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# HCV Advocate

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## Pegasys Plus Ribavirin - An Analysis: Will this Combination become the Next Standard of Care?

By Alan Franciscus  
Editor-in-Chief

As I wrote in October 2001 for the HCV Advocate, every person affected by hepatitis C, including me, has been waiting for many years for the approval of the pegylated interferons in combination with ribavirin. There were four reasons promised for a long time suggesting that this new combination would be a major advance over the then standard of care, Rebetron (standard interferon alpha2b plus ribavirin). Patients and healthcare providers dealing with hepatitis C were hoping for increased sustained virologic response (SVR). SVR means HCV RNA negative at six months after treatment. Secondly, the pegylated interferon would show a further improvement in liver histology (the health of the liver) and a slowing of the progression to cirrhosis. Thirdly, the new therapy would be easier to tolerate and have fewer side effects, and finally, it would be more convenient and easier to administer.

When Peg Intron/Rebetol (pegylated interferon alfa 2b 1.5mcg plus ribavirin) was approved in 2001, I analyzed the package insert focusing on these four areas of hope for patients with hepatitis C. Now that Pegasys/Copegus (Roche's ribavirin) is approved, I will share with you a similar analysis of the Pegasys combination package insert that I have completed.

In regards to efficacy or effectiveness, the overall SVR for Pegasys 180µg plus Copegus 1000/1200mg in clinical trials ranged from 53% in the 801 trial published in September, 2002 in the NEJM, to 44% to 61% when compared to Rebetron in the 942 trial presented at EASL this year—which is the overall highest SVR ever reported in the treatment of hepatitis C. In pooled data from both trials, for patients with

high viral load and HCV genotype 1 the SVR was 43% for Pegasys/Copegus, and for those patients with low viral load and HCV genotype 1, the SVR for Pegasys/Copegus was 56%. (In the 801 trial the SVR for genotype 1 was 44% for Pegasys/Copegus versus 36% for Rebetron, and the SVR for genotype 2-6 was 70% versus 59%. The 942 trial did not have Rebetron as a comparator.) The Pegasys/Copegus package insert confirms what we already have long suspected, and that is that genotype, age, degree of fibrosis and weight are all host factors affecting the overall sustained virologic response in the treatment of hepatitis C. In pooled data of the two trials, treatment responses were lower in patients older than 40 years (50% vs. 66%), in patients with cirrhosis (47% vs. 59%), and in patients weighing over 85kg (49% vs. 60%). Unfortunately, these host factors dominate the treatment pool in the United States, hence adding to treatment challenges.

The next area I analyzed was whether there was a histological improvement from the Pegasys component of therapy. This is especially important for those patients who do not clear the virus, but at least could have an improvement in liver health. The Pegasys/Copegus package insert is the first pegylated interferon to be indicated in patients with both compensated liver

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# National Harm Reduction Conference:

## Focus on Hepatitis C

By Alan Franciscus

Editor-in-Chief

The National Harm Reduction Conference is one of the most important meetings concerning hepatitis C because it is the only national conference that focuses on the needs of drug users—the population at highest risk for acquiring HCV. This year's conference, held December 1–4, 2002 in Seattle, attracted over 1,000 attendees including community health outreach workers, needle exchange advocates, health-care providers, and others working to provide education, support, and services for many different communities. While the conference did not specifically focus on hepatitis C, there was plenty of information presented on this topic. Part one of this report will focus on the opening keynote address and a session on HCV in prison.

The keynote speaker was Dr. Joycelyn Elders, former Surgeon General during the Clinton administration. Dr. Elders talked about a variety of topics including harm reduction, HIV, HCV, needle exchange, overdose, and drug treatment. Dr. Elders spoke about her term as Surgeon General and commented that her only regret about being fired is that she was not able to get the ban on federal funds to support needle exchange programs lifted. In addition, she stated that legalization of drugs should be seriously studied because she views drug use and addiction as a public health issue, not a legal or criminal issue. Dr. Elders also commented on the huge rise in the prison population, an increase of between 200,000 and 300,000 since 1985 to the current estimate of two million. Sixty percent are in prison for non-violent drug-related crimes, and an effort should be made to establish drug treatment programs to effect positive change.

