

# HBV JOURNAL REVIEW

Volume 4, Issue 5

May 01, 2007

## Hepatitis B

Christine Kukka

### **Pegylated Interferon Plus Adefovir Lowers Viral Load Faster Than Interferon Alone**

More hepatitis B virus (HBV)-infected patients treated with a combination of pegylated interferon plus adefovir (Hepsera) achieved undetectable HBV DNA (viral load) after 24 weeks of treatment than patients treated with just interferon, according to a report presented at the European Association for the Study of the Liver (EASL) in April.

The researchers focused on patients who tested negative for the hepatitis B e antigen (HBeAg-negative) and had moderately elevated alanine aminotransferase (ALT) levels and viral load at

the start of treatment. HBeAg-negative patients tend not to respond well to either antivirals or interferon.

But the 30 treated with interferon and the antiviral adefovir experienced a more rapid HBV DNA decline—some up to a 100-fold drop—and a higher rate of undetectable viral load after 24 weeks of combination treatment than the 30 patients treated with only interferon.

There were no significant differences between the two groups in terms of ALT changes or loss of the hepatitis B surface antigen (HBsAg). An increase in ALT indicates damaged or dying liver cells.

The study is continuing to see what long-term differences emerge from the two groups. Researchers are

trying to determine if a combination of antiviral and interferon treatment is more effective in hepatitis B treatment, as is the case with hepatitis C. To date, most studies of combination antiviral and interferon therapy have been inconclusive.

### **Patients Who Do Not Respond to Lamivudine Do Better on Telbivudine**

A global study of 246 patients who failed to improve after 12 months of treatment with the antiviral lamivudine (Epivir-HBV) found their health improved more when they were switched to the antiviral telbivudine (Tyzeka) than if they continued with lamivudine.

HBV Journal Review

*A publication of the Hepatitis C Support Project*

Executive Director

Editor-in-Chief,  
HCSP Publications  
Alan Franciscus

Contributor

Christine Kukka

Managing Editor,

Webmaster  
C.D. Mazoff, PhD

Contact Information:

The Hepatitis C Support Project

PO Box 427037

San Francisco, CA 94142

[www.hbvadvocate.org](http://www.hbvadvocate.org)

© 2007

Hepatitis C Support Project

The report, presented at the EASL meeting, tracked patients for 24 weeks. The 122 patients who were switched to telbivudine experienced significantly greater declines in HBV DNA (viral load or the amount of virus in their blood), and also had reduced, and healthier ALT levels, compared to the 124 patients who continued on lamivudine.

However, researchers noted that lamivudine-resistant patients did not benefit from the switch to telbivudine, because HBV that can resist lamivudine appears able to also resist the antiviral telbivudine as well.

### ***Entecavir Reduces HBV DNA Faster Than Adefovir After One Year***

Researchers compared the effectiveness of one year of treatment with the antiviral entecavir (Baraclude) in 33 patients against treatment with adefovir in 32 patients. They reported at EASL that entecavir was more effective in decreasing HBV DNA in patients who had never been treated. All patients

were positive for HBeAg.

Differences in HBV DNA declines were noted even at Day 10, and by Week 48, 58% of entecavir-treated patients had achieved undetectable HBV DNA compared with 19% of adefovir-treated patients.

### ***Viral Resistance to Entecavir Still Low after Four Years of Treatment***

Nearly all patients who had never been previously treated with an antiviral did well when treated with entecavir, researchers reported at EASL, and only about 1% developed viral resistance after four years of treatment.

In contrast, previously treated patients who already had developed resistance to lamivudine had a high rate of entecavir resistance (39%) after four years of treatment.

Development of entecavir resistance is rare in previously untreated patients, researchers noted, because entecavir, “produces potent antiviral activity and sustained suppression of HBV DNA,” and in

order for HBV to resist entecavir, it must develop at least three mutations to escape entecavir's antiviral effects. Antivirals work by meddling with the virus' genetic material, which makes it difficult for the virus to replicate.

