Evaluating anti-viral drug selection and treatment duration in HBeAg-negative chronic hepatitis B: a cost-effectiveness analysis

Veenstra D L, Spackman D E, Bisceglie A, Kowdley K V, Gish R G

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 evaluate the clinical and economic outcomes of potential treatment strategies and durations for patients with hepatitis B e antigen-negative chronic hepatitis B. The authors concluded that a five year on followed by one year off treatment strategy with entecavir was the most cost-effective, but additional clinical data were needed to optimise therapy. The quality of the study was satisfactory, and the results were generally well reported, but they should be interpreted with their limitations in mind.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to evaluate the clinical and economic outcomes of a number of potential anti-viral strategies for the treatment of patients with hepatitis B e antigen (HBeAg)-negative chronic hepatitis B (CHB).

Interventions
The anti-viral strategies were initial therapy with lamivudine, adefovir or entecavir, with the addition of adefovir or entecavir for patients who developed virological breakthrough because of resistance. Each therapy was evaluated over a variety of time horizons, including five years, 10 years, and lifetime. The authors also evaluated a strategy of treating patients for five years and then stopping treatment for one year, for those who responded, or re-initiating lifetime therapy, for those who relapsed. In total, 12 strategies were evaluated.

Location/setting
USA/ambulatory and in-patient care.

Methods
Analytical approach:
A disease simulation model was devised using both decision analytic and state-transition (Markov) models, which were based on ones published by these authors. The time horizons were five years, 10 years, and lifetime. The health states included CHB, HBeAg seroconversion, hepatitis B surface antigen loss, flare, resistance, compensated cirrhosis, non-replication cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, and after liver transplantation. The authors reported that the perspective was that of the US payer.

Effectiveness data:
The disease progression and clinical efficacy data came from a critical review of the literature. The main clinical efficacy parameters were the response and resistance rates of the different regimes, and these data were derived mainly from randomised controlled trial (RCT)s.

Monetary benefit and utility valuations:
The majority of the utility data came from a US study which used the standard gamble technique to elicit valuations from 100 members of the general population. The estimate for HBeAg seroconversion was obtained from a previous study that was not described.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the main benefit measure and life-years were also evaluated. These outcomes were discounted at 3% per annum.

Cost data:
Direct medical costs were included for all the model health states. These were mainly obtained from a retrospective cohort analysis, using health claims data, but also from smaller published studies. Drug costs were obtained from 2007 average wholesale prices. All health state costs were adjusted to 2006 US dollars ($) using the consumer price index for medical care. The costs were discounted at 3% per annum.

Analysis of uncertainty:
One-way sensitivity analyses were performed on all the model parameters. A probabilistic sensitivity analysis was conducted, and reported a cost-effectiveness acceptability frontier. A number of scenario analyses with different starting ages, discount rates, and treatment durabilities were also tested.

Results
The results for the non-dominated, cost-effective strategies were as follows.

Over five years, lamivudine produced an additional 16.07 QALYs at a cost of $47,346; entecavir produced an additional 16.71 QALYs at a cost of $57,758; and the incremental cost-effectiveness ratio (ICER) for entecavir over lamivudine was $16,272.

For the five years on and one year off strategy, entecavir, produced an additional 19.21 QALYs at a cost of $117,958 and, compared with entecavir over five years, the ICER was $24,080.

The sensitivity analyses showed that the key drivers were the lamivudine resistance rate, the baseline risk of cirrhosis, entecavir drug cost, and response to salvage therapy. If the relapse rate was under 10%, the optimal treatment strategy was to stop treatment for one year to identify the durable (non-relapsing) responders before continuing treatment for those who did not show a sustained response.

In the probabilistic sensitivity analyses, the entecavir five years on and one year off strategy had the greatest expected net health benefit from a threshold willingness to pay of $1,000 up to $150,000 per QALY.

Authors' conclusions
The authors concluded that, in HBeAg-negative CHB infection, a five years on and one year off treatment strategy with entecavir improved the health outcomes at a reasonable cost compared with the alternative strategies.

CRD commentary
Interventions:
The authors generally justified the inclusion and the exclusion of the chosen comparators. Some judgement is required in deciding if these justifications are acceptable. They also acknowledged the complexity of this issue and that sequencing, which may have been relevant, was outside the scope of this study.

Effectiveness/benefits:
The disease progression data were derived from what the authors referred to as a critical review of the literature. The clinical efficacy data were taken from RCTs, which appear to have been selected by the authors using their best judgement. No details were provided on how the included studies were identified or chosen. No details of any quality assessment or statements about the internal validity of the included studies were reported. These facts suggest that no systematic review of the literature was undertaken. It is therefore not possible to ascertain if the best available evidence has been used to populate the model.

Costs:
The authors stated that they included all the direct medical costs that were relevant to the perspective. However, the costing was only presented in an aggregated manner for each health state, which makes it difficult to assess which unit costs were considered and limits the transferability to other settings. The sources of the health state costs and drug costs...
were presented, along with details of relevant adjustments.

Analysis and results:
The analysis and the results were clearly and transparently presented by the authors. The impact of uncertainty seemed, generally, to be well addressed, but details of the probability distributions assigned for the probabilistic analysis would have been useful. The authors highlighted a number of limitations, which included the uncertainty in the long-term progression rate of CHB; the sensitivity to the discount rate; the small study that served as the basis for defining the durable response; the exclusion of strategies that did not have direct comparisons; and the absence of long-term control data. The authors discussed differences with previous studies and provided some justification for why these differences might have arisen.

Concluding remarks:
The quality of the study was satisfactory, and the results were generally well reported. These results should be interpreted bearing their limitations in mind.

Funding
Funded by a grant from Bristol-Myers Squibb.

Bibliographic details

PubMedID
18373637

DOI
10.1111/j.1365-2036.2008.03691.x

Original Paper URL
http://onlinelibrary.wiley.com/journal/120088375/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Adenine /analogs & derivatives /economics /therapeutic use; Antiviral Agents /economics /therapeutic use; Cost-Benefit Analysis; Epidemiologic Methods; Guanine /analogs & derivatives /economics /therapeutic use; Hepatitis B e Antigens /metabolism; Hepatitis B, Chronic /drug therapy /economics; Humans; Lamivudine /economics /therapeutic use; Organophosphonates /economics /therapeutic use

AccessionNumber
22008100997

Date bibliographic record published
13/05/2009

Date abstract record published
12/08/2009