The keynote session ended with an inspiring message that moved the audience to a standing ovation: "Not to know is bad, not to want to know is worse, not to hope is unthinkable, but not to care is unforgivable."

### HCV in Prisons

A session on hepatitis C in prisons brought together people with different approaches and viewpoints on prisoners with HCV. It included information from activists and an overview of two testing and education programs within California prisons.

Judy Greenspan, from the HIV/HCV in Prison Committee of California Prison Focus, talked about her work within prisons and about the lack of testing, education, and support. Greenspan commented that very few prisons offer any type of HCV education, and noted that she frequently hears from prisoners who learn they are HCV positive only after demanding to see their medical records. Greenspan closed her presentation with a plea to the audience to become involved in these issues and to push for

education, free and confidential testing, and medical care for prisoners with hepatitis C.

Brenda Goldhammer, MPH, from the State of CA-STD/HIV Prevention Training presented information from a study that tested and interviewed 472 prisoners entering three California prisons. The focus of the program was to provide appropriate health education that would be integrated into other trainings that currently exist in prison settings. In addition, informal focus groups with recently released parolees and a needs assessment of community-based providers were conducted. Goldhammer concluded that a successful hepatitis training and skills-based model based on harm reduction principles had been developed, and that the preliminary analysis of the program indicated that prisoners improved their knowledge about hepatitis and their skills to help prevent transmission.

Sue Currie, Project Director of HEPCAP at the University of California, San Francisco, presented data from a recently completed study of the prevalence and independent correlates of HCV among prisoners entering California correctional institutions. The researchers interviewed 469 prisoners entering three California prisons and tested them for HCV. They found that 34% of this group tested positive for HCV antibodies. HCV was most highly associated with gender (38% female vs. 33% male), race (60% white, 53% Latino, 20% African American), and injection drug use (65% IDU vs. 10% non-IDU). The authors of this study concluded that there was a high prevalence of HCV among persons entering prison, the majority of whom were not aware of their infection status. Almost all HCV infections in this study were established rather than incident (new) infections; only one new infection occurred while in prison. The majority of hepatitis C in correctional institutions is attributable to injection drug use; tattooing, piercing, snorting drugs, and being cut or assaulted were not independently associated with HCV. Among those with no history of injection drug use, HCV infection was associated with a longer history of incarceration and a history of blood transfusion or receipt of blood products during surgery or organ transplantation. The authors recommended that HCV education should be provided to prison populations, including prevention education and information specifically targeting juveniles, first-time offenders, and first time drug offenders. Prevention programs should focus on risk reduction within prisons, and should also be targeted to the communities where prisoners will be released. A history of incarceration should be considered an indication for HCV screening, and screening and management of HCV may need to be addressed during incarceration.

*Part two* will focus on integrating viral hepatitis into existing harm reduction programs, designing clinical hepatitis programs, and more.

# What Did We Learn From AASLD ?

## Part 2

By Alan Franciscus  
Editor-in-Chief

Currently, the standard of care for the treatment of chronic hepatitis C infection in naïve (previously untreated) patients, as recommended by the 2002 NIH Consensus Statement on Hepatitis C developed last summer, is once-weekly pegylated interferon alfa either 2a (Pegasys – Roche) or 2b (Peg Intron – Schering Plough) in combination with daily ribavirin.

At AASLD 2002, Rosenberg et al (abstract #859) reported the results of a retrospective analysis looking at the pivotal pegylated interferon/RBV phase 3 trials in an endeavor to establish which pegylated interferon is better since to date there has not been a head to head controlled trial. Rosenberg and colleagues looked at the 2 large trials (Fried and Manns) which compared each of the pegylated interferons plus ribavirin with combination standard interferon plus ribavirin (Rebetron). The authors evaluated the results of the 2 trials in an attempt to determine if any differences between the efficacies of the products could be attributed to chance, confounding, or bias. They reported that the lower overall response rates seen with pegylated interferon alfa 2b may be secondary to the inclusion of a greater percentage of patients with hepatitis C virus genotype 1 infection, more severe fibrosis, and heavier weight. Therefore, until a better trial is designed to compare the efficacy of the two pegylated interferons a decision to utilize one pegylated interferon over the other should be based upon sub-genotype efficacy analysis if significant, ease of use, tolerability and cost.

