

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

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Week Ending: January 19th 2008

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January 12th, 2007

Healthcare Help for the Burmese

<http://www.indianasnewscenter.com>

By Jessica Toumani

40 percent of their adult population is infected with latent TB and Hepatitis. [Watch the story:](#)

We're talking about the Burmese refugee population in Fort Wayne and it will soon get some big help when it comes to healthcare.

One foundation, though, hopes to make their transition to our country easier.

Just this year 800 new Burmese refugees are expected to make their way to Allen County.

The St. Joseph Community Health Foundation announced today they will spend more than \$133,000 to help refugees who've suffered through particularly unhealthy conditions get the healthcare they need.

More than 98 thousand will go to Catholic Charities so they can establish a program to aid with medical follow-ups, and hire a case coordinator to get the refugees connected with the right care.

Almost \$35,000 more will be used to arrange for translation services.

Britain's transplant crisis: Poor lifestyle fuels big rise in waiting lists

<http://news.independent.co.uk>

By Nina Lakhani

Binge drinking is blamed for a 76 per cent increase in 10 years in those needing a new liver, while the demand for kidney replacements is up 55 per cent. This week, a 14-point plan will try to tackle the donor shortage.

The UK is in the grip of a chronic organ donation crisis which is set to get worse as Britain's culture of excess drives a burgeoning obesity epidemic. The gap between the numbers of suitable donor organs and patients desperately needing them is getting wider every year.

Official figures show that three people a day are dying for want of an organ, but experts believe this is the tip of the iceberg, as many others are not put on transplant lists and are "dying silently". Figures show the numbers waiting for a transplant in the past 10 years has increased by 40 per cent to almost 9,700. Patients waiting for kidney transplants have increased by 55 per cent, while those hoping for livers are up 76 per cent. The situation is particularly critical for people from black and minority ethnic (BME) groups who make up nearly a quarter of those waiting, but must wait twice as long for organs as their white counterparts.

Experts warn that the chronic shortages will get worse, with greater longevity, soaring rates of diabetes, obesity, hepatitis C and the consequences of binge drinking leading to increasing demands for healthy donor organs.

The revelations come on the eve of a publication by a government task force set up to examine ways to help to solve the donor crisis. The task force report, to be published on Tuesday, recommends a 14-point plan to increase the number of registered donors by 50 per cent in five years by doubling the number of specialised staff, standardising training across the UK and strengthening out-of-hours services to get organs to where they are needed quickly. Strategies to reduce current inequalities with ethnic minorities are also included. Doctors believe thousands of lives could be saved if the Government implements all 14 recommendations.

However, some experts warn they do not go far enough in recognising the importance of healthier lifestyle choices to curb the demand for transplants, and improving the detection and treatment of conditions that can lead organ failure.

The report will not refer to the opt-out system recommended by the Chief Medical Officer, Sir Liam Donaldson, last July. Currently no organs or tissue can be taken for transplant without the consent of the deceased or their relatives – an opt-in scheme. Under the opt-out system, organs automatically become available for transplant unless a specific objection is made beforehand. Instead of carrying a donor card, objectors would carry non-donor cards. The task force's

findings on Sir Liam's proposal are expected to be published in a second report this summer.

Gordon Brown last night threw his weight behind the call for a move to a policy of presumed consent. "A system of this kind seems to have the potential to close the aching gap between the potential benefits of transplant surgery in the UK and the limits imposed by our current system of consent," the Prime Minister said in *The Sunday Telegraph*.

Spain, which has Europe's best organ donation rate, introduced an opt-out scheme in 1979, but it had little impact until highly trained transplant co-ordinators were placed in every intensive care unit 10 years later. The success is attributed more to trained staff and a change in ethos, according to Rafael Matensaz, director of the Spanish National Organisation for Transplants.

According to doctors, our ageing population and the obesity epidemic are the two main reasons behind the increase in kidney failure, and both trends seem set to continue.

Mr Argiris Asderakis, transplant surgeon and transplant programme director at the University Hospital of Wales, Cardiff, said: "An ageing population brings an increase in chronic disease. Second, we have a society with more blood pressure problems and more obesity, which is linked to the type 2 diabetes epidemic and can lead to kidney failure.

"The population will continue to age, but improvements in diet and avoiding obesity could halve the number of people developing kidney failure and inadvertently reduce the need for kidney transplants."

