Cost-effectiveness of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitor in the treatment of acute ST-segment elevation myocardial infarction

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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 objective was to assess the cost-effectiveness of bivalirudin, for patients receiving primary percutaneous coronary intervention, for acute ST-segment elevation myocardial infarction. The authors’ concluded that bivalirudin was a cost-effective alternative to heparin plus a glycoprotein IIb/IIIa inhibitor. UK clinical practice appeared to be slightly different to that used in the trial that supplied the data, but the results were robust and the authors’ conclusions are appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of bivalirudin, for patients receiving primary percutaneous coronary intervention, for acute ST-segment elevation myocardial infarction.

Interventions
Bivalirudin was compared with heparin plus glycoprotein IIb/IIIa inhibitor. The treatments were described as equivalent to those used in the Harmonising Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial.

Location/setting
UK/hospital.

Methods
Analytical approach:
Two analyses of overall survival were presented. The main analysis used a decision tree to model the clinical events for one year after initial treatment. These outcomes were extended to a lifetime horizon (maximum 100 years) by a two-state (alive or dead) Markov model. The alternative analysis used a decision tree for three years, followed by the same Markov model. The perspective was stated to be that of the UK NHS.

Effectiveness data:
The key clinical data were survival and the risk of adverse events, including bleeding, ischaemic stroke, or repeat myocardial infarction. These data were from the HORIZONS-AMI trial, which was an international, prospective, randomised, open-label, phase III clinical trial. The authors stated that this was the only appropriate trial available in the literature. An intention-to-treat analysis was conducted. The prevalence of radial arterial access was higher in the UK, than in other countries, so the estimates from the HORIZONS-AMI trial were adjusted to reflect UK data. Long-term survival was based on data from the Nottingham Heart Attack Register. These were adjusted to the mean age of the HORIZONS-AMI patients, and for the increase in life expectancy, since the data were collected, using life-tables for England and Wales and the declining exponential approximation of life expectancy (DEALE) method.

Monetary benefit and utility valuations:
Two utility values were used one for the first year after an acute ST-segment elevation myocardial infarction, and the other for subsequent years. These were from a study of 229 consecutive myocardial infarction survivors at a UK centre. The EQ-5D was used, with UK tariffs and the time trade-off method.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs). Benefits were discounted at a rate of 3.5% per annum.

Cost data:
The economic analysis included the costs of drugs, treatment procedures, adverse events (bleeding, ischaemic stroke, repeat myocardial infarction, and death), ward use, and long-term annual cardiovascular treatment. Most of the resource use was from the HORIZONS-AMI trial. The estimates for alternative glycoprotein IIb/IIIa inhibitors and hospital length of stay were adjusted to represent UK practice, using UK sources and authors' assumptions. Allowances were made for treatment wastage. The costs were from UK sources and were reported in UK £. The price year was 2009 to 2010, with costs inflated where necessary. Future costs were discounted at a rate of 3.5% per annum.

Analysis of uncertainty:
Deterministic sensitivity analysis was conducted by varying the key model parameters within given ranges. Probabilistic sensitivity analysis assessed the impact of overall uncertainty in the model inputs, by drawing parameter values from assigned distributions. Several scenario analyses were performed to assess the applicability of the main results to UK practice.

Results
In the main analysis, the total cost was £12,843 for bivalirudin and £13,110 for heparin plus glycoprotein inhibitor. The total QALYs per patient were 6.26 for bivalirudin and 6.17 for heparin. In the alternative analysis, the total cost was £13,480 for bivalirudin and £13,730 for heparin. The total QALYs were 6.43 for bivalirudin and 6.32 for heparin.

Bivalirudin was found to dominate heparin, as it was less costly and more effective, in both analyses.

In the deterministic sensitivity analysis, bivalirudin remained dominant for all parameter changes, except when the difference in length of stay, between strategies, on a normal ward and in intensive or coronary care, were both varied to their 95% confidence intervals. In this case, the incremental cost-effectiveness ratio was $415 per QALY gained.

In the probabilistic sensitivity analysis, bivalirudin was dominant in 95.0% of the 10,000 simulations. At a willingness-to-pay threshold of £20,000 per QALY gained, bivalirudin was cost-effective in 99.2% of simulations. The alternative analysis yielded similar results.

Dominance was maintained over a wide range of scenarios. Even under very unfavourable assumptions (100% eptifibatide use; 100% radial arterial access with reduced survival advantage for bivalirudin; and no difference in initial hospital length of stay), the incremental cost-effectiveness remained better than £6,000 per QALY gained.

Authors' conclusions
The authors concluded that bivalirudin was a cost-effective alternative to heparin plus a glycoprotein IIb/IIIa inhibitor.

CRD commentary
Interventions:
The interventions appear to have been appropriate. The authors justified their choice of comparator, as it was the preferred option in the UK. There was no discussion of other comparators. The detailed dosages and treatment strategies were available in another publication (see Other Publications of Related Interest).

Effectiveness/benefits:
The details of effectiveness parameters were clearly reported. The choice of the HORIZONS-AMI trial as the main source for the effectiveness data appears to have been justified, but only 2.8% of participants were from (representative of) the UK. The authors stated that no other relevant trials were available and they tried to adjust the estimates to the UK. Variations in the estimates were explored in the sensitivity and scenario analyses, and the results were stable. The authors acknowledged these potential problems in generalising the estimates to the UK. The derivation of the utility weights was clearly reported and appropriate, and the utility values were clearly reported.

Costs:
The costs appear to have been appropriate for the perspective adopted, and the values were clearly reported. Cost adjustments were made for the UK setting. An appropriate discount rate was applied, and on the whole, the costing methods were well reported.

Analysis and results:
The analysis was clearly described and a model diagram was supplied. The ranges of parameter values and distributions used for the sensitivity analyses were clearly reported. For some model parameters, the choice of the range of values explored in the sensitivity analysis was not justified. The authors did not justify their choice of distributions for the probabilistic sensitivity analysis, and triangular distributions did not accurately reflect the uncertainty in the model, but the results were robust in many scenarios. The results were clearly reported, with appropriate diagrams.

Concluding remarks:
UK clinical practice appeared to be slightly different to that used in the trial, but the results were robust and the authors' conclusions are appropriate.

Funding
Funded by The Medicines Company, USA.

Bibliographic details

PubMedID
22313548

DOI
10.1136/heartjnl-2011-301323

Original Paper URL
http://heart.bmj.com/content/98/7/544.abstract

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Anticoagulants /economics /therapeutic use; Cost-Benefit Analysis; Drug Therapy, Combination; Electrocardiography; Female; Follow-Up Studies; Heparin /economics /therapeutic use; Hirudins /economics; Humans; Male; Middle Aged; Myocardial Infarction /drug therapy /economics; Peptide Fragments /economics /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /economics /therapeutic use; Quality-Adjusted Life Years; Recombinant Proteins /economics /therapeutic use; Retrospective Studies; Time Factors; Treatment Outcome

AccessionNumber
22012013773

Date bibliographic record published
05/12/2012

Date abstract record published
19/03/2013