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Hepatitis B

Christine Kukka

Doctor Warns Against Using Lamivudine as First Antiviral to Treat Hepatitis B

Renowned hepatitis B doctor and researcher Dr. Stephen Locarnini warned against using the antiviral lamivudine (Epivir-HBV) as the first line of treatment for hepatitis B virus (HBV) infection in a lecture at the XV International HIV Drug Resistance Workshop.

For years, lamivudine was the only antiviral available to treat hepatitis B, and it is still used as the first line of treatment in many countries.

The antiviral disrupts the virus' genetic material so it cannot replicate. However, HBV easily mutates and over time the virus is able to

“resist” lamivudine’s antiviral impact and the infection rapidly rebounds. Viral resistance occurs with other antivirals, but not as quickly as with lamivudine.

Once HBV is able to resist lamivudine, it is predisposed to “resist” other antivirals that are now on the market. To sidestep this lamivudine-induced resistance, Locarnini recommends that doctors avoid prescribing lamivudine as the first line of treatment. Instead, other antivirals should be employed first, such as entecavir (Baraclude) or tenofovir (a successful HIV drug that is currently in Phase III trials to treat hepatitis B). These two antivirals have a very low rate of resistance.

After 24 weeks of

treatment with one of these antivirals, doctors should test a patient’s viral load (which measures the quantity of HBV DNA circulating in the bloodstream) to see if the antiviral has been effective. If the viral load remains detectable, another antiviral with low viral resistance should be added to the treatment regimen.

Early Study Shows Tenofovir Successful when Lamivudine and Adefovir Fail

Many patients who develop viral resistance to lamivudine find they also quickly develop resistance to adefovir (Hepsera). A group of German researchers, searching for an effective antiviral to use in patients

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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

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who have developed this dual drug resistance, tried the antiviral tenofovir. Tenofovir (brand name Viread when used for HIV) has not yet been approved by the U.S. Food and Drug Administration (FDA) to treat hepatitis B.

The researchers treated 20 lamivudine- and adefovir-resistant patients (18 were HBeAg-positive) with 300 mg daily of tenofovir. According to the report published in the August 2006 issue of *Hepatology*, within four months 19 out of 20 patients had undetectable HBV DNA, and 10 of 14 patients achieved normal ALTs after an average of 12 months. Four patients lost HBeAg by 16 months and one patient developed surface antibodies (anti-HBs) after 16 months.

No lamivudine or adefovir mutations were found, and there were no adverse side effects.

“These preliminary observations strongly suggest that (tenofovir) might be a highly effective rescue drug for HBV-infected patients with altered responsive-

ness to treatment with lamivudine and adefovir,” researchers wrote.

Entecavir Outperforms Lamivudine in HBeAg-Negative Patients

Entecavir outperformed lamivudine in a Phase 3 study of 648 HBeAg-negative patients, according to a report published in the September 2006 issue of the *Journal of Hepatology*.

The patients were treated with either 0.5 mg of entecavir or 100 mg of lamivudine once daily for at least 52 weeks. Researchers wanted to gauge the impact of treatment on liver health. Liver biopsies were performed before and after treatment.

After 48 weeks, liver health improvements were noted in 208 of 296 entecavir-treated patients compared with 174 of 287 lamivudine-treated patients.

More patients in the entecavir group had undetectable HBV DNA (90% vs. 72%), and normal ALT levels (78% vs. 71%). Reduction of viral load was five-fold in

the entecavir group, vs. 4.5-fold in the lamivudine group.

There was no evidence of viral resistance to entecavir, and both drugs had similar safety records.

Emergency of Mutations after Three Months of Lamivudine Indicates Treatment Success or Failure

South Korean researchers, writing in the July 23, 2006 journal of *Antiviral Therapies*, suggest that detecting the emergence of the HBV YMDD mutation in patients treated with lamivudine three months after treatment begins can signal whether the drug will succeed or not.

YMDDs mutation in HBV allows it to resist lamivudine’s antiviral effects. While initially beneficial in decreasing viral load, lamivudine-treated patients with the YMDD mutation can experience a resurgence of viral load, as the HBV with YMDD mutations continue to replicate freely.

Researchers followed 30 HBeAg-

positive patients and analyzed their HBV after lamivudine treatment began. Those who had the YMDD mutations in their HBV at three months fared less well than those without the mutation. After three years, 75% of those with the early-identified YMDD mutation experienced a rebound of infection, compared to 14% without the YMDD mutations.

“In conclusion, early detection (of) HBV YMDD mutation at three months may be useful to predict the long-term outcomes of (lamivudine) therapy in patients with HBeAg-positive chronic hepatitis B,” researchers wrote.

