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Pegasys Granted Priority Review

By Liz Highleyman
Contributing Editor

On July 15, the U.S. Food and Drug Administration (FDA) put Pegasys—Hoffman-LaRoche's brand of pegylated interferon—in combination with ribavirin on its agenda for priority approval. The FDA is expected to review and make a decision about Pegasys in combination with ribavirin by the end of the year.

Pegylated interferon is a chemically altered version of standard interferon in which a polyethylene glycol molecule is added to extend the life of the drug within the body. This allows pegylated interferon to be injected once per week, instead of the three times per week recommended for standard interferon. Pegasys is a pegylated form of interferon-alpha 2a.

Schering-Plough's Peg-Intron—which has been on the market for a year and a half—is a pegylated version of interferon-alpha 2b.

Pegasys is a ready-to-use solution that is injected under the skin. In contrast, Peg-Intron comes as a powder that must be reconstituted before use. Pegasys has a standard dosage (Peg-Intron is dosed by weight). Roche is seeking approval for 12-month Pegasys combination treatment duration for genotype 1 and six-month treatment duration for genotypes 2 and 3.

Studies have shown that combination therapy with Pegasys plus ribavirin is more effective than treatment with standard interferon plus ribavirin, especially in patients with genotype 1 HCV, high viral load which is the majority of HCV patients in the U.S..

The recently revised National Institutes of Health draft consensus statement on management of hepatitis C recommends combination therapy with pegylated interferon plus ribavirin as the most effective treatment for chronic HCV.

At the European Association for the Study of the Liver conference in April 2002, researchers presented

much-anticipated data on Pegasys.

The Roche Global 942 Phase III study, which compared combination treatment with Pegasys to combination therapy with standard interferon, included over 1,200 participants. Using an intent-to-treat analysis, patients who received Pegasys obtained the highest sustained virological response rate (SVR, undetectable HCV viral load six months after the end of therapy) seen to date—61% overall. Breaking this down, SVR was achieved in 51% of those with genotype 1, 78% of those with non-1 genotypes, 50% of those with liver cirrhosis, and 65% of those without cirrhosis.

Side effects of Pegasys combination therapy in the two clinical trials cited in the application were less than seen with standard interferon combination therapy. In contrast, studies of Peg-Intron combination therapy demonstrated greater side effects than standard interferon combination therapy in Schering-Plough's pivotal trial.

The most common side effects of Pegasys include flu-like symptoms, fever, fatigue, headache, nausea, diarrhea, loss of appetite, partial hair loss, muscle and joint aches, and pain at the injection site. Potentially more serious adverse effects include low white blood cell counts due to bone marrow suppression—which can raise the risk of infections—and mental symptoms such as irritability and depression. Pegasys and Peg-Intron have not yet been directly compared in head-to-head trials. In clinical studies comparing pegylated interferon with standard interferon, combination therapy using Pegasys appears

See Pegasys on page 5

In This Issue:

- A Positive Approach.....page 2**
- HIV Co-Infection Report.....page 3**
- Quality of Life Part 3.....page 7**

The Wait -- A Positive Approach

By Lucinda K. Porter, RN, CCRC

One of the most enlightening opportunities is talking to others who have chronic hepatitis C virus infection (HCV). It is intriguing to hear how we integrate this diagnosis into our lives.

Recently I spoke to someone who was impatient about the unavailability and limitations of current treatment. Initially he was interested in treatment with Pegasys and ribavirin. Tired of waiting for this product to be available, he decided to try Peg-Intron. He was put on a waiting list for Peg-Intron and experienced a longer than expected delay before receiving his medication.

During the long wait, he expressed to me his frustration and told me he “felt like he was sitting around and doing nothing while the hepatitis C was eating away at his liver.” This is a powerful image.

I am sure others have felt helpless and discouraged by some aspect of living hepatitis C. It is quite understandable that this man would feel helpless and like he was “doing nothing.”

However, in the face of powerlessness, it may be essential to challenge the way one looks at a particular situation. This person assumed he was “doing nothing.” In fact, he was actually doing a great deal. Between maintaining a healthy diet and exercise regimen, he was plowing the way towards a favorable outcome. Now, when I use the term “favorable outcome,” I am not speaking about response to treatment. I am referring to a larger concept.

