

HCV ADVOCATE

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HealthWise

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Report on Annual Meeting of the American Association for the Study of Liver Diseases (AASLD)

This year's annual meeting of the AASLD met in Dallas. This article will focus on my overall impression and provide a brief summary. I want to emphasize that my perspective and opinion are subjective. My interest evolves around hepatitis C viral (HCV) infection. Consequently, I attended the presentations that were pertinent to this issue. In spite of this, it appeared that as a single disease, HCV dominated the meeting. Looking ahead to the next millennium, this virus is generating a great deal of concern. As both a nurse and patient, I find this enormously reassuring. The sheer numbers of people, time, money, and personal sacrifice devoted to HCV-

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AASLD Conference

Alan Franciscus

This was the first year that we (HCSP) participated in the AASLD conference which is **THE** liver conference of the year. Liver specialists from all over the world attend this conference to hear about the latest information on liver related disease. It was a wonderful experience and the information presented on hepatitis C was extraordinary.

The following list contains my choices (in no particular order) for the most interesting or important Hep C related issues discussed at the AASLD Conference. One of the benefits of attending this conference is the hope and optimism it generates about therapies that will some day offer better treatment options or even a cure.

Pegylated Interferons - The big buzz this year in Hep C circles is pegylated interferon. FDA approval of Schering's Peg-Intron and Roche's Pegasys are expected by mid to end of year 2000.

Pegylated interferon is a time-released interferon injected once weekly. It is believed this long acting interferon will help the body fight the hepatitis C virus by keeping constant levels of interferon in the blood stream. Additionally, initial reports indicate that patients may experience less side-effects than the traditional dosage of injecting 3 times weekly. Early results promise a 40- 45 % response rates.

Combination of pegylated interferon and ribavirin are even more encouraging. Some studies suggest end of treatment response rate as high as 60%-70% and the studies are proving

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HCV ADVOCATE

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related issues is phenomenal. It gives me a tremendous amount of hope.

There was nothing earth shattering presented at the meeting. Treatment for chronic HCV infection has come a long way and still has some distance to go. Approaches to treatment appear to be somewhat individualized. Although there are some general guidelines for treatment, there is no one universal recipe.

The posters and presentations on “complementary and alternative” therapies were of great interest. It is well known that interferon, with or without ribavirin, often causes side effects. With this in mind, many patients look to other sources to help manage HCV. Although there do not seem to be any promising cures on the horizon, there were a number of potentially beneficial substances that were presented. Two of these are vitamin E and milk thistle (silymarin). Both of these may have an antifibrotic effect on the liver. Whether or not this will prevent disease progression is unknown. If you decide to include either of these substances in your regimen, do not exceed the recommended doses. Use products that have been standardized and discuss this with your doctor.

In addition to looking for a cure for HCV, there is quite a bit of research being conducted using other approaches. Simply stated how can fibrosis be prevented or delayed for those with progression of liver disease. Again, nothing definitive was presented, but a number of substances are being researched. In addition to “alternative treatments”, some of the interleukin agents are being investigated. Interferon is also being studied.

Some of the pegylated (timed-release) interferon data presented shows promise. Both Schering and Roche have pegylated interferons. The speculation is that both will be available within 8 to 18 months, with Schering’s version coming out first. Roche appears to have a better pegylation process, possibly giving their version some advantages over Schering’s. The facts are still in the future.

Regarding completely new treatments, ribozymes seem to be one of the next rising stars. Ribozymes are viral specific whereas interferons target the immune system. Excerpts from a press release about this is included in this newsletter.

Although we still have a long way to go, it is important to put the journey in perspective. Treatment

for chronic HCV infection is not perfect. However, compared to HIV it offers far more hope and is much more tolerable. I realize that we are people and not numbers, but statistics are on our side. Until there is a cure, take responsibility for what you able.

- Abstain from alcohol
- Practice the healthiest lifestyle you can
- Continue to see your doctor on a regular basis

May your holidays and New Year be filled with hope and contentment.

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DALLAS--(BW HealthWire)--Nov. 8, 1999--In a study presented Monday at the AASLD annual scientific conference, a novel approach utilizing a ribozyme to directly attack Hepatitis C virus RNA was shown to inhibit viral replication.