Other interesting information presented on the pegylated interferons at AASLD 2002 included an abstract by Bruno (abstract # 159) which looked at hepatitis C virus dynamics during therapy with pegylated interferon alfa-2a, compared to pegylated interferon alfa-2b in naïve patients with hepatitis C. The authors conclude that “Although the trend in viral decay was similar between the groups in the first four weeks of treatment, pegylated interferon alfa-2a induced a more significant viral clearance when compared with pegylated interferon alfa-2b after 12 weeks of therapy. This finding may reflect a different drug exposure of the two drugs.” Another abstract by E. Formann and

others (abstract #502) studied twice weekly administration of pegylated interferon alfa 2b to see if it improves the viral kinetics in patients with hepatitis C genotype 1. The authors concluded: “To achieve continuous drug exposure and to improve initial viral clearance, Peg Intron must be given at least 2 times weekly.” These two abstracts were extremely interesting as they may shine some initial light on why Peg Intron/RBV is not anymore effective than Rebetron in patients with high viral load regardless of genotype. Maintaining constant antiviral pressure on the hepatitis C virus is crucial during therapy because of the short virion half-life (2.7 hours) and the estimated production and clearance rate of  $10^{12}$  virions/day. In the case of Peg Intron the pharmacokinetic parameters do not maintain this constant pressure on the virus as there is no drug left in the system by day 5-6 of the 7 day dosing regimen, and in many patients this is the case for the entire treatment duration.

At AASLD 2002 we also learned some treatment information by genotype. Hepatitis C viral genotype has consistently been shown to be the most important predictor of response to any form of combination interferon and ribavirin therapy. Firstly, regarding genotype 2 and 3. Pegylated interferon alfa 2a has already reported superior sustained response rates compared to standard interferon alfa and ribavirin after only a 24 week treatment course with a low (800mg) dose of ribavirin (EASL 2002). At AASLD 2002, Hinrichsen and colleagues (abstract #594) reported the sustained response rates of genotype 2 and 3 patients treated with standard interferon alfa plus ribavirin or pegylated interferon alfa-2b plus ribavirin 800 mg per day, for a total treatment course of 24 weeks. The sustained viral response rates for the standard treatment and pegylated interferon groups were 84% and 86%, respectively. It was therefore determined that Peg Intron in combination with low dose (800mg) ribavirin can also be given for a 24 week treatment course in genotype 2 or 3; however, it does not appear to be superior in efficacy to standard interferon alfa and ribavirin. The study authors concluded that for genotype 2 and 3 patients, pegylation of the interferon in the case of pegylated interferon alfa 2b does not affect treatment outcome or quality of life during the 24-week treatment period. Secondly, regarding treatment outcomes in genotype 4. Until AASLD 2002 there was minimal data on treatment efficacy in genotype 4

# Being an Effective Patient:

## Part 1 of a Three-Part Series on Health Self-Advocacy

By Lucinda K. Porter, RN, CCRC

When I was five years old, I had a high fever and sore throat. My mother did not drive and our family doctor did not think sick people should have to get out of bed to see him. This man made house calls throughout my childhood. These days, with the financial crisis in healthcare, it is considered fortunate to have ten minutes with our doctors. Given these time constraints, this article provides some suggestions on how to maximize the time with your care provider.

1. Be prepared. Take the time before your appointment to write down all of your medications, any pertinent allergies, a brief medical history, and your chief health complaints. It can also be helpful to include the names, addresses, and phone numbers of your primary care provider and any specialists who might be linked to your current medical issue.

2. Maintain your own health records – It can really help expedite matters if you bring copies of your most recent pertinent diagnostic test results.

3. Make eye contact before speaking to your physician. Once you begin speaking, your doctor may take notes. This does not mean s/he is not listening.

4. Prioritize your health issues and be brief but clear. Start with the most important details and, if there is time, you can add the less important information in at the end.

5. When describing your symptoms, begin with the general picture and end with the specifics. Example: My stomach hurts. I feel nauseous in the morning.