Hepatitis C is only one factor that can have a negative impact on one’s health. There are other conditions, such as heart disease and cancer that can confront us. We are whole entities, not separate organs. It can be emotionally consuming to think that hepatitis C is our major problem. This can cause us to neglect the rest of our needs. Whether you are waiting for better treatment options, the availability of a particular drug, or have decided not to undergo treatment, here are some suggestions to help optimize your health:

Try to maintain a healthy weight. Obesity can have a negative impact on the liver, heart, and overall health.

Reduce your intake of fat. In particular, avoid trans-fatty acids and saturated fats. Choose “heart-friendly” oils such as olive and canola. Foods that are high in omega-3 fatty acids are particularly good choices.

Increase your intake of fruits and vegetables. Vary the color of your produce. In other words, eat something green (such as broccoli, greens), orange (cantaloupe, carrot), red (such as tomato or red pepper), etc.

Keep moving. The word “exercise” is limited in its scope. It is recommended to include at least thirty minutes of daily activity such as walking, bicycling, gardening, dancing, swimming or tennis. Walking is my personal favorite because it is simple.

Maintain strong bones. Resistance exercises and sufficient calcium intake are cornerstones for this. Check with your doctor to evaluate if you are at risk for osteoporosis.

Avoid alcohol, smoking, and recreational drug use. We all know this. No lectures are necessary. If you can’t quit, get help.

Get sufficient sleep. The function of sleep is to restore our bodies. Insufficient sleep can negatively impact daily performance, immune function, and has been linked to traffic accidents.

Drink at least 8 glasses of water every day.

Finally, it is worth mentioning **visualization**. Although I do not have evidence-based research to support this claim, I believe what we think influences us. The patient who felt that “hepatitis C was eating away at his liver” was holding on to a very powerful image of self-destruction. I do not know what HCV was doing to his liver. However, it can’t be helping his health. Substituting an image of his immune system defending his liver may strike a more comfortable balance. If nothing else, it is an image that calms rather than provokes fear.

What do you say to yourself? Are you sending negative messages to your body, mind, and spirit? What can you do to take control of your life? Pick one goal you can start practicing today.

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HealthWise

Hepatitis & HIV Co-Infection Report

Updates from the International AIDS Conference in Barcelona

By Liz Highleyman
Contributing Editor

The 14th International AIDS Conference took place July 7-12, 2002, in Barcelona, Spain. The biannual conference is one of the premier forums for new research on HIV and AIDS. Several presentations at the conference dealt with HCV or HBV coinfection in people with HIV.

How HCV and HIV Interact

Mark Sulkowski and colleagues from Johns Hopkins University (abstract ThPeC7496) reported that in their cohort of nearly 900 HIV/HCV coinfecting people, those with both viruses were not more likely to experience accelerated HIV disease progression, develop AIDS-defining illnesses, or die from AIDS. Use of combination anti-HIV therapy (HAART) was safe in people with HCV coinfection, and HCV did not appear to reduce the effectiveness of HAART. The researchers concluded that HCV should not be seen as a barrier to HIV treatment.

Similarly, A. Barrasa and colleagues from Madrid (abstract WePeC6058) found that coinfection with HCV is not associated with faster progression to AIDS compared to HIV alone. However, J.A. Pineda and colleagues (abstract ThPeA7158) presented evidence suggesting that CD4 cell recovery after starting HAART may be slower in HIV/HCV coinfecting patients compared to those with HIV alone.

In related research, C.L. Thio of Johns Hopkins University and colleagues (abstract WePeB6016) found that the risk of developing AIDS or dying from AIDS-related causes also was not increased in people coinfecting with HBV and HIV, and that HBV coinfection does not reduce the likelihood of responding to HAART.

