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Title **Adefovir Dipivoxil and Pegylated Interferon Alpha for the Treatment of Chronic Hepatitis B: An Updated Systematic Review and Economic Evaluation**

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Aim

To update and extend a 2006 report on the clinical and cost effectiveness of adefovir dipivoxil (ADV) and pegylated interferon alpha (PEG-a) in treating chronic hepatitis B (CHB).

Conclusions and results

Of the 8 randomized controlled trials (RCTs) included in the systematic review, 3 evaluated ADV, 4 evaluated PEG-a -2b, and 1 (from the original literature search) compared PEG-a -2b plus lamivudine (LAM) with PEG-a -2b monotherapy. No RCTs of PEG-a -2a were identified. One ADV trial showed a statistically significant difference between ADV and placebo in terms of ALT response and HBV DNA levels, favoring ADV. Following withdrawal of ADV, HBV DNA, and of ALT, response declined to levels similar to those observed in placebo patients. In the ADV versus ADV plus LAM trial in patients with LAM resistance, a statistically significant difference favored combination treatment. In the PEG-a trials, statistically significant differences favored PEG-a -2b plus LAM compared with either one of the drugs given as monotherapy. In the comparison between PEG-a -2b and IFN-a, and the comparison between different staggered regimens of the commencement of PEG-a -2b and LAM, there were no statistically significant differences between groups. Four full economic evaluations were identified in addition to one identified in the original report. Two assessed PEG-a -2a; the remainder assessed ADV. PEG-a -2a was associated with increased treatment costs and gains in quality-adjusted life expectancy. In a UK study, the incremental cost-effectiveness ratio (ICER) for PEG-a -2a was 10 444 pounds sterling (GBP) per QALY gained compared with LAM. The ICERs in our updated economic model were generally less favorable than those in the original assessment report. However, this primarily arises from a change in discounting practice. The sequential treatment strategy (interferon [pegylated or conventional] followed by LAM with ADV as salvage for patients who develop LAM resistance) identified as optimal in our original report remained optimal in the updated model. In a probabilistic sensitivity analysis, when compared with conventional interferon, PEG-a -2b had a probability of being cost-effective of 79% at a willingness-to-pay threshold of GBP 20 000 per QALY, and 86% at a willingness-to-pay threshold of GBP 30 000 per QALY.

Recommendations

Both ADV and PEG-a appear beneficial for patients with CHB in suppressing viral load, reducing liver damage-associated biochemical activity, inducing HBeAg seroconversion, and reducing liver fibrosis and necroinflammation. Overall, the evidence from RCTs suggests that the effects of long-term treatment with ADV are generally durable, with relatively low rates of resistance. Beneficial effects are lost once ADV is withdrawn. In LAM-resistant HBeAg-negative patients there were no significant differences between adding ADV to ongoing LAM or switching from LAM to ADV, except for viral resistance where the combination was more favorable. PEG-a -2b was associated with some benefit, relative to comparators. However, not all differences were statistically significant.

Methods

See link www.hta.ac.uk/project/1718.asp.

Further research/reviews required

Further research should assess the clinical and cost effectiveness of newer antiviral agents in relation to existing drugs, including the role of initiating treatment with combination therapy.

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