Chronic Hepatitis B: Update 2009

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The 2009 update of the American Association for the Study of Liver Diseases (AASLD) Practice Guidelines for Management of Chronic Hepatitis B are now posted online at www.aasld.org. This is the fourth version of this guideline; the last version was published in 2007.[1]

The key changes in the 2009 version are new recommendations for first-line and second-line antiviral agents. Since the last update, tenofovir disoproxil fumarate (Viread) was approved by the U.S. Food and Drug Administration for treatment of chronic hepatitis B based on the results of two double-blind randomized trials showing a superiority of tenofovir compared to adefovir. In the trial on patients positive for hepatitis B e antigen (HBeAg), 48 weeks of treatment with tenofovir resulted in a significantly higher proportion of patients with undetectable serum hepatitis B virus (HBV) DNA assay by polymerase chain reaction (76% versus 13%), alanine aminotransferase normalization (68% versus 54%), and hepatitis B surface antigen loss (3% versus 0%), with similar rates of histologic response (74% versus 68%) and HBeAg seroconversion (21% versus 18%) compared to treatment with adefovir.[2] In the trial on HBeAg-negative patients, 48 weeks of treatment with tenofovir resulted in significantly more patients with undetectable serum HBV DNA by polymerase chain reaction assay (93% versus 63%) than adefovir and similar proportions of patients achieving alanine aminotransferase normalization (76% versus 77%) or histologic response (72% versus 69%).[2] Tenofovir resistance was not detected in any of the patients after up to 96 weeks treatment, but patients at the greatest risk of drug resistance—those who remained viremic at week 72—received additional therapy with emtricitabine. Therefore, data on resistance to tenofovir monotherapy beyond 72 weeks cannot be determined from the two pivotal trials. The primary resistance mutation has not been determined. An alanine-to-threonine substitution at position 194 (rtA194T) has been reported to be associated with tenofovir resistance,[3] but additional studies are needed to confirm the association. Tenofovir had similar safety profile as adefovir in the phase III trials. Tenofovir has been reported to cause Fanconi syndrome and renal insufficiency, as well as osteomalacia and decrease in bone density. Monitoring of serum creatinine and phosphorus is recommended.[4] The recommended dose of tenofovir is 300 mg daily. Dose adjustments should be made in patients with impaired renal function.

Based on these new findings, the recommendation for first-line oral antiviral medications has been changed to tenofovir or entecavir, and adefovir has been moved to second-line oral antiviral medication. Interferon remains one of the first-line options for patients who do not have cirrhosis. Please refer to recommendations 15, 16, 20-24, 31 and 40, and tables 8, 9, 10e, and 11-13.

Since the last update in 2007, additional data on activity of entecavir against human immunodeficiency virus (HIV) became available.[5] Therefore, entecavir is no longer recommended in persons with HBV/HIV coinfection, who are receiving treatment for HBV alone. Please refer to recommendations 34 and 35.

The guidelines were also updated to include recent changes in Centers for Disease Control and Prevention recommendations on HBV screening.[6] The new recommendations expanded HBV screening to persons born in intermediate endemic areas and those who will be receiving cancer chemotherapy or long-term immunosuppressive therapy. Please refer to recommendations 1 and 39, and table 2.

Abbreviations: HBeAg, hepatitis B e antigen; HBV, hepatitis B virus; HIV, human immunodeficiency virus.

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