

AASLD Conference Highlights: *Part 2*



Alan Franciscus, Editor-in-Chief

Part two of this report will focus on the projected future HCV-related public health burden, as well as on some promising new HCV therapies.

In the United States, hepatitis C is estimated to be four times more common than HIV. Prior to highly active antiretroviral therapy (HAART) deaths from HIV exceeded those from liver disease. Now HIV related deaths have declined significantly but HCV remains largely undiagnosed in the vast majority of people infected with HCV. Estimating the future burden of these two diseases will help health care policy makers plan for future needs.

Sylvie Deuffic-Burban and colleagues compared the future public health burden of HIV and hepatitis C in the United States. In this study, a complex backcalculation method was developed and incorporated medical treatment (prior to pegylated/ribavirin therapy) into these estimates.

These models were based on US epidemiological data (CDC, WHO) on prevalence, incidence of infection, age and gender of incident cases, AIDS, deaths related to liver disease and general population mortality. Models were developed separately for HIV and hepatitis C. After this model was established, the authors projected future HIV and HCV related

deaths until 2070.

The authors estimated that the HCV epidemic peaked in 1984 at 149,000-224,000 new infections and then fell to about 33,000-46,000 in 1998. HIV incidence reached its maximum in 1989 at 132,000-162,000 new infections and then declined to 38,000-49,000 in 1995 before rising again.

The model forecasts that deaths related to HCV (liver failure or liver cancer) will rise from about 3,800 – 4,200 in 1998 to peak at 14,000-19,000 in 2030. This compares with HIV related deaths of 16,000 in 1998 and projected at 4,200-6,700 in 2030.

The authors concluded that due to the availability of effective HAART for HIV infection, deaths from HIV appear to have declined substantially. The stability of that decline will depend on epidemiological trends and the rate of development of HAART resistance. Their projection model is consistent with other models that suggest HCV related deaths and the public health burden of HCV will rise over the next 10-30 years.

HCV medical treatment can effectively eradicate the virus in up to 50% of people treated with current medications. However, as deaths related to HCV continue to rise, it is even more important that new therapies are developed.

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INVESTIGATIONAL DRUGS

Schering-Plough released data from a report on a novel protease inhibitor that showed promise as a new drug candidate. SCH6 was shown to inhibit HCV replication and expression in vitro.

In another report released, two new molecules showing HCV inhibition (BC2125 and BC2329) were identified by S. Dagan and colleagues. The authors concluded from the results that BC2125 and BC2329 are potential oral drug candidates for treating hepatitis C.

Vertex released pre-clinical data on a newly discovered HCV protease inhibitor VX-950. Three separate posters were presented that discussed the potential for VX-950. Ann Kwond, Ph.D., reported on one experiment in which treatment with VX-950 for nine days reduced HCV RNA by almost 10,000 fold (4 log10). In another experiment, HCV replicon cells treated with VX-950 for 13 days exhibited viral clearance at day thirteen, and no rebound of HCV viral load was observed at day twenty-seven. In addition, there was data pre-

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HealthWise:

■■■
Lucinda K. Porter, RN, CCRC

“Sometimes a wound is the place where we encounter life for the first time, where we come to know its powers and its ways. Wounded, we may find a wisdom that will enable us to live better than any knowledge, and glimpse a view of ourselves and of life that is both true and unexpected.” – Author unknown

This has been an especially memorable year for me. Working with patients infected with chronic hepatitis C virus (HCV) is a rich experience. The patients I encounter are unusually brave. I say brave, not fearless. Courage is when we carry on in spite of the fear in our hearts. I witnessed patients coping with the trials and tribulations of antiviral therapy, organ transplantation, pain and death. Some tears were shed, but they were outweighed by laughter.

This year among the HCV patients I worked with, I saw more sustained responders to peginterferon/ribavirin therapy than in any previous year. It is wonderful when patients learn that they no longer have detectable HCV. Delivering this “news” is pure pleasure. Unfortunately, the results are not always what everyone hopes for.

To those of you who are nonresponders, responder-relapsers, or could not complete peginterferon/ribavirin therapy, you did not waste your time. Do not regret the effort. There may be other benefits to antiviral therapy besides sustained viral eradication. It has been shown that patients have improved liver histology with or without total HCV suppression. Some nonresponders and responder-relapsers report an enhanced quality of life after treatment. We need to follow and collect long term data on these patients, but what we have seen up to this point is favorable.

