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December 2000's Advocate:

HCV Treatment Reaches the Next Level Schering-Plough Reports Phase III Results at AASLD: 54% Sustained Response Rates for all Genotypes

By Alan Franciscus
Editor

The results of Phase III clinical trial with the combination of Peg-Intron and ribavirin were reported at the annual AASLD conference held in Dallas, Texas in October. This study showed that the combination of Peg-Intron (peginterferon alfa-2b) injection plus daily Rebetol (ribavirin) capsules achieved a overall 54% sustained virologic response (SVR) in previously untreated adult patients with chronic hepatitis C.

This study enrolled 1,530 patients worldwide and were randomized to three treatment arms:

1. Peg-Intron - 1.5 mcg/kg once weekly (QW) plus ribavirin capsules- 800 mg/daily for 48 weeks.
2. Peg-Intron -1.5 mcg/kg QW plus ribavirin - 1000-1200 mg/daily for four weeks followed by Peg-Intron .5 mcg/kg QW plus ribavirin 1000-1200 mg/daily for 44 weeks
3. Intron A - 3 MIU/three times weekly plus ribavirin 1000-1200 mg/daily for 48 weeks. (Current Rebetron therapy). The study participants were: 66% male; average age - 44 years old; average weight - 83 kg. Genotype - 1 - 68%; Genotype 2 and 3 - (29%); other genotypes - (3%). Pretreatment viral load >2 million copies-68%.

The most successful SVR was obtained from the first treatment arm (Peg - 1.5 mcg/kg plus ribavirin 800 mg/daily for 48 weeks) with an overall response rate of 54%. The SVR breakdown by genotype was genotype 1 - 42% SVR; genotype 2 & 3 - 82% SVR. This compares to SVR of 47% for the treatment arm 2 and 3. Additionally, when analyzed on a dose/body-weight basis that is tailored to weight (10.5 mg/kg of ribavirin daily plus Peg - 1.5 mcg/kg once weekly) an estimated 61% SVR would be achieved for all genotypes, 48% for genotype 1 and 88% for genotype 2 and 3.

The SVR from the second arm were similar to the current treatment with Rebetron (third arm).

The safety profile of both doses of Peg-Intron plus ribavirin were similar to Rebetron, with no new types of adverse events (side effects) observed. Discontinuation of therapy was 14% (trial arm - #1), 13% (trial arm #2) and 13% (trial arm #3). Dose modifications were 42%, 36% and 34% respectively.

"These results are especially encouraging given the increasing interest physicians in tailoring treatment doses to an individual patient's needs," said Michael P. Manns, M.D., professor and chairman, department of gastroenterology and hepatology, Hannover Medical School, Hannover, Germany. "We have learned from this study and previous studies with alpha interferon that, in addition to genotype, body weight is an important factor in determining optimal clinical outcome. These results demonstrate that the dosing flexibility provided by Peg-Intron plus Rebetol has the potential to take combination therapy to the next level of hepatitis C treatment," Manns said.

Source: company press release

December 2000's Advocate:

Healthwise: How the Hepatitis C Virus is Transmitted

By Lucinda K. Porter, RN

How is the hepatitis C virus (HCV) transmitted? This simple question should warrant an equally simple response. However, the answer is complicated because there is still more research to be accomplished to thoroughly understand this issue. Basically, HCV is a blood-borne pathogen. This means that the virus may be passed person-to-person when the blood of an HCV-infected person comes in contact with the blood of an uninfected person.

The most common route of HCV exposure is among individuals with a history of injection drug use. Shared drug paraphernalia (needles, syringes, drug, water, cotton, straw, etc) bring with it an unintended risk, i.e., shared blood that might contain HCV or other viruses such as hepatitis B virus or human immunodeficiency virus. The same is true for the risk of HCV transmission by blood transfusions prior to 1992. Dialysis, organ transplantation, and health care exposure account for smaller percentages of the overall risk factors.

Two common areas of concern regarding transmission center on infection via sexual contact and the spread from mother to child (via pregnancy, childbirth, and breastfeeding). Patients want to know if they can pass HCV on to their loved ones. The good news is that with minimal precautions, the chances of passing HCV sexually or perinatally are low. Unfortunately the risk is not zero which would make us all feel more comfortable. The purpose of this article is to help find a way to navigate through the statistics regarding sexual and perinatal transmission.

