Cost-effectiveness analysis of roadmap models in chronic hepatitis B using tenofovir as the rescue therapy

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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 cost-effectiveness of roadmap models for lamivudine and telbivudine was compared with that of tenofovir or entecavir monotherapy, and lamivudine without a roadmap, in patients with chronic hepatitis B. The roadmaps were cost-effective in achieving undetectable hepatitis B virus deoxyribonucleic acid for patients who were hepatitis B e antigen (HBeAg) positive, while monotherapy was preferred for patients who were HBeAg negative. The methods were valid, but the sensitivity analyses and the reporting were limited and the conclusions need confirmation.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness, in a global market, of roadmap models for lamivudine and telbivudine compared with tenofovir and entecavir monotherapies, and lamivudine without a roadmap, for the treatment of chronic hepatitis B.

Interventions
There were five strategies.

The reference strategy was lamivudine monotherapy 100mg daily, with the addition of tenofovir 300mg daily if viral resistance developed after one year.

Tenofovir monotherapy was given at 300mg daily for two years and it was assumed that there was no viral resistance. Similarly, entecavir monotherapy was given at 0.5mg daily for two years and no viral resistance was assumed.

With the lamivudine roadmap, lamivudine 100mg was given daily, with a switch to tenofovir 300mg daily if hepatitis B virus deoxyribonucleic acid (DNA) was detected at week 24, or the addition of tenofovir 300mg daily if viral resistance developed after one year.

Similarly with the telbivudine roadmap, telbivudine 600mg was given daily, with a switch to tenofovir 300mg daily if hepatitis B virus DNA was detected at week 24, or the addition of tenofovir 300mg daily if viral resistance developed after one year.

Separate analyses were performed for patients who were hepatitis B e antigen positive and those who were negative.

Location/setting
USA, Germany, and Asian countries/hospital.

Methods
Analytical approach:
The analysis was based on a decision-tree model and the time horizon was two years. The authors reported that the perspective was that of the public health care provider.

Effectiveness data:
The clinical data were identified by a systematic review of the literature. Where more than one study was found for a model parameter, the mean, weighted by study sample size, was calculated. Some assumptions were needed. Drug
Resistance was the key input for the model.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The summary benefit measures were the rate of undetectable hepatitis B virus DNA at two years and the rate of hepatitis B e antigen seroconversion.

Cost data:
The economic analysis included only the direct treatment costs for the drugs. All other direct medical costs were assumed to be similar for each treatment strategy. The US costs were found on the Internet, while the drug costs for Asian countries and Germany were provided by the authors. The cost of tenofovir was not available in Asia and it was assumed to be equal to the local cost of entecavir. All costs were in US dollars ($).

Analysis of uncertainty:
A deterministic analysis was carried out to consider variations in the treatment costs, while the probabilities remained unchanged. For Asian countries, the cost of tenofovir was varied to equal the local cost of telbivudine rather than entecavir.

Results
In patients with chronic hepatitis B, who were hepatitis B e antigen positive, compared with the reference strategy (lamivudine with tenofovir for viral resistance), the incremental cost per patient with undetectable hepatitis B virus DNA at two years, in the USA was $31,500 with tenofovir, $58,000 with entecavir, $15,300 with lamivudine roadmap, and $29,600 with telbivudine roadmap. In Germany, it was $55,700 with tenofovir, $80,500 with entecavir, $29,100 with lamivudine roadmap, and $51,900 with telbivudine roadmap. The lamivudine roadmap was the most cost-effective option both in the USA and in Germany.

In the Asian countries, the ICERS were lowest with the lamivudine roadmap and the telbivudine roadmap, and highest with tenofovir and entecavir monotherapies, regardless of the assumptions for the price of tenofovir.

With the rate of hepatitis B e antigen seroconversion as the outcome, the reference strategy had the best incremental cost-effectiveness ratios, while the two monotherapy strategies were less effective and more expensive, and the two roadmap strategies were not cost-effective.

In patients who were hepatitis B e antigen negative, per patient with undetectable hepatitis B virus DNA, tenofovir monotherapy was most cost-effective in Germany and in the USA, while in Asia it was cost-effective, depending on its price.

Authors’ conclusions
The authors concluded that the lamivudine roadmap and the telbivudine roadmap were cost-effective in achieving undetectable hepatitis B virus DNA for patients who were hepatitis B e antigen positive, while tenofovir or entecavir monotherapy was preferred for patients who were hepatitis B e antigen negative.

CRD commentary
Interventions:
The strategies compared appear to have been appropriate and the recommended treatments for chronic hepatitis B were considered. The authors stated that pegylated interferon was not considered to be relevant because the benefit measure of undetectable hepatitis B virus DNA was too stringent for this treatment and it did not have the problem of drug resistance.

Effectiveness/benefits:
The authors provided extensive details of the clinical inputs, but did not describe their sources (study design, patient population, follow-up, etc). The systematic review to identify the available sources appears to have been appropriate.
No head-to-head studies were found, which might be a weakness in the clinical sources. The authors justified their selection of the benefit measure: the short-term virological outcome was chosen over benefit measures, such as life-years or quality-adjusted life-years, due to a lack of published evidence, which would have required many assumptions.

Costs:
The economic analysis was restricted to the costs of drugs and their sources and patterns of consumption were reported. The unit costs were not given. The authors justified their exclusion of some cost items, on the basis of equal values for all treatment arms. The price year and currency conversions were not reported. Some costs were varied in the sensitivity analysis.

Analysis and results:
An incremental approach was used to synthesise the costs and benefits, which were clearly reported for all strategies and for all countries. The uncertainty was not extensively investigated as the analysis focused exclusively on the cost of drugs. The fact that the analysis was conducted in several countries increases the generalisability of the results. The authors stated that their results should be validated in further long-term studies.

Concluding remarks:
The methods appear to have been valid, but the sensitivity analyses and the reporting of the data sources were limited. The authors’ conclusions need to be confirmed by further studies.

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