There may be other benefits besides eradication of HCV. Ask yourself what you learned about during this process. Although not FDA-approved or found listed in the product information, there may be some positive aspects that can be gained from a journey of antiviral therapy. You might learn about love and the people in your life. You might discover unknown strengths and weaknesses. You might come to see how valuable life is.

Do not expect yourself to bounce back immediately from this experience. Give yourself all the time you need. Be gentle with yourself. Questioning if you did everything you could have or should have done is only useful if you can use it positively. It can be destructive if you use it to blame yourself about the current outcome. The past cannot be changed. It can be useful to analyze the past to change the present. Just skip the guilt and blame.

To those who are no longer HCV positive, do not forget your wounds. Do not forget to give back to those who may be suffering. To those who are considering HCV treatment or choosing other options, focus on the process rather than the outcome. Life is not a goal, but a series of moments. As James Thurber said, “The secret of life is enjoying the passing of time.”

There is a difference between being cured and being healed. To me, there is much more value in being healed than in being cured. Bacon can be cured. Healing is what occurs when we open our hearts to all possibilities.

As this year ends, I would like to publicly thank the many people who have graced my life. There is not enough paper in the world to list you all. I especially want to mention my family, friends, and colleagues. Thank you for tolerating my many sides. I also want to thank my physicians, especially Paul and Patty. Brian and Alan, you give me a perspective no one else can. Last, but certainly not least, I want to thank Ginny, the Redwood City HCV Support Group, and “my” patients. You have taught me the meaning of hope.

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sented that VX-950 was able to inhibit HCV replicons containing the dominant mutation observed for BILN 2061 to the same degree as inhibition of wild type replicons. Based on the data from these studies, the authors concluded that VX-950 is a potential new HCV therapy that will now be evaluated in humans.

BILN 2061

The 2003 AASLD Conference presented data on a new HCV protease inhibitor (BILN 2061) that showed great promise as a new treatment for HCV. BILN 2061 is the first direct antiviral agent against HCV.

At this year's conference, Heiner Wedemeyer and colleagues reported on a randomized, double-blinded study of 10 patients with HCV genotype 1 with cirrhosis. Patients were treated with 200 mg BILN 2061 (8 patients) or a placebo (2 patients) in an oral solution for two days and were followed up to 12 days (+/- 2 days). A viral load decrease of greater than or equal to a 2 log₁₀ decrease was seen in the patients treated with BILN 2061. No viral load decrease was observed in the 2 patients receiving the placebo. After treatment the viral load returned to baseline levels in 2-7 days. ALT levels remained unchanged except that an increase of 69 to 98 IU/mL was noted in one patient receiving BILN 2061. No safety issues were identified and the authors commented that tolerability was "good" in all patients.

Markus Reiser and colleagues reported results from another study on BILN 2061 that compared BILN 2061 (8 patients) to a placebo (2 patients) in HCV genotype 2 and 3 patients with minimal liver fibrosis. Ten male patients were given an oral solution

of 500 mg BILN 2061 or a placebo over 2 days. All patients completed the study and were followed up for 12 (+/- 2) days).

The authors found that the viral load decreased by greater than or equal to 1 log₁₀ in 4 of 8 patients treated with 500 mg BILN 2061 without detectable difference between genotypes 2 and 3. A weak response was observed in one patient treated with BILN 2061, whereas 2 of 8 BILN 2061 treated patients and 2 of 2 patients given placebos experienced no response. Viral load returned to baseline levels within 1-7 days after treatment was stopped. No safety issues were identified. The authors noted that the tolerability was rated "good" in 9 patients and satisfactory in 1 BILN 2061 treated patient.

The authors concluded that BILN 2061, given over 2 days at 500 mg, demonstrated antiviral activity in 5 non-genotype 1 patients. However, in contrast to the previous results in genotype 1 patients, the antiviral activity was not uniform and was less pronounced.

Albupheron

Albupheron consists of recombinant interferon alfa that is genetically fused to recombinant human serum albumin allowing the interferon to remain in the body longer. V. Balan and colleagues reported on the data from an ongoing phase 1/2 study. Of the 63 patients currently enrolled, 96% were infected with HCV genotype 1 with a mean baseline viral load of 2 million copies/mL. Seventy-eight percent of the study participants had previously failed pegylated interferon therapy.