While HCV infection does not appear to accelerate AIDS progression, the reverse is not the case. A.H. Mohsen and colleagues from the University of London (abstract MoOrB1057) presented results confirming that HIV/HCV coinfecting people experience more rapid liver disease progression than those with HCV

alone. In this study the estimated time from HCV infection to the development of liver cirrhosis was about 20 years in the coinfecting patients compared with about 30 years in those with HCV alone. Accelerated fibrosis was especially apparent in those with a CD4 T-cell count below 250. Mohsen and colleagues concluded that HIV was significantly associated with faster fibrosis progression. C. Arizcorreta and colleagues from Cadiz, Spain (abstract WePeB6036) found that both higher HIV viral loads and lower CD4 cell counts were associated with worse liver damage.

Treatment of Coinfecting Patients

Christian Perronne and colleagues from Paris (abstract LbOr16) reported results from a study of pegylated interferon in HIV/HCV coinfecting people. Combination therapy with Peg-Intron (Schering-Plough's brand of pegylated interferon-alpha 2b) plus ribavirin was compared to standard interferon plus ribavirin. Thirty-seven percent (53 out of 143) in the Peg-Intron arm had a virologic response after 48 weeks of therapy and 34 discontinued treatment. In the standard interferon arm, 24% (37 out of 152) had a response and 34 also stopped therapy. Among those taking Peg-Intron, 25% of those with genotype 1 and 45% with genotypes 2 or 3 had an end-of-treatment response. The researchers concluded that combination therapy with Peg-Intron is better than combination treatment with standard interferon. However, the response rates in this study were lower than those typically seen in trials of people with HCV alone. This may be due in part to the high rate of treatment dropout in this study—considerably higher than in similar trials in patients with HCV alone. The data suggests that people with HIV/HCV coinfection may not tolerate HCV treatment as well as those with HCV alone, and may require increased monitoring, support, and adjunct therapy.

Rafael Esteban and colleagues from Barcelona (abstract LbPeB9022) also presented data comparing Peg-Intron plus ribavirin to standard interferon plus ribavirin in HIV/HCV coinfecting patients. Sustained virological response rates were higher in patients in the Peg-Intron arm (42%) compared to

See Co-Infection on page 4

Co-Infection

Continued from page 3

those receiving standard interferon (33%). Among patients with HCV genotypes 1 or 4, the respective response rates were 31% and 13%. In this trial also adverse effects were common, mostly mild to moderate. The researchers reported several cases of hyperlactatemia. (Hyperlactatemia, or lactic acidosis, is a rare but serious complication of nucleoside analog therapy related to mitochondrial toxicity).

D.M. Smith from the University of California at San Diego and colleagues (abstract MoOrB1059) also reported on symptomatic hyperlactatemia in participants in the Apricot Study, which is looking at treatment with Pegasys (Roche's brand of pegylated interferon-alpha 2a) or standard interferon plus ribavirin. Out of more than 750 patients, eight developed hyperlactatemia. Most of these had been on stable anti-HIV therapy including (Zerit) or ddI (Videx), and developed the condition when HCV therapy including ribavirin was added. Although rates of symptomatic hyperlactatemia in this study were not significantly higher than rates seen in people taking d4T or ddI without concurrent HCV therapy, there remains a concern that ribavirin could heighten the risk of mitochondrial toxicity.

Adverse side effects of HAART are of increasing concern to people with HIV and their caregivers. One of the most worrisome is high blood fat levels, which are known to lead to heart disease. J.T. Stapleton and colleagues from the Veteran's Administration Medical Center in Iowa (abstracts ThPeC7517, ThPeC7519) found that HIV/HCV

coinfected people taking HAART were significantly less likely to have high cholesterol levels than those with HIV alone. The researchers also presented laboratory data (abstract WePeB6041) suggesting that the difference may be due to the way HCV binds to lipoproteins.

Tenofovir for HBV

Several researchers reported on the safety and effectiveness of tenofovir (Viread), a drug used to treat both HIV and hepatitis B. D. Cooper and colleagues (abstract WePeB6015) added tenofovir or placebo to the existing HBV and HIV treatment regimens of HBV/HIV coinfecting patients. At 48 wks, HBV viral load decreased by 10,000-fold and was sustained for 48 weeks; no decrease in HBV viral load was seen in the placebo group. HBV viral load decreases were similar with both wild-type and lamivudine-resistant HBV. Marina Nunez and colleagues from Madrid, Spain (LbPeB9015) also reported decreases in HBV viral load with tenofovir in HBV/HIV coinfecting patients who were failing or only partially responding to lamivudine therapy. These researchers reported that the drug is generally well tolerated and does not appear to promote the development of resistance.