He added: "Fifteen to 20 per cent of people who are obese will end up with kidney failure." Nearly 108,000 people were treated in hospital for kidney failure in England and Wales in 2006-07, more than double the number eight years ago.

Gurach Randhawa, professor of public health at Bedfordshire University and a task force member, believes disease prevention is vital to address the disproportionate donor shortage in black and ethnic minority groups. "In the short term we need to increase the number of donors from these groups," said Professor Randhawa. "But in the long term we have to address the fact they are six times more likely to become diabetic and then 10 times more likely to develop complications. We have to address long-term lifestyle and diet issues with individuals but also ensure they have equal access to services."

The number of people treated in hospital for liver diseases in England in 2006-07 increased by nearly 80 per cent over eight years to reach a record high of 45,557. Experts warn of a liver disease time bomb as rates of obesity, excessive drinking and hepatitis C continue to soar. "The striking increases we are seeing in chronic liver disease, both alcoholic and non-alcoholic fatty disease, which is caused by obesity, will increase the need for liver transplants. The rise in alcohol-related damage seems set to continue as we have not found a way to reduce the nation's drinking habit," Dr Ian Gilmore, president of the Royal College of Physicians, said. The numbers of people treated for alcoholic liver disease has doubled to more than 26,000 since 1998.

The third high-risk group is people with hepatitis C: one in five will need transplants. "We know of 65,000 hepatitis C cases but between 80 to 90 per cent of infected people are undiagnosed.

Hepatitis C and alcohol are both likely to burden the transplant services further," Dr Gilmore said.

Carol Beckett, 37, from Manchester has a rare form of cancer and will die unless she receives a liver transplant soon. But with the competition for organs high, the average wait at her transplant centre is six to 12 months. She refuses to criticise people whose diet or alcohol use may have contributed to organ failure.

She said: "We don't all live healthy lifestyles, but we all pay our taxes and should have access to the same treatment. I am not going to pass moral judgement on people but everyone should be aware this is a life-or-death situation."

A series of surveys has revealed that while nine out of 10 people say they are willing to donate their organs, only 20 per cent are registered. Furthermore, four out of 10 families of potential donors – people diagnosed brain dead – who are asked to donate the organs refuse. Their refusal, which can be at odds with the donor's personal wishes, is seldom overruled.

It was thought this was because relatives are unaware of the dead person's wishes but new research contradicts this. "Our research has totally overturned this as we found donations did not happen despite the views of the deceased. When it comes down to it, many people cannot go through with it, often because they do not want to disfigure or violate the body," said Magi Sque, senior lecturer at Southampton University.

"There has been too much emphasis on the plight of people waiting for organs, and not enough promotion of donation as an incredible achievement for the deceased, a way of leaving a legacy."

January 13th, 2007

SF med center to use gene therapy

<http://abclocal.go.com>

Bay City News

California Pacific Medical Center in San Francisco announced this week that it has reportedly become the first medical research institute to use a gene-silencing therapy to treat hepatitis B.

California Pacific teamed up with Pennsylvania-based Nucleonics Inc., along with other investigators, to test a method of helping people suffering from the hepatitis B virus, which is the second leading cause of cancer worldwide.

"This is an exciting time, and a potentially important new way of helping people battle what can be a deadly disease," said Robert Gish, medical director of the Liver Disease Management & Transplant Program at California Pacific Medical Center.

When hepatitis B infects a liver cell it creates a strand of genetic material called RNA and then uses that material to turn the cell into a mini hepatitis B factor, essentially churning out new copies of the virus, which spread throughout the liver.

This new therapy prevents the virus from multiplying by effectively paralyzing it and making it unable to create infectious virus particles.

An estimated 2 million Americans are chronically infected with hepatitis B, according to the Centers for Disease Control and Prevention. Most people who have chronic hepatitis B infections undergo life-long therapy to keep the virus at bay. If left unchecked, it can cause cirrhosis or scarring of the liver, liver cancer, liver failure and even death in one out of four people infected with the virus.

Studies from University of California in the area of cancer vaccines published

<http://www.newsrx.com>

According to recent research from the United States, "Viral hepatitis due to chronic hepatitis B and C virus (HBV/ HCV) infects more than 500 000 000 individuals worldwide. These chronic viral diseases are highly linked to the development of hepatocellular carcinoma (HCC), the fifth most common cause of cancer death worldwide."