6. Ask for clarification. If your doctor uses words or explanations you do not understand, ask her to clarify or simplify her words.

7. Take notes – If the doctor makes suggestions, write them down. Ask him to spell any words you might want to refer to later, such as a diagnosis, medication or procedure.

8. Take a friend – This is especially important for appointments that may be long, complicated, or not routine. Ask your companion to take notes for you.

9. Express your reservations – If your doctor suggests a treatment plan that you have some concerns about, let her know. Sometimes these concerns can be easily addressed.

10. Ask if there are any alternatives – If your doctor makes a treatment suggestion and it is not one that you are prepared to follow, ask about the alternatives.

11. Keep an open mind – This can be your strongest ally. It is amazing how many people will not try a medication because of their fear of side effects, only to find out later that the reality was not anywhere near what they imagined.

12. Discuss the follow-up plan – If you are scheduled to have diagnostic tests, ask the doctor when you can expect the results and how these results will be conveyed to you. If the results are going to be disclosed at your next appointment and if there is going to be a long interval between appointments, ask how you can obtain earlier results. Additionally, ask the physician what the best way to contact his office is, should a need arise that may not require an office visit.

*Coming next month: Questions to ask your medical provider*

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# Sleep and Hepatitis C

By Ian Campsall, MA

“If hepatitis C makes me feel so tired, surely sleeping more would help, wouldn’t it?” How many persons with hepatitis C have asked themselves this question, and how many have come to the conclusion that no matter *how much* they sleep, they just can’t sleep enough—that sleep, itself, doesn’t seem to work?

There has been little if any research done on the question of the effects of hepatitis C on sleep, and, as a result, patients and doctors must grapple with the problem without the benefit of solid data. Sleep, itself, is not fully understood, and, while advances are being made in the diagnosis and treatment of hepatitis C, there is still much that remains to be discovered. The result, as with many issues and symptoms related to hepatitis C, is that patients are faced with a confusing and frustrating set of symptoms on which medical science can currently shed little light. However, it is possible to bring some greater measure of clarity to the subject by examining the facts concerning sleep, and by relating the experiences of persons with hepatitis C in that context.

Sleep is, quite simply, as fundamental to life as water, air, or food. In the first stage of sleep the muscles relax and the brain waves become irregular and rapid; in the second stage the brain waves grow in size and are accompanied by bursts of electrical activity. During the third and fourth stages, deep sleep, characterized by large slow waves, occurs.

Approximately an hour later dream state, or REM (rapid eye movement), sleep begins. Your eyes are in constant motion, and your brain waves are almost the same as when you are awake. REM sleep may comprise only 25% of the total hours we spend sleeping, but it is vital to feeling well-rested and alert.

When a disruption in a person’s sleep pattern or rhythm occurs, he or she may experience an inability to concentrate or focus, irritability or moodiness, loss of energy or fatigue, and a general decline in quality of life—symptoms surprisingly similar to those produced by hepatitis C itself. Sleep related problems have reached epidemic proportions in North America. A recent Gallup Poll found that one in two Americans suffers from sleeplessness or insomnia at some point in their lives, and, furthermore, that 30-40 million Americans are afflicted with serious sleep disorders.

For the person living with hepatitis C the situation is further complicated by the fact that they are already coping with an illness that has serious physical and psychological consequences, both of which have repercussions on a person’s ability to rest. The interrelated array of systems that regulate sleep are affected by the damage inflicted by hepatitis C to the body, and the trauma wreaked on the mind by the fear, frustration, and stress of having to cope with the disease. As one hepatitis C sufferer stated, “I can’t tell

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## AASLD

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which is most prevalent in the Middle East and Northern Africa. Two studies were presented during the conference that specifically examined the sustained viral response rates of this patient population when treated with combination pegylated interferon and ribavirin. Esmat and colleagues (abstract 803) reported on the use of combination pegylated interferon alfa-2b plus ribavirin in patients infected with HCV genotype 4. Preliminary data show a 76% on-treatment response rate at week 24 with combination pegylated interferon alfa-2b plus ribavirin. The 24-week on-treatment response rate with standard interferon alfa 2b plus ribavirin therapy is 59%. This study is an ongoing trial that offers encouraging results for the treatment of patients infected with HCV genotype 4. The second study by Diago and colleagues (abstract 804) reported a sustained viral response rate of 79% following a 48-week course of pegylated interferon alfa-2a plus ribavirin 1-1.2 g daily in genotype 4 patients. Based on the data presented in the above 2 studies, the perception that genotype 4 is a “difficult-to-treat” disease may need to be looked at more closely in the future since results, especially as seen in the second trial with pegylated interferon alfa-2a where the SVR rates look closer to that seen with genotype 2 and 3, appear better than expected.