Transmission and Prevention

Two studies shed light on mother-to-child (vertical or perinatal) transmission of HCV. B.L. Pappalardo of the Blood Centers of the Pacific in San Francisco (abstract ThPeC7503) conducted a meta-analysis of several studies of vertical transmission in HIV/HCV

See Co-Infection on page 5

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Co-Infection

Continued from page 4

coinfecting mothers and those with HCV alone. He found an overall perinatal HCV transmission rate of 3.48% for HIV/HCV coinfecting mothers—higher than the rates found in several studies of women with HCV alone. Rates of vertical HCV transmission were higher in women with detectable HCV viral load. E. Mariné Barjoan and colleagues (WeOrC1379) also reported on vertical transmission. In her study of 283 HCV infected women in France—27% of whom were coinfecting with HIV—seven cases of vertical transmission occurred. Six HCV transmissions were from HIV/HCV coinfecting women (four were Cesarean births) and one was from a woman with HCV alone. The researchers concluded that HIV infection appears to be the main risk factor for vertical HCV transmission and that Cesarean delivery does not prevent transmission.

In terms of sexual transmission, S. Garcia and colleagues (abstract ThPeC7491) followed a cohort of 165 sexually transmitted disease clinic clients (147 women and 18 men) who started out with neither HIV nor HCV, but whose steady sexual partners had both viruses. During the follow-up period the researchers recorded over 5,200 instances of unprotected vaginal or anal intercourse and over 22,000 acts of unprotected oral sex. One woman contracted HIV, but none contracted HCV. In addition, A.

Neaigus and colleagues (abstract MoPeC3528) looked at transmission of HIV, HCV, and HBV among a network of non-injecting drug users. The researchers found that contracting HIV and HBV were associated with unprotected sex, but that contracting HCV was only associated with starting to inject drugs. Both studies confirm previous research showing that sexual transmission of HCV is rare.

Pegasys

Continued from page 1

to have an overall effectiveness similar to that of combination therapy using Peg-Intron in terms of achieving a sustained virologic response. However, studies of Pegasys have shown more effectiveness in treating people with genotype 1, including those with a high viral load and patients with cirrhosis—the most difficult patients to treat. There also is evidence that Pegasys may be more easily tolerated and have fewer side effects than Peg-Intron. While it remains to be seen which version of pegylated interferon is better, patients surely will benefit from having another treatment option available once the FDA approves Pegasys.

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Hepatitis C and Injection Drug Users – Part Two

By Alan Franciscus
Editor-in-Chief

Interferon alpha 2b coupled with ribavirin has become the standard of treatment for naïve non-addicted patients with hepatitis C. For patients who are currently injecting drugs or drink excessive amounts of alcohol, HCV treatment with interferon alpha and ribavirin is still not recommended either by the 1999 EASL International Consensus Conference on Hepatitis C or the 1997 National Institutes of Health Consensus Development Panel on the grounds that the compliance of IDUs is poor and the risk of reinfection is high if they continue to do drugs. However, the recent preliminary draft of the 2002 NIH Consensus Statement on Management of Hepatitis C has revisited treatment guidelines and opens the door to treatment consideration for many special populations, including active injection drug users. Please see last month's issue.

To date, there have been very few studies looking at treatment of this patient population, but hopefully the new consensus statement will provide opportunities to further expand our understanding of treating active IDUs. Even though there have been limited data on treating active injection drug users, there have been some small studies that have looked at treatment among people who have reinitiated injection drug use during HCV treatment.