However, patients who have already developed lamivudine resistance have already developed two of those mutations and quickly develop the third mutation required to resist entecavir.

In the study, 91% of treatment-naive patients assessed over four years achieved undetectable HBV DNA at some point during the study period.

### ***Significant Liver Damage Can Occur Even When ALT Is Only Moderately Elevated***

A study of patients enrolled in a Phase III drug study suggests that HBV-infected patients can still have significant liver damage even when ALT levels are elevated less than twice the normal level.

These patients had liver biopsies prior to enrolling in a drug

study, and researchers compared their ALT levels to their actual liver damage revealed by the biopsies. They were surprised to find that even with normal or moderately elevated ALT levels, some patients had significant liver fibrosis and scarring (cirrhosis).

They suggested that current criteria governing when to treat patients should be modified so treatment is recommended if ALT levels were moderately elevated and patients were:

- HBeAg positive with HBV DNA greater than 20,000 IU/mL, or
- HBeAg negative with HBV DNA greater than 2,000 IU/mL and if patients were 40 years of age or older, had high/normal ALT levels and a family history of liver cancer.

Currently, the American Association for the Study of Liver Disease recommends that normal ALT levels should be 30 IU/mL in men and 19 IU/mL in women.

A liver biopsy remains an important tool to identify patients with chronic hepatitis B, researchers noted. If patients have ALT levels

that are twice normal and if significant liver damage is found, they could benefit from antiviral therapy.

### **Few Benefits Gained When Adefovir Added to Lamivudine Treatment after Lamivudine-Resistance Develops**

In another EASL report, researchers investigated whether adding adefovir to ongoing lamivudine treatment after lamivudine-resistance developed, was more effective than replacing lamivudine with adefovir.

In a study that followed 479 Korean patients, doctors found no long-term benefits gained among 94 lamivudine-resistant patient treated with a combination of lamivudine and adefovir for eight weeks before switching to only adefovir, compared with 385 patients who were immediately switched from lamivudine to adefovir with no overlap.

Current guidelines recommend overlapping lamivudine with adefovir for two to

three months before switching to just adefovir.

But researchers reported no significant differences in ALT levels or viral load changes in the two groups of patients 12 months after adefovir was added.

### **Pegylated Interferon Effective in HBeAg-Negative Patients Three Years after Treatment**

Researchers followed three groups of HBeAg-negative patients who had been treated for at least 48 weeks with just pegylated interferon (116 patients), pegylated interferon plus lamivudine (114), and 85 patients treated with just lamivudine, over three years.

Patients treated with interferon with or without lamivudine experienced significantly higher rates of ALT normalization, HBV DNA suppression, HBsAg loss and development of HBsAg antibodies, which signifies eradication of the virus, compared with the lamivudine-only-

treated group.

(HBsAg loss occurred in 8% of patients receiving interferon.)

Researchers focused on HBeAg-negative patients because they are the ones who most frequently develop viral resistance to antivirals and experience rebounds in both viral load and ALT levels.

To date, when researchers monitor HBeAg-negative patients after 24 weeks of treatment, pegylated interferon therapy is usually more effective than lamivudine alone, but researchers have yet to find any benefit from a combination of interferon plus lamivudine in these patients.

This study was unique because it monitored patients' response to interferon with or without lamivudine for three years after treatment ended.

After three years, according to their report presented at the EASL conference, patients who received interferon with or without lamivudine had higher rates of sustained low viral load and normal ALT levels than those treated with just lamivudine.

### **K2 Vitamin Slows Bone Loss in Women with Hepatitis-Related Cirrhosis**

Women with osteoporosis who also have hepatitis-related cirrhosis, benefit from treatment with vitamin K2 (menatetrenone), according to a report by Japanese researchers published in *The American Journal of Gastroenterology*.