Hepatitis C Treatment (Ribavirin and Pegylated Interferon) Also Worked against Hepatitis B in Coinfected Man

French doctors, who treated a man coinfecting with both HCV and HBV, made a surprising discovery after they treated the man with the antiviral ribavirin, commonly

used only to treat hepatitis C, and pegylated interferon, which is approved to treat hepatitis B.

The patient, according to their report published in the September 2006 issue of the *European Journal of Gastroenterology and Hepatology*, cleared HCV RNA, and surprisingly his HBV DNA became undetectable and he lost HBeAg and developed “e” antibodies (anti-HBe) after two years of treatment.

“HCV RNA became undetectable at week 17,” researchers wrote. “At the end of the 48 weeks of treatment, HCV RNA was still undetectable, HBV DNA was reduced and HBeAg remained positive. Twelve weeks after the end of treatment, HBV DNA reduction was followed by HBeAg to anti-HBe seroconversion.”

“We conclude that the combination of pegylated interferon plus ribavirin may induce suppression of both viral infections,” they wrote.

To date, the hepatitis C antiviral ri-

bavirin (Rebetol) has not been used, even experimentally, to treat hepatitis B.

Doctor Recommends Liver Biopsy in Healthy Patients If Viral Load Is Slightly Elevated

In an “Ask the Experts” column published in *Medscape Gastroenterology* in July 2006, Dr. Rowen K. Zetterman, chief of staff of the NWI Health Care System in Omaha, discussed how to monitor a 33-year-old patient who tests positive for the hepatitis B surface antigen (HBsAg), negative for the “e” antigen (HBeAg), and has normal liver enzymes (alanine aminotransferase - ALT). ALT levels rise when liver cells are damaged or die.

Zetterman recommends that ALT should be tested every 3-6 months in these patients to make sure the patient consistently has normal liver tests. If the patient has normal ALTs and has undetectable HBV DNA or a viral load of less than 100,000 copies per

mL, the patient does not require treatment.

If the patient has a viral load exceeding 100,000 copies per mL (and normal ALT levels), the patient should have a liver biopsy. If there is significant fibrosis or scarring found, then the patient should be treated.

Dr. Zetterman also recommended a test for alpha fetoprotein test (AFP), which can signal liver cancer, every six months, and an ultrasound examination of the liver every 12 months.

Survey of College Students Shows No Link Between Tattoos and Hepatitis, but HBV Infection Is 5.2%

Researchers have long suspected that tattoos and body piercings, performed with unsafe equipment, may increase the risk of hepatitis B or C. A study by U.S. Centers for Disease Control and Prevention (CDC) and the University of Texas School of Public Health that surveyed 5,282 Houston area college students explored this link.

The students, considered at low risk for injecting drug use, completed anonymous surveys and provided blood samples. About 62% of those studied were female, 42% were white, 26% were black, 2% Hispanic, and 10% were of Asian descent. About 21.2% reported having body piercings and 25.2% reported having tattoos.

The results, published in the August 2006 issue of *Hepatology*, found no risk between tattoos and piercings and hepatitis infection. However, researchers did discover:

5.2% of the students were infected with HBV. Hepatitis B infection was highest in those who practiced high-risk sexual behaviors or who were black or of Asian descent.

0.9% were infected by the hepatitis C virus (HCV). Hepatitis C infection was associated with injecting drug use, a blood transfusion before 1991 and previous incarceration.

The authors concluded, “There was

no increased risk for HCV or HBV infection in low-risk adults based solely on history of cosmetic procedures or snorting drugs. However, proper infection control practices for cosmetic procedures should be followed, illegal drug use discouraged, and hepatitis B vaccination provided to adolescents and sexually active adults.”

Hepatitis C-Infected Liver Cancer Patients Live Longer than Hepatitis B-Infected Cancer Patients

A study, published in the Aug. 18, 2006 *European Journal of Cancer*, compared survival in 2,820 liver cancer patients who were infected with either HBV or HCV.

Surprisingly, the Taiwanese researchers found that even though the hepatitis B patients in their study tended to be 10 years younger on average than the hepatitis C patients and had smaller tumors and lower ALT levels, it was the hepatitis C patients who on average lived 12 months longer.

“Compared with HBV-(related liver cancer) patients, HCV-(related liver cancer) patients were older, had a lower male/female ratio, lower white blood cell count, lower serum albumin level, higher serum ALT level, lower serum alpha-fetoprotein level, smaller tumor size and survived longer,” the researchers concluded.

Severe Acute Hepatitis B Treated Successfully with Lamivudine and Liver Dialysis

A case study, published in the July 2006 issue of the *Journal of Infection*, described how a patient suffering from life-threatening acute hepatitis B was treated successfully with lamivudine and the molecular adsorbent recirculating system (MARS), which is a liver dialysis process to remove toxins.

