

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

*Alan Franciscus
Editor-in-Chief*

Week Ending: November 7, 2009

In This Issue:

- [AASLD: HCV-Related News](#)
- [AASLD: HBV-Related News](#)
- [Hundreds in Denver, Colorado Springs Still Need Hepatitis C Testing](#)
- [How Long Does Hepatitis B Vaccine Protection Last?](#)
- [Combination Drugs Are the Future for Hepatitis C](#)
- [US Lawmakers Push to Ramp Up Hepatitis Battle](#)
- [Non-Response to HBV Vaccine a Sign of Possible Celiac Disease](#)
- [New Hepatitis C Protease Inhibitors Achieve 80% ‘Cure’ Rate in Patients with Genotype 1 Infection](#)
- [Idenix Pharmaceuticals Initiates Phase II Clinical Trial of IDX184 in Combination with Pegylated Interferon and Ribavirin for the Treatment of Hepatitis C Virus \(HCV\)](#)
- [HBV Reduces Recurrence-Free Survival after Surgery for Hepatocellular Carcinoma](#)
- [Low Factor V Levels Signal Poor Prognosis with Hepatitis B-Induced Acute Liver Failure](#)
- [HCV Vaccines, TLRs Advance Away from Protease Spotlight](#)
- [Hepatitis C Workshop Set for Nov. 18](#)
- [Speaker Pelosi Says Hepatitis B Prevention at Core of Healthcare Reform](#)
- [AASLD: HCV Now an STD in New York](#)
- [AASLD: Direct Antivirals Can Beat HCV without Interferon](#)
- [AASLD: Treating before Transplant Cuts HCV Recurrence](#)
- [Bipartisan Support Grows for Addressing Nation’s Hepatitis Scourge](#)

Hundreds in Denver, Colorado Springs Still Need Hepatitis C Testing

<http://www.denverpost.com>

By Jennifer Brown

The Denver Post

Four months after a terrorizing and high-profile hepatitis C outbreak linked to hospital drug theft, hundreds of patients who might have been exposed to the liver disease still may not have been tested.

But for the thousands who have tested negative, there is relief: Enough time has passed since the breach that exposure to the virus would have surfaced in blood tests, health officials said.

Rose Medical Center is still trying to track down 375 patients who were in the Denver hospital when surgical technician Kristen Diane Parker, who was infected with hepatitis C, worked there.

Parker pleaded guilty in September to stealing the liquid painkiller fentanyl, then refilling her dirty syringes with saline solution for patients.

Audubon Surgery Center of Colorado Springs, where Parker worked after leaving Rose, has not been able to reach 57 patients.

The patients who haven't surfaced represent a fraction of about 5,700 people the two hospitals set out to test. Rose tested or received test results from private physicians for 4,158 patients, according to the hospital. Of those, 15 contracted the potentially fatal hepatitis C from Parker, genetic testing shows.

About 50 others were found to have hepatitis C that has not been linked to Parker.

Rose is trying to find patients who had surgery from Oct. 21, 2008, to April 13, 2009, in the hospital's main operating room or outpatient surgery center.

Audubon has test results from 1,167 patients. Although 16 of them tested positive for the disease, none got it from Parker, according to genetic tests.

Three Audubon patients were found to have hepatitis C antibodies in their blood, meaning their bodies fought off the virus. For those patients, there is no way to tell whether they were exposed by Parker, said Brent Ashby, an Audubon administrator.

"We're feeling very confident at this point that none of our patients has been exposed," Ashby said. "We'd like to think that maybe we were doing some good things to prevent her from doing here what she was doing at Rose."

Parker told authorities, though, that she stole painkillers during the seven weeks last spring that she worked at Audubon.

Ashby said the surgery center closed its hepatitis C help line about a month ago and doesn't

expect to find the 27 patients who, as far as hospital officials know, never were tested or the 30 additional patients who should have had follow-up testing but did not.

"At this point, we've done just about everything we can to get ahold of all the patients," he said. "We've sent letters. We've made phone calls."

Rose sent certified letters and attempted to call patients in each of the past three months, said Rose communications coordinator Cara Harshberger.

Among the 375 who have not responded are some who refused testing and some who sought testing through a private physician but have not shared those results. Rose does not have current or correct phone numbers for about 100 of the patients.

In response to the outbreak, the Colorado Hospital Association created a task force to investigate hospital "drug diversion" — drug theft by staff, patients or others.

The group is reviewing hospital hiring and drug policies, plus state and federal laws, as it looks for ways to strengthen patient safety, said association president Steven Summer.

Rose also is installing new drug-dispensing machines in its operating rooms and training managers and employees to recognize drug theft, Harshberger said.

Hepatitis C would have shown up in patients' blood six weeks after surgery had they been exposed and if they had submitted to a series of blood tests offered by the hospitals, health officials said.

Parker was arrested in June. She will be sentenced in December, and prosecutors are recommending 20 years in prison.

It can take up to six months after exposure for hepatitis C antibodies to show up in a person's blood. More extensive blood work produces conclusive results after six weeks.

Rose and Audubon each are facing one lawsuit so far as a result of the outbreak.

"This has been a very challenging experience for everybody," Ashby said. "We're certainly glad we're at the end of the road."

Some fought off the virus

- 5,700 Patients potentially exposed to hepatitis C while surgical technician Kristen Diane Parker worked at Rose Medical Center and Audubon Surgery Center in Colorado Springs
- 15 Rose patients who tested positive; 50 others were found to have hepatitis C not linked to Parker
- 0 Audubon patients whose positive tests were linked to Parker
- 375 Rose patients not yet tested
- 57 Audubon patients not yet tested

How Long Does Hepatitis B Vaccine Protection Last?

www.reuters.com

NEW YORK (Reuters Health) - The hepatitis B vaccine - given to protect against infection by a virus that can cause severe liver damage and cancer - may protect for more than two decades, according to a new study.

In 1981, Dr. Brian J. McMahon, from the Alaska Native Medical Center, Anchorage, and his colleagues gave more than 1500 Alaska Native adults and children over age 6 months three doses of hepatitis B vaccine. Before the hepatitis B vaccine was licensed for U.S. use in 1981, as many as one in 12 Alaskan Natives were infected.

In 2003, the team checked with almost 500 of those given the shots and had a response to them at the time to see who was still showing evidence of an immune system response. Blood tests found that more than half - 60 percent -- were still considered immune to the virus.

To test whether the other 40 percent were immune, they were given a booster dose of the vaccine, to simulate infection. Most of those people - more than 80 percent - showed a response.

Overall, the researchers estimate that more than 90 percent of the original group was protected. There were no long-term hepatitis B infections in the group, which also suggests a high level of protection, they note in a report in the *Journal of Infectious Diseases*.

They conclude, "in light of the strong evidence we present here, hepatitis B vaccine booster doses are not currently indicated."

SOURCE: Journal of Infectious Diseases, November 1, 2009.

Combination Drugs Are the Future for Hepatitis C

<http://www.xconomy.com/>

Steve Worland

Combination therapy has been a central component of treatment for certain viral diseases for more than 15 years. The benefits of combination therapy can arise from activation of multiple host pathways, suppression of mutational variants that can lead to viral escape, or perhaps both.