These small studies can provide us with some insight from which we can draw a few conclusions. A study published in the HCV Advocate Medical Writers' Circle, May 2002, titled "Treatment of HCV in the Methadone Patient" by Dr. Diana Sylvestre of the Organization to Achieve Solutions In Substance-Abuse (O.A.S.I.S.), showed a trend towards positive treatment outcomes. The sustained virological response (SVR) for methadone patients treated with Rebetron (interferon and ribavirin) depended on the participant's sobriety prior to treatment and the amount of alcohol and drugs used during treatment. To date, there have been 59 methadone patients who have completed the study. The overall SVR for all participants was 28%, which is moderately lower than the results from larger

clinical trials in the non-using population. When the data were analyzed further, participants who achieved sobriety prior to initiation of therapy (even if that period was somewhat short) achieved similar SVR to non-drug users, whereas someone who was not clean and sober prior to treatment attained an SVR of only 17%. If we look at behaviors further, participants who used drugs intermittently during treatment and whose relapses were aggressively managed, achieved an SVR similar to non-users. None of the patients who used drugs regularly (on a daily basis) during treatment achieved an SVR. From this data it is clear that it is very important for sobriety issues to be addressed prior to treatment and that signs of relapse be aggressively managed so that patients can be maintained on therapy and achieve optimum results. A crucial part of a successful outcome in this study population was the availability of medical and social/behavioral support. The conclusion was that intervention before a patient relapsed to regular drug use helped to keep people in therapy which led to more successful treatment outcomes.

Backmund, et al studied 50 patients who were treated with interferon or interferon and ribavirin while undergoing detoxification. Treatment response was 36% at 24 weeks post treatment, and the authors concluded that there was no significant difference whether or not the patients who continued to be treated with HCV medications had started using again during therapy. Hopefully, some prospective studies on active injection drug users will be conducted as a result of the new consensus guidelines that will finally shed some light on this complicated issue. Even if the issue of treatment can be definitively answered, it is obvious that better HCV prevention strategies need to be taught to injection drug users.

The following guidelines have been recommended: IDUs should be advised of the risks of sharing needles or works and discouraged from doing so. Any paraphernalia used to heat up or prepare drugs can be contaminated with infected blood. IDUs should be advised to use new needles/works every time. Spoons and other injecting paraphernalia should be bleached and washed thoroughly with

See IDUs on page 7

Part III: The Impact of Treatment on HRQOL in Hepatitis C

By Alan Franciscus
Editor-in-Chief

The impact of hepatitis C on quality of life plays an important role in the evaluation of patients with hepatitis C and whether or not each patient should pursue treatment. Many practitioners are under the misconception that patients with hepatitis C are largely asymptomatic (do not have any symptoms as a result of their disease), and therefore their disease rarely impacts their quality of life. As discussed in Part II this is truly a misconception as hepatitis C itself does negatively affect a patient's quality of life both from the clinical manifestations of the disease as well as the social impact of being diagnosed, infectious and having a highly stigmatized disease.

Additionally, it is widely known that hepatitis C therapy significantly impacts quality of life which can be debilitating for some patients but what effect does treatment have on overall quality of life? As previously discussed, until recently, quality of life instruments were not endorsed for routine use in patients with chronic hepatitis C. Several instruments, such as the hepatitis quality of life questionnaire (HQLQ) and the short-form 36 (SF-36) have now been corroborated for use in this setting and specifically for hepatitis C. As

IDUs

Continued from page 6

dishwasher detergent and hot water.

Users should not share cocaine straws for snorting the drug because this could also pose a potential risk. IDUs should be advised to avoid anyone else's blood and thoroughly wash their hands before and after any contact. IDUs should be informed of the dangers posed by using lemon juice to dissolve heroin. The lemon juice may not be sterile and at the very least, the individual may get fungal infections. Vitamin C or citric acid powder are a preferred alternative. New filters should be used each time the individual intends to take drugs. Old or used filters can have traces of dirt or old blood on them. Individuals should be told to dispose of used equipment in a sharps bin or, if this is not possible, then they should put all of their paraphernalia in a sealed container (e.g., a jar or a bottle) before disposing of it.

a reminder, the SF-36 is a simple questionnaire that includes 36 questions that evaluate 8 domains of general well-being. Higher SF-36 scores represent better quality of life.

The early treatment protocols for HCV-infected patients focused on such variables as normalization of ALT, loss of HCV RNA from serum, and histological improvement and never even looked at the impact that treatment of hepatitis C might have on a patient's quality of life. However, more recent clinical trials are now including assessments of HRQOL.