The authors reported that Albupheron was well tolerated with no discontinuations. The most common side effects were injection site redness/irritation, headache, fatigue, muscle and joint pain. Fifty-two per-

cent of patients showed a maximal 0.55 log or greater reduction in HCV viral load during the first two weeks. Also, 20% or greater reductions in ALT levels were observed in 36% of patients in these single dose cohorts.

The authors concluded that in this ongoing phase 1/2 study, Albupheron demonstrated a favorable safety and immunogenicity profile. The pharmacokinetic profile supports dosing every 2-4 weeks due to Albupheron's reduced clearance and extended half-life of up to 158 hours. All cohorts showed evidence of antiviral activity.

Viramidine

Viramidine is a prodrug of ribavirin (converts to ribavirin in the liver) and is believed to have lower red blood cell toxicity compared to ribavirin. L-T Yeh and colleagues studied how viramidine is converted into ribavirin in the liver. Cynomolgus monkeys were given an oral dose of 10 mg/kg of viramidine or ribavirin once daily for 10 days. The authors reported that after oral dosing, viramidine in the liver was slowly converted to ribavirin and that following prolonged administration, viramidine may have greater effectiveness and less red blood cell toxicity than ribavirin. Valeant Pharmaceuticals International (formerly ICN Pharmaceutical) recently announced that they would commence phase III clinical trials of viramidine.

Amantadine

The benefit of amantadine and interferon therapy has been controversial. The majority of studies show little benefit from the addition of amantadine to interferon therapy. Two studies presented at AASLD reported on the amantadine and pegylated interferon therapy.

Eric J Lawitz and colleagues re-

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Nutrition and Cirrhosis



Kara Wright, PA-C

Patients with cirrhosis need to maintain a healthy, liver-friendly diet. Different stages of the disease require different nutritional counseling. It is recommended that patients speak to a registered dietician for the best advice regarding the particular stage of liver disease and nutritional requirements of each individual. Some general guidelines are outlined here.

A high calorie diet is normally recommended in patients with hepatitis. A person's daily calorie needs can be calculated by multiplying body weight (in pounds) by a factor of 14-16.

Example: 150 pound man x 14-16 = 2100 to 2400 calories per day.

Patients with cirrhosis need a diet rich in complex carbohydrates. Complex carbohydrates include breads, cereals, grains, legumes, beans, pastas and rice. This is important because these foods provide glucose (sugar) to the body and are a good source of energy. Patients with cirrhosis often experience fluctuations in blood sugar and the body is better able to maintain healthy sustained energy levels from complex carbohydrates than from simple carbohydrates. Simple carbohydrates include things such as candy, milk, and pastries. These foods provide energy as well, but the body uses them too quickly which leads to a rise in sugars and then a quick drop.

Proteins are an important part of the diet. Proteins are needed for repair and maintenance of blood

and body tissues, including liver tissue. Proteins also make up important parts of the immune system called antibodies which help fight off infections. Patients need to maintain adequate but not excessive amounts of protein in the diet. A damaged liver cannot process as much protein as a healthy liver. When a damaged liver gets overloaded with protein, encephalopathy (a state of mental confusion that can lead to coma) may occur. This occurs because a toxic chemical called ammonia can no longer be properly processed in the liver, and builds up in the blood stream causing numerous problems.

Protein intake must be adjusted in accordance with a person's body weight and degree of liver damage. It is best to discuss this with a physician or dietician, but as a general rule, approximately 0.8 grams of protein per kilogram (2.2 pounds) of body weight is recommended for someone with stable liver disease. People with unstable liver disease or de-compensated cirrhosis need to lower the percentage of protein content in the diet so that it falls

between 10-15%. A diet high in animal protein (which typically contains a lot of ammonia) may precipitate an episode of encephalopathy. Patients with cirrhosis tend to better tolerate protein from dairy and plants sources than from meat sources since a vegetarian diet has a low ammonia content and is less likely to cause encephalopathy.

Some patients with cirrhosis

may begin to experience difficulty digesting and absorbing fat. The liver produces bile, which helps in the digestion and absorption of fat. When fat is not absorbed, the result is steatorrhea (undigested fat in the stool). If this occurs, patients should reduce the fat to

25% of total calories (about 40-70 grams of fat a day). When the liver is no longer producing adequate bile, a type of fat called medium-chain triglycerides (MCT) can be used in place of other fats. MCT does not require bile for absorption and can be found in some oils and nutritional supplements.