Ribozyme Pharmaceuticals Inc.'s (NASDAQ:RZYM - news) Dr. Lawrence Blatt, Research vice president, Biopharmacology, showed data that demonstrated highly specific and dramatic inhibition of replication of a chimeric HCV-poliovirus by an Anti-HCV ribozyme in cell culture experiments. These studies indicate that the ribozyme therapeutic has potent antiviral activity and its effects are dependent on a ribozyme mechanism of action. In addition, the Anti-HCV ribozyme is expected to be effective against all known HCV genotypes. RPI anticipates filing an IND for the Anti-Hepatitis C ribozyme with its partner Eli Lilly before the end of 1999.

The Anti-Hepatitis C ribozyme was also reported to demonstrate a synergistic effect when combined with a current therapy, Infergen(TM) (interferon alfacon1), inhibiting viral replication in this model system up to 99%.

In another presentation at the AASLD meeting, Dr. Patrice Lee, Senior Scientist, Pharmacology, described the results of experiments that demonstrated significant uptake of the Anti-HCV ribozyme by liver cells following either subcutaneous or intravenous injection. This

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high as 60%-70% and the studies are proving that the combination of pegylated with ribavirin is safe and effective.

Complementary Therapies - This was another hot topic at the conference. Leonard B. Seeff, MD, talked on past, present and future of complementary therapies. Research is finally being conducted and some of the compounds such as Milk Thistle, Glycyrrhizin (licorice root extract), Sho-saiko-to (TJ-9) and Compound 861 look promising, but need further research. Jacquelyn J. Maher, MD, presented very encouraging data that showed Vitamin E may reduce liver scarring. It is very encouraging that many medical doctors are now interested in studying the effects of different herbal preparations.

Interleukin-10 - more promising news about another drug - Interleukin-10. One study suggested that interleukin-10 therapy reduced inflammation and lowered liver enzyme levels in almost all the patient (19) out of 22 patients enrolled in the study. Even more exciting is the news that many patients (14) showed improvement in the amount of scar tissue in the liver prior to treatment in just 3 months. Additionally, few side effects were reported, but larger

studies are needed.

Methadone - A small study of 26 patients with HCV on Methadone maintenance supported the inclusion of stable methadone maintenance patients in therapeutic trials of hepatitis C.

HIV / HCV Co-infection - A study of 30 HIV/HCV co-infect patients taking protease-inhibitors found that the HIV medications were well-tolerated in patients with HCV. However, patients must be monitored very closely for potential liver damage.

In a study from Spain a group of 19 hemophiliac showed that patients on HAART tolerated the combination therapy of interferon and ribavirin. Even though this clinical trial has not been completed, it gives promise for treating co-infected individuals with both HIV medications and the combination therapy of interferon and ribavirin. Another study conducted in New York, found similar results and recommended treating co-infected patients with interferon and ribavirin in combination with HAART is safe and effective, but patients need to be closely monitored for anemia.

Don't forget to make your plans early! See you there in 2000.

[Ribozymes - continued from page 2 -](#)

presentation was selected for an AASLD President Choice Poster Award. "These observations demonstrate that ribozymes targeting HCV RNA are able to effectively enter cells and further supports the feasibility of ribozyme therapy in patients with Hepatitis C," said Willis C. Madrey, M.A.C.P., a renowned Hepatologist and Professor of Internal Medicine, UT Southwest Medical Center, Dallas.

Hepatitis C is considered an epidemic in the United States by the Centers for Disease Control, with a four-fold higher prevalence than HIV. Over four million people are infected in the U.S. and 125 million people are reported to be infected worldwide. Chronic infection can lead to liver inflammation, cirrhosis, cancer and death. Current treatment options for patients are limited, clearing virus in only 20-40% of the patients and are associated with serious side effects. The ribozyme approach has the potential to treat all known types of Hepatitis C virus with a benign side effect profile.

Ribozymes are the product of Nobel Prize winning science and are synthetically engineered to act as "molecular scissors" capable of cleaving target RNA in a highly specific manner.

Joe Shaw

The following articles are results of studies and other news from the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD).

