

Hepatitis C

Interferon Response in Asians

Response to interferon-based therapy is similar in Asian-Americans and whites people with chronic hepatitis C, according to a California study reported in the May 2010 *American Journal of Gastroenterology*. It is well known that people of African descent do not respond as well as whites to interferon; there is less research on other racial/ethnic groups, but some previous data suggest Asians may have more favorable response.

P. Vutien and colleagues compared sustained virological response (SVR) rates among 112 Asian-American and 157 white treatment-naïve patients with HCV genotypes 1 and 2/3 treated with pegy-

lated interferon plus ribavirin. The researchers took care to accurately classify genotypes using viral core sequencing, since the less accurate INNO-LiPA test can mistakenly classify easier-to-treat genotype 6 as genotype 1, leading to a falsely high response rate. Genotype 6 is predominant in Southeast Asia but rare in the U.S. and Europe.

In an intent-to-treat analysis, genotype 1 SVR rates were 52% for Asians and 45% for whites, not a statistically significant difference. Genotype 2/3 SVR rates were 77% and 74%, respectively. In a multivariate analysis adjusting for other factors including HCV genotype, baseline viral load, and treatment adherence, Asian ethnicity was not

(Continued on page 2)

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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

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an independent predictor of sustained response. However, a separate analysis of patients classified as genotype 1 using the INNO-LiPA test did find a significantly higher SVR rates for Asians compared with whites (64% vs. 45%, respectively).

When to Predict Nonresponse

Early virological response (EVR), or HCV viral load decline of at least 2 logs at week 12, is typically used as a stopping rule to predict which hepatitis C patients are likely to go on to achieve SVR with interferon-based therapy and which are unlikely to benefit from continued treatment. As described in the May 2010 *Journal of Viral Hepatitis*, E. Lukasiewicz and colleagues assessed whether response before week 12 is also an accurate predictor, which could spare patients additional weeks of futile therapy.

The researchers used a technique called longitudinal discriminant analysis to create mathematical models that included baseline patient characteristics and HCV viral load at weeks 4, 8, and 12. Lack of sustained re-

sponse was best predicted by a single HCV RNA measurement at week 8, together with patient sex, age, and body mass index. Predictions at week 8 were better than those based on week 4 viral load, but just as good as those made at week 12. "These results indicate that lack of sustained viral response is best predicted after eight weeks of treatment and that waiting until 12 weeks does not improve the prediction," the investigators concluded.

Relapse Risk Factors

A related study in the May 2010 *European Journal of Hepatology* looked at predictors of viral relapse after completing treatment. M. Deschênes and colleagues performed a retrospective analysis of data from 432 treatment-naïve genotype 1 patients in the Canadian Pegasys Expanded Access Program who had undetectable HCV RNA at the end of a 48-week course of pegylated interferon plus ribavirin.

Among 405 participants with adequate data, 81% achieved SVR—or continued undetectable HCV RNA six months

post-treatment—while 19% experienced viral relapse. Overall early virological response rates at week 12 were the same in sustained responders and relapsers (both 99%). Relapsers, however, were three times more likely than sustained responders to experience partial rather than complete EVR, that is, HCV RNA decreased by at least 2 logs but still detectable (16% vs. 5%). Furthermore, among the patients with partial EVR, average and maximum viral load levels were higher in relapsers compared with sustained responders. In a multivariate analysis, factors significantly associated with relapse included older age, white race/ethnicity, higher baseline viral load, and a smaller drop in HCV RNA between baseline and week 12.

Adjuvant Therapy

Standard chronic hepatitis C treatment produces a suboptimal overall sustained response rate of approximately 50%, in part because many people reduce their drug doses or stop treatment prematurely due to side effects. Adjuvant or supportive therapies—such as antide-

(Continued on page 3)

pressants and hormones to increase blood cell production—can help patients stay on treatment.

As described in the April 2010 *Journal of Viral Hepatitis*, W.J. Cash and colleagues studied the effects of blood-boosting adjuvant therapies during hepatitis C treatment. These include erythropoietin (Procrit or Epogen), which increases production of red blood cells to manage anemia caused by ribavirin, and granulocyte colony-stimulating factor (Neupogen), which boosts infection-fighting white blood cells to manage neutropenia caused by interferon. The study included 132 mostly treatment-naive chronic hepatitis C patients receiving pegylated interferon plus ribavirin; about 40% had hard-to-treat HCV genotypes 1, 4, or 6.