Vitamin deficiencies can occur in cirrhosis. The fat-soluble vitamins (A, D, E, and K) may need to be taken in their water-soluble form by prescription from a doctor. Deficiencies in the

***Patients with cirrhosis
tend to better tolerate
protein from dairy
and plant sources
rather than from meat
sources***

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minerals zinc, calcium and magnesium can also occur and require supplementation. Blood potassium levels need to be monitored and supplementation should only occur with the prescription of a physician. Do not take vitamins and minerals without first asking a physician.

In patients with advanced liver disease, sodium typically needs to be restricted. Cirrhotics should limit sodium to 2500 milligrams per day. Sodium acts like a sponge causing the body to hold on to more fluid predisposing you to fluid retention called ascites (fluid build up in the abdomen). Patients should avoid processed foods since they generally contain large amounts of sodium.

Although anemia may be common in liver disease, iron deficiency is not. Iron is stored in the liv-

er; therefore patients with liver disease should not supplement iron because of the potential for toxicity. There is a concern of iron overload in the liver, which may cause further damage and scarring in the liver.

Last, but not least, patients should absolutely avoid alcohol. Alcohol speeds up the rate of liver damage tremendously and is particularly hard on patients who have hepatitis.

Patients with cirrhosis should monitor their diets carefully in order to avoid complications or any further damage to the liver. Each patient should consider speaking to a nutrition expert who works closely with a physician in order to determine the best diet for his or her needs.



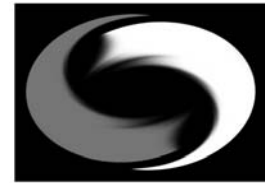
FOODS TO AVOID

Foods High in Ammonia

Aged cheese, salami, bacon, ham, ground beef, gelatin

Foods High in Sodium

Salt, garlic salt, onion salt, soy sauce, MSG, canned soup, canned vegetables and meats, cured meats (bacon, sausage, ham, lunchmeat), processed cheese, frozen meals, salty snacks(chips, pretzels, popcorn), pickled foods (sauerkraut, pickles, olives)



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Pregnancy and Hepatitis



Liz Highleyman

Much discussion about viral hepatitis in pregnant women focuses on the risk of mother-to-child transmission. While this is a pressing issue, it is also important to look at how hepatitis affects pregnant women themselves.

In general, most research indicates that viral hepatitis does not have a major adverse effect during pregnancy. The primary exception to this rule is hepatitis E. The hepatitis E virus (HEV) is transmitted much like hepatitis A, usually through contaminated food or water or poor hygiene practices. In most adults, the disease course is similar to that of hepatitis A, but in pregnant women, HEV infection is associated with fulminant hepatitis and a maternal death rate as high as 20%. However, hepatitis E occurs mostly in developing countries, and is rare in the United States.

Likewise, most research indicates that pregnancy does not have a serious impact on the progression of viral hepatitis, although it may affect levels of certain biochemical markers of liver function. Because the placenta (the tissue in the womb that provides oxygen and nutrients to the fetus) produces alkaline phosphatase, blood levels of this enzyme may increase during pregnancy. Albumin levels often decrease, while transaminases (ALT and AST) may remain stable or vary with the stage of pregnancy.

Although pregnancy does not greatly increase demands on the

liver, the extra blood produced to provide for the developing fetus circulates through the portal vein and the inferior vena cava, which can lead to complications in women who already have liver cirrhosis (scarring) and compromised hepatic blood flow.

In addition, some pregnant women develop acute fatty liver of pregnancy, which involves deficiencies in an enzyme that metabolizes fatty acids, gallstones (due to a build up of bile acids in the gall bladder), or a syndrome called HELLP characterized by hemolysis (blood cell destruction), elevated liver enzymes, and low platelet count. Women with existing liver problems may be at higher risk for these conditions.

HEPATITIS A

Hepatitis A rarely causes major pregnancy complications, although the rate of premature delivery is somewhat higher. Transmission of the hepatitis A virus (HAV) from mother to baby is uncommon; if it occurs, the infant usually has mild disease and develops lifelong immunity. If a woman is exposed to hepatitis A during pregnancy, use of HAV immunoglobulins (injected antibodies) can protect both the woman and her baby from contracting the disease. The hepatitis A vaccine is not recommended for children under two years of age, but is considered safe for pregnant women.