PEG-Intron Study

In a dose-ranging study designed to assess the biologic activities, pharmacokinetics, pharmacodynamics and tolerance of PEG-Intron, previously untreated patients chronically infected with the hepatitis C virus (HCV) received the drug subcutaneously once weekly for 24 weeks. Intron A 3 MIU administered subcutaneously three times a week was used as a comparator. In vitro activity was assessed using an HCV-surrogate cell-based assay. In this study, PEG-Intron was shown to be a biologically active molecule and demonstrated antiviral activity in vitro. PEG-Intron also demonstrated delayed clearance characteristics consistent with once weekly dosing.

In an oral presentation of results of a dose-ranging study of PEG-Intron in combination with Rebetol, investigators assessed the tolerance, pharmacokinetics and efficacy of the combination therapy in patients with chronic hepatitis C and evaluated its antiviral activity. In this study, the tolerance profile of PEG-Intron / Rebetol was comparable to the known tolerance profile of Rebetron Combination Therapy.

Pegasys May Work Better Than Combo Therapy, Says Roche

A new anti-viral drug developed by Hoffmann-La Roche appears to be better than the existing treatment for potentially fatal hepatitis C while having fewer severe side-effects. Hoffman-La Roche said clinical trials showed the drug peginterferon alpha-2a was much more effective than the main (combo) treatment now used against hepatitis C. Until now, two drugs are used to treat it, usually in combination -- interferon alfa-2b, sold under the brand name Intron A, and ribavirin, sold under the brand name Rebetol. Both are sold by Schering-Plough Corp. and the combination is sold under the name Rebetron.

But the combination only helps about 40 percent of patients and can have severe side-effects, mainly due to ribavirin, which can cause such problems as anemia and birth defects. Hoffman-La Roche said its Pegasys, a chemically-altered version of interferon alpha, when taken alone appears to be much more effective than interferon without risking the potentially drastic side effects of ribavirin.

In trials with 271 hepatitis C patients with cirrhosis, Pegasys caused a sustained reduction of the virus to undetectable levels in 29 percent of patients, while interferon had the same effect on just 6 percent. This followed results announced earlier from a trial with hepatitis C patients who had not developed the added complication of cirrhosis. In that test, 36 percent of those treated with Pegasys saw a sustained reduction in their viral load as against 3 percent of those on interferon. When combined with ribavirin, Pegasys also had a higher success rate of 70 percent as opposed to about 40 percent for the standard combination of interferon and ribavirin.

Besides Roche, rival Schering-Plough is also working on a version of peginterferon. The drug is created by chemically attaching a long hair-like strand of a synthetic substance to the molecules that make up interferon.

Researchers believe that attaching the strands, or pegylation, increases the effectiveness of interferons in two ways, by hiding the protein from the body's immune system and by making it larger and therefore slower to pass out of the body. The longer interferon remains in the body, the more time it has to attack the hepatitis C virus, researchers say.

Veterans May Have Higher Rate of HCV Infection

U.S. military veterans may have a far higher rate of infection with potentially deadly hepatitis C than the general population, researchers said.

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A study of blood samples in the San Francisco area found 19 percent of veterans using the San Francisco Veterans Affairs (VA) hospital were infected with the hepatitis C virus, compared to two percent in the broader population.

The San Francisco study looked at blood samples taken from 791 veterans, 95 percent of them men, who were also interviewed about potential risk factors in their backgrounds such as duty as a combat medic, frequent sexual contact or getting tattoos.

Although the study was limited to San Francisco, the results raise serious questions about the prevalence of hepatitis C among military men and women nationally, VA doctors Megan Briggs and Teresa Wright said.

“Even if the national prevalence is half that seen in San Francisco, with 2.7 million users of the VA, this represents a substantial financial burden to this federally funded health care system,” they said at the annual meeting of the American Association for the Study of Liver Diseases in Dallas.

Study Says Long-Term Costs of HCV in U.S. More Than \$81 Billion

A study presented at the AASLD meeting concluded that long-term damage from hepatitis C infections may cost the U.S. economy more than \$81 billion by 2019.

The study, by researchers from the New England Medical Center and Tufts University School of Medicine, looked at what costs can be expected in the ten years from 2010 to 2019 as a result of the long-term effects of hepatitis C infections. The study used a computer model to estimate the level of disease and death expected in the period 2010-2019 from existing and future infections.