In HIV, the benefit of combination therapy is due to suppression of viral resistance, which is the result of using multiple agents acting at distinct sites within the virus life cycle. In hepatitis C (which I'll abbreviate as HCV) the addition of ribavirin to interferon turned what was primarily an on-treatment lowering of viral titers into the first significant rate of viral clearance that persisted even after therapy was stopped. This sustained virological response, known as SVR, has become the primary measurement of clinical benefit in HCV. The mechanism underlying the dramatic effect of combining ribavirin with interferon is not clear. The benefit could be due to a pharmacologic interaction between pathways activated by interferon and pathways activated by ribavirin, or it may be the result of a modest ribavirin antiviral effect added to an "antiviral state" induced by interferon.

Just this year, companies in the HCV field began exploring the use of direct antiviral combinations. It is hoped that by appropriately choosing complementary targets, benefits of combination similar to what was seen in HIV may soon be seen in HCV therapy. Whether or not the combination of direct antivirals will permit the elimination of interferon and/or ribavirin remains unknown at this time, and is perhaps the most highly anticipated answer in the HCV field today.

Combinations of antivirals today

Three companies have moved into the clinical stage of exploring direct antiviral combinations for HCV.

Roche is most advanced in combination studies of direct antivirals with its INFORM-1 study. In this study, HCV patients were treated for 14 days with various dose levels of two drug candidates that inhibit different parts of the virus life cycle. These drug candidates are **RG7128**, a nucleoside polymerase inhibitor licensed from **Pharmasset**, and **RG7227**, a protease inhibitor licensed from **Intermune**. Data from the first several dosing cohorts was disclosed this past April at the annual meeting of the European Association for the Study of the Liver. Additional data, including responses at higher doses and in patients who previously failed interferon/ribavirin, will be reported at the annual meeting of the American Association for the Study of Liver Diseases conference in Boston.

The INFORM-1 study clearly shows that two antiviral agents can act in concert to produce a greater antiviral effect over 14 days than either agent produced alone. At the same time, critical questions remain for longer studies — Can direct antivirals alone retain viral titers at undetectable levels over longer periods of treatment? Even more important, will a state of virus negativity elicited by a direct antiviral combination afford the same rate of SVR once therapy is stopped as when virus negativity is induced by the interferon/ribavirin combination? Is there anything special about the mechanism(s) relied upon to reach negativity, or once arrived at, are all virus negativities created equal?

Two other companies have taken the first steps toward a combination study of two direct antivirals in HCV patients. **Gilead Sciences** has conducted a study in healthy volunteers to assess any interactions between a non-nucleoside polymerase inhibitor and a protease inhibitor (**GS-9190** and **GS-9256** respectively). Likewise, **Vertex Pharmaceuticals** is conducting a similar study using the same two classes of therapeutics. This study includes telaprevir, a protease inhibitor currently in late stage clinical trials, and **VX-222**, a non-nucleoside Vertex gained through its acquisition of ViroChem earlier this year. For both of these companies, assessing interactions between the drugs precludes studying these combinations in HCV patients.

Standard of care plus antivirals

In addition to the clinical trials testing combinations of two direct antivirals, drug developers are expected to test combinations of two direct antivirals with pegylated interferon and/or ribavirin, with various objectives for various trial designs.

In patients who have not been previously treated, there is a possibility that treatment with two antivirals added to interferon/ribavirin may further increase SVR beyond that seen when a single antiviral was added to interferon/ribavirin, although a more likely outcome is an increase in the percentage of patients who can successfully be treated with shorter course interferon.

In patients who previously failed to achieve SVR on interferon/ribavirin, the situation may be different. Vertex's PROVE 3 clinical trial showed that adding a single antiviral on top of interferon/ribavirin enhanced SVR rates, but with plenty of room for further improvement. In this case, adding a second direct antiviral to create a four drug combination may indeed improve SVR. There is also interest in testing the ability to remove interferon and/or ribavirin through the use of two direct antivirals.

Many trial designs to test combinations involving multiple direct antivirals have been discussed. There will be a significant advantage to companies who have access to the agents required to conduct such combination trials and whose trial design creativity is coupled to effective interactions with regulatory agencies such that they can efficiently move through the complex space of potential trials to arrive at optimum combination regimens.

Impact on biotech business

The benefits of combinatorial therapy may drive significant business activity as well. As the HIV field approached combination clinical trials in the early 1990s, it became clear that the challenge of getting two or more sponsors who owned individual drug candidates to agree to specific trial designs represented a significant hurdle to moving forward. Cooperative groups such as AIDS Clinical Trials Group (ACTG) and government sponsored trials struggled to provide efficient paths to combination trials.

Gilead Sciences utilized a business combination to solve this puzzle. By acquiring Triangle Pharmaceuticals in 2003, for approximately \$460 million, the company gained access to the product FTC. On its own, FTC was a thoroughly undifferentiated product. However, by controlling the asset Gilead could efficiently develop combinations with its attractive agent tenofovir, which ultimately led to the fixed dose combination products tenofovir emtricitabine (Truvada) and tenofovir emtricitabine efavirenz (Atripla). Many would argue that the acquisition of Triangle was a critical step in Gilead's path to its current market cap of approximately \$40 billion.

In HCV, the first business combination directed at clinical exploration of antiviral combinations was seen earlier this year when Vertex acquired ViroChem for approximately \$375 million.

The medical community will watch closely as companies test antiviral combinations, and the investment community will watch closely to see which companies are most adept at establishing compelling combination regimens, and to see if the need for assets to create combinations leads to additional combinatorial business activity.

Steve Worland is the president and CEO of San Diego-based Anadys Pharmaceuticals.

November 3, 2009

US Lawmakers Push to Ramp Up Hepatitis Battle

<http://www.google.com>

(AFP)

WASHINGTON — US lawmakers led by Asian Americans on Monday pushed to ramp up spending to fight hepatitis B and C, warning that the disease is causing a long-term burden for

the costly US health care system.

Hepatitis B and C are liver diseases commonly spread by blood that can lead to early death if untreated. Hepatitis disproportionately affects Asian Americans, in part due to its prevalence in parts of East Asia.

The bill led by Representative Mike Honda, head of the Asian American caucus in Congress, would devote 90 million dollars as of 2011 to help prevent and immunize people against hepatitis and step up research.

The California lawmaker said that efforts against the disease were underfunded, with 18.3 million dollars devoted to hepatitis in the current fiscal year compared with 692 million dollars for domestic efforts against HIV.

"We have a wave of chronic liver disease that will crash like a tsunami on the United States health care system if we do not address this problem now," said Lorren Sandt, chair of the National Viral Hepatitis Roundtable, an umbrella organization of groups fighting the disease.

"This simple legislation will help identify the people who are chronically infected and get them into treatment, which can save millions in future health care costs," Sandt said.

Some five million people in the United States are infected with hepatitis B or hepatitis C but many are unaware, according to the Centers for Disease Control and Prevention.

The hepatitis bill spearheaded by Honda, a Democrat, is also supported by Republican lawmakers including Bill Cassidy of Louisiana, a physician.

