The exclusion of these costs might have biased the results in favour of one of the three treatment alternatives. The resource quantities and the costs were not reported separately and no details were given of the cost items included in the analysis. This would prevent the analysis being reworked for other settings. The price year and the dates corresponding to the cost data were not reported. A sensitivity analysis was performed on the costs. Discounting was reported.

Other issues
The generalisability of the results was not addressed. The authors did not compare their findings with those from other studies. The authors highlighted some limitations of their study and do not appear to have reported their results selectively. In terms of the cost estimates, the reproducibility of the results to other settings may be questioned.

Implications of the study
The authors did not report any recommendation or need for further research. However, a cost-effectiveness analysis using data from randomised controlled trials is needed to demonstrate the cost-effectiveness of anagrelide, and also to validate the results of this study.

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**Other publications of related interest**

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