"HCC is much more common in Asia and Africa than in the USA and Europe, although HCC is one of the few cancers with a rising incidence in the USA. There are 530 000 cases of HCC worldwide of which 82% are related to viral hepatitis. 316 000 cases of HCC are HBV-associated, 118000 are HCV-associated. The most effective way to prevent HCC is to prevent viral infection through immunization. Currently there are effective vaccines against hepatitis B and A, but not against HCV, the virus that accounts for most HCC in the USA. The published work supporting the use of antiviral therapy in preventing liver cancer is limited. Data supporting the use of antiviral therapy in preventing recurrence of HCC after initial anticancer approaches is even less available," wrote T.L. Wright and colleagues, University of California.

The researchers concluded: "Nevertheless, the weight of evidence suggests that treatment of HBV/HCV-related fibrosis will reduce the risk of developing HCC."

Wright and colleagues published their study in *Hepatology Research* (Antiviral therapy and primary and secondary prevention of hepatocellular carcinoma. *Hepatology Research*, 2007;37(Suppl. 2):S294-S298).

For additional information, contact T.L. Wright, University of California, Dept. of Medical, San Francisco, CA 94143, USA.

January 14th, 2007

Court Declines Experimental Drugs Case

<http://www.therapeuticsdaily.com>

AP Online

WASHINGTON (AP) - The Supreme Court refused Monday to review a ruling that terminally ill

patients have no constitutional right to be treated with experimental drugs – even if that means the patient will likely die before the medicine is approved. A federal appeals court, siding with the Food and Drug Administration, last year said the government may deny access to drugs that have not gone through extensive testing and received FDA approval. The process can take years.

Schering-Plough Reports Top-Line Results of the Ideal Study

www.schering-plough.com

Press Release

- *First Large Study Comparing Leading Hepatitis C Therapies Shows Similar Sustained Response Rates;*
- *Fewer Patients Relapsed Following PEGINTRON Combination Therapy*

KENILWORTH, N.J., Jan. 14, 2008 – Schering-Plough Corporation (NYSE: SGP), a leader in hepatitis research, today reported top-line results of the IDEAL study, the first large, randomized, clinical study comparing the leading therapies for chronic hepatitis C: PEGINTRON™ (peginterferon alfa-2b) and REBETOL® (ribavirin, USP) combination therapy vs. Pegasys (peginterferon alfa-2a) and Copegus (ribavirin, USP) combination therapy,¹ as well as a lower dose of PEGINTRON in an investigational combination regimen. The results showed that sustained virologic response (SVR),² the primary endpoint of the study, was similar for the two leading combination therapies for hepatitis C; and that using a lower dose of PEGINTRON with REBETOL also resulted in a similar SVR. The study also showed that fewer patients treated with both PEGINTRON regimens relapsed after the end of treatment compared to those receiving Pegasys and Copegus.

In the IDEAL (Individualized Dosing Efficacy vs. Flat Dosing to Assess optimal pegylated interferon therapy) study, both PEGINTRON regimens utilized investigational weight-based ribavirin dosing. The three treatment regimens studied were:

- (1) PEGINTRON 1.5 mcg/kg/week and REBETOL 800-1,400 mg/day;
- (2) PEGINTRON 1.0 mcg/kg/week and REBETOL 800-1,400 mg/day; and
- (3) Pegasys 180 mcg/week and Copegus 1,000-1,200 mg/day

In the study, 3,070 previously untreated U.S. patients with HCV genotype 1, the most common form of the virus worldwide and most difficult to treat, were randomized to one of the three treatment regimens and received up to 48 weeks of combination therapy with 24 weeks of follow-up. SVR, the primary endpoint of the study, was similar for the three treatment regimens (40 vs. 38 vs. 41 percent, respectively). Importantly, while end of treatment response was higher in the Pegasys combination therapy arm, IDEAL showed that fewer patients receiving PEGINTRON combination therapy relapsed after the end of treatment (24 vs. 20 vs. 32 percent, respectively).

Overall adverse events reported for the three treatment regimens were similar and, as seen in other studies with these treatments, a range of “flu-like symptoms” were the most commonly reported adverse events for all three treatment regimens. Discontinuation rates due to adverse events also were similar (13 vs. 10 vs. 13 percent, respectively).