"As a hepatologist, I have witnessed firsthand the consequences hepatitis can inflict on a patient's health, their families and the nation's health care budget," he said.

Honda's office is seeking additional supporters of the legislation and is hoping the bill can move forward after legislation on reforming the health care system.

President Barack Obama has made health care reform his top priority. Some 47 million Americans lack medical insurance although the United States spends more per Gross Domestic Product on health care than any other wealthy nation.

Non-Response to HBV Vaccine a Sign of Possible Celiac Disease

www.medscape.com

NEW YORK (Reuters Health) Oct 30 - Celiac disease patients often don't respond to hepatitis B virus (HBV) vaccination, leading Italian researchers to recommend that monitoring responses to the vaccine be routine in celiac patients.

In other populations, they advise, a non-response to the vaccine "must be considered...a sign of...possible undiagnosed celiac disease."

"Unresponsiveness of celiac patients to HBV vaccine may represent a significant public health problem that needs to be addressed," Dr. S. Leonardi and colleagues at the University of Catania write in the October issue of *Vaccine*. "In fact a large reservoir of HBV-susceptible people will persist since frequency of celiac disease is worldwide."

The finding that HBV vaccine fails to elicit protective antibody levels in many people with celiac disease is not new, but neither is it well studied. Dr. Leonardi's group compared 60 children with celiac disease who had been vaccinated before their first birthday, and 60 controls.

Anti-hepatitis B surface antibody (anti-HBs) levels were measured in all children, with levels below 10 mIU/mL considered to be negative and levels between 10 and 100 IU/L considered a low response. Anything above that was a high response.

In the general population, according to the authors, rates of non-response to the HBV vaccine range from 4% to 10%. In this study, however, at an average age of 9 years, 30 of the celiac children, or 50%, were unresponsive to the vaccine, compared to 7 (11.6%) in the control group ($p < 0.0001$).

Among the celiac children who did have responses, 15 were high responders and 15 were low responders. In the control group, by contrast, 34 patients were high responders and 19 were low responders.

All of the patients with celiac disease were adhering to gluten-free diets, as determined by tests for serum markers of gluten ingestion. Years of gluten intake before diagnosis could not be correlated with responder versus nonresponder status. There were, however, significantly more responders among the youngsters diagnosed before age 18 months and significantly fewer responders among children who were not diagnosed until adolescence.

"This study confirms again that celiac patients have a lower percentage of response to hepatitis B vaccination than healthy subjects but the underlying mechanism remains unclear," the researchers conclude.

"Probably new modalities to enhance vaccine response in celiac disease patients should be investigated," perhaps an intra-dermal route or additional doses, they add.

Vaccine 2009;27:6030-6033.

New Hepatitis C Protease Inhibitors Achieve 80% 'Cure' Rate in Patients with Genotype 1 Infection

www.aidsmap.com

Gus Cairns

A course of hepatitis C (HCV) combination therapy including the experimental HCV protease inhibitor telaprevir (VX-950) has produced a sustained viral response (SVR) in over 80% of treatment-naïve, hepatitis C-mono-infected patients with HCV genotype 1.

Another study found similar rates achieved by another protease inhibitor, boceprevir. The

findings were announced on Tuesday at the American Association for the Study of Liver Disease (AASLD) meeting in Boston, USA.

This response rate is at least 30% higher than the best SVR rates achieved in trials of patients with genotype 1 mono-infection treated with the standard pegylated interferon/ribavirin regimen.

Eighty-two per cent of patients achieved an SVR in 24 weeks (12 weeks on telaprevir plus interferon/ribavirin and 12 on interferon/ribavirin alone), when standard treatment for G1 lasts 48 weeks.

SVR, which is regarded as equivalent to a cure, is defined as the lack of detectable hepatitis C in the blood six months after the cessation of therapy.

The results were superior to results achieved in the previous PROVE studies of telaprevir - see this report - where SVR rates of nearly 70% were achieved compared with under 50% in patients taking telaprevir placebo.

Final results from the present study, VX950-C208, were announced in a press release from the two companies developing the drug, Tibotec and Vertex, to accompany the conference presentation. This study had four differences from the PROVE study:

- There was no placebo-controlled arm: all patients took telaprevir;
- Half the patients took pegylated interferon-alfa-2a (Pegasys) and half took pegylated interferon-alfa-2b (PegIntron);
- Half the patients took 750mg of telaprevir three times daily, as in the PROVE studies, while half took 1250mg twice daily;
- If patients achieved an undetectable viral load by week four of the trial and maintained it till week 20, they were allowed to stop treatment at week 24. The 18% of patients who were exceptions to this carried on treatment till week 48.

Eighty-five per cent of patients taking telaprevir three times a day plus Pegasys achieved an SVR, and 82.5% of those on twice-a-day telaprevir.

In those taking PegIntron an SVR was achieved in 81% of those on thrice-daily telaprevir, and 82.1% twice-daily. These differences were not statistically significant. Interestingly, at week 12 there had appeared to be a difference in results, with 93% with undetectable HCV on thrice-daily telaprevir and 84% on twice-daily.

Regarding side-effects, the press release accompanying the trial results commented that “adverse events were similar to those observed in other trials with telaprevir.” The only figures given were for “serious adverse events leading to permanent discontinuation of all drugs,” which is a very restrictive definition. Three per cent discontinued the study due to rash by this criterion and 2% due to anaemia. In the PROVE 1 and 2 trials 21% and 12% of patients on telaprevir respectively discontinued therapy versus 11% and 7% on placebo. The main side effect of telaprevir is rash, with was classed as ‘severe’ in 7% and 15% of patients respectively in PROVE 1 and 2.

Final figures for viral breakthrough were not specified. Interim figures given in the abstract showed that nine patients (5.6%) had experienced an initial fall but then rebound of HCV by week 12 and that all nine had telaprevir resistance mutations.

The AASLD conference heard a lot of other news about new hepatitis C drugs. The results were also announced of PROVE 3, a trial of telaprevir in patients who have previously failed hepatitis C therapy. In this trial, nearly 40% of patients who previously failed to respond to pegylated interferon/ribavirin and nearly 70% who had responded but relapsed achieved an SVR with 24 weeks of treatment, while 76% of relapsers had an SVR with 48 weeks.

A study of Schering-Plough's boceprevir, the first hepatitis C protease inhibitor to be trialed, found SVR rates of 82% in patients with genotype 1 who had an undetectable viral load by week four, and 79% by those who had not achieved one by week four but had by week 16. And a second boceprevir study found an SVR rate of 55% among patients who had previously failed to respond to pegylated interferon/ribavirin. In these studies, pegylated interferon/ribavirin is given for four weeks then boceprevir added for 24 weeks (in naïve patients) and 44 weeks (in previous non-responders).

References

Marcellin P et al. Virological analysis of patients receiving telaprevir administered q8h or q12h with peginterferon-alfa-2a or -alfa-2b and ribavirin in treatment-naïve patients with genotype 1 hepatitis C: study C208. AASLD Conference, Boston, abstract 194. 2009.