The first such study that looked at measurements of quality of life was by Davis et al using a Sickness Impact Profile questionnaire to measure changes in HRQOL in patients treated with alpha interferon as therapy for hepatitis C. The authors of this study found an improvement in HRQOL in the interferon treated patients compared with untreated patients. What was interesting from this study is that similar improvements in HRQOL were observed in responders and non-responders to interferon therapy, suggesting that interferon treatment alone improved HRQOL in patients with hepatitis C. Next Foster and colleagues assessed the quality of life in non-cirrhotic patients prior to starting interferon treatment. In all 8 domains of the SF-36 short form, hepatitis C patients reported a significantly lower quality of life than did the controls. Additionally of interest is that the subgroup of patients with hepatitis C who had used intravenous drugs in the past showed the greatest impairment in their quality of life scores. The amount of inflammation on liver biopsy was not found to be associated with the magnitude of impairment of quality of life.

However, different results with respect to changes in HRQOL were obtained by Bonkovsky et al in a trial of interferon monotherapy in 642 hepatitis C infected patients. The study found that treated patients who were sustained virological responders had improvements in HRQOL (experienced significant improvements in perceived wellness and functional status) which exceeded those observed in relapsers and non-responders to treatment in the majority of HRQOL scales tested. The study also regrettably found that

See HRQOL on page 8

HRQOL

Continued from page 7

HRQOL scores even in sustained virological responders did not completely normalize even with the hepatitis C virus eradicated. These results led the authors to suggest that a sustained response to interferon treatment (i.e. loss of virus from blood) leads to an improvement in HRQOL over baseline. Since the study protocol ended at the six-month post-interferon treatment period it is not known whether this improvement in HRQOL is persistent beyond this period. Anecdotally, some patients report that it can take longer to fully recover from HCV therapy. The results of the Bonkovsky et al study were very exciting to patients and practitioners because it appeared that not only could interferon treatment successfully clear the hepatitis C virus but could also potentially improve a patients' HRQOL. There is however a factor in the design of this trial that has the potential to dilute the results. Treated patients were not blinded with respect to their ALT values (this means that each patient was aware what their ALT level was while enrolled in the trial). At the time this study was performed, patients and physicians were well aware that if an individual's ALT did not normalize on treatment, or became abnormal after treatment, then these patients were unlikely to be sustained responders to treatment. Therefore, awareness of an individual's ALT results would be expected to directly affect their perceived health status and therefore their quality of life measurements.

Ware and colleagues used the quality of life measurements to evaluate changes in quality of life in IFN monotherapy relapse patients treated with combination IFN and ribavirin therapy. A sustained virologic response was associated with improvements in vitality, social functioning, and health distress. It should be noted that the improvements in quality of life that all these investigators found in these studies with interferon are post-treatment (a comparison of how a patient perceived their quality of life prior to the treatment versus 6 months post treatment).

Antiviral therapies are associated however with deterioration in a patient's quality of life during therapy. This deterioration returns to baseline when therapy is ceased. Medication side effects are one of

the most difficult aspects of the treatment of people with hepatitis C. Hepatitis C treatments, especially interferon, are notorious for their adverse effects, including fatigue, myalgia (tenderness or muscle pain), flu-like symptoms, depression and other psychological changes. These adverse effects negatively impact the patient's overall sense of well-being and quality of life. Treatment side effects are an important factor in the patient's decision to start, continue and adhere to therapy.

Patients and medical providers have hoped that the development of pegylated interferons would cause less deterioration in a patient's quality of life during treatment for a few factors. Firstly with pegylated interferons the patient only has to inject themselves once a week versus three times with standard interferon. In addition because the drug levels are more consistent in the body with pegylated interferon, the side effects associated with each dose theoretically should be lower. These factors potentially could contribute to less of a decline in quality of life while on treatment as well as have a positive effect on adherence to therapy.

