Marker of Active Hep B Infection Declines in Those Coinfected with HIV, Treated with Tenofovir

March 20, 2012 By Tim Horn

Prolonged therapy with antiretroviral regimens containing tenofovir is associated with a decline in hepatitis B surface antigen (HBsAg) levels in people coinfected with HIV and hepatitis B virus (HBV), according to a report presented by Dutch researchers at the 19th Conference on Retroviruses and Opportunistic Infections on Tuesday, March 6, in Seattle.

Loss of HBsAg is the ultimate chronic HBV infection treatment goal, as it signals that the immune system has ramped up and gained control of HBV replication. Among people with chronic HBV infection who experience a spontaneous loss in HBsAg, rates of cirrhosis and liver cancer are significantly lower than those who remain positive for the antigen, considered to be one of the most important markers of active infection.

Unfortunately, the rate of HBsAg loss in people undergoing hepatitis B treatment is very low. Among those not coinfected with HIV, HBsAg loss occurs in up to 8 percent of those with hepatitis B envelope antigen (HBeAg)-positive infection, compared with up to 5 percent of those with "mutant" HBeAg-negative infection, after three to five years of antiviral therapy.

Because rates of HBsAg loss associated with treatment are so low, declines in these antigen levels are not widely recognized as an achievable goal by liver disease specialists. Instead, the focus is on keeping hepatitis B viral loads undetectable, normalizing liver enzymes and—at least among those with HBeAg-positive infection—either loss of HBeAg or HBeAg-to-HBe antibody seroconversion.

But interest in therapies that can achieve both HBeAg and HBsAg loss remains high, particularly in people coinfected with HIV. In those coinfected with both viruses, the presence of HBsAg is associated with even greater risks of cirrhosis and liver cancer, compared with those with HBV monoinfection. Consequently, there is demand for research defining positive treatment outcomes for HIV/HBV-coinfected patients, particularly those using HIV treatment regimens containing antiretrovirals with the double distinction of being active against HBV: tenofovir (found in Viread, Truvada, Atripla and Complera), emtricitabine (found in Emtriva, Truvada, Atripla and Complera) or lamivudine (found in Epivir, Combivir and Trizivir).

Focusing specifically on tenofovir, one of the most widely used ARVs, Theodora de Vries-Sluijs, MD, of Erasmus Medical Center in Rotterdam, the Netherlands, and her colleagues looked at HBsAg declines and rates of HBsAg loss in a study of 104 people coinfected with HIV and HBV undergoing therapy with a tenofovir-inclusive regimen.

At the time of Vries-Sluijs's presentation, the patients had been followed for an average of 57 months. Sixty-six were HBeAg positive upon starting therapy, and 38 had mutant HBeAg strains of HBV. HBeAg-positive individuals were more likely to be male (99 versus 71 percent), white (70 versus 32 percent) and to have higher pre-treatment HBV viral loads and HBsAg levels.

About 17 percent who entered the study with HBeAg-positive infection lost their HBeAg after one year, with 47 percent estimated to have lost the antigen after six years of treatment. The estimated rate of HBeAg seroconversion to HBeAg antibodies was about 23 percent after six years.

Declines in HBsAg levels were documented by Vries-Sluijs's team. Among those in the HBeAg-positive group who lost their HBe antigen during treatment with tenofovir, HBsAg levels declined by 2.5 log. Among those who remained HBeAg positive after six years, HBsAg declines averaged 1.8 log.

Though Vries-Sluijs did not discuss HBsAg declines among those who entered the study with HBeAg-negative HBV infection, the accompanying abstract notes that decreases were less pronounced among these patients.

Five patients (8 percent) who entered the study with HBeAg-positive HBV infection lost their HBs antigen during the study. The researchers also noted in the abstract that three patients (8 percent) who entered the trial with HBeAg-negative HBV infection also achieved HBsAg loss.

In cases where HBsAg clearance occurred, it was usually during the first year of treatment. The researchers noted that HBeAg-positive patients with HBsAg levels below 100 after six months of treatment had a 71 percent probability of achieving HBsAg loss.

High pre-treatment HBsAg levels in addition to higher CD4 cell counts six and 12 months after starting antiretroviral therapy were both correlated with steeper HBsAg declines in the study.

As for long-term outlooks, Vries-Sluijs and her colleagues estimated that the average time to HBsAg loss among all patients who entered the trial with HBeAg-positive HBV infection was 18.2 years. More sobering was the estimate for those who entered the trial with HBeAg-negative HBV infection: 41 years of HBV-suppressive treatment would be necessary, on average, to achieve HBsAg loss.

"Tenofovir for HIV/HBV patients up to six years leads to significant HBsAg decline in the HBeAg-positive population," the researchers concluded. "Early HBsAg kinetics"—the slope of HBsAg loss—"were predictive for HBsAg clearance in HBeAg-positive patients and correlated with increases in CD4 cell counts." Along with the observation that "HBsAg clearance mainly occurred

within the first year of therapy," Vries-Sluijs added, "these findings underline the importance of immune restoration in HBV clearance."

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