Half of 50 women with hepatitis-related cirrhosis, which can also contribute to bone loss, were treated with K2. The women's bone mineral density in their lumbar vertebrae was measured at the beginning of treatment and one and two years later.

Bone loss was slower in the K2-treated group, 0.1% and 2.6% at years 1 and 2, compared to 0.5% and 3.9% respectively in the control group, who received no K2.

"Vitamin K2 can prevent bone loss and may therefore be useful in the management of bone disease in women with cirrhosis of the liver," researchers wrote.

## **Antiviral Mutations Could Alter HBsAg So It Evades Both Antibodies and Detection by Labs**

Researchers, presenting reports at the recent 14th Conference on Retroviruses and Opportunistic Infections, discussed the increase in “occult” or hidden hepatitis B infections in people coinfecting with HBV and HIV.

An occult hepatitis B infection can occur when the virus mutates due to antiviral treatment, they noted. Often a mutated HBV that can continue to replicate despite antiviral treatment emerges and becomes the majority HBV. One of these mutations may involve the cover of the virus, the surface antigen (HBsAg). If this occurs, medical tests that look for non-mutated HBsAg fail to identify the “mutated” or changed virus. As a result, doctors fail to identify an HBV infection.

At the conference, researchers noted it was not surprising that long-term antiviral therapy, vaccination with only the HBsAg to cause the body to produce surface antibodies (anti-HBs),

or treatment with hepatitis B immunoglobulin (HBIG) could lead to mutations in the HBV.

Spanish and Australian researchers followed 71 patients (52 were coinfecting with HIV) with chronic hepatitis B who were treated with antivirals for more than one year.

Remarkably, three coinfecting patients harbored HBV strains with mutations that allowed the HBsAg to escape attack by surface antibodies and detection by most medical lab tests. This could explain the phenomenon of “occult” hepatitis B, researchers noted.

### **Researchers Explore Coexistence of Surface Antigens and Antibodies**

Researchers are trying to determine how both surface antigens and antibodies can both be present at the same time in some people infected with HBV. Usually, the presence of anti-HBs indicates the body’s immune system has eradicated the infection, including all HBsAg.

Researchers in China studied the presence of both surface antigens and antibodies in 411

people, 20 of whom had surface antibodies. They concluded that some people developed two different types of HBsAg, the “normal” HBsAg and an HBsAg subtype.

In these people, who represented about 4.9% of patients monitored, the immune system produced an antibody for one HBsAg, but not the other. The dual presence of HBsAg and anti-HBs did not result from an HBsAg mutation, they reported in the April 2007 issue of the *Journal of Clinical Infectious Diseases*, given the fact that many of these patients had not been treated with an antiviral.

### **Unvaccinated Korean-Americans Have 6.1% HBV Infection Rate**

Between November of 1988 and May 1990, researchers screened 6,130 Korean-Americans to determine the rate of HBV infection in immigrants and their U.S.-born offspring.

The HBsAg-positive rate was 6.1% (8% for males and 4.4% for females), and was highest in those between ages

21 and 40. The HBsAg rate for 452 U.S.-born children, none of whom had been immunized at birth, was lower (2.7%) than that of 623 Korean-born (5.5%). The transmission rate was 30.3% in children born to HBsAg-positive mothers and 100% in those born to HBeAg-positive mothers.

In contrast, children with HBsAg-positive fathers had a 10.3% infection rate and those with HBeAg-positive fathers had a 19.2% infection rate. HBeAg-positive people usually have high viral loads, which makes their blood and body fluids more infectious. What surprised researchers was that among 139 asymptomatic adult carriers, 42% had elevated ALT levels and 11% had developed liver cirrhosis.

“These findings strongly suggest the need for active HBV screening of immigrants from endemic regions and, most importantly, the need for careful monitoring of the carriers,” researchers wrote in the April 2007 issue of *The American Journal of Gastroenterology*.