After three eight-hour sessions of MARS treatment in one week, the patient had a remarkable improvement. On the 14th day, he devel-

oped surface antibodies.

MARS treatment has helped patients experiencing liver failure from different causes including acute exacerbation of chronic hepatitis B, poisoning, post transplantation and Wilson's disease. This case suggests it may be beneficial when combined with lamivudine in treating patients with acute, life-threatening hepatitis B.

New U.S. Treatment Guidelines Identify What HBV DNA Levels Merit Treatment

New treatment guidelines that hinge on a patient's viral load, were recently written by a prominent hepatitis B doctor and published in the August 2006, journal of *Clinical Gastroenterology and Hepatology*.

Dr. Emmet B. Keeffe, a hepatologist, developed the new guidelines (also called algorithm) due to recent refinements in measuring HBV DNA and an increase in antiviral drugs used to suppress the virus.

Keeffe pointed out that HBV DNA can now be detected at levels as low as 10 IU/mL, and should be used to identify a baseline viral load level before treatment; monitor response to treatment, and determine when and if drug resistance develops.

The primary aim of antiviral therapy, he noted, is to lower HBV DNA to the lowest levels possible. His recommendations include:

The level of HBV DNA at which therapy should be considered is 20,000 IU/mL or more for patients with HBeAg-positive chronic hepatitis B.

A lower HBV DNA threshold of 2,000 IU/mL or more is recommended for patients with HBeAg-negative hepatitis B, and 200 IU/mL or more for those with decompensated (advanced) cirrhosis.

HBIG Plus Antivirals Help HBV-Infected Transplant Patients with High Viral Load

Usually, hepatitis B patients with high vi-

ral load are denied liver transplants because doctors believe the virus will continue to replicate and quickly damage the new organ. However, recently a group of doctors successfully transplanted a patient who had high viral load due to lamivudine-resistant HBV after treating him with both adefovir and HBIG (hepatitis B antibodies).

The doctors, reporting in the journal of *Transplant Infectious Diseases*, added adefovir to the patient's lamivudine treatment, and added HBIG.

One year after the liver transplant was performed, there was no evidence of HBV infection recurring. "This observation suggests that persistent high HBV replication might not be a contra-indication to liver transplantation, providing adequate and effective (preventive treatment) is given, using HBIG and antiviral drug combination therapy," they wrote.

Hepatitis B and C Infections Cause Majority of Liver Disease Deaths Worldwide

Globally, liver disease causes one in 40 deaths

each year. Researchers attempted to determine how much HBV and HCV infections contribute to deaths from liver disease.

According to the article published in the June 2006 issue of *Journal of Hepatology*, 57% of cirrhosis was caused by either HBV (30%) or HCV (27%) and 78% of liver cancer was attributable to HBV (53%) or HCV (25%).

Applied to 2002 worldwide death rates, these estimates represent 929,000 deaths due to chronic HBV and HCV infections, including 446,000 cirrhosis deaths (235,000 from HBV and 211,000 from HCV), and 483,000 liver cancer deaths (328,000 resulting from HBV and 155,000 from HCV).

Gallstones More Prevalent in Older Women with Cirrhosis

Gallstones, apparently, are more common in older people who also suffer cirrhosis, according to a report by Chinese researchers published in the September 2006 issue of the *Journal of Gastroenterology and Hepatology*.

Blood samples and ultrasound were used to

study 90 cirrhotic patients and 300 who served as controls. Gallstones were found more often in cirrhotic patients (23.7%) than in controls (7.33%). The prevalence of gallstones in seriously cirrhotic patients was higher than those with milder cirrhosis.

Advanced age, female gender, family history of gallstones, gallbladder wall thickness and inside diameter of the portal vein all played a role in development of gallstones.

Chemotherapy Drug Fludarabine Can Revive HBB in Patients with Resolved Infections

Greek researchers, reporting in the September 2006 issue of the *Journal of Viral Hepatitis*, explored the role mutations in the HBV core region play when eight patients with resolved HBV infections received chemotherapy and experienced a return of hepatitis B infection.

They studied eight patients who received chemotherapy treatment, including corticosteroids (CSs), the new chemotherapy drug fludarabine used to treat leukemia and some lymphomas, and cyclophos-

phamide/adriamycine. All tested negative for HBsAg and HBeAg before chemotherapy.

Four survived and two died from liver failure. At the time of HBV reactivation, all six patients carried the precore mutations and five had other mutations in the core region of their virus.

Fludarabine, researchers recommended, should be added to the list of drugs inducing HBV reactivation.

