A cost-effectiveness analysis of currently approved treatments for HBeAg-positive chronic hepatitis B

Spackman DE, Veenstra DL

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 examined the cost-effectiveness of adefovir, entecavir, lamivudine, telbivudine, and pegylated interferon, for the treatment of hepatitis B e antigen-positive chronic hepatitis B. The authors concluded that four years of treatment with regimens that had good seroconversion, viral suppression, and low resistance such as entecavir and pegylated interferon was cost-effective. The study appears to have been based on valid methodology and the authors' conclusions should be robust, despite limited reporting around the data sources.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of adefovir, entecavir, lamivudine, telbivudine, and pegylated interferon, for the treatment of patients with hepatitis B e antigen (HBeAg)-positive chronic hepatitis B.

Interventions
The analysis considered the antivirals adefovir, entecavir, lamivudine and telbivudine, and the immune modulator pegylated interferon. Adefovir was added to the treatment regimen for those resistant to entecavir, lamivudine, or telbivudine. Entecavir was used as salvage therapy for those resistant to adefovir, and as second-line treatment for those treated with pegylated interferon, who were not seroconverted after two years. Treatment duration was four years.

Two additional strategies were considered: no intervention (best supportive care) and drug switching for patients, who had not responded to therapy after one year.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model with a lifetime horizon. The authors stated that the perspective was that of the third-party payer.

Effectiveness data:
Most of the clinical data were from the Markov model publication (Veenstra, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details), which has been assessed. The baseline characteristics of the patient population and the drug efficacy data were derived from recent clinical trials. Most of the efficacy data were based on pairwise comparisons and no study was found that compared all the interventions. The transition probabilities for disease progression were taken from published studies, the details of which were provided in an online appendix. A number of key assumptions regarding the clinical estimates and patterns of transition among health states were also made. The key clinical endpoint was the probability of transition from chronic hepatitis B to compensated cirrhosis or hepatocellular carcinoma, for each treatment.

Monetary benefit and utility valuations:
The utility values were derived from published sources and the details of these were not reported.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at 3% per annum. Other clinical outcomes were life-years, cumulative incidence of treatment-induced seroconversion, cumulative incidence of resistance, and 10-year cumulative incidence of cirrhosis.

Cost data:
The economic analysis included the costs of drugs and treatment of specific health conditions such as chronic hepatitis B, HBeAg seroconversion, flare, drug resistance, cirrhosis, hepatocellular carcinoma, and liver transplantation. Monitoring costs were assumed to be similar across treatments. The costs were presented as macro-categories. Previously published cost estimates were used and the details were not given. All costs were in US dollars ($) and were discounted at an annual rate of 3%. The price year was 2008.

Analysis of uncertainty:
The model uncertainty was assessed initially by a series of one-way sensitivity analyses using published ranges of data. Scenario analyses were also conducted to explore those parameters found to be influential or uncertain, such as the baseline seroconversion rates and the impact of viral suppression on cirrhosis risk. A probabilistic Monte Carlo simulation was performed to generate cost-effectiveness acceptability curves.

Results
The expected QALYs were 17.88 with no treatment, 18.25 with adefovir (entecavir at follow-up), 18.38 with lamivudine (adefovir at follow-up), 18.55 with telbivudine (adefovir at follow-up), 18.64 with pegylated interferon (entecavir at follow-up), and 18.70 with entecavir (adefovir at follow-up). The costs were $28,017 with no treatment, $51,914 with adefovir, $46,176 with lamivudine, $53,618 with telbivudine, $53,482 with pegylated interferon, and $50,264 with entecavir.

The incremental analysis revealed that adefovir was dominated by lamivudine; lamivudine, telbivudine, and pegylated interferon were dominated by entecavir; and the incremental cost per QALY gained with entecavir over no treatment was $27,184.

The deterministic analysis showed that extreme seroconversion rates for patients treated with entecavir in years two to four favoured pegylated interferon. As did extreme seroconversion rates, in years three to four, for patients initially treated with pegylated interferon, but subsequently treated with entecavir. In general and in the scenario analyses, seroconversion rates were the most influential model inputs.

The probabilistic analysis showed that no treatment was the preferred option at cost-effectiveness thresholds lower than $27,000. Above this figure, entecavir was the most economically attractive strategy. The probabilities of the interventions being cost-effective at a threshold of $50,000 per QALY were 57% for entecavir, 37% for pegylated interferon, and 2% for telbivudine, as initial treatments.

Authors' conclusions
The authors concluded that four years of treatment with regimens that had good seroconversion, viral suppression, and low resistance, such as entecavir and pegylated interferon, was cost-effective for HBeAg-positive chronic hepatitis B patients.

CRD commentary
Interventions:
The selection of the comparators was appropriate in that the currently approved antiviral treatments for HBeAg-positive chronic hepatitis B and pegylated interferon were examined. The authors stated that lamivudine was no longer a first-line therapy, but it was included because it has been a standard comparator in most clinical trials. Tenofovir was excluded because it had not been approved at the time of the study.
The clinical evidence came from published sources that were known to the authors. Drug efficacy data were taken from randomised controlled trials, which should ensure good internal validity. Since no trial that compared all the interventions was found, some assumptions were required and these were subjected to extensive sensitivity analysis. Other data were taken from published studies, the details of which were not given, as most of them were obtained from the previous modelling study. The use of QALYs as the summary benefit measure was appropriate as they capture the full impact of the interventions on the patients' health and allow comparisons to be made with the benefits of other health care technologies.

Costs:
The cost categories were appropriate and consistent with the economic viewpoint. The sources of data were mentioned, but were not described in detail, which limits the transparency of the economic estimates. The details on unit costs and quantities of resources used were not reported separately. More details on the economic analysis could presumably be found in the online appendix.

Analysis and results:
The costs and benefits were appropriately synthesised, using an incremental approach. The issue of uncertainty was extensively investigated using various approaches. In general, the results were clearly presented and discussed. Recommended discounting was performed for both costs and benefits. The authors assumed a treatment duration of only four years, because there was little evidence available on the long-term efficacy of these drugs. It was also stated that limited evidence was available for drug switching. The authors compared their results with those from other published studies, which found similar conclusions.

Concluding remarks:
The study appears to have been based on valid methodology and the authors' conclusions should be robust, despite limited reporting around the data sources.

Funding
Supported by a grant from Bristol-Myers Squibb.

Bibliographic details

PubMedID
18850763

Original Paper URL
http://www.ingentaconnect.com/content/adis/pec/2008/00000026/00000011/art00006

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Antiviral Agents /economics /therapeutic use; Cost-Benefit Analysis; Disease Progression; Drug Costs; Drug Resistance, Viral; Hepatitis B e Antigens /immunology; Hepatitis B, Chronic /complications /drug therapy /economics; Humans; Liver Cirrhosis /etiology /prevention & control; Markov Chains; Quality of Life; Quality-Adjusted Life Years; Treatment Outcome; United States

AccessionNumber
22008102088