Sexual Transmission

In the July/August issue of the Hep C Connection newsletter, there was an excellent article by Dr. Gregory Dore, Lecturer in Epidemiology, Infectious Diseases Physician, National Centre in HIV Epidemiology and Clinical Research, University of New South Wales. (This was an abridged version originally published in the Australian Hepatitis Chronicle, Issue 4 March 2000:2-5.) Dr. Dore presented a very well reasoned argument stating his belief that the level of risk of HCV transmission via sexual contact is low to negligible. He bases his belief on the following:

1. There are flaws in recent Centers for Disease Control and Prevention (CDC) epidemiologic study. This study (Alter et al. New England Journal of Medicine, 341:556-62 1999) neglected to ask questions regarding history of injection drug use.
2. Injection and illicit drug use in the United States is highly stigmatized. In our country, people may be less willing to answer truthfully to direct questions about illegal drug use. Thus, reporting sexual history may become a more likely shared "risk" factor. All but one person in an Australian study of 467 people reported possible blood exposure (injection drug use, 85%; pre-1990 blood transfusion, 6%; blood exposures, 8%) (Sladden et al Medical Journal of Australia 166:290-293, 1997)
3. Sexual transmission may be possible, such as in the situations of trauma to membranes or during menstruation. However, semen and vaginal secretions contain little or no HCV. (Caldwell et al. Liver Transplant Surgery 2:124-9, 1996)
4. Review of longitudinal couples' studies offers encouraging data. These studies look at couples in which one member is HCV-positive and the other is negative. Two European studies found no cases of probable sexual transmission. (Meisel et al. Lancet 345:1209-11, 1995; Power et al. Lancet 344:1166-7, 1994) Other European studies support these findings.

The CDC recommendations regarding sexual transmission are as follows:

Persons with Monogamous Partners

"...a low prevalence of HCV infection has been reported by studies of long-term spouses of patients with chronic HCV infection who had no other risk factors for infection. Five of these studies have been conducted in the United States, involving 30-85 partners each, in which average prevalence of HCV infection was 1.5%...

HCV-positive persons with long-term steady partners do not need to change their sexual practices. Persons with HCV infection should discuss with their partner the need for counseling and testing. If the partner chooses to be tested and tests negative, the couple should be informed of available data regarding risk for HCV transmission by sexual activity to assist them in making decisions about precautions. If the partner tests positive, appropriate counseling and evaluation for the presence or development of liver disease should be provided."(ii)

Persons with a History of Multiple Sex partners or Sexually Transmitted Diseases (STDs)

Although persons with a history of multiple sex partners or treatment of STDs and who deny injecting drug use appear to have an increased risk for HCV infection, insufficient data exist to recommend routine testing based on these histories alone.

Dr. Dore's advice to patients is in alignment with the CDC's recommendations. He adds that sexual activity during menstruation warrants the use of barrier protection or abstinence from vaginal sex. Naturally, for those in multiple or non-monogamous relationships, the practice of safe sex is strongly advised.

Perinatal Transmission

The transmission of HCV from mother to unborn child (vertical transmission) is rare. The CDC states the transmission rate is around 5 to 6 %. (iii) Infants and children often resolve the infection.(iv) The CDC makes no recommendations regarding the mode of childbirth delivery.(v)

There seem to be no differences between infants who are breastfed and those who are bottle-fed.(vi) The CDC makes no specific precautions regarding breastfeeding. I advise practicing good nipple care when breastfeeding. There are many community resources that can advise new mothers about how to take good care of their breasts to avoid painful cracks in the skin. Self-care is important for all new mothers, not just those who want to practice extra precautions.

The possibility of sexual and perinatal transmission of HCV does exist, but with simple precautions these risks are very minimal. Reassurance, backed up by the facts, is the best approach.

This article can be found at: <http://www.hepc-connection.org> (This was an abridged version originally published in the Australian Hepatitis Chronicle, Issue 4 March 2000:2-5.)

ii Centers for Disease Control and Prevention. Recommendations & Reports MMWR 1998; 47: 7-9.

iii *ibid.*

iv Okamoto, H Blood Weekly, 9/29/97, p15

v Centers for Disease Control Recommendations and Reports MMWR October 16, 1998

vi *ibid.*

December 2000's Advocate:

Synopsis of Roche Pegasys Studies from the AASLD Combination Therapies with Pegasys - Data from 4 Weeks of Treatment

By Alan Franciscus
Editor

In a small study of 81 previously untreated HCV positive patients, results of Pegasys in combination with different medications was discussed. Please note the paper discussed data from only 4 weeks of treatment in a 48-week study.

