

HBV JOURNAL REVIEW

Volume 2, Issue 6

June 01, 2005

Hepatitis B

Christine Kukka

Interferon Most Cost Effective Treatment Option for HBeAg-Negative Hepatitis B

A commentary in the May 2005 issue of the *Annals of Internal Medicine* examined the cost effectiveness of conventional interferon and two leading antivirals and found neither lamivudine (Epivir-HBV), which is well known for causing viral resistance, nor adefovir (Hepsera), which is extremely expensive, to be economical when used individually.

In their cost comparison, researchers compared the cost of the following strategies to treat hepatitis B “e” antigen-negative patients

with elevated alanine aminotransferase (ALT) levels and no cirrhosis.

- No treatment at all
- Treatment with conventional interferon
- Treatment with lamivudine
- Treatment with adefovir

And treatment with lamivudine, later replaced with adefovir once viral resistance appeared.

Compared with the ineffective “do nothing” strategy, using interferon cost \$6,337 to gain one additional healthy year. Compared with interferon, the adefovir salvage strategy (prescribed once viral resistance to lamivudine develops) cost \$8,446 dollars per year gained. Both the lamivudine and adefovir monotherapy strategies were more expensive and less effective.

Researchers found in-

terferon was more cost-effective for cash-strapped health care systems that treat many HBeAg-negative patients. However, the salvage strategy using adefovir once lamivudine resistance occurs, “may be highly cost-effective across most health care settings.”

People with Past Hepatitis B Infections Can Still Be Organ Donors

Surgeons at the University of Pittsburgh Medical Center have successfully transplanted livers from donors

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

© 2005
Hepatitis C Support Project

who had past hepatitis B infections, and report that survival rates are similar to patients who received hepatitis B-free organs.

Their findings, reported at the American Transplant Congress in May, prove that using these previously-infected organs are safe and that people with resolved hepatitis B infections can be organ donors.

Because of a shortage of suitable organs, some transplant centers are using organs that would have been discarded 10 years ago. In this study, doctors found that 65 percent of the transplanted hepatitis B livers survived at least two years, and that the patients who received these livers had a 76 percent survival rate.

The average three-year survival rate of an organ for liver transplant recipients is 71.3 percent, according to the United Network for Organ Sharing.

Valtorcitabine Effectively Suppresses HBV DNA Levels in Early Studies

In laboratory and animal experiments, valtorcitabine has been shown to work well with telbivudine in preventing HBV replication. Valtorcitabine is now being evaluated for development as anti-viral drug to be given in combination with telbivudine.

In a randomized, double-blind, controlled, Phase I/II study, the effects of seven different daily doses of valtorcitabine given for four weeks were evaluated. Each dosage group included seven patients who had been randomized 6:1 to receive valtorcitabine or placebo.

Reductions in HBV DNA levels at Day 28 was found in doses that ranged from 50 mg/day to 900 mg/day, which produced a 1,000-fold drop in HBV DNA or viral load.

No safety issues were reported.

Researchers con-

cluded that valtorcitabine appeared safe and effective. The dose of 900 mg/day was selected for ongoing clinical evaluation in combination with telbivudine.

ALT Flares Less Frequent with Entecavir Than Lamivudine in HBeAg Patients

Researchers compared increases in ALT, an enzyme released by liver cells when they are damaged or die, in patients who received either entecavir (Baraclude) or lamivudine.

Flares can occur when patients stop taking antivirals, and HBV rebound in large numbers. The flares can be dangerous and even life-threatening.

ALT elevations were analyzed in two Phase III trials in 709 patients, who all tested positive for HBeAg, who were given either entecavir or lamivudine for up to 96 weeks, according to researchers reporting at the Digestive Disease Week 2005 conference in

May.

Patients in both groups who achieved HBeAg loss and undetectable HBV DNA at 48 weeks discontinued treatment and were followed for 24 weeks. ALT flares were defined as a two-fold increase in ALT.

ALT flares during treatment were observed in 12 (3%) of entecavir patients and 23 (6%) of lamivudine patients. All entecavir flares were associated with a 100-fold reduction in HBV DNA, which continued throughout the treatment period. Twelve of 13 entecavir-related flares were resolved during treatment.

Eight patients discontinued lamivudine due to flares.

Researchers concluded that flares during entecavir therapy were uncommon and generally associated with a drop in viral load HBV DNA, and caused no serious liver damage. In contrast, ALT flares during lamivudine treatment were frequently associated with loss of therapeutic effectiveness.

