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Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B.

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BACKGROUND: Tenofovir disoproxil fumarate (DF) is a nucleotide analogue and a potent inhibitor of human immunodeficiency virus type 1 reverse transcriptase and hepatitis B virus (HBV) polymerase. METHODS: In two double-blind, phase 3 studies, we randomly assigned patients with hepatitis B e antigen (HBeAg)-negative or HBeAg-positive chronic HBV infection to receive tenofovir DF or adefovir dipivoxil (ratio, 2:1) once daily for 48 weeks. The primary efficacy end point was a plasma HBV DNA level of less than 400 copies per milliliter (69 IU per milliliter) and histologic improvement (i.e., a reduction in the Knodell necroinflammation score of 2 or more points without worsening fibrosis) at week 48. Secondary end points included viral suppression (i.e., an HBV DNA level of <400 copies per milliliter), histologic improvement, serologic response, normalization of alanine aminotransferase levels, and development of resistance mutations. RESULTS: At week 48, in both studies, a significantly higher proportion of patients receiving tenofovir DF than of those receiving adefovir dipivoxil had reached the primary end point ($P<0.001$). Viral suppression occurred in more HBeAg-negative patients receiving tenofovir DF than patients receiving adefovir dipivoxil (93% vs. 63%, $P<0.001$) and in more HBeAg-positive patients receiving tenofovir DF than patients receiving adefovir dipivoxil (76% vs. 13%, $P<0.001$). Significantly more HBeAg-positive patients treated with tenofovir DF than those treated with adefovir dipivoxil had normalized alanine aminotransferase levels (68% vs. 54%, $P=0.03$) and loss of hepatitis B surface antigen (3% vs. 0%, $P=0.02$). At week 48, amino acid substitutions within HBV DNA polymerase associated with phenotypic resistance to tenofovir DF or other drugs to treat HBV infection had not developed in any of the patients. Tenofovir DF produced a similar HBV DNA response in patients who had previously received lamivudine and in those who had not. The safety profile was similar for the two treatments in both studies. CONCLUSIONS: Among patients with chronic HBV infection, tenofovir DF at a daily dose of 300 mg had superior antiviral efficacy with a similar safety profile as compared with adefovir dipivoxil at a daily dose of 10 mg through week 48. (ClinicalTrials.gov numbers, NCT00116805 and NCT00117676.)

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