McHutchison JG et al. PROVE3 Final Results and 1-Year Durability of SVR with Telaprevir-Based Regimen in Hepatitis C Genotype 1-Infected Patients with Prior Non-response, Viral Breakthrough or Relapse to Peginterferon-Alfa-2a/b and Ribavirin Therapy. AASLD Conference, Boston, abstract 66. 2009.

Kwo PY et al. Response-Guided Therapy (RGT) for Boceprevir (Boc) Combination Treatment? – Results from HCV SPRINT-1. AASLD Conference, Boston, abstract 1582. 2009.

Idenix Pharmaceuticals Initiates Phase II Clinical Trial of IDX184 in Combination with Pegylated Interferon and Ribavirin for the Treatment of Hepatitis C Virus (HCV)

CAMBRIDGE, Mass., Nov. 3 /PRNewswire-FirstCall/ -- Idenix Pharmaceuticals, Inc. (Nasdaq: IDIX - News), a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral diseases, announced today that it has initiated a Phase II clinical trial evaluating **IDX184**, a liver-targeted nucleotide prodrug candidate for the treatment of HCV, in combination with pegylated interferon and ribavirin, in treatment-naïve hepatitis C genotype 1-infected patients. Antiviral activity, safety and tolerability of the triple combination will be assessed at 14 days. Patients will continue on treatment with pegylated interferon and ribavirin for 14 days and Rapid Viral Response (RVR), the proportion of patients with undetectable virus at week 4, will be determined at Day 28.

"IDX184 was well tolerated and exhibited favorable antiviral activity in the initial 3-day, proof-of-concept study," said Douglas Mayers, M.D., chief medical officer of Idenix. "We look forward to evaluating IDX184 over a longer treatment period and as a component of combination therapy. This trial will also help us determine the optimal doses for broader clinical development."

The clinical trial is a Phase II, randomized, double-blind, placebo-controlled, sequential dose-escalation study evaluating the safety, tolerability, pharmacokinetics and antiviral activity of IDX184 in combination with pegylated interferon and ribavirin in treatment-naïve HCV genotype 1-infected patients. Patients will receive a daily dose of IDX184 or placebo plus pegylated interferon and ribavirin for 14 days and then continue on pegylated interferon and ribavirin for an additional 14 days. Antiviral activity will be assessed at the 14-day and 28-day timepoints. All patients in the study will have the option to continue pegylated interferon and ribavirin for up to 48 weeks. Four doses of IDX184 ranging from 50 to 200 mg per day will be evaluated. Each cohort of the study will evaluate twenty patients randomized 16 to IDX184 and 4 to placebo. This study is being conducted at multiple centers in the United States and Argentina.

About IDX184

IDX184 is a novel, liver-targeted nucleotide prodrug of 2'-methyl guanosine, which includes Idenix's proprietary liver-targeting technology. This technology enables the delivery of nucleoside monophosphate to the liver, leading to the formation of high levels of nucleoside triphosphate, thus potentially maximizing drug efficacy and limiting systemic side effects.

About Idenix

Idenix Pharmaceuticals, Inc., headquartered in Cambridge, Massachusetts, is a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral diseases. Idenix's current focus is on the treatment of infections caused by the hepatitis C virus. For further information about Idenix, please refer to www.idenix.com.

November 5, 2009

HBV Reduces Recurrence-Free Survival after Surgery for Hepatocellular Carcinoma

www.medscape.com

By David Douglas

NEW YORK (Reuters Health) Nov 04 - In cirrhotic patients, hepatitis B virus (HBV) infection is associated with a poorer long-term prognosis after hepatectomy for hepatocellular carcinoma, according to Italian researchers.

Infection with HBV, lead investigator Dr. Matteo Cescon told Reuters Health, "is a strong predictive factor for tumor recurrence after liver resection for hepatocellular carcinoma in patients with cirrhosis."

In the October issue of the *Archives of Surgery*, Dr. Cesco of the University of Bologna and colleagues report that they came to this conclusion after analyzing data on 240 cirrhotic patients who underwent hepatectomy. All had hepatocellular carcinoma with single nodules no greater than 5 cm in diameter.

At 5 years, recurrence-free survival was 38% in patients who were HBV-negative and hepatitis C virus (HCV)-positive at the time of resection. Recurrence-free survival was similar - 34% -- in patients without HBV or HCV infection at operation. Among HBV-positive, HCV-negative patients, only 9% were recurrence-free at 5 years.

Factors independently associated with recurrence-free survival were HBV infection (OR, 1.79) and poor tumor differentiation (OR, 2.01).

Recurrence-free survival at 5 years in those with neither factor was 49%. For patients with one factor, it was 20% and for those with both, it was 8%.

The findings, Dr. Cescon continued, add more support for use of adjuvant antiviral treatment.

"Given the high risk of recurrence after resection in patients who are seropositive for hepatitis B virus and have poorly differentiated cancers," he concluded, "this population should be considered as a major candidate for a policy of salvage liver transplantation."

Dr. David M. Levi of the University of Miami, co-author of an accompanying editorial, remarked to Reuters Health that "through a simple but thorough analysis, the authors have demonstrated that for patients with cirrhosis and hepatocellular carcinoma, a diagnosis of HBV infection negatively affects disease-free survival."

Arch Surg 2009;144:906-913.

Low Factor V Levels Signal Poor Prognosis with Hepatitis B-Induced Acute Liver Failure

www.medscape.com

Caroline Helwick

November 5, 2009 (Chicago, Illinois) — In patients with acute hepatic failure resulting from hepatitis B, factor V level on day 3 of diagnosis can help predict the risk for mortality, and thus can help triage patients for liver transplantation, according to a study from India reported here at the American Society for Clinical Pathology 2009 Annual Meeting.

"Factor V level signifies the regenerative capacity of the remaining hepatocytes," explained Naveen Gupta, MD, from the Institute of Liver and Biliary Sciences, New Delhi, India.

The study was performed at the All India Institute of Medical Sciences, New Delhi.

Levels of factor V lower than 10% vs those higher than 10% can distinguish which patients need transplant and which can recover with supportive therapy, Dr. Gupta said.

Acute hepatic failure is mainly caused by viral hepatitis, toxic substances, acetaminophen overdose, and metabolic disorders such as Wilson's disease. It is frequently fatal, and liver transplantation is the only curative treatment.

"The All India Institute of Medical Sciences treats about 75 cases of acute hepatic failure each year, almost all due to viral hepatitis. We wanted to determine the prognostic implications of various parameters in hepatitis B-induced liver failure in order to help us triage patients for liver transplantation," Dr. Gupta said. "In India, due to the extreme shortage of donor livers, our task is to know which patients to allocate to transplant and which may have an acceptable course

without a liver transplant."

The study was performed in a cohort of 40 patients with viral hepatitis–induced acute liver failure, 26 of whom died (65%), and 14 of whom survived (35%).

Investigators examined variables that were hypothesized to predict survival, including age, interval between onset of jaundice and encephalopathy, coagulation factor level, and various metabolic parameters. They excluded patients with liver failure caused by paracetamol poisoning or Wilson's disease, drug overdose, history of recent (within 1 week) alcohol use, and possible infiltrating tumor.

Patients were evaluated on day 1 and day 3 of admission. Evaluations included factor V, arterial blood gases, and serum lactate estimation.