Pradefovir (Remofovir) Shows Promise in Early Phase I Studies

The antiviral pradefovir (formerly remofovir) is a promising antiviral that appears to be far less toxic to the kidneys than the antiviral adefovir.

A Phase I study was performed on 40 patients (65% of whom were of Asian origin), with ALT levels ranging from slightly above normal to twice normal levels, detectable HBV DNA, and either positive or negative for HBeAg. The group was given 5, 10, 30 or 60 mg/day of pradefovir or placebo for 28 days, and followed for 12 weeks after.

HBV DNA declines ranged from 100-fold at doses of 5 mg/day to nearly 1,000-fold at 60 mg/day. Side effects were mild. The most frequently reported adverse event was a headache.

Researchers reported pradefovir was safe, well tolerated, and induced significant decreases in viral load. Phase II studies com-

paring pradefovir in combination with adefovir are currently underway.

The Longer Patients Take Adefovir, the Better the Response

Researchers who followed 309 hepatitis B patients who received adefovir for 144 weeks found that the longer the patients received adefovir, the better their chances of developing the “e” antibody and achieving normal ALT and undetectable viral load, according to a report presented at the European Association for the Study of the Liver (EASL).

About 91% of patients experienced HBeAg seroconversion, which endured even after treatment ended. As treatment continued, an increasing number of patients achieving undetectable HBV DNA and normal ALT.

Male Gender, Old Age and Basal Core-Promoter Mutation Increase Cancer Risk

Writing in the June 2005 issue of *Liver International*, a team of Taiwanese researchers reported that old age and the presence of a viral mutation in the HBV called a basal core-promoter mutation together increase the risk of cirrhosis and liver cancer in HBeAg-negative hepatitis B patients.

This basal core-promoter HBV mutant might also play a role in why men more than women develop cirrhosis and liver cancer, the authors noted.

The researchers examined the virus of 174 HBeAg-negative chronic hepatitis B patients.

Male patients older than 50 who had the HBV mutation had a higher rate of liver damage and cancer.

Lamivudine May Hurt Children’s Pancreas and Ability to Process Sugar

The most common toxic side effect from the antiviral lamivudine is pancreatitis, in which the ability to process glucose (sugar) is impaired. Turkish researchers followed 23 children, eight of whom were treated with lamivudine, to see what impact the drug had on their glucose metabolism.

An oral glucose tolerance test was performed before and after treatment. After six and 12 months of the treatment, four (18.4%) and eight (34.8%) patients had impaired glucose tolerance.

Researchers found no relationship between impaired glucose tolerance and any other factors, such as age or gender or liver disease. However, insulin concentrations were not different between treated and untreated children.

Because at least 8.7% of the patients had persistently impaired glucose tolerance during the first year of the therapy, researchers suggest that

children should be screened before lamivudine therapy begins.

Peg. Interferon-Lamivudine Combo Has Slight Edge in Long-Term Response

A group of Hong Kong researchers, writing in the May 2005 issue of *Hepatology*, found that pegylated interferon and lamivudine combination treatment has a slight advantage over just lamivudine in producing a sustained response, including HBeAg loss and low HBV DNA.

Forty-eight patients who completed 32 weeks of peginterferon plus 52 weeks of lamivudine were compared to 47 patients who completed 52 weeks of only lamivudine. Patients were followed for up to three years after treatment ended.

At the end of treatment, HBeAg loss occurred in 63% of patients in the combination group and 28% of patients in the lamivudine group. Response for the combination and lamivudine groups respectively were

33% and 13% at week 24, 31% and 11% at week 52, and 29% and 9% at week 76.

Doctor: Use Tenofovir and Lamivudine for HBV-HIV Coinfected Patients

In a Medscape Expert Interview on how to treat someone coinfecting with HIV and hepatitis B, David L. Thomas, MD, MPH, explained his preference for tenofovir and either lamivudine or emtricitabine. "In many instances the individual's HBV is already resistant to emtricitabine and/or lamivudine, but nonetheless, there is no reason not to include lamivudine or emtricitabine as a part of the treatment," he explained.

"Response rates dramatically improve when tenofovir is added to emtricitabine or lamivudine," he added, "but that's principally because tenofovir is a much more potent anti-hepatitis B drug than

either emtricitabine or lamivudine and has a much higher threshold for (preventing) resistance."

Dr. Thomas admitted that while there are no studies demonstrating that a drug combination that combines tenofovir with emtricitabine or lamivudine would be superior to tenofovir alone, "...I think that the experience that we have with treating HIV and the experience we have with treating most chronic infectious diseases suggests that it would be advisable, whenever possible, to use a second drug, especially when it confers very little additional toxicity."