It found that the medical costs of treating such liver damage as cirrhosis and cancer would total at least \$10.3 billion in those ten years. Productivity lost to the work force from hepatitis C complications and death would equal another \$71.5 billion, the researchers, led by Dr John Wong, said.

Sustained Response to Treatment

In a study designed to assess durability of viral response to Rebetron Combination Therapy or Intron A in patients with chronic hepatitis C, results suggested that few patients who still have undetectable levels of HCV RNA* six months after completing treatment (sustained response) with either therapy will subsequently relapse. In this study, late relapse was less common following treatment with Rebetron Combination Therapy than with Intron A.

Study Suggests U.S. Rates of Hepatocellular Carcinoma May Increase

In a study of the health impact of HCV in Japan versus the United States as estimated by molecular evolutionary analysis, researchers noted that the incidence of HCV infection in Japan is approximately the same as in the United States, yet the incidence of HCV-related hepatocellular carcinoma is eight times greater in Japan. Researchers estimated that in Japan the divergence of genotype 1b infection, the most prevalent genotype in that country, started between 1943-1949. In the United States, the divergence of genotype 1a infection, the most prevalent genotype in the United States, started between 1966-1970. The incidence of hepatocellular carcinoma in Japan was observed to increase in 1975, approximately three decades after the spread of HCV infection there. Projecting from these dates, researchers estimated that the incidence of hepatocellular carcinoma in the United States may start to increase soon (three decades after 1966-1970).

Should Patients With Mild HCV Be Treated?

In a study to determine whether treatment with Rebetron Combination Therapy is justified in patients with mild chronic hepatitis C based on virologic response and improvement in quality of life, patients with mild disease responded equally as well to Rebetron Combination Therapy as patients with non-mild disease in terms of virology and quality-of-life burden. Investigators concluded that given the unpredictable natural history of chronic hepatitis C in individual patients, the combination therapy should be offered to informed patients regardless of disease activity.

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Hepatitis C (HCV) at the Central California Women's Facility (CCWF)

Judy Ricci

PJ was looking forward to her parole date in April, 2000. Looking forward to spending some quality time with her family. This was especially important, because PJ had AIDS and HCV, and not much time. Needless to say, she did not make it out of CCWF, and passed away over the Labor Day weekend.

If we are to believe "inmate rumor," when the autopsy was done, it was discovered that her abdominal cavity was filled with blood. I would venture to say that "inmate rumor" was right on the money.

PJ's death was not sudden, not unexpected. Any untrained eye could clearly see her dying a little more each day. I only wonder why the medical staff at CCWF could not (or would not) see!

For months prior to her death, there was a constant flow of blood from her nose. She was constantly sniffing (as if she had a cold) the blood back into her nose so that it would not run down her face. Her abdomen was swollen so that it appeared that she was in her second or third trimester of pregnancy. In the last days before her passing, PJ was so jaundiced that her eyes were the florescent yellow of a caution sign. She was obviously in liver failure, but was still being given handfuls of liver toxic HIV medications at the med window. She should have been pulled off of all medications and hospitalized until she could have (possibly) been stabilized. PJ's story, I know, is horrifying to hear. Trust that it was horrifying, heartbreaking and frustrating to see.

PJ's story, sadly, is not unique. There are two other women currently here that will soon be in her position, and are alas. . . receiving little, and in one case, NO care!

When a woman enters this institution, a routine battery of tests is run, including a hepatitis panel. This is how an inmate is cleared for food handling (or not).

Recently, many women (who have already been incarcerated for a period of years) are "finding out" about their HCV status. In a few cases, because they have started displaying symptoms that are severe enough to request medical attention, only to find that a positive HCV result was recorded in their medical files all along. Now they are cirrhotic and will never be considered for treatment here. You have to wonder, how much of this could have been avoided with early intervention?

The numbers are numbing - 69% of female inmates, 54% of male inmates, 63,500 inmates (estimated) statewide!

Who cares about a bunch of prisoners that are already safety locked away? Imagine 63,500 people unaware of the infection they carry, uneducated, untreated, being released to unsuspecting families and into communities. I wonder how many future infections could be avoided with an effective education/treatment program here?

I read somewhere that \$300,000 was allocated for HCV treatment in the California Department of Corrections this year. Enough to treat about 15 people for one year. I wonder, which 15?