HEPATITIS B

Hepatitis B also rarely leads to

major complications during pregnancy but, as with HAV, premature delivery is more common. The hepatitis B virus (HBV) is easily transmitted from mother to child. The vertical transmission rate is 20% or less if the woman only has HBs surface antibodies, but as high as 90% if she has detectable HBe antigen (indicating active viral replication). Although only about 10% of adults infected with HBV develop chronic hepatitis, the virus persists in about 90% of infected infants. Fortunately, vertical transmission of HBV is almost completely preventable. The Centers for Disease Control and Prevention (CDC) recommend that all pregnant women should be screened for hepatitis B during pregnancy (since only about half of those infected have no known risk factors). If the mother is infected, the newborn should receive HBV immunoglobulins (HBIG) and the first dose of the hepatitis B vaccine within 12 hours of birth. The other two vaccine doses should be given at one month and at six months. With these measures, the HBV transmission rate may be reduced to less than 10%. Even if the mother does not have HBV, the CDC now recommends that all infants should start the hepatitis B vaccine series soon after birth. For women at risk for HBV, vaccination during pregnancy is considered safe. Breast-feeding has not been associated with HBV transmission.

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HEPATITIS C

While hepatitis C virus (HCV) is rarely associated with serious pregnancy complications, research indicates that being pregnant can affect HCV viral load and biochemical markers of liver function. For example, Dario Conte, MD, and colleagues found that ALT decreased during the third trimester (last three months) of pregnancy, often to normal levels, but increased again after delivery. This may occur because immune function is altered during pregnancy to prevent the mother's immune system from rejecting the fetus. As immune activity is dampened, liver inflammation may be reduced, resulting in lower ALT levels.

Study results are mixed concerning how pregnancy affects HCV viral load. Some researchers have found that HCV RNA increases in the second and third trimester, but falls again after delivery, while others have reported no change. In one recent study, Yuko Hattori and colleagues

Most research indicates that pregnancy does not have a serious impact on the progression of viral hepatitis

reported that pregnancy and delivery may actually promote HCV clearance. In this study, two out of 22 pregnant HCV positive women cleared HCV permanently after delivery, and one temporarily cleared the virus (an overall 14% clearance rate). In comparison, just one permanent and one temporary clearance were seen in 120 non-pregnant women with HCV (a 2% clearance rate). The researchers suggested that viral clearance may be due to the immune system "rebound" that occurs after giving birth. In another small study, HCV-infected women who received liver biopsies before and after delivery showed worse liver tissue damage after giving birth, which may also be related to post-delivery immune rebound.

It is recommended that women

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not receive hepatitis C treatment during pregnancy. Ribavirin has been associated with birth defects and fetal death, and interferon is also contraindicated. In fact, women and men must use effective birth control while being treated with interferon/ribavirin and for six months thereafter to ensure that pregnancy does not inadvertently occur. It is even recommended that men should not take ribavirin if their female partners are pregnant. Women also should not take interferon/ribavirin while breast-feeding.

Compared with HBV, HCV is not commonly transmitted from mother to child. Most studies have found an overall vertical transmission rate of about 5%. The risk of transmission is greater in women with higher HCV viral loads. Transmission is most likely in women with over 1,000,000 HCV RNA copies/mL, and very rare in women with undetectable HCV viral loads. The transmission rate is also increased—three or more times higher—in women who are coinfecting with HIV or HBV in addition to HCV. Although study results are mixed, some research suggests that elective Cesarean (surgical) delivery may reduce the chances of HCV transmission, especially in HCV/HIV coinfecting women. However, as Eve Roberts and Latifa Yeung discussed at the National Institutes of Health Consensus Development Conference on the Management of Hepatitis C in 2002, since data is inconsistent and Cesarean section itself carries some risk, most experts encourage normal vaginal deliveries for women with HCV. Because they increase the baby's

exposure to the mother's blood and genital fluids, some studies suggest that amniocentesis and forceps delivery may also slightly increase the risk of HCV transmission.

While some studies have found small amounts of HCV in breast milk, there is no evidence that breast-feeding leads to hepatitis C transmission (although some research suggests it may occur if the mother is coinfecting). Unfortunately, unlike with HBV, there is currently no effective vaccine or immunoglobulin therapy to prevent HCV transmission.

CONCLUSION

In summary, hepatitis A, B, and C generally do not cause major pregnancy complications. Pregnancy also does not appear to adversely affect hepatitis disease progression. While results are still inconsistent and preliminary, there is some evidence that immune changes during pregnancy and after delivery may help some women clear HCV. HBV is easily transmitted from mother to baby, but transmission can be reduced by 90% using HBV immunoglobulins and the HBV vaccine. Mother-to-child HCV transmission currently cannot be prevented, but is not common. Even if women have high HCV viral loads or HCV/HIV coinfection, a majority will not transmit HCV to their babies. Women with viral hepatitis, and those at risk for infection, should consult their doctors if they are pregnant or wish to become pregnant.