Serum lactate levels and average arterial blood glasses were largely similar between patients who died and those who survived. However, factor V level on day 1 of admission was significantly lower in patients who died — in the range of 0% to 5% — whereas one quarter of patients who survived had factor V levels higher than 5%. Factor V level on day 3 was even more highly associated with survival. The level ranged from 0% to 10% among those who died compared with 7% to 25% for those who survived ($P < .034$), Dr. Gupta reported.

Altogether, maximum factor V levels were 12% for patients who died and 25% for those who lived, he noted.

Univariate analyses on all the other variables showed no statistically significant differences. Metabolic parameters, therefore, were not helpful in predicting outcomes, Dr. Gupta said.

"We feel that coagulation factor levels predict survival and help us allocate scarce resources for patients who have poor survival rates, such as those whose factor V level is moderate to severely deficient," he said. "Other patients with high levels can be managed with supportive therapy."

Dennis P. O'Malley, MD, from Clariant Diagnostics, Inc, Aliso Viejo, California, one of the session moderators, said the results are not particularly applicable to US populations of patients with acute liver failure, but he applauded the study from a global perspective.

Dr. O'Malley said the concept was important to study, especially for the Indian acute liver failure population. "You cannot necessarily apply standards developed in the United States to an Indian population, because the pathophysiology is different, and this requires different standards," he said. "But it is important to recognize, from the standpoint of global healthcare, that there are differences in patient populations and practice concerns among regions."

Dr. Gupta has disclosed no relevant financial relationships. Dr. O'Malley is an employee of Clariant Diagnostics, Inc, which was not involved in this study.

American Society for Clinical Pathology 2009 Annual Meeting: Abstract 83. Presented October 31, 2009.

HCV Vaccines, TLRs Advance Away from Protease Spotlight

<http://www.therapeuticsdaily.com>

BioWorld International

Protease inhibitors like Vertex Pharmaceuticals Inc.'s telaprevir and Schering-Plough Corp.'s boceprevir tend to take center stage at the American Association for the Study of Liver Disease (AASLD) annual meeting.

They are, after all, the most advanced alternative to the hepatitis C standard of care, ribavirin plus pegylated interferon, which often comes under fire for its 40 percent to 50 percent cure rate and significant side effects. But beyond protease inhibitors and their direct-acting antiviral cousins, polymerase inhibitors, other HCV approaches like therapeutic vaccines, Toll-like receptor agonists and cyclophilin inhibitors showed progress at this year's conference.

In the vaccine department, GlobeImmune Inc., of Louisville, Colo., presented Phase IIb data with **GI-5005**, a yeast-based vaccine expressing HCV NS3 and Core antigens. The vaccine plus standard of care was well tolerated and increased treatment responses by 15 percent compared to standard of care alone in treatment-naive HCV patients. After 48 weeks, 70 percent of patients receiving the vaccine plus standard of care compared to 55 percent of those receiving standard of care alone had a response, as defined by HCV RNA < 25IU/mL.

Vienna, Austria-based Intercell AG presented somewhat mixed data with **IC41**, its peptide vaccine containing CD4 and CD8 T-cell epitopes. In a Phase II study of treatment-naive HCV patients, those receiving the vaccine plus the approved TLR7 drug **Aldara** (imiquimod, Graceway Pharmaceuticals LLC) showed viral load reductions, while those receiving more vaccine but no Aldara did not. Intercell, however, said 40 percent to 60 percent of patients showed T-cell responses in both treatment groups.

More vaccine data came from Strasbourg, France-based Transgene SA. The company is developing **TG4040**, a Modified Vaccinia Ankara viral vector incorporating the gene sequences for NS3, NS4 and NS5B. Interim Phase I data in treatment-naive HCV patients showed T-cell responses as well as some cellular immune responses, with the strongest vaccine-specific T-cell responses corresponding to the highest decreases in viral load following vaccination.

Additionally, Rome-based Okairos AG presented Phase I data with its adenovirus vector-based vaccine expressing HCV NS3-5 proteins. Treatment was well tolerated and induced both CD4 and CD8 HCV-specific T-cell responses.

Another immune-stimulating approach making headway in HCV is Toll-like receptor agonists, which trigger an innate immune response. The TLR field has suffered setbacks in multiple indications, including HCV: Coley Pharmaceutical Group Inc. (now part of Pfizer Inc.) previously dropped its TLR9 agonist Actilon due to limited efficacy seen in early HCV trials.

Yet another TLR9 agonist is moving forward in the hands of Cambridge, Mass.-based Idera Pharmaceuticals Inc. The company's IMO-2125 is being studied in two Phase I trials, one combining the drug with ribavirin in treatment-naive patients, and the other looking at the drug as a monotherapy in nonresponders. At AASLD, Idera presented preclinical data showing that **IMO-2125** induced the production of cytokines and chemokines, including endogenous

interferon-alpha, which may indicate the potential to spare patients at least somewhat from harsh interferon treatments.

Also in the TLR space is San Diego-based Anadys Pharmaceuticals Inc. The company presented data from a dose-ranging Phase I trial showing that TLR7 agonist **ANA773** was well tolerated and significantly reduced serum HCV RNA levels at the highest dose, with reductions ranging from 0.10 log₁₀ to 2.52 log₁₀ (p = 0.04). The reductions correlated with markers of interferon induction. Anadys said earlier this year it is looking to outlicense ANA773 as it focuses on its non-nucleoside polymerase inhibitor, **ANA598**.

Another new approach to HCV is inhibition of cyclophilins, a family of enzymatic proteins that assist with protein folding and transport.

Scynexis Inc., of Research Triangle Park, N.C., is planning to start Phase II trials with its cyclophilin inhibitor, **SCY-635**, next year. In the interim, the company presented preclinical data at AASLD evaluating the drug in combination with ribavirin, interferon, protease inhibitors, nucleoside polymerase inhibitors and non-nucleoside polymerase inhibitors. Each of the combinations showed additive to synergistic activity, and evidence of hepatoprotection was seen when SCY-635 was combined with protease inhibitors.

Enanta Pharmaceuticals Inc., of Watertown, Mass., also presented data with a cyclophilin inhibitor, **EP-CyP282**. Preclinical data showed the drug is synergistic when combined with a non-nucleoside polymerase inhibitor and led to less frequent development of resistance than with either drug alone. In a separate preclinical study, the drug showed synergy with an NS5A inhibitor.

Hepatitis C Workshop Set for Nov. 18

<http://www.kauaiworld.com>

By The Garden Island

Malama Pono in partnership with the state Department of Health HIV/STD Branch presents the "Hepatitis C Training Workshop" on Nov. 18, a news release says.

Nationally renowned Hepatitis C instructor Alan Franciscus returns to Kaua'i to support and augment the knowledge and skills of people working directly with Kaua'i's estimated 1,500 Hepatitis C infected individuals. Hepatitis C is the major cause of liver failure and liver cancer on Kaua'i, the release says.

Both Malama Pono and the Department of Health HIV/STD Branch express concern that the liver cancer rate on Kaua'i may well double in the next nine years as a result of Kaua'i's high infection rate.

