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Entecavir

A Viewpoint by Robert G. Gish

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Chronic hepatitis B virus (HBV) infection continues to pose a very serious healthcare problem worldwide; 20–30% of hepatitis B surface antigen (HBsAg) carriers will die of complications of chronic liver disease including cirrhosis and liver cancer.[1] Patients with elevated ALT and high HBV DNA levels are the leading candidates for therapy since they are at greatest risk of progressive liver disease.

Current options for the treatment of HBV are encouraging, although resistance, partial suppression and adverse effects impact the use of lamivudine, adefovir and interferon therapy.

Entecavir, an oral antiviral medication, inhibits viral replication by HBV polymerase at three points, concentrates to very high levels in hepatocytes and results in powerful suppression of HBV in animal models, including the prevention of liver cancer in woodchucks. These three mechanisms of viral suppression provide an explanation for the powerful suppression seen in studies of both hepatitis B e antigen (HBeAg)-positive (67% of patients HBV DNA negative by polymerase chain reaction [PCR] at 48 weeks, and 81% during a second year of therapy), and HBeAg-negative patients (90% of patients HBV DNA negative by PCR at 48 weeks, and 94% during a second year of therapy). Furthermore, in lamivudine resistant, HBeAg-positive patients, viral suppression was achieved by 19% of patients after 48 weeks and 30% of patients during a second year of therapy.

The absence of resistance seen in HBeAg-positive and -negative patients after 2 years of therapy in lamivudine-naive patients is also very encouraging. Except in the most extenuating circumstances, i.e. long-term lamivudine exposure with resistance due to multiple point mutations, where 9% of patients with pre-existing lamivudine resistance who are changed to entecavir will have genotypic resistance to entecavir with rising DNA levels (rebound), entecavir resistance has not been seen to date.

Exciting new data demonstrate the safety and potency of entecavir in a wide variety of patients, with demonstrable histological improvements compared with lamivudine.[2] The adverse-effect profile of entecavir is similar to that of lamivudine, except for fewer flares of liver disease (ALT increases) in patients treated with entecavir because of the markedly lower rate of resistance.

In summary, exciting new treatments for the management of HBV continue to push viral levels to lower thresholds; improvements in histology, even in the short term, are remarkable and the safety of emerging agents remains very favourable. ▲

References

1. Dodd RY, Nath N. Increased risk for lethal forms of liver disease among HBsAg-positive blood donors in the United States. J Virol Methods 1987; 17 (1-2): 81-94.

2. Locarnini S. Molecular virology of hepatitis B virus. Semin Liver Dis 2004; 24 Suppl. 1: 3-10