

## Cost Effectiveness of Treating Chronic Hepatitis B and C

Based on presentations by J. Robert Beck, MD; Raymond S. Koff, MD; and William Bennett, MD

### *Presentation Summary*

Based on Centers for Disease Control and Prevention (CDC) data, more than 1 million people in the United States have chronic hepatitis B and nearly 4 million have chronic hepatitis C. Both illnesses typically persist for decades before causing serious complications, such as cirrhosis and hepatocellular carcinoma. Treatment with interferon alfa-2b results in loss of detectable markers of hepatitis B infection and normalization of liver function. Whether interferon therapy is cost effective, given the slowly progressive nature of chronic hepatitis, was the focus of two studies, one examining the use of interferon alfa-2b in patients with chronic hepatitis B who were posi-

tive for the hepatitis B e antigen (HBeAg) and the other examining use of the drug in patients with mild chronic hepatitis C. Both studies used similar methodology, employing well-designed computer modeling and decision analysis to project long-term clinical and economic outcomes for a cohort of simulated patients. Results from both studies indicated that interferon alfa-2b increases life expectancy and quality-adjusted life expectancy and decreases lifetime costs associated with chronic hepatitis. Thus, unless results of controlled clinical trials prove otherwise, these data support the routine use of interferon alfa-2b for patients with chronic hepatitis B and C.

**B**ased on Centers for Disease Control and Prevention (CDC) data, in the United States, more than 1 million individuals have chronic hepatitis B and approximately 4 million have chronic hepatitis C. Although most older children and adults infected with the hepatitis B virus recover spontaneously,<sup>1</sup> recovery is much less likely with hepatitis C infection, with the majority of individuals developing chronic disease.<sup>1</sup> Chronic hepatitis may progress to cirrhosis and liver failure and greatly increases the risk of developing

hepatocellular carcinoma.<sup>1</sup> Yet the slowly progressive nature of chronic hepatitis means that patients may live for decades before becoming seriously ill.

In some patients with chronic hepatitis B, treatment with interferon alfa-2b results in loss of detectable markers of hepatitis infection<sup>2</sup> and normalization of levels of alanine aminotransferase (ALT). Interferon therapy is expensive and can cause short-term side effects, the most common of which are flu-like symptoms. Because the course of chronic viral hepatitis

runs over decades, conducting controlled clinical trials on the long-term effects of interferon alfa-2b is difficult and costly, with the results unavailable for 20 or 30 years. Yet healthcare providers and managed care organizations must decide today whether patients should receive interferon alfa-2b. By drawing on the power of well-designed decision analysis tools and computer projections, researchers have examined the cost effectiveness of interferon alfa-2b treatment in patients with chronic hepatitis B or C. The results of these studies were described by: J. Robert Beck MD, Vice President, Medical Illustration and Telecommunications Information Technology program, Baylor College of Medicine, Houston, Texas; Raymond S. Koff, MD, Professor of Medicine, University of Massachusetts Medical School; and William Bennett, MD, gastroenterologist, Internal Medicine Associates of Tupelo, Starksville, Mississippi.

### Methodology

Similar methodology was used in the cost-effectiveness studies of chronic hepatitis B<sup>2</sup> and chronic hepatitis C.<sup>3</sup> In both studies, investigators used decision analysis software to perform a Markov computer simulation, a technique in which cohorts of patients move through various states of health over time until all patients have died.<sup>4</sup> The likelihood of moving from one state of health to another was estimated from data in published studies, which were identified through a comprehensive literature search. An expert panel provided additional input on the probability of certain events occurring; they also provided quality-of-life estimates for each health state. Data on the effectiveness of interferon alfa-2b were derived from a meta-analysis of controlled clinical trials (nine in the chronic hepatitis B study and five in the chronic hepatitis C study).

For calculations of cost, investigators used variable cost estimates (the

amount spent by the hospital to care for one additional patient with the illness), approximate physician fees, and the wholesale price of interferon alfa-2b. In the chronic hepatitis B study, the cost of 16 weeks of treatment with interferon alfa-2b (the standard regimen) was estimated at \$5570 (\$4595 for the drug itself and \$975 for office visits and laboratory fees); in the chronic hepatitis C study, the total

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cost of 6 months of treatment with interferon alfa-2b (the standard regimen) was estimated at \$2511. In both studies, investigators had to make certain assumptions to account for variations in data in the literature.

"Once the data are inputted, the computer can then project long-term outcomes for, say, 1000 simulated patients. The simulation program keeps running until the last patient has died," explained Dr. Koff. The computer simulation data are then analyzed to estimate the lifelong clinical and economic outcomes resulting from treatment.

### Cost Effectiveness of Treating Chronic Hepatitis B

The study conducted by Dr. Wong and colleagues<sup>2</sup> evaluated the cost effectiveness of interferon alfa-2b in patients with chronic hepatitis B who tested positive for the hepatitis B e antigen (HBeAg), an indication that the virus is actively replicating. Patients who test positive for HBeAg are more likely than those who test negative to develop decompensated

cirrhosis or hepatocellular carcinoma.<sup>2</sup> These two conditions are costly to treat, with estimates of \$22,100 per year for decompensated cirrhosis and \$19,600 per year for hepatocellular carcinoma, compared with \$740 per year for an HBeAg-positive patient whose disease does not progress.<sup>2</sup> "The nine controlled clinical trials we analyzed all showed that treatment with interferon significantly reduced the risk of remaining HBeAg positive. Subsequent data have shown that

HBeAg positivity is a superb marker for predicting outcome of disease progression and response to treatment," said Dr. Koff.