Nearly 45% of participants used adjuvant therapies during treatment. The overall sustained response rate was 67% (50% for genotypes 1/4/6 and 78% for genotypes 2/3). Looking only at treatment-naive participants, the overall sustained response rate was 69% (49% for genotype 1 and 83% for genotypes 2/3). "In genotype 1 patients, SVR rates of up to 46% have been

reported in previous studies without the use of erythropoietin and granulocyte colony-stimulating factor," the researchers concluded. "We have demonstrated the SVR for genotype 1 can be improved to 50% overall."

Trends in Liver Cancer

New cases of hepatocellular carcinoma (HCC)—a type of primary liver cancer that may develop in people with long-term chronic hepatitis B or C—have increased over the past several years in the U.S., according to an analysis from the Centers for Disease Control and Prevention (CDC) published in the May 7, 2010 *Morbidity and Mortality Weekly Report*. Although new HBV and HCV infections have decreased dramatically in recent decades, liver cancer rates continue to rise as people infected years ago reach the stage of advanced disease.

Researchers analyzed data for 2001-2006 from the CDC's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results system. They compiled reports from 45 cancer registries, covering

just over 90% of the U.S. population. A total of 48,596 new HCC cases were reported during this period, for an average annual incidence rate of 3.0 per 100,000 persons. Incidence rose significantly over the study period, from 2.7 per 100,000 in 2001 to 3.2 per 100,000 in 2006—an average annual percentage increase of 3.5%.

Men were about three times more likely than women to develop HCC (5.0 vs. 1.3 per 100,000). Asian/Pacific Islanders had the highest HCC incidence (7.8 per 100,000)—reflecting their high hepatitis B prevalence—followed by Hispanics, blacks, Native Americans, and whites (5.7, 4.2, 3.2, and 2.6 per 100,000, respectively). But blacks and whites had the largest annual percentage increases (4.8% and 3.8%, respectively), while Asian incidence remained stable.

Older people were more likely to be diagnosed with HCC, as expected because liver cancer typically takes a long time to develop. The median age at HCC diagnosis was 64 years (62 for men, 69 for women). People in the 70-79 age

(Continued on page 4)

group had the highest HCC incidence (13.7 per 100,000), followed by age > 80 (10.0 per 100,000) and age 60-69 (9.6 per 100,000). The 50-59 age group had an incidence of 6.8 per 100,000, but showed the largest percentage increase, at 9.1%. Incidence then dropped to 2.1 per 100,000 in the 40-49 age group and even lower for younger people. The authors of an accompanying editorial note explained that HCC rates were highest among people born during 1946-1964, particularly black men. "In the absence of testing and care, the risk for HCC is expected to increase with aging of the cohort of persons with HCV infection," they wrote.

HCV Uncommon in HIV Negative Gay Men

In the early 2000s, researchers began reporting outbreaks of apparently sexually transmitted acute HCV infection among HIV positive men who have sex with men in the U.K. and Europe; similar outbreaks have since been reported in the U.S. People with HIV routinely undergo liver function monitoring for drug toxicity, which can signal

HCV infection at its earliest stages. But HIV negative people typically do not receive regular liver monitoring, leading some to suggest that hepatitis C among HIV negative gay men was not being detected because clinicians were not looking for it.

As reported in the May 2010 *Journal of Infection*, C. Scott and colleagues analyzed data from urban sexual health clinics in the U.K. that began routine testing for HCV regardless of risk profile starting in 2007. Over six months, a total of 3,365 gay and bisexual men attended the clinics for sexually transmitted disease screening; 2,309 agreed to be tested for HCV. Among these men, HCV prevalence was just 0.65%, similar to that of the general population in England. Researchers in Europe, the U.S., and Australia also have not seen unusually high hepatitis C rates among HIV negative men who have sex with men, even though HCV incidence among HIV positive men is high and rising.



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