Although a clinical response at study day 7 was reported, the clearest indication of the treatment efficacy was shown by post-treatment stool analysis: *Cryptosporidium* oocysts were absent in similar proportions of patients who received nitazoxanide as either tablets or oral suspension (93% and 90%, respectively), compared with 37% of patients who received placebo. Notably, patients given placebo who were symptomatic on study day 7 were still symptomatic 7 days later. Only mild and transient adverse effects of treatment were reported.

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Original article Rossignol JF *et al.* (2006) Effect of nitazoxanide in diarrhea and enteritis caused by *Cryptosporidium* species. *Clin Gastroenterol Hepatol* **4:** 320–324

Entecavir shows promise as primary treatment for chronic hepatitis B

Hepatitis B e-antigen (HBeAg)-positive and HBeAg-negative chronic hepatitis B are highly prevalent worldwide, and collectively account for more than two million deaths annually, which are caused by related hepatic complications. The principal goal of therapy for chronic hepatitis B is to suppress replication of the hepatitis B virus (HBV); for patients with the HBeAg-negative strain, in whom response to treatment cannot be measured by seroconversion, treatment efficacy is assessed by monitoring viral DNA load and alanine aminotransferase levels in serum.

Lamivudine (Epivir-HBV®, GlaxoSmithKline) has been widely used for treating both types of chronic hepatitis B infection, but is associated with a high rate of emergence of drug-resistant mutant strains. Entecavir (Baraclude®, Bristol-Myers Squibb), a guanosine analog capable of highly selective inhibition of HBV DNA polymerase, has proven to be efficacious and tolerable at a dose of 0.5 mg once daily in Phase II and III trials in patients with either HBeAg-positive and HBeAg-negative hepatitis B. Two Phase III, double-blind multicenter trials that investigated the efficacy and safety of entecavir at this dose compared with lamivudine have recently been conducted; one by Chang and coworkers in HBeAg-positive patients, and the other by Lai and coworkers in HBeAg-negative patients with no history of nucleoside analog treatment.

In the first study, 715 HBeAg-positive patients were randomly assigned to receive entecavir 0.5 mg once daily or lamivudine 100 mg once daily. After 48 weeks of treatment patients were evaluated for histologic improvement, HBeAg loss and seroconversion, normalization of alanine aminotransferase levels, and a reduction in serum HBV DNA levels compared with baseline values. The results revealed that entecavir was markedly more effective than lamivudine for all outcome measures, apart from seroconversion, for which similar data were recorded for the two groups.

The second study reported similar benefits of entecavir in 648 HBeAg-negative patients, who were randomly assigned to receive entecavir or lamivudine using the same treatment regimens as in Lai *et al*.'s study. At the 48-week evaluation, entecavir was more effective than lamivudine for all outcome measures (histologic improvement, normalization of alanine aminotransferase levels, and reduction in serum HBV DNA levels compared with baseline). In addition, there was no evidence of resistance to entecavir in either study, and the safety profile of the two drugs was comparable.

These studies demonstrate that entecavir is associated with higher rates of histologic improvement and virologic response than lamivudine, in patients with either HBeAg-positive or HBeAg-negative chronic hepatitis B. The authors conclude that entecavir is beneficial as a primary treatment for patients with these hepatitis B subtypes.

Katy Cherry

Original articles Chang TT *et al.* (2006) A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. *N Engl J Med* **354:** 1001–1010
Lai CL *et al.* (2006) Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. *N Engl J Med* **354:** 1011–1020