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IT'S THAT TIME OF YEAR AGAIN! INFLUENZA - FLU SHOT

The flu season upon us and this year it is expected to be a particularly bad strain. See your healthcare provider for this vaccine as well as for others listed below.

Other vaccines to consider include:

Hepatitis A

Recommended for people with liver disease if they have not been previously exposed.

Hepatitis B

Recommended for people with liver disease if they have not been previously exposed.

Pneumococcal

Recommended for people with liver disease.

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ported the final results of the Tri-Star Trials study to determine if the addition of amantadine to pegylated interferon alpha 2b plus weight based ribavirin improves the sustained response rate of treatment naïve patients with hepatitis C. Patients were treated with either triple therapy (pegylated interferon, plus amantadine, plus weight based ribavirin) or double therapy (pegylated interferon plus weight based ribavirin). The authors concluded that amantadine does not improve the response rates when added to pegylated interferon plus ribavirin.

Gaetano Ideo and colleagues reported the final results of a study comparing the effectiveness and tolerability of pegylated interferon alpha 2a plus ribavirin or pegylated interferon alpha 2a plus amantadine. Patients were treated with pegylated interferon alpha 2a (180 µg once weekly) plus ribavirin (1.1.2 g/daily) or amantadine (200mg/daily) for 48 weeks with a 24 week follow-up. As expected, the authors found that pegylated interferon alpha 2a plus ribavirin was more effective than pegylated interferon alpha 2a plus amantadine.

TREATMENT FOR NON-RESPONDERS

Effective treatments for previous non-responders are limited. However, some medications or combinations of medications show promise in treating this difficult to treat population.

Thymalfasin

Thymalfasin is a synthetic preparation of thymosin alpha 1, a natural substance of our body which helps the body's immune response fight viral infections. Jorge L. Poo and col-

leagues reported on *interim data* on a pilot study investigating the effects of thymalfasin in combination with pegylated interferon alpha 2a in patients who did not respond to a previous course of interferon plus ribavirin. To date the investigators have enrolled 24 patients. Of the 23 patients who had completed 12 weeks of therapy, 48% tested negative for HCV RNA. Thymalfasin was well tolerated with no obvious side effects. The authors concluded that thymalfasin improves the effectiveness of pegylated interferon plus ribavirin. While the results are encouraging, interim data can be misleading. The sustained virological response rates when the trial is completed are eagerly awaited.

Consensus Interferon

Recent data from trials using consensus interferon to treat previous interferon plus ribavirin non-responders has been encouraging. Stephan Kaiser and colleagues reported on a trial using daily induction consensus interferon (CIFN) followed by CIFN plus ribavirin in previous non-responders to combination therapy. One hundred and twenty patients—mean age (46.1 yrs), male (79%), genotype 1 (91%), bridging fibrosis or cirrhosis (28%)—were enrolled. Patients were either treated with CIFN at a dosage of 18 µg for 4 weeks, followed by 9 µg for 8 weeks or with CIFN 27 µg for 4 weeks, followed by 8 weeks of CIFN 18 µg. Following the induction phase, treatment was continued in all treatment groups with CIFN at a dose of 9 µg QD with ribavirin (at 10 - 15 mg/kg/d) for another 36 weeks.

The results of the study found that the subset of patients having reached end-of-treatment and 24 week follow-up showed response rates of 59-66% (ETR) and 37-43% (SR), respectively.

No growth factors (adjunct therapies) were used in this trial. Sixteen percent of patients required dose reductions and 7% of patients discontinued therapy. The most common cause for dose reductions was significant reductions in WBC and platelet counts, especially in the 27 µg CIFN group. The overall tolerability of the CIFN 18/9 µg regimen was of comparable tolerability to a standard therapy with pegylated interferon and ribavirin, while the CIFN 27/18/9 µg regimen was less tolerable during the high dose induction period, but discontinuance rates were not different between the two dosing regimens.

The authors concluded that CIFN daily dosing/induction therapy together with combination CIFN plus ribavirin shows promise with a 3-fold higher rate of response when compared to rates observed with pegylated interferon.



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