This clinical trial was designed to establish the safety and effectiveness of Pegasys in combination with three different drugs -- ribavirin (antiviral), amantadine (antiviral), and CellCept (medication used for prevention of organ rejection for liver, heart and kidney transplants).

The study participants were on average 46 + 5.6 years old, male 50 (62%), average ALT 103 + 60.3 U/L, high viral load 53 (65%), low viral load 28 (35%), genotype 1 - 61 (75%), non-1 genotype 20 (25%).

The results are as follows:

Therapy	HCV RNA Negative After 4 Weeks
Interferon plus ribavirin	11%
Pegasys plus CellCept	17%
Pegasys plus amantadine	33%
Pegasys plus ribavirin, plus amantadine	18%

There were no unexpected side effects reported and no patients dropped out after 4 weeks.

While it is too early to predict sustained virologic response rates, it is interesting that the arm with Pegasys and amantadine reported the most favorable outcome even when compared to Pegasys plus ribavirin, plus amantadine.

Adrian M. Di Bisceglie, MD and others. AASLD, Abstract 1139

Improved Virologic Response Rates with Pegasys compared to Roferon-A (standard interferon) in Blacks

By Alan Franciscus
Editor

Current data suggests that HCV positive Blacks are less likely to respond to HCV antiviral therapy than Caucasians.

The goal of this study was to compare the effectiveness of Pegasys compared to Roferon (standard interferon) among Blacks.

The data from this presentation was compiled from a database of 1205 patients from randomized phase II and III international studies comparing treatment with Pegasys (40kDa) IFN a-2-a (180 µg) with Roferon (3MIU or 6 MIU - 3 times a week). Within this database there were 55 Blacks studied-- 50% males, 80% genotype 1 and 25% with cirrhosis or transition to cirrhosis. Twenty-seven patients received Pegasys and 28 received Roferon. The sustained virologic response (SVR) rate after 72 weeks of treatment was 15% for the group treated with Pegasys and 0% for the group treated with Roferon. In contrast, the Caucasian group reported 35% SVR for patients treated with Pegasys and 13% SVR for the group treated with Roferon. Histological improvements were similar in both groups treated -- Pegasys (31%), Roferon (28%).

This results from this study indicate that treatment with Pegasys increases the SVR for Blacks when compared to standard interferon.

Mitchell L. Shiffman, MD and others. AASLD, Abstract 753

Improving Liver Health with Antiviral Therapy

By Alan Franciscus
Editor

The current goal of HCV antiviral therapy (interferon or interferon/ribavirin) is elimination of the hepatitis C virus. If an individual is on antiviral treatment for 3 months and does not clear the virus, it is unlikely that they will achieve a sustained virologic response (SVR). At this point, many physicians will stop treatment due to the side effects and/or cost of therapy.

Now a growing body of evidence indicates that antiviral therapy can actually reverse scarring of the liver. This improvement in liver health can occur even if an individual does not clear HCV while on treatment with standard interferon or standard interferon and ribavirin. This is very good news for patients and challenges the current goal of therapy.

Now we have the addition of pegylated interferon and the combination of pegylated interferon/ribavirin that has the potential to increase both the virologic and histologic response. The following study compares the virologic and histologic response of pegylated interferon (Pegasys) versus standard interferon (Roferon).

Pegasys is Superior to Standard Interferon in Improving Liver Histology

This study reported on the relationship between virologic and histologic response following treatment with either Pegasys (180 µg) or INF a-2a (Roferon - standard interferon) 3 MIU, 3 times a week for 48 weeks. Four hundred and thirty patients were biopsied before and after treatment. Histologic response was defined as a 2 point improvement in the Histology Activity Index (HAI) score to baseline on a liver biopsy obtained 24 weeks following the completion of treatment, as judged by a blinded central pathologist.

Results reported:

	Pegasys	Roferon (standard interferon)
Overall response (all patients)	57%	41%
Patients with SVR	83%	79%
Patients without SVR	44%	36%

SVR = sustained virologic response

This trial also concluded that a virologic response predicted a histological response.

Jenny Heathcote, MD and Others. AASLD, Abstract 246

December 2000's Advocate:

HCV News Briefs Interleukin-11 Study - Treating Low Platelet Levels

A small study of 4 patients treated with Neumega (interleukin-11 platelet growth factor, FDA approved for chemotherapy patients at risk for thrombocytopenia) was presented at the AASLD that may provide help for HCV+ patients with low platelet levels (thrombocytopenia) prior to and while undergoing interferon and ribavirin antiviral therapy.