“While the sustained response rates were similar in the IDEAL study, we were pleased to see that fewer patients relapsed following PEGINTRON combination therapy,” said Robert J. Spiegel, M.D., chief medical officer and senior vice president, Schering-Plough Research Institute. “With these results, we now have, for the first time, a large body of well-controlled clinical data demonstrating how the similarities and differences of the two leading combination therapies for hepatitis C affect outcomes for patients. These findings provide important clinical-based evidence that will help physicians in making treatment decisions and in guiding their patients through what is a long and challenging course of therapy. We look forward to further analyses of this large data set to gain additional clinical insights into the management of this serious disease.”

In IDEAL, the combination regimen of Pegasys and Copegus used the recommended doses in accordance with their approved U.S. labeling, which includes a flat dose of Pegasys (180 mcg/week) for all patients regardless of body weight, and 1,000 or 1,200 mg/day of Copegus, adjusted for two weight categories. PEGINTRON was dosed either at 1.5 mcg/kg/week or an investigational combination dose of 1.0 mcg/kg/week with REBETOL at an investigational dose of 800-1,400 mg/day, adjusted by four weight categories. As a result, the majority of patients (1598/3070, 52 percent) were assigned the same dose of ribavirin (either REBETOL or Copegus) based on their weight groups. In the study, 39 percent of patients in the Pegasys arm were assigned a higher dose of ribavirin, while 9 percent of patients in the PEGINTRON arms were assigned a higher dose of ribavirin. Among those who were assigned equivalent doses of ribavirin based on their weight group, SVR also was similar (40 vs. 38 vs. 38 percent, respectively). Also, fewer of these patients treated with PEGINTRON and REBETOL relapsed after the end of therapy compared with those treated with Pegasys and Copegus (22 vs. 20 vs. 35 percent, respectively).

Complete results of the IDEAL study will be submitted for peer-reviewed publication and for presentation at upcoming medical meetings, as well as to Health Authorities worldwide.

About IDEAL

The IDEAL study was undertaken by Schering-Plough as an important step in meeting the needs of the hepatitis C medical and patient communities to identify improved treatment strategies to optimize outcomes for patients. IDEAL, a Phase IIIb, randomized, parallel-group study, was conducted at 118 academic and community centers across the United States. The study treated 3,070 adult patients with chronic HCV genotype 1. Of these, 82 percent of patients had high viral load (greater than or equal to 600,000 IU/mL),³ 11 percent had grade F3/4 fibrosis/cirrhosis, and 19 percent were African Americans. There were no significant differences in patient demographics or disease characteristics across the three treatment arms.

The comparison of the two PEGINTRON combination therapy doses (1.5 vs. 1.0 mcg/kg/week) was conducted as a post-approval commitment to the U.S. Food and Drug Administration (FDA). The comparison of the PEGINTRON and Pegasys combination therapy regimens was added to the study because no randomized, controlled head-to-head study of the two available peginterferon regimens had been conducted to date. Cross-study comparisons and retrospective analyses of previous data are difficult to interpret because of differences in study designs, patient populations and assay limits.

John McHutchison, M.D., and Mark Sulkowski, M.D., are the co-principal investigators of the IDEAL study. They also are co-chairmen of the IDEAL Publication Committee, which also includes three independent expert members not associated with the study to assure an unbiased evaluation of the data. The Publication Committee was responsible for the preparation of the prespecified data analysis plan for the statistical analysis conducted for the primary publication of the study results.

About Hepatitis C

Hepatitis C is a serious and potentially life-threatening disease. It is the most common blood-borne infection in America and the most common form of liver disease, affecting nearly 5 million people in the United States and some 170 million people worldwide. It is the leading cause of cirrhosis and liver cancer, and the number one reason for liver transplants in the United States.

About PEGINTRON

In the United States, PEGINTRON is indicated for use alone or with ribavirin for the treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alpha and who are at least 18 years of age.

Important Safety Information Regarding U.S. Labeling for PEGINTRON and REBETOL

Alpha interferons, including PEGINTRON and INTRON® A, may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolve after stopping PEGINTRON and/or INTRON A therapy.

Use with Ribavirin: Ribavirin may cause birth defects and/or death of the unborn child. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin causes hemolytic anemia. The anemia associated with REBETOL therapy may result in a worsening of cardiac disease. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen.