African-American patients have lower response rates to antiviral therapy than do Caucasian patients. Recently, although the treatment numbers are low, African American patients have been shown to have better response rates to pegylated interferon plus ribavirin than to standard interferon plus ribavirin. It is the hope that the NIH trial called the Vira-HepC trial will shed a lot more light on hepatitis C and treatment in the African American community. The Vira-Hep C trial is utilizing pegylated interferon alfa-2a (Pegasys) in combination with ribavirin. At AASLD 2002, Dr. Lennox Jeffers presented an interim report on a comparative study of non-Hispanic black patients and non-Hispanic white patients with HCV genotype 1 infection treated with pegylated interferon alfa-2a plus ribavirin (abstract # 784). One hundred and six previously untreated patients with genotype 1 disease are enrolled in the study: 78 are non-Hispanic black and 28 are non-Hispanic white. To date, no unexpected side effects have been seen. At the

conference, the authors reported the 48-week end-of-treatment viral response data. End-of treatment viral response rates for non-Hispanic black patients and non-Hispanic white patients were 32% and 52%, respectively. Although the virologic response rate seen in black patients is lower than that seen in whites, these rates are higher than those reported in previously published trials with standard interferon in combination with ribavirin. We will anxiously await the sustained virologic rates that will be released in the future.

Well, what about patients who have relapsed from previous therapy? Herrine and colleagues (abstract # 781) reported on the use of various combinations of antiviral therapies for the treatment of relapse and breakthrough to standard interferon and ribavirin therapy. One hundred twenty-four patients were randomized to receive once-weekly pegylated interferon alfa-2a plus either daily ribavirin at a dose of 800-1000 mg, daily mycophenolate mofetil (Cellcept) at a dose of 1000 mg twice daily, daily amantadine at a dose of 100 mg twice daily, or a combination of daily ribavirin at a dose of 800-1000 mg plus amantadine at a dose of 100 mg twice daily. Eighty-three patients completed 48 weeks of therapy and 24 weeks of follow-up. Sustained viral response was 37.5% for the group treated with pegylated interferon alfa-2a plus ribavirin; 17.2% for the group treated with pegylated interferon alfa-2a plus mycophenolate mofetil; 9.7% for the group treated with pegylated interferon alfa-2a plus amantadine; and 45.2% for the group treated with the triple combination of pegylated interferon alfa-2a, ribavirin, and amantadine. No significant safety issues were noted in the treatment groups, although a significant number of dose reductions secondary to anemia were required in the ribavirin-treated arms, and all groups required significant numbers of dose reductions secondary to neutropenia. These results confirm again that amantadine as well as mycophenolate mofetil add no additional efficacy in the hepatitis C patient population. The study does, however, show promising results in relapse and breakthrough patients who are receiving pegylated interferon alfa-2a plus ribavirin. In a second abstract, Goncalves and colleagues (abstract #794) reported an interim analysis on the retreatment of patients who relapsed following an initial 24-week course of pegylated interferon alfa-2a plus ribavirin,

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if I am exhausted, or sick, or just sleep-deprived and crazy. [Sleeplessness] has interfered in an EXTREME manner with my ability to work. I do not remember the feeling of being totally rested, and energetic.”

People with hepatitis C suffer from the same sleep disorders as anyone else, but the combination of general stress and the mayhem caused throughout the body by the hepatitis virus seems to make the symptoms more erratic and disruptive. Reported symptoms include constantly having to get up to urinate, being unable to sleep for more than an hour, sudden violent awakenings without any apparent cause, feeling extremely hyper, and sleep terrors. Not surprisingly, many people also find that the pain caused by hepatitis C makes falling asleep difficult. One man found that his liver was so swollen that he was unable to sleep on his left side. However, the most common sleep symptom reported is not feeling rested or refreshed in the morning, but, rather, feeling even more exhausted than before going to bed.