Interferon and ribavirin can cause a significant reduction in platelets. Platelets are large cells found in the bone marrow that help blood to clot by plugging injured blood vessels. Many patients cannot start or stay on HCV antiviral therapy if their platelet count is low.

In this study, 2 patients were treated with Neumega and were able to increase their platelet count to levels that permitted initiation of antiviral therapy. The two other patients were successfully treated with Neumega when thrombocytopenia developed as a result of treatment with interferon /ribavirin and were able to complete antiviral therapy.

The most notable side effect was fluid retention that ranged from mild to moderate, but reversed once treatment was stopped.

Further large scaled studies are needed.

Source: Medscape

Does Hep C Cause Diabetes?

According to a report published in the Annals of Internal Medicine, Johns Hopkins University reported the results of a study which found that people over forty who are infected with hepatitis C are 3 times more likely to have type 2 diabetes than people without hepatitis C. Diabetes is a disease that is marked by an inability of the body produce or process insulin. Type 2 diabetes is usually seen in individuals over 40 years of age and can be controlled with proper diet and/or medication. This study showed an association between type 2 diabetes and HCV, but does not prove that HCV causes diabetes. However, it has been suggested that type 2 diabetes may be caused by progressive liver damage.

Source: Annals of Internal Medicine - 2000 Volume 133 Number 8

Herb dose, price can vary widely with brand

While most brands of three popular mood-altering supplements--St. John's wort, Sam-e and kava kava--contain dosages of herbs that are close to those listed on the label, a report from the Consumer Union, publisher of Consumer Reports, found the prices of a daily dose can vary widely between brands, anywhere from 15 cents to \$1.20 a dose for St. John's wort, and \$1.80 to \$8.75 per dose for Sam-e.

Also the report found that there is no way of verifying if products such as chicken soup with echinacea and corn chips with kava kava-products known as functional foods-actually contain herbal ingredients in safe or effective amounts.

"The reasonable consumer should not expect these products to provide any benefit and should not assume that they are safe," said Ronald Buchheim, associate health editor for Consumer Reports.

Thirteen brands of St. John's wort, 12 brands of SAM-e, and 15 brands of kava were tested in the study.

The majority of products, which are touted to treat depression or anxiety, contained the amount of ingredients listed on the labels, according to the article in the December issue of Consumer Reports.

Some of the labels on SAM-e supplements were deemed vague and misleading. Four brands said that each pill contained 200 milligrams (mg) of the compound when they actually contained about 110 mg.

December 2000's Advocate:

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December 2000's Advocate:

Advocate Staff Notes Noted Canadian HCV Activist Joins Advocate Staff

Please join us in welcoming David Mazoff to the editorial staff of the HCV Advocate.

David was instrumental in helping us load up all the 1999 HCV Advocate to our website and other projects. His input and guidance has been invaluable over the last couple of months.

Here's David:

C.D. Mazoff, PhD, DipTh, Executive Director, HepCBC

David, the author of two books, and numerous essays, articles, and reviews, has taught at several universities, including Concordia, McGill, and University of Northern BC, where his interests were critical thinking and ethics. David (aka "squeaky") was also an active recreational triathlete and community volunteer. In 1994, David became quite ill, and was subsequently diagnosed with hepatitis C. He is now at Stage 2-3 fibrosis, and has suffered a few serious complications from treatment, including a minor stroke in one eye, and the development of inner ear disease and fibromyalgia. He is now on a disability pension. Since his diagnosis with HCV, David has been involved with HeCSC in Montreal and in Victoria, where he was Chair. David and his partner, Joan King, helped found HepCBC, of which he is now Executive Director. He designed the HepCBC website, established the HepCAN list, put the hepc.bull online, designed an effective database, and manages the computer network. David is also co-author of the HepCBC pamphlet series and designed the Bus Ad campaign.

He has been active in the community as an educator and fundraiser. Recently, David took over the FAQ project from Peppermint Patti and has updated it to version 4. It is available at www.hepcbc.org.

Volunteer of The Year: Joe Shaw

It is a real pleasure to announce that Joe Shaw was recently named the '2000 Volunteer of The Year.' Joe has been instrumental in our efforts to improve the HCV Advocate newsletter by (as Joe says) taking it to the next level. Even more impressive is his efforts along with Richie Lam in the design and maintenance of the HCV Advocate website. Please join us in recognizing Joe's many talents and his extraordinary efforts in our mission to help educate and inform the HCV community. Thanks Joe!