Contraindications

PEGINTRON is contraindicated in patients with hypersensitivity to PEGINTRON or any other component of the product, autoimmune hepatitis, and hepatic decompensation (Child-Pugh score greater than 6 [class B and C]) in cirrhotic CHC patients before or during treatment. INTRON A (Interferon alfa-2b, recombinant) for Injection is contraindicated in patients with hypersensitivity to INTRON A or any component of the product, autoimmune hepatitis, and decompensated liver disease. PEGINTRON or INTRON A in combination with REBETOL therapy is additionally contraindicated in patients with hypersensitivity to ribavirin or any other component of the product, women who are pregnant, men whose female partners are pregnant, patients with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia), and patients with creatinine clearance less than 50 mL/min.

Avoid Pregnancy

REBETOL therapy should not be started until a report of a negative pregnancy test has been

obtained immediately prior to planned initiation of therapy. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients during therapy and 6 months post-treatment. Patients should use at least two effective forms of contraception and have monthly pregnancy tests during therapy and for 6 months after completion of therapy. A Ribavirin Pregnancy Registry has been established to monitor maternal-fetal outcomes of pregnancies in female patients and female partners of male patients exposed to ribavirin during treatment, and for 6 months following cessation of treatment. Physicians and patients are encouraged to report such cases by calling 1-800-593-2214.

Incidence of Adverse Events

There are no new adverse events specific to PEGINTRON as compared to INTRON A; however, the incidence of some (e.g., injection site reactions, fever, rigors, nausea) were higher. The most common adverse events associated with PEGINTRON were “flu-like” symptoms, occurring in approximately 50% of patients, which may decrease in severity as treatment continues. Application site disorders were common (47%), but all were mild (44%) or moderate (4%) and no patient discontinued, and included injection site inflammation and reaction (i.e., bruise, itchiness, irritation). Injection site pain was reported in 2% of patients receiving PEGINTRON. Alopecia (thinning of the hair) is also often associated with alpha interferons including PEGINTRON.

Psychiatric adverse events, which include insomnia, were common (57%) with PEGINTRON but similar to INTRON A (58%). Depression was most common at 29%. Suicidal behavior including ideation, suicidal attempts, and completed suicides occurred in 1% of patients during or shortly after completing treatment with PEGINTRON.

The following serious or clinically significant adverse events have been reported at a frequency less than 1% with PEGINTRON or interferon alpha: Severe decreases in neutrophil or platelet counts, hypothyroidism, hyperglycemia, hypotension, arrhythmia, ulcerative and hemorrhagic colitis, development or exacerbation of autoimmune disorders including thyroiditis, RA, systemic lupus erythematosus, psoriasis, pulmonary disorders (dyspnea, pulmonary infiltrates, pneumonitis and pneumonia, some resulting in patient deaths), urticaria, angioedema, bronchoconstriction, anaphylaxis, retinal hemorrhages, and cotton wool spots.

In the PEGINTRON/REBETOL combination trial, the incidence of serious adverse events was 17% in the PEGINTRON/REBETOL groups compared to 14% in the INTRON A/ REBETOL group. The incidence of severe adverse events in the PEGINTRON/REBETOL combination therapy trial was 23% in the INTRON A/REBETOL group and 31-34% in the PEGINTRON/REBETOL groups. Dose reductions due to adverse reactions occurred in 42% of patients receiving PEGINTRON (1.5 mcg/kg)/REBETOL and in 34% of those receiving INTRON A/REBETOL.

Additional Safety Information

Relapse of drug addiction/overdose has occurred in patients on PEGINTRON therapy. Aggressive behavior sometimes directed towards others has occurred in patients with and without a previous psychiatric disorder during PEGINTRON and/or INTRON A treatment and follow-up. If patients develop psychiatric problems, including clinical depression, it is recommended that patients be carefully monitored during treatment and in the 6-month follow-

up period. If psychiatric symptoms persist or worsen, or suicidal ideation or aggressive behavior towards others is identified, it is recommended that treatment with PEGINTRON and/or INTRON A be discontinued, and the patient be carefully followed with psychiatric intervention, as appropriate. Cases of encephalopathy have been observed in some patients, usually elderly, treated with higher doses of PEGINTRON and/or INTRON A. Ischemic and hemorrhagic cerebrovascular events have been observed in patients treated with interferon alpha therapies, including PEGINTRON and INTRON A. Dental and periodontal disorders have been reported in patients receiving PEGINTRON or INTRON A in combination with REBETOL therapy.

