

Reply:

We agree that patients with hepatitis B e antigen (HBeAg)-positive chronic hepatitis B and normal aminotransferase levels (immune-tolerant phase) are at risk for developing hepatocellular carcinoma although it is unclear what the risk is compared with patients with HBeAg-positive chronic hepatitis B and elevated aminotransferase levels. Therefore, we recommended that these patients be monitored every 6 months and more frequently when aminotransferase levels became elevated. In addition, as per our Practice Guideline, physicians should consider periodic alpha-fetoprotein testing in these individuals. We also recommended that liver biopsy examination be considered and antiviral treatment initiated if the patients remained HBeAg positive with hepatitis B virus-DNA levels greater than 10^5 copies/mL after a 3- to 6-month period of elevated aminotransferase levels. We did not recommend the initiation of antiviral treatment when the aminotransferase level was persistently normal because of the low rate of response to currently approved treatment (almost identical to placebo). Our recommendation was based on the lack of evidence that current treatment could alter the outcome of these patients and not on any misguided assumption that these patients would not develop any adverse sequelae in the future. We agree that clinical trials of new treatment that is more potent and/or effective in overcoming the lack of host immune response should include patients with HBeAg-positive chronic hepatitis B and normal aminotransferase levels. Practice Guidelines are evidence-based documents. Until data supporting that treatment can result in virologic response and/or improve clinical outcome are available, we feel that it would be inappropriate to revise the Practice Guidelines with regard to treatment of HBeAg-positive patients with normal aminotransferase levels.

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