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Title **Adefovir Dipivoxil and Pegylated Interferon Alfa-2a for the Treatment of Chronic Hepatitis B: A Systematic Review and Economic Evaluation**

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Aim

To assess the clinical and cost effectiveness of adefovir dipivoxil (ADV) and pegylated interferon alfa-2a (PEG) in treating adults with chronic hepatitis B (CHB) infection.

Conclusions and results

The results showed that ADV was significantly more effective than placebo. For patients resistant to lamivudine (LAM), response rates were significantly higher for those treated with ADV in addition to ongoing LAM than those who continued on LAM with placebo. All studies reported significant alanine aminotransferase (ALT) reductions to normal levels. For treatment-naïve patients, seroconversion rates were statistically significant, rates were higher for LAM-resistant patients who received ADV in addition to on-going LAM than those who continued on LAM with placebo, and rates were higher for LAM-resistant patients who switched to ADV than those who continued on LAM with placebo. HBsAg loss or seroconversion was observed in less than 5% of patients taking ADV. Histological improvement and necroinflammatory activity/fibrosis scores were significantly for ADV than placebo. Dose discontinuations for safety reasons were low for patients receiving ADV. With the exception of headache, the most commonly reported adverse events were often seen in the placebo groups in similar proportions to the ADV groups (different trials reported conflicting results). PEG/LAM dual therapy and PEG monotherapy were similar in effect on HBV DNA and ALT levels, and both were significantly superior to LAM monotherapy. Response rates were higher for HBeAg-negative patients than for HBeAg-positive patients. HBeAg seroconversion rates at followup were significantly higher in PEG monotherapy than in either a combination of PEG and LAM or LAM monotherapy. Comparing PEG and IFN-2a showed a significant difference in combined outcome of ALT normalization, HBV DNA response, and HBeAg seroconversion at followup. No statistically significant difference was found in histological improvement between PEG monotherapy groups, LAM monotherapy groups, and dual therapy groups. Health-related quality of life (HRQoL) decreased during treatment, but returned at followup. For HBeAg-positive patients, there were no significant differences in scores between treatment groups. Dose discontinuations for safety reasons were significantly higher for patients receiving PEG than those receiving LAM monotherapy. Adverse events in the PEG studies were headache, pyrexia, fatigue, myalgia, and alopecia. Our model estimated incremental cost per QALY at GBP 5994 for IFN compared with best supportive care, GBP 6119 for PEG compared with IFN, GBP 3685 for LAM compared with best supportive care, and GBP 16 569 for ADV compared with LAM.

Recommendations

ADV and PEG improve several biochemical, virological, and histological outcomes in HBeAg-positive and -negative patients. In a small proportion of patients this is associated with resolution of infection. For another proportion it leads to remission and reduced risk of progressing to cirrhosis, hepatocellular carcinoma, liver transplant, and death. For others who do not respond or who relapse, retreatment with another agent is necessary. Our cost-effectiveness analysis shows that incremental costs per QALY fall within the range the NHS considers as good value.

Methods

Electronic databases were searched, a model was developed to estimate cost effectiveness, a Markov state transition model was constructed, and changes in HRQoL were estimated. (See executive summary link above.)

Further research/reviews required

Further RCT evidence of the effectiveness of anti-viral treatment is required, particularly for subgroups of patients with different genotypes, patients with cirrhosis, patients from different ethnic groups, patients with co-infections (eg, HIV, HCV) and comorbidities, liver transplant patients, and children and adolescents.

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