When asked if he would ever prefer adefovir over tenofovir, he commented, "The only scenario in which I can see adefovir being preferred to tenofovir is when you don't want to treat HIV, and in that situation entecavir now may represent another, superior alternative. Personally, I don't see adefovir playing a major role in the treatment of chronic hepatitis B infection in HIV-infected individuals."

HIV Patients May Need HBV Vaccine, Despite Presence of Core Antibody

HIV-infected individuals who test positive for the hepatitis B core antigen (anti-HBc) may be producing "false positives" and still require vaccination against hepatitis B, according to a study published in the May 1, 2005, issue of *The Journal of Infectious Diseases*.

Researchers analyzed the response rate in 69 HIV-infected subjects who tested negative for hepatitis B surface antigen (HBsAg) and antibody and were then immunized with hepatitis B vaccine.

Twenty-nine subjects (42%) tested positive for anti-HBc and 40 (58%) tested negative for anti-HBc.

According to the team, the overall response to hepatitis B vaccination was low (16%) and did not differ significantly between subjects who tested positive for anti-HBc (24%) and those who tested negative for anti-HBc (10%) before vaccination.

This suggests that testing for anti-HBc alone may not be reliable in this population.

Another surprise finding, was that HIV and hepatitis C coinfecting people were less likely to develop hepatitis B antibodies after immunization than were those injected with HIV alone.

Entecavir Improves Quality of Life More so Than Lamivudine

Entecavir, approved by the U.S. Food and Drug Administration to treat hepatitis B in late March 2005, improves patient's quality of life after 48 weeks, according to a report presented to the Digestive Disease Week 2005 conference.

Entecavir outperformed lamivudine in areas of patient mobility, self-care and pain relief.

"In this study we found that the larger proportion of patients on entecavir achieved positive quality-of-life effects, and notably for pain and discomfort, compared with the lamivudine group," said presenter Jun Su, MD, clinical researcher and group manager of Bristol-Myers Squibb, which markets entecavir.

Peg Interferon Effective in Treating HBeAg-Negative HBV

A German researcher, writing in the May 2005 issue of *Hepatology*, compared the success of peg interferon plus placebo, peg interferon + lamivudine, and lamivudine alone respectively in 177, 179, and 181 patients with HBeAg-neg chronic HBV.

Patients were treated for 48 weeks and followed for 24 more weeks. The percentage of patients with normal ALT and undetectable HBV was significantly higher with peg interferon (59% and 43% respectively) and peg interferon plus lamivudine (60% and 44%) than with just lamivudine (44% and 29%).

Rates of sustained suppression of HBV DNA to below 400 copies per milliliter were 19% with just interferon, 20% with combination therapy, and 7% with lamivudine.

Loss of surface antigen occurred in 12 patients in the two interferon groups.

Patients with HBeAg-negative chronic hepatitis B had significantly higher rates of response, sustained for 24 weeks after treatment ended, with peg interferon than with lamivudine.

HBV FACTSHEETS

HCSP Factsheet Series

- Getting Social Security Disability Benefits
- HBV/HIV Coinfection: What You Need to Know
- HBV: Drugs in Current Clinical Development
- HBV: Grading and Staging a Liver Biopsy
- HBV: How to Interpret (and Understand) Your Liver Tests
- HBV: How to Interpret Hepatitis B Viral Tests
- HBV: Preventing Hepatitis B at Home and in Personal Care Settings
- HBV: Preventing Mother-to-Child Hepatitis B Infection
- HBV: What is Acute Hepatitis B?
- Hepatitis B: The Basics
- How Frequently to Monitor Your Hepatitis B
- How to Tell Children They Have Hepatitis
- Managing HBV Treatment Side Effects
- Testing Positive for Hepatitis B: Now What?
- What Are the Occupational Risks of Hepatitis B?
- What's New in Hepatitis B Treatment
- When to Disclose Your HBV Infection

- Acute Hepatitis B
- Biopsy
- Core Antigen
- HBeAg-Negative Hepatitis B
- Hepatitis B and Alcohol
- Hepatitis B Treatment
- Sex and Hepatitis B
- Tattoos
- The Liver
- What Are Antivirals?
- What Do Antigens & Antibodies Mean?
- What Is AFP?
- What Is Alt?
- What Is the "e" antigen (HBeAG)?
- What Is Interferon?

All of our Factsheets are available for download at www.hbvadvocate.org

Easy B's

- 100 Infants
- 100 People