

# Hepatitis C

By Liz Highleyman

## **New HCV Therapies Show Promise: Etanercept and Lambda Interferon**

Given that a considerable proportion of patients do not achieve sustained virological response after treatment with pegylated interferon-alpha plus ribavirin, researchers are continually searching for new and potentially more effective therapies.

In the March 2005 *Journal of Hepatology*, researchers looked at whether adding etanercept to a standard interferon/ribavirin regimen could improve response rates. Etanercept (Enbrel) is a medication that blocks tumor necrosis factor (an immune system chemical messenger) that is used to treat rheumatoid arthritis. In

this Phase II trial, 50 subjects were randomly assigned to receive interferon/ribavirin plus etanercept or interferon/ribavirin plus placebo. After 24 weeks, 63% (12 out of 19) in the etanercept arm achieved undetectable HCV RNA, compared with 32% (8 out of 25) in the placebo arm. The authors concluded that adding etanercept “significantly improved virologic response...and was associated with decreased incidence of most adverse effects associated with interferon and ribavirin.” While these results appear promising, further study with longer follow-up is needed to see if response is sustained over time and if similar results are also seen using today’s standard of care, pegylated interferon plus ribavirin.

In the March *Journal of*

### **Hepatitis Journal Review**

*A publication of the Hepatitis C Support Project*

Executive Director  
Editor-in-Chief,  
HCSP Publications  
**Alan Franciscus**

Contributor:  
**Liz Highleyman**

Managing Editor, Webmaster  
**C.D. Mazoff, PhD**

Design/Production  
**Alan Franciscus**

**Contact Information:**  
The Hepatitis C Support Project  
PO Box 427037  
San Francisco, CA 94142

**[www.hcvadvocate.org](http://www.hcvadvocate.org)**

© 2005  
Hepatitis C Support Project

*Virology*, M.D. Robek and colleagues reported on the use of a new type of interferon  $\frac{3}{4}$  interferon-lambda  $\frac{3}{4}$  in the treatment of hepatitis B and C. Interferons promote the body's immune response and protect cells from infection. Interferon-alpha is standard therapy for chronic hepatitis C, while interferon-gamma and consensus interferon are under study for the treatment of HCV nonresponders and relapsers. Interferon-lambda is a newly discovered member of this family that appears to induce an intracellular antiviral response similar to that of interferon-alpha, but using a different cell receptor. In laboratory studies, the researchers found that interferon-lambda inhibited HBV replication in mouse liver cells and blocked HCV replication in human liver cells. While much more study is needed, the authors suggest that interferon-lambda may one day join the armamentarium of treatments for hepatitis B and C.

### ***HIV/HCV Coinfection News Roundup***

Several recent journal articles have reported on various aspects of HIV/HCV coinfection. It is known that

coinfection with HIV leads to worse progression of hepatitis C. For example, J.A. Pineda and colleagues reported in the April issue of *Hepatology* that survival with decompensated cirrhosis or end-stage liver disease was considerable shorter among HIV/HCV coinfecting patients than among those with HIV alone. But research continues to turn up contradictory data about whether HCV adversely affects HIV disease. A study by R.C. Hershow and colleagues reported in the March *Clinical Infectious Diseases* looked at 625 HIV positive subjects in the Women and Infants Transmission Study; 190 (29%) were coinfecting with HCV. The coinfecting women did not progress to an AIDS-defining illness or death faster than those with HIV alone. HIV viral load levels were similar in both groups, but CD4 cell percentages were slightly higher among the coinfecting women. "In this cohort, the rate of clinical progression of HIV-1 infection was not greater for HCV-infected women," the authors concluded.

According to the March *Journal of Hepatology*, coinfecting individuals taking highly active antiretroviral therapy for HIV

(HAART) are more likely to develop fulminant hepatic failure (severe, rapid liver failure) than those with HIV alone. In a retrospective analysis of medical records from 11,678 veterans with HIV alone and 4,761 with HIV/HCV coinfection, R.J. Kramer and colleagues determined that the cumulative incidence of fulminant hepatic failure was 1.1 per 1,000 person-years in the HIV-only group compared with 2.5 per 1,000 person-years the coinfecting group. They also noted that the risk of fulminant hepatitis was considerably higher since the advent of HAART, suggesting that antiretroviral drug toxicity plays a role. However, the risk remains quite low: in this study only 92 total cases were seen between 1991 and 2000.

In the April 8 issue of *AIDS*, Mark Sulkowski and colleagues reported that hepatic steatosis (fatty liver) was seen in 40% of 112 coinfecting subjects (99% with HCV genotype 1), most of whom were taking HAART. Steatosis was more common in patients with advanced liver disease (higher fibrosis scores), patients with hyperglycemia (high blood glucose), obese individuals, and those receiving the anti-HIV drug

stavudine (d4T, Zerit); only 4 subjects had never taken stavudine, none of whom had steatosis.

### **More Data on Sexual Transmission**

Over the past year, clusters of HCV infections among gay men in London and Paris have led some experts to suggest that sexual transmission of HCV may be more common than previously believed. However, to date no similar outbreaks have been reported in North America. According to an article in the March *American Journal of Public Health*, a recent Canadian study found sexual transmission of HCV to be rare among HIV negative gay men. M. Alary and colleagues studied a cohort of more than 1,000 gay men in Montreal. During eight months of follow-up (2,653 person-years), only one new HCV infection was detected (in a man who reported sharing drug injection equipment), even though 63% of men said they had engaged in unprotected anal sex. After controlling for injection drug use, sexual behavior was not significantly linked to HCV infection. Notably, the suspected sexually

transmitted HCV cases in Europe occurred among HIV/HCV coinfecting men, who may be at higher risk for HCV transmission.

A related study by V. Tahan and colleagues reported in the April *American Journal of Gastroenterology* confirms that HCV sexual transmission is rare among monogamous heterosexual couples. The researchers studied 216 HIV negative heterosexual spouses of individuals with chronic hepatitis C; the spouses were tested each year for HCV antibodies. They found that none of the initially HCV negative spouses seroconverted during an average follow-up period of about three years, which included an average of 257 instances of sexual intercourse.



### **CHECK OUT THE LATEST FACTSHEETS**

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

- *Alcohol and HCV*
- *HCV Disease Progression  
Cirrhosis  
Fibrosis  
Steatosis*
- *HCV and Mental Health  
Overview of Depression  
Depression: Self-Help Tips  
HCV and Depression  
Managing Depression  
Mental Health Resources*
- *Side Effect Management:  
Hemolytic Anemia  
Mouth Sores  
Nausea  
Neutropenia  
Rashes  
Water*
- *Advocates and Activists Needed!*
- *African Americans and HCV*
- *Dispelling Myths about HCV*
- *Extrahepatic Manifestations*
- *How Long Does HCV Live on Surfaces*
- *How to Tell Children They Have Hepatitis*
- *Interferon*