Sleep apnea is one of the most common sleep disorders and affects nearly 10 million Americans. Persons who have this disorder experience a temporary stoppage of breath that may last up to ten seconds and causes the person to awaken briefly as he or she gasps for breath.

Many hepatitis C patients suffer from sleep apnea; however, as it is also related to age and weight, apnea is most likely more closely linked to peripheral symptoms of hepatitis C, such as weight gain, than the disease itself. A device known as a CPAP (continuous positive airway pressure) can be placed in the mouth before sleep to prevent the airway from closing and allow the patient to sleep normally.

Another disorder that many hepatitis C patients have to contend with is restless legs syndrome (RLS), which is characterized by an urge to move the legs in order to relieve uncomfortable sensations that are often described as a creeping or crawling, or tingling, cramping, burning or just pain. Some patients have no definite sensation other than the need to move their legs. RLS is an often reported incident on many of the hepatitis C internet chat and support groups, and has been in quite a few cases the symptom that led to the diagnosis of hepatitis C. Several studies have linked RLS with the neurological complications associated with hepatitis C virus infection, either directly or through hepatitis C related fibromyalgia, as

well as with nerve damage in the legs due to diabetes, kidney problems or alcoholism. RLS can also be the result of a pinched nerve root caused by arthritis in the lower back. Most cases of RLS respond well to medical treatment.

Other symptoms of RLS include: a need to move the legs to relieve the discomfort by stretching, bending, rubbing the legs, tossing and turning in bed, or getting up and pacing the floor. The discomfort increases when lying down, especially while trying to fall asleep or during other forms of inactivity, but is at its worst late in the day and at night.

Various drugs have been used successfully in the treatment of RLS: benzodiazepines, the L-Dopa family, and, in serious cases, opiates and methadone. However, as some of these drugs can be harmful to the liver, make sure that your doctor is aware of your medical condition when discussing possible forms of treatment.

The use of *melatonin* to relieve sleep disorders has become something of a recent fad, and has received a great deal of coverage and hype from the media, but scientists remain sceptical about its current status as a “wonder drug.” The exact nature of how melatonin affects how sleepy we feel is not yet clear, but it has been proven that it is effective in quickly relieving jet lag. However, as so little is known about its function in sleep, and as it has been linked to autoimmune hepatitis, melatonin remains a drug that should be monitored for further developments and studies.

Recently, however, scientists have shown that another natural substance, *jasmine*, is quite effective in inducing sleep. According to Reuters, “researchers found that when people slept in a jasmine-infused space, they moved less during the night. Although people slept the same amount each night, jasmine-smellers reported feeling less anxiety when they woke up.” The study also showed that lavender as well “appeared to help with sleep and later awareness . . . but its benefits were not as noticeable as those seen with jasmine.”

The most effective strategy for maximizing energy levels and minimizing sleep related problems is establishing a consistent sleep schedule. The importance of being consistent is evident in the fact that many people living with hepatitis C have reported that getting up so much as five minutes too early can leave them feeling fatigued for several days afterwards. That is not to say that you should be a prisoner of your schedule. Design your day to allow as much flexibility as possible, while still allowing time to rest,

## Pegasys

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disease and histological evidence of cirrhosis (Child-Pugh Class A). This addition of cirrhotics to the indication is due to the mono cirrhotic trial which enrolled patients with a histological diagnosis of cirrhosis (78%) or bridging fibrosis (22%) as well as the fact that the 942 combination trial had about 25% cirrhotics, which is considerably higher than the other pegylated phase III combination trials. The Pegasys/Copegus package insert states that there were similar reductions in inflammation across all treatment arms, and the fibrosis improvements listed in the mono Pegasys label were not recognized in the combination label for Pegasys/Copegus.