This full day training session is provided free for attendees under a grant from Roche Pharmaceuticals and includes continental breakfast, lunch and all snacks and refreshments. Topics to be covered include Hepatitis C transmission and prevention, diagnostic tools, symptomatology and disease progression, disease management, treatment and the role of complementary medicine.

A comprehensive course manual will be provided to all attendees and their successful completion of the course will result in certification as a Hepatitis C instructor. The course is also certified for six hours of Certified Substance Abuse Counselor (CSAC) credits.

The workshop takes place in the Orchid Room at the Hilton Kaua‘i Beach Resort beginning at 8 a.m. and finishing at 5 p.m. Seating is limited and reservations are required. To register or for more information contact Malama Pono at 246-9577.

Speaker Pelosi Says Hepatitis B Prevention at Core of Healthcare Reform

<http://www.asianweek.com/>

Connie Zheng

SAN FRANCISCO - In her first public appearance since the health care reform bill rollout last Thursday, House Speaker Nancy Pelosi addressed the need for community-based health care reform in a press conference at the Chinese Hospital on Oct. 31, highlighting the San Francisco Hep B Free campaign as a model for the nation.

With one in ten Asian American Pacific Islanders (AAPIs) chronically infected with the hepatitis B virus, Hep B Free is a citywide campaign to turn San Francisco into the nation’s first city free of the disease.

Joined by local, state and federal officials, community and health care leaders, citizen activists, corporate executives and family associations, Pelosi lauded the Hep B Free campaign’s success as an inspiration and blueprint for the national campaign.

“It certainly would not be possible without the local leadership as models for us in San Francisco,” Pelosi said. “The campaign has led thousands of individuals to get screened and treated.”

Hepatitis B is responsible for up to 80 percent of all liver cancers worldwide, and AAPIs have the highest rates of liver cancer for any racial or ethnic group.

“The Hep B campaign hits the core of our national drive for health insurance,” Pelosi said. “The hepatitis B virus is preventable and treatable. Yet too many in the AAPI community across the nation suffer from this disease. We must protect everyone from hepatitis B.”

Pelosi underscored the need for culturally sensitive health care that ends discrimination against individuals with pre-existing conditions, such as hepatitis B. The end of this type of discrimination is one of the proposed bill’s three main principles, along with affordable health care and fiscal responsibility.

Assemblywoman Fiona Ma has chronic hepatitis B infection and is a leading advocate for legislation to reduce the disease.

“Hepatitis B is a pre-existing condition,” Ma said. “We desperately need policy reform to make sure nobody gets kicked off health insurance for pre-existing conditions.”

Congresswoman Jackie Speier (D-CA) echoed Pelosi's sentiment regarding health care discrimination at the press conference.

"It is very appropriate that we send a message to everyone in the city that you have nothing to fear about hepatitis B," Speier said. "Pre-existing conditions will no longer be a fear for anyone, whether they have hepatitis B, HIV, cancer, or bunions - you name it."

Additionally, Pelosi discussed how the proposed reforms will remove health disparities among ethnic communities, such as hepatitis B, the greatest health disparity for Asians.

"With reform in place when we pass this legislation, the AAPI community will have access to treatments, the vaccine, screening and care that will help end those disparities, keep families healthy, and ensure our success in fighting hepatitis B and making San Francisco a hepatitis B-free city."

The spotlight on health disparities affecting ethnic communities, such as hepatitis B for Asian Americans, is part of a growing national awareness from health care reform to the White House.

On Oct. 14, President Obama re-established the advisory commission and White House initiative created by President Clinton ten years ago to address concerns affecting AAPIs. While acknowledging the many contributions of AAPI communities to the country, Obama recognized the challenges faced by AAPIs in health disparities like hepatitis B.

"The more than 16 million AAPIs across our country have helped build a strong and vibrant America," Obama said. "It's tempting, given the strengths of AAPI communities, for us to buy into the myth of the 'model minority,' and to overlook the very real challenges that certain AAPI communities are facing: from health disparities like higher rates of diabetes and hepatitis B."

Under the House Democrats' proposed health care legislation, the government will give new grants for prevention and wellness services to communities with special emphasis on health disparities, expand coverage for vaccines, and eliminate co-payments and deductibles for preventive services such as the hepatitis B vaccine.

"We will have an opportunity in San Francisco and across the country to change our health insurance system for the better, whether it's making this city as a hepatitis B-free city or expanding access to quality, affordable, accessible health care for all Americans," Pelosi said.

Dr. Garth Graham, deputy assistant secretary for minority health for the Department of Health and Human Services, said the department supported a national strategy aiming to address the issues of prevention of new infections by promoting screening, immunization, education; promotion of early detection; appropriate follow-up and clinical management of individuals with chronic hepatitis B infection with linguistically and culturally appropriate prevention care and treatment; and increased awareness and support of hepatitis B and liver cancer research among national and state policymakers.

"We recognize chronic hepatitis B's disproportionate impact on the AAPI community is a national problem," Graham said.

Since the San Francisco Hep B Free Campaign's inception in 2007, the campaign has developed significant partnerships with over 50 public and private health care organizations, businesses, and educational institutions, as well as Major League Baseball's San Francisco Giants. It has created seven low-cost public access hepatitis B screening and vaccination sites.

"Our goal is to try to get everyone screened and tested in San Francisco," Ma said. "We wanted to spread the message we can eradicate hepatitis B, just like smallpox. But we had no money when we started, just a goal. Now two and a half years later, all our community partners, public and private hospitals, doctors, insurance and pharmaceutical companies, non-profit organizations and the community have gotten together to ensure that everyone can get screened, tested and treated here in San Francisco."

The campaign's success has inspired other communities to follow its model.

"It is a model that is being replicated in San Mateo, San Jose, Orange County and Los Angeles," Ma said. "We believe that we are on the way to a movement."

Graham lauded the campaign's use of community partnerships, academia, community-based organizations and local government to increase education and awareness and recommended adoption of its model as part of a national strategy.

"The San Francisco Hep B Free Campaign is an excellent demonstration of what the Department of Health and Human Services is trying to see happen across the country," Graham said. "We want to broaden this model, use it as a model of community engagement and go across the country in terms of national strategy."

Pelosi added that it was no surprise the Centers for Disease Control and Prevention would look to San Francisco for leadership and to take its success as a blueprint for the national campaign.

Officials and leaders urged the public to get tested, treated and vaccinated for hepatitis B at the press conference.

"We are so fortunate in spite of the extraordinary infection rates that there is a hepatitis B vaccine that the World Health Organization has called the world's first anti-cancer vaccine," said Senator Mark Leno.

"It is treatable, it is preventable, we can eradicate it," Ma said. "We just need everybody's help."

David Chiu, San Francisco Board of Supervisors President, voiced the hope that the day will soon come when San Francisco will be a hepatitis B-free city.

"We are all here today united in the Hep B Free Campaign," Chiu said. "Chinatown in San Francisco is the Asian American capital of not just our city, not just California, but the entire country. Half of the deaths that arise from hepatitis B come from our community. This is our disease, this is our campaign, and this is our cause."