In their baseline analysis, the investigators compared the effects of interferon alfa-2b therapy with those of standard care (ie, observation) for a 35-year-old HBeAg-positive man without cirrhosis. They found that interferon treatment increased life expectancy and quality-adjusted life expectancy and decreased lifetime costs (Table 1).<sup>2</sup> "In my experience as an analyst, it is very unusual to see results like this. Ordinarily, quality adjustment of life expectancy reduces the raw differences between treatment strategies. In this case, it increases the difference between strategies because, with interferon alfa-2b therapy, so much less time is spent in the clinical states that experience deleterious qualities of life," noted Dr. Beck. "Even when future costs are discounted, interferon therapy reduces the total cost burden associated with illness: Standard care was both less effective and more costly." Indeed, not treating hepatitis B patients with interferon alfa-2b may be the more expensive alternative, with lifetime costs for untreated patients greater than those for patients receiving interferon alfa-2b.<sup>2</sup>

In this study, the cost per quality-adjusted life year with interferon alfa-2b therapy did not exceed \$12,000,<sup>2</sup> which compares favorably with that for other well-accepted life-saving medical interventions (\$16,000 to \$32,000 for antihypertensive treatment, \$22,000 for postsurgical chemotherapy for breast cancer, and \$17,000 for beta-blocker therapy in low-risk myocardial infarction survivors).<sup>5,6</sup>

Dr. Koff concluded that interferon alfa-2b could result in considerable cost savings for managed care organizations. "Based on prevalence rates, a managed care organization with 500,000 covered lives would have approximately 1000 persons with chronic hepatitis B within that group.

**Table 1.** Baseline Analysis for a 35-Year-Old HBeAg-Positive Man Without Cirrhosis

Treatment	Life Expectancy	Quality-Adjusted Life Expectancy	Lifetime Costs (Discounted)*
Standard care	24.8 y	22.4 y	\$60,200 (\$32,700)
Interferon alfa-2b	27.9 y	25.8 y	\$53,600 (\$30,600)

Source: See reference 2.

\*Discounting accounts for the potential impact of future medical advances.  
HBeAg = hepatitis B e antigen

**Table 2.** Baseline Analysis for a 35-Year-Old Man With Mild Chronic Hepatitis C

Treatment	Life Expectancy	Quality-Adjusted Life Expectancy	Lifetime Costs (Discounted)*
Standard care	35.3 y	27.4 y	\$20,233 (\$5630)
Interferon alfa-2b	37.0 y	31.2 y	\$16,630 (\$6103)

\*Discounting accounts for the potential impact of future medical advances.

The lifetime cost of providing standard care for these patients is about \$60 million, compared with \$53 million for interferon, a savings of \$7 million," he said. Thus for each patient with chronic hepatitis B treated with interferon alfa-2b, the managed care organization would save \$7000.

### Cost Effectiveness of Treating Chronic Hepatitis C

The goal of the study conducted by Dr. Bennett and colleagues<sup>3</sup> was to determine whether treating histologically mild or early chronic hepatitis C infection with a single 6-month course of interferon alfa-2b affects life expectancy and the lifelong costs associated with the illness. "Based on our meta-analysis of primary data from five clinical trials, the sustained response rate to interferon alfa-2b is very dependent on the histology," Dr. Bennett noted. Among patients with mild chronic hepatitis C, about 27% will normalize serum alanine aminotransferase levels and remain negative for the hepatitis C virus after completing a 6-month course of interferon alfa-2b therapy.

In the baseline analysis, interferon alfa-2b was shown to increase life expectancy and quality-adjusted life expectancy and decrease lifetime costs for a 35-year-old man with mild chronic hepatitis C (Table 2). "Overall, the gain in life expectancy was greater in the younger patients, about 3.5 years for those aged 20 and 7.5 months for those aged 50," observed Dr. Bennett.

The investigators calculated the cost per year of life gained at \$214 for a 20-year-old patient and \$5038 for a 50-year-old patient. A sensitivity analysis revealed that if the total cost of interferon therapy is lowered from \$2514 (a cost that includes office visits and laboratory tests, as well as the drug) to \$2000, interferon alfa-2b becomes cost saving (Table 3). "In other words, it would cost you not to treat these patients," Dr. Bennett said.

**Table 3.** Sensitivity Analysis of Interferon Alfa-2b Treatment for Chronic Hepatitis C

Variable	Value	Marginal Cost-effectiveness Ratio (Cost Per Year of Life Gained)
Cost of interferon alfa-2b	\$2514	\$1199
Low	\$2000	cost saving
High	\$3000	\$2374

The cost of treating patients with mild chronic hepatitis C with a single 6-month course of interferon alfa-2b compares favorably with that for many well-accepted therapies, such as providing pneumococcal vaccine for the elderly, treating mild to moderate hypertension, screening blood donors for human immunodeficiency virus, performing coronary artery bypass grafting, and screening the elderly for breast and colorectal cancer. These interventions range from \$18,000 to \$74,000 per year of life gained. Dr. Bennett concluded that using interferon alfa-2b to treat mild chronic hepatitis C appears justified despite the typically slow clinical progression of the disease.

### Conclusion

Both chronic hepatitis B and chronic hepatitis C are slowly progressing illnesses that may persist for years before causing serious complications. Using powerful computer modeling, researchers have been able to project long-term outcomes for patients in the absence of clinical trial data. Results of these studies indicate that treatment of chronic hepatitis with interferon alfa-2b is cost effective, both increasing life expectancy and decreasing overall costs of care. Thus, unless results of controlled clinical trials prove otherwise, routine use of interferon alfa-2b for patients with chronic hepatitis is highly recommended.

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