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Week 24 Testing During Treatment Predicts Non-Response

In a study assessing the accuracy of testing serum HCV RNA levels at various time points during Rebetron Combination Therapy to predict eventual nonresponse or sustained response in chronic hepatitis C patients, testing at week 24 of therapy was shown to be most accurate and correctly identified 98 percent of nonresponders to combination therapy.

Does Ribavirin Have An Antiviral Effect?

In a study to determine whether ribavirin and its triphosphate metabolite (RTP) have any direct antiviral effect against HCV, RTP was shown to inhibit HCV polymerases derived from all HCV genotypes. Researchers concluded that in addition to its reported immunomodulatory effect, ribavirin also has a direct antiviral effect against HCV, possibly through its misincorporation into viral RNA products as a result of its inhibition of the HCV polymerase enzyme.

Source: Company Press Releases

The Hepatitis C Support Project offers information about various forms of intervention in order to serve our membership at large. By providing information about any form of medication, treatment, therapy or diet we are neither promoting nor recommending use, but simply offering information in the belief that the best decision is an educated one. Additionally, views expressed in the HCV Advocate do not necessarily reflect the views of the HCV Advocate or the Hepatitis C Support Project.

For more information about hepatitis C, please contact the following organizations:

- American Liver Foundation 800-223-0179 <http://www.liverfoundation.org/>
 - Hepatitis Foundation International 800-891-0707 <http://www.hepfi.org/>
 - Hep C Connection 800-522-4372 <http://www.hepc-connection.org>
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*Scholarships are available for \$6.00.

Lahey Clinic Surgeons Perform Unprecedented Operation; Liver and Kidney Transplanted Simultaneously from Two Living Donors

BURLINGTON, Mass., Nov. 23 /PRNewswire/ via NewsEdge Corporation—In an unprecedented 14-hour operation, doctors at the Lahey Clinic have transplanted simultaneously a kidney and a large portion of the liver from two living donors to save the life of a 45-year-old Plymouth man. The operation involved six surgeons, three operating rooms, and about 20 additional medical staff.

Albert Duarte will leave Lahey Clinic today with a new lease on life. “I feel a thousand percent better,” said Albert, as he prepared to leave. His two nieces, who each donated an organ, went home shortly after the operation and have resumed nearly all their normal activities. Karen Silvia, who donated 60 percent of her liver, is back working at a school for troubled children, and Roxanne Guisti-Lavoie, who gave one of her kidneys, is back with her four children and once again coaching track at a local high school.

Duarte had a rare liver disease that was destroying his kidneys. At the time of the operation his kidneys had failed and he was on dialysis six days a week. He needed the double transplant to save his life, and he did not have enough time to wait for a cadaver liver, which sometimes can take years. The liver is one of the few organs that can regenerate, and, at this time, the livers of both the donor and recipient are almost full size, according to doctors at Lahey Clinic.

Although adult-to-child liver transplants have been performed for a decade, adult-to-adult transplants have only been performed in the US for the past two years. Less than 100 procedures have been done nationwide. Lahey’s liver transplant team performed the first adult-to-adult living donor liver transplant in New England last December at Beth Israel Deaconess Hospital in Boston.

Liver surgeons who participated in the ground-breaking operation include Roger L. Jenkins, MD, and W. David Lewis, MD, co-directors of Lahey’s Liver Transplantation Team, Elizabeth A. Pomfret, MD, and James J. Pomposelli, MD. John A. Libertino, MD, and Michael J. Malone, MD, performed the kidney transplant. Fredric D. Gordon, MD, is director of hepatology at Lahey Clinic.

Although the only biological requirements for being a living liver donor are the individual’s size and blood type, potential donors are carefully screened. At Lahey Clinic, psychologists, ethicists and social workers, as well as surgeons and specialists, evaluate each potential donor.

“We want to make sure donors have freely offered to undergo the surgery, “ said Pomfret, who directs the Living Donor Transplantation Program.

Living donor programs developed as a result of a shortage of available organs for transplantation. Nationwide, almost 14,000 people are waiting for livers, and only 4500 will get them. In New England, more than a thousand wait for a new liver. Approximately, 25 percent of those patients will die while waiting for a liver.

SOURCE Lahey Clinic