Pelosi urged everyone to "take the (Hep B Free) campaign theme to heart: B a Hero. See a doctor who tests for Hepatitis B."

About San Francisco Hep B Free Campaign:

The San Francisco Hep B Free Campaign is a “first-in-the-nation” effort calling on the collaboration of a wide spectrum of organizations to educate the public about the health risks of the hepatitis B virus (HBV) and to promote routine HBV screenings and vaccinations for the city’s Asian and Pacific Islander (API) population. For more information, please visit www.sfhepbfree.org.

About the Hepatitis B Virus (HBV):

Hepatitis B is a serious disease of the liver caused by the hepatitis B virus (HBV) that can lead to acute illness and chronic infection including cirrhosis, liver failure or liver cancer. It is a silent killer affecting approximately 1.4 million Americans, of which more than half are of API descent.

HBV is an epidemic within San Francisco’s API community. An estimated one in ten APIs have an undiagnosed infection. APIs are up to 100 times more likely to suffer from chronic HBV infection and four times more likely to die from liver cancer compared with the general population. Hepatitis B is responsible for 80 percent of all liver cancers among APIs, who have the highest rates of liver cancer for any racial or ethnic group. San Francisco’s liver cancer rate is the highest in the U.S.

Hepatitis B is 100 times more infectious than HIV and is easily transmitted - from an infected mother to her child at birth, through unprotected sex or by contaminated blood.

For more information, please visit www.sfhepbfree.org.

November 5, 2009

AASLD: Direct Antivirals Can Beat HCV without Interferon

www.medpagetoday.com

By John Gever, Senior Editor, MedPage Today

Reviewed by Robert Jasmer, MD; Associate Clinical Professor of Medicine, University of California, San Francisco and

Dorothy Caputo, MA, RN, BC-ADM, CDE, Nurse Planner

BOSTON -- The first clinical trial of direct antiviral drugs against hepatitis C virus (HCV) without interferon was a success, researchers said, although the FDA currently won't permit such a strategy in the U.S.

A combination of two investigational antivirals, one an HCV protease inhibitor and the other targeting the HCV polymerase, led to dramatic reductions in viral loads during a 13-day pilot trial, according to Edward Gane, MD, of Auckland Clinical Studies in Auckland, New Zealand, where the study took place.

The drugs' lead developer, Roche, announced that Phase II testing would begin in early 2010. But for now, the studies must be conducted outside the U.S. because of an FDA policy requiring HCV drug testing to include interferon-alfa.

Action Points

- *Explain to interested patients that neither drug is FDA approved for any purpose.*
- *Explain that treating patients only with direct antiviral agents without interferon is controversial and could provoke resistance to drugs that might otherwise remain effective.*
- *Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered preliminary until published in a peer-reviewed journal.*

Along with ribavirin (Rebetol), interferon is the only agent currently proved to control HCV infection. The FDA believes it is unethical to withhold it from infected patients, though researchers close to the situation said Roche was talking with the agency about relaxing its stance.

Gane, speaking here at the American Association for the Study of Liver Diseases' annual meeting, reported data from a placebo-controlled Phase Ib trial called INFORM-1, testing various dosing regimens of two oral drugs co-developed by Roche and two other companies.

The drugs were RG7128, a nucleoside agent inhibiting the HCV polymerase enzyme, and RG7227, a small-molecule compound that inhibits the virus's protease enzyme.

Gane said the combination was attractive for several reasons. The differing targets and mechanisms discourage development of resistance, and in vitro studies confirmed that RG7128 suppressed emergence of resistance to the protease inhibitor.

There is no cross-resistance between molecules, he added, and the drugs have different routes of elimination and no signs of pharmacokinetic interaction or overlapping toxicities.

The clinical study encompassed seven treatment arms, four of which involved RG7128 given twice daily and RG7227 three times daily in treatment-naive patients. Gane reported results from those regimens earlier this year at a European liver disease meeting.

He focused his presentation here on the other three treatment arms, in which both drugs were given twice daily and the 30 patients involved included people who had previously shown incomplete (partial or relapsing) or null responses to standard treatment with interferon and ribavirin as well as previously untreated patients.

Eight patients in each group received active drugs for 13 days, and two received placebo pills. The RG7128 dose was 1,000 mg twice daily in all groups. RG7227 was given at 600 mg twice daily to the incomplete initial responders, while those with null responses or who were treatment-naive received 900 mg twice daily.

Median reductions in HCV viral loads from baseline, measured in log₁₀ increments on day 13, were as follows:

- Incomplete initial responders: 4.0 (range 2.5 to 6.0)
- Null initial responders: 4.9 (range 3.5 to 5.3)
- Treatment-naive: 5.1 (range 3.0 to 5.9)

Gane said half of the previously-treated patients in both groups had viral loads suppressed below the lower limit of quantification. This level of virologic response was seen in seven of eight treatment-naïve patients.

HCV RNA was undetectable in five treatment-naïve patients, two of the null responders, and one of the partial responders.

Gane said there was no evidence of resistance to the drugs in any of the seven INFORM-1 treatment groups. Adverse effects did not appear to differ between placebo and the active drug, although the study was not powered to detect differences. No severe adverse events were noted, Gane said.

Scott Friedman, MD, president of AASLD and a hepatologist at Mount Sinai School of Medicine in New York City, said the prospect of an interferon-free, all-oral drug regimen for HCV was intriguing.

"Interferon is a nasty drug," he said, adding that patients with advanced disease often can't tolerate it.

On the other hand, Friedman said, there is some chance that treatment based solely on direct antiviral drugs could provoke resistance to those agents -- resistance that would not develop if interferon were also given.

That outcome could leave patients worse off, even taking the toxicities of interferon into account, he suggested.

The study was funded by Roche, Pharmasset, and InterMune.

Gane reported no potential conflicts of interest other than the research funding. Several co-authors were employees of Roche, Pharmasset, or InterMune.

Friedman reported relationships with Exalenz, sanofi-aventis, Axcan, Angion, Intercept, 7TM, Stromedix, and Celera.

Primary source:

Hepatology

Source reference:

Gane E, et al "Combination therapy with a nucleoside polymerase (R7128) and protease (R7227/ITMN-191) inhibitor in HCV: Safety, pharmacokinetics, and virologic results from INFORM-1" *Hepatology* 2009; 50: 394A-395A.

AASLD: Treating before Transplant Cuts HCV Recurrence

www.medpagetoday.com

By John Gever, Senior Editor, MedPage Today
Reviewed by Zalman S. Agus, MD; Emeritus Professor
University of Pennsylvania School of Medicine

BOSTON -- In patients with advanced liver disease related to hepatitis C, a course of pegylated interferon and ribavirin (Rebetol) before liver transplant may help them avoid recurrence of infection, a researcher said here.

Nearly 30% of patients receiving the drugs showed no signs of the hepatitis C virus (HCV) three months after receiving a new liver, reported Gregory T. Everson, MD, of the University of Colorado in Denver.

He presented results of a prospective, semirandomized component of a larger study called A2ALL at the American Association for the Study of Liver Diseases meeting.

"This experience supports the concept that pretransplant therapy can prevent allograft reinfection," he said.