When I looked at the side effect profile of Pegasys/Copegus compared to that of Rebetron, I was pleasantly surprised. Across almost every type of annoying side effect having an impact on adherence, in clinical trials Pegasys/Copegus had a significantly lower percentage of side effects than Rebetron. The more common adverse events in the Pegasys/Copegus patients were myalgia: (muscle pain) - 40%, a 9% decrease compared to Rebetron; irritability/anxiety/nervousness - 33%, a 5% decrease compared to Rebetron; insomnia (inability to sleep) - 30%, a 7% decrease compared to Rebetron, and depression - 20%, an 8% decrease compared to Rebetron. It should be noted that side effect profiles in package inserts can be misleading because there is no severity scale which would record how often a patient experienced a side effect, or how severe it was. Keep in mind, though, that this theory would also hold for reported Rebetron side effects (as it was a head-to-head trial), so the difference in percentages from a trend perspective is accurate. Even with this in mind, the side effect profile of Pegasys/Copegus appears much easier to tolerate than that of Rebetron, and therefore is likely to have a positive impact on a patient's ability to stay on therapy or be compliant with therapy.

The last benefit that we had come to expect from the pegylated interferon combination was ease of use and convenient dosing. A benefit that patients will have from Pegasys/Copegus is that they will only have to administer the interferon once per week, versus three times per week for Rebetron.

Additionally there are other considerable benefits as it relates to ease of use and convenient dosing. Pegasys does not have to be weight based dosed as does Peg Intron so all patients get one dose, 180µg subcutaneously weekly. Pegasys also comes in a ready-to-use solution that needs to be refrigerated and there is no reconstitution; therefore the opportunity for patient error is very much reduced and the process obviously much simpler for the patient. Additionally, patients with genotype 2 and 3 only require a 24 week treatment duration and low dose ribavirin (800mg) when treated with Pegasys/Copegus.

The title of this article poses the question as to whether Pegasys/Copegus will become the next standard of care. For years the pegylated interferons have been hyped to be a major improvement over Rebetron for the four reasons I listed earlier—increased SVR, improved histology (liver health), improved tolerability and, lastly, convenience and ease of use. In prospective clinical trials Pegasys/Copegus, across all patient genotypes including cirrhotics, has demonstrated efficacy surpassing Rebetron especially in difficult to treat patient populations including genotype 1, high viral load and cirrhotics. Even though no fibrosis improvement data was listed in the combination package insert, Pegasys/Copegus is indicated in cirrhotics and has been widely studied in this population. Furthermore, the HALT-C trial should answer many of the remaining questions. Pegasys/Copegus has consistently demonstrated a tolerability profile better than that of Rebetron in both pivotal phase 3 trials, and lastly, what could be more convenient than a ready to use solution, once a week and one dose for all?

Based upon what is available today I believe that Pegasys/Copegus will become the next standard of care—but a word of caution. There are still many patients who are going to have to be patient and wait for the first non-interferon based drug to come to market for the treatment of hepatitis C. Keep in mind that the results presented in the pegylated interferon package inserts are based on naïve patients and there are many hepatitis C patients awaiting treatment, including me, who are either multiple relapsers or non-responders, and for whom the results will not nearly be as favorable as for the naïve patient.

## Sleep

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and make sure that you get to bed ON TIME. Be open and frank about the importance of being consistent with friends, family, and co-workers to avoid misunderstandings.

Furthermore, eat a nutritional diet including a variety of vegetables, fruit, and fibre-rich carbohydrates. Try to avoid animal proteins (especially those high in fat), and foods that are high in saturated fat and sugar. Maintain a regular exercise regimen, but do not exercise just before bed. Drink at least eight full glasses of water daily. Your doctor can recommend vitamins that you can take on a regular basis including multi-vitamins and minerals without iron, such as vitamin E (400-800 IU), selenium (100-200mcg), omega (fish) oil (1000mg). However, never take high doses of supplements. Tobacco, street drugs, and alcohol are all linked to many sleep disorders and should be avoided.

There is one final recommendation. Laugh. Research

conducted by William Fry, M.D., a professor emeritus in psychiatry at Stanford University Medical School, has demonstrated that laughter stimulates the immune system. Spend time doing things that you enjoy, and that give you pleasure. Remember, nothing will help you fall asleep faster than knowing that you have accomplished something with your day, and feeling that you are an active contributor to the community in which you live.