The impact of pegylated interferon therapy on quality of life was reviewed by Drs. Bernstein, Perrillo and colleagues and published recently in *Hepatology*. In this study the objectives were to evaluate the effect of SVR on quality of life in patients with HCV and determine whether impairment of quality of life during treatment contributes to early treatment discontinuation. The authors of the study used a pooled secondary analysis of 1,441 patients from across 3 international, multicenter, open-label, randomized studies that compared Pegasys (peginterferon alfa-2a) with interferon alfa-2a. Quality of life was evaluated using the SF-36 Health Survey and the Fatigue Severity Scale (FSS), both of which were completed by patients at baseline and at weeks 2, 12, 24, 48, and 72. During treatment, patients receiving Pegasys had better scores on 7 of 8 SF-36 domains regarding quality of life, both SF-36 summary scores, and had less fatigue as measured by the FSS assessments. Baseline to 24-week changes in fatigue and mental and physical compromise significantly predicted treatment discon-

See HRQOL on page 9

HRQOL

Continued from page 8

tinuation. Therapy was discontinued in 141 patients (10%) before 24 weeks of therapy, and worsening fatigue scores and declines in SF-36 mental and physical component summary scores were found to be significant predictors of treatment discontinuation. The authors found that SVR was associated with marked improvements from baseline to end of follow-up in all subjects, including patients with cirrhosis. The authors conclude, "Sustained virologic response is associated with improvements in disabling fatigue and patient functioning and well-being in patients with chronic HCV with and without evidence of cirrhosis as measured by both the SF-36 and FSS scales...Maintaining an acceptable quality of life on therapy is vital to patient compliance and acceptance of these therapies. Minimizing the adverse impact of therapy on quality of life should help lessen the degree of early treatment discontinuation".

"Peginterferons seem to offer an advantage over standard therapies in maintaining an acceptable quality of life. Quality of life issues should be considered in conjunction with safety and efficacy concerns in choosing optimal therapy for the treatment of patients with chronic HCV."

Furthermore, Rasenack reported, that in a 72-week multinational trial with patients (n=264) randomized to either Pegasys 180 mg weekly or IFN a-2a 6 MIU tiw for 12 weeks followed by 3 MIU tiw for 36 weeks, quality of life and fatigue were studied by the standardized 36-question short form health survey (SF-36) as well as a fatigue severity scale (FSS). At weeks 2 and 12 of therapy patients in the Pegasys group had statistically better QOL scores. Pegasys was associated with less profound fatigue as measured by FSS scores relative to their standard IFN counterparts (P<0.05) indicating that Pegasys therapy is better tolerated than currently available interferon therapy.

Additionally, quality of life (QoL) treatment benefits were assessed in a multinational trial headed by T.I. Hassanein from San Diego, California, that compared the effects of pegylated interferon alfa-2a (Pegasys) plus ribavirin versus standard interferon alfa-2a plus ribavirin treated for 48 weeks and followed for an additional 24 weeks. QoL was assessed using the SF-36 and Fatigue Severity Scale. For both

groups, QoL scores declined from baseline to week 2, declined further by week 12, then remained stable through week 48. QoL was better for the pegylated interferon alfa-2a plus ribavirin on almost all scores throughout the study, several of the differences reaching statistical significance, such as for bodily pain, vitality and social functioning. The patients in the pegylated (40 kD) interferon alfa-2a plus ribavirin group also complained of less pain and fatigue interfering with activities such as work.

Lastly, pegylated interferon alpha 2b (PEG-Intron) plus fixed or weight based dosing of ribavirin compared to standard combination therapy Rebetrone (Intron A plus ribavirin) has been shown to increase survival time and improve quality of life for the initial treatment of chronic hepatitis C, according to study results presented by Dr. U. Siebert. Furthermore, when compared to standard combination therapy, PEG-Intron plus fixed or weight-based dosing of ribavirin was shown to increase life expectancy by 0.5 and by 1.0 years.

In summary, treating hepatitis C with interferon therapy has consistently demonstrated that it can improve a patient's HRQOL especially if treatment results in eradicating the virus. Pegylated interferons offer additional hope since studies have demonstrated that while on treatment a patient's quality of life is less significantly impacted than with standard therapy. Additionally, poor adherence and discontinuation to therapy are substantially less with pegylated interferon which ultimately leads to a higher likelihood of a sustained virological response, which ultimately improves a patient's overall quality of life.

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