Action Points

- *Explain to interested patients that hepatitis C virus infection can persist after liver transplant.*
- *Explain that the pretransplant drug regimen used in this study had significant toxicities and did not benefit all patients.*
- *Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered preliminary until published in a peer-reviewed journal.*

Not surprisingly, the best results were achieved in patients whose HCV viral loads were reduced to undetectable levels at the time of transplant, Everson reported. Among 14 patients in whom this was achieved, eight remained virus free at the post-transplant evaluation.

Duration of the pretreatment regimen was also a significant predictor of post-transplant response, Everson reported.

Some 44% of patients who received the interferon-ribavirin treatment for more than 15 weeks before transplant had a postprocedure response, compared with 18% of those treated for 10 to 15 weeks and 15% of those getting the drugs for less than 10 weeks (P=0.04).

Other factors -- such as baseline HCV viremia, viral genotype, type of donor (live versus dead), and toxicity-related dose limitations -- were not significantly associated with post-transplant response, although the study may not have been powered adequately to detect such associations.

Of the 79 patients enrolled in the trial, 47 with HCV genotypes 1, 4, 5, or 6 were randomized in a 2:1 ratio to receive the pretransplant drug regimen or no treatment. All of the 32 other patients with HCV genotypes 2 or 3 received the treatment.

The treatment consisted of starting doses of 0.75 mcg/kg/week of pegylated interferon-alfa-2b (PEGIntron) and 600 mg/day of ribavirin, which were both escalated as tolerated over several weeks to standard target levels.

Median treatment duration was 11.4 weeks for the 44 dead-donor candidates and 14.6 weeks for

the 35 able to receive live-donor organs.

Transplant was actually performed in 41 patients, 25 of whom were dead-donor candidates.

Everson characterized the effectiveness of the pretransplant drug regimen as "limited."

He said it should be considered only for selected patients, particularly those with relatively less severe disease.

In the trial, those were the patients who were live-donor candidates along with the dead-donor candidates who received a so-called MELD upgrade because of hepatocellular carcinoma.

"If you take all the patients with HCV going to liver transplant, many of them are too sick to treat with [pegylated interferon] and ribavirin," he said.

Data from the study indicated that the treatment was significantly toxic. Three-quarters of the treated patients suffered serious adverse events, compared with half of untreated patients (P=0.04). These were seen both before and after transplant.

However, mortality rates were the same in treated and untreated patients, at about 15%.

Everson said it might be possible in the future to try pretreatment in sicker patients when direct antiviral drugs for HCV become available.

In the meantime, he said, patients who can tolerate the treatment need to stay on it for at least 12 weeks.

The study was funded by the National Institutes of Health.

Everson reported relationships with Schering-Plough and Ortho Biotech. Other co-authors reported relationships with Roche, Salix, Gilead, Vertex, Pfizer, GlaxoSmithKline, Amgen, Bayer, Novartis, and Human Genome Sciences, among others.

Primary source:

Hepatology

Source reference:

Everson G, et al "Interim analysis of a controlled trial of pretransplant peginterferon alfa-2b/ribavirin (PEG/RBV) to prevent recurrent hepatitis C virus (HCV) infection after liver transplantation (LT) in the Adult-to-Adult Liver Transplantation (A2ALL) Study" *Hepatology* 2009; 50: 302A.

Bipartisan Support Grows for Addressing Nation's Hepatitis Scourge

<http://www.rollcall.com>

By Lorren Sandt

Special to *Roll Call*

While lawmakers, budget experts and health care policy gurus have long known that chronic

illnesses like diabetes, hypertension and cancer threaten to overwhelm our health care system, too few in Washington, D.C., have recognized that chronic liver

disease deserves to be part of the conversation. Left unchecked, chronic liver disease stemming from hepatitis B and hepatitis C is projected to cost our nation's health care system more than \$85 billion annually within 15 years and ravage minority populations, including millions within the African-American, Latino and Asian-American communities.

[IMGCAP(1)] Admirably, leading Members of Congress from both sides of the aisle have taken an important step in the past week to help address this public health crisis. H.R. 3974, the Viral Hepatitis and Liver Cancer Control Act, was introduced Oct. 29 in the House. Spearheaded by Rep. Mike Honda (D-Calif) in strong partnership with Reps. Charlie Dent (R-Pa.), Edolphus Towns (D-N.Y.), Bill Cassidy (R-La.), David Wu (D-Ore.) and Anh “Joseph” Cao (R-La.), the legislation would help establish, promote and support a comprehensive prevention research and medical management referral program under the Public Health Service Act for chronic hepatitis B and chronic hepatitis C virus infection. The legislation would provide a relatively modest \$90 million in funding in 2011 — with additional funding in subsequent years — that would increase the ability of the Centers for Disease Control and Prevention to support state health departments in their prevention, immunization and surveillance efforts.

At a time of polarized health care debates, this legislation has already enlisted prominent bipartisan support that spans the political spectrum. Reps. Todd Platts (R-Pa.), Barbara Lee (D-Calif.), Bobby Rush (D-Ill.), Judy Chu (D-Calif.) and G.K. Butterfield (D-N.C.) and Del. Donna Christensen (D-Virgin Islands) have all signed on to the legislation as original co-sponsors. The depth and breadth of political support for increased funding for detection, prevention and treatment is testament to the gravity and urgency of this crisis.

Each of these Members is to be applauded for recognizing the human and economic costs that chronic liver disease inflicts on our nation. As many as 5.4 million Americans are infected with chronic hepatitis B or chronic C virus infection — and most don't even know they are infected. With most cases undiagnosed, millions of Americans are not receiving preventative, life-saving and cost-effective treatment. For many individuals, the first time they become aware of their viral hepatitis infection is when it has advanced irrevocably to cirrhosis, liver cancer or liver failure.

The absence of meaningful prevention, detection and treatment programs means that chronic liver disease threatens to overwhelm federal, state and local health programs. Annual medical costs for patients with hepatitis C virus infection alone are expected to skyrocket from \$30 billion in 2009 to \$85 billion annually by 2024, according to a recent Milliman analysis. Many of these costs in the coming years will be borne by already-stretched Medicare and Medicaid programs, which makes action now even more critical.

Three demographic groups are at highest risk of infection. The baby boom generation — those born between 1946 and 1964 — are most likely to be infected with chronic hepatitis C virus infection. African-Americans are twice as likely as the general population to contract hepatitis C. One in 10 Asian-Americans has contracted hepatitis B. Again, given that most are unaware of their infection, few even know they have a virus, let alone that it can be treated or even cured.

In the coming decades, the complexion of our nation will rapidly diversify — and with it, so too will our health care challenges. It is vital that our entire health care system embrace and prepare for this historic shift. By modernizing our approach here and now to increased prevention, detection and management of hepatitis B and hepatitis C, policymakers will lay the foundation for an infrastructure designed to meet this challenge head on. And that’s something all Members of Congress can rally around.

Lorren Sandt is executive director of the Caring Ambassadors Program, based in Portland, Ore., and is chairwoman of the National Viral Hepatitis Roundtable, a coalition of more than 150 public, private and voluntary organizations dedicated to reducing the incidence of infection, morbidity and mortality from viral hepatitis.