The following organizations offer support and advocacy services:

*The National Sleep Foundation*

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

*The Restless Legs Foundation* [www.rls.org](http://www.rls.org)

*The American Sleep Apnea Organization*

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

## AASLD

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with a 48-week course of pegylated interferon alfa-2a plus ribavirin. Sixty-four patients were enrolled in the study; 69% were genotype 1 and 31% were genotype non-1. The overall sustained viral response rate was 53% in all patients, and 49% and 64% in patients with genotype 1 and non-1, respectively. It is important to remember that the patients included in this study were all initial end-of-treatment responders to a previous course of therapy. Perhaps some of these relapse patients, especially the genotype 1 patients who require a 48-week course of therapy, had an inadequate initial course of treatment, which contributed their relapse.

Lastly, did we learn anything more about the role of maintenance interferon therapy in preventing advanced fibrosis and delaying hepatocellular carcinoma in hepatitis C patients who do not respond to treatment? In order to evaluate maintenance therapy in patients with cirrhosis with hepatitis C, the NIH is conducting an ongoing trial called Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C). Dr. Mitchell Shiffman presented an interim analysis of this study (abstract #527) at AASLD 2002. Eight hundred and sixty-three patients have been enrolled in the trial. The patient population is 73% male, 83% white, and 6% African-American, and 88% have genotype 1 disease. Mean patient age is 49 years. All patients were nonresponders to either interferon monotherapy or

combination standard interferon and ribavirin. All patients included in this study are initially treated with pegylated interferon alfa-2a plus ribavirin for 20 weeks. Patients who do not achieve viral clearance at 20 weeks are randomized into the HALT-C maintenance trial. The information presented was the results of 293 patients for whom sustained viral response data were available. 90% of these patients are HCV genotype 1 and 12% are African-American. Patients infected with HCV genotypes 2 and 3 had a sustained viral response rate of 52%; the sustained viral response rate of patients with genotype 1 disease was 14%. The sustained viral response rates in interferon monotherapy and combination therapy nonresponders were 30% and 11%, respectively. 64% of nonresponders had an initial HCV-RNA level > 1.5 million international units. Caucasian, African-American, and Hispanic patients achieved sustained viral response rates of 20%, 6%, and 17%, respectively. Dose reduction of pegylated interferon did not influence sustained viral response rates, however dose reduction of ribavirin had a significant adverse effect on sustained response rates. 16 of the 293 (5.5%) of patients required discontinuation of therapy for varying reasons.

**What Did We Learn About Hepatitis C From AASLD 2002? Part III will cover information presented at the conference on future therapies for hepatitis C**

## **Clinical Trials**

### ***National Trials***

**ROCHE - 866-GO-WINGS**  
**NIH - HALT-C (Cirrhosis)**  
800-411-1222

### ***Northern California***

**University of California, Davis**  
Dr. Rossaro (916) 734-8696  
**University of San Francisco Medical Center**  
Stephanie Straley, PA (415) 353-2328  
**VA Hospital-UCSF**  
(415) 750-2105  
**California Pacific Medical Center**  
(415) 600-1100 or (415) 600-1106  
**San Francisco General Hospital**  
Athiana (415) 206-3725  
**San Francisco**  
Dr. Cazen (415) 565-6288  
**Stanford University Hospital**  
Stanford Liver Research Clinic (650) 724-7057

**Quest Medical Research (HIV/HCV Coinfection)**  
Dr. Lalezari (415) 353-0800  
**East Bay Liver Clinic**  
Oakland, CA - Grant Young (510) 208-1777  
**Dr. John J. Jolley - San Rafael**  
Contact: Lynn Jolley  
(415) 257-3030

### ***Southern California***

**USC Hepatitis Research Clinic**  
Dr. Karen Lindsay, Susan Milstein, RN  
(323) 442-5550  
**UC Irvine Medical Center**  
Dr. John Hoefs, Barbara Walker, RN  
(714) 456-7821  
**VA Medical Center - Long Beach**  
Dr. Timothy Morgan, Julia Sanborn, RN  
(562) 494-5933  
**Santa Barbara/Ventura Counties**  
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