About Schering-Plough

Schering-Plough is an innovation-driven, science-centered global health care company. Through its own biopharmaceutical research and collaborations with partners, Schering-Plough creates therapies that help save and improve lives around the world. The company applies its research-and-development platform to human prescription and consumer products as well as to animal health products. In November 2007, Schering-Plough acquired Organon BioSciences, with its Organon human health and Intervet animal health businesses, marking a pivotal step in the company's ongoing transformation. Schering-Plough's vision is to "Earn Trust, Every Day" with the doctors, patients, customers and other stakeholders served by its approximately 50,000 people around the world. The company is based in Kenilworth, N.J., and its Web site is www.schering-plough.com.

SCHERING-PLOUGH DISCLOSURE NOTICE: The information in this press release includes certain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements relating to the IDEAL study and the potential market for PEGINTRON and REBETOL. Forward-looking statements relate to expectations or forecasts of future events. Schering-Plough does not assume the obligation to update any forward-looking statement. Many factors could cause actual results to differ materially from Schering-Plough's forward-looking statements, including market forces, economic factors, product availability, patent and other intellectual property protection, current and future branded, generic or over-the-counter competition, the regulatory process, and any developments following regulatory approval, among other uncertainties. For further details of these and other risks and uncertainties that may impact forward-looking statements, see Schering-Plough's Securities and Exchange Commission filings, including Part II, Item 1A, "Risk Factors" in the company's third quarter 2007 10-Q.

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References:

- (1) 1 Pegasys and Copegus are registered trademarks of Hoffmann-La Roche Inc. Please see the Pegasys and Copegus product inserts for information on these products.
- (2) 2 SVR, the protocol specified primary efficacy endpoint, is defined as achievement of undetectable HCV-RNA at 24 weeks after the end of treatment. Per protocol, if a patient did not have a 24-week post-treatment assessment, the patient's 12-week post-treatment assessment was utilized.
- (3) 3 Roche Cobas Taqman 1.0 assay; lower limit of detection is 15 IU/mL.

Roche Responds to Announcement of “IDEAL” Hepatitis C Trial Results

<http://www.rocheusa.com>

Press Release

Following an announcement from Schering-Plough, Roche today affirmed the value of PEGASYS® (peginterferon alfa-2a) in combination with ribavirin as the market-leading treatment for patients with hepatitis C, in the United States and globally. Despite clear biases in the design of the “IDEAL” study that potentially favored patients taking Peg-Intron™ (peginterferon alfa-2b) regimens – particularly the ribavirin dose reduction protocol – the study results have shown that patients treated with a PEGASYS regimen had a similar chance of being successfully treated for hepatitis C.

“I do not expect that the results of the IDEAL study will meaningfully impact clinical practice, except to inform physicians on the appropriate dosing of Peg-Intron and to reinforce the already widely-accepted view that optimizing ribavirin dosing throughout treatment is critical to achieving success and preventing treatment relapse in hepatitis C,” said Douglas Dieterich, M.D., Professor of Medicine in the Division of Hepatology at Mt. Sinai School of Medicine in New York, New York.

In 2001, the U.S. Food and Drug Administration (FDA) required Schering-Plough to conduct a post approval commitment trial to determine if a lower dose of Peg-Intron (1.0 mg/kg) was as effective as the approved dose of 1.5 mg/kg, both in combination with identical ribavirin regimens. A third arm was added to the study in which patients received PEGASYS 180 mcg with a different ribavirin dosing schedule. This mismatch of ribavirin dosing introduces several potential biases into the study because experts agree that an optimized dose of ribavirin, with either pegylated interferon, is critical to achieving success in hepatitis C treatment. In particular, maintaining a full dose of ribavirin has shown an important ability to reduce relapse following the end of treatment.

“PEGASYS quickly became the market leader after its launch, based on robust clinical data and patient and physician preference. We are convinced that physicians and patients will continue to choose PEGASYS/ribavirin combination therapy based on positive experience and sound clinical evidence,” said George Abercrombie, President and CEO, Hoffmann-La Roche. “Our current focus at Roche is on advancing the treatment of hepatitis C by optimizing doses and duration of PEGASYS/ribavirin in patients with unmet medical need, while developing new compounds that have the potential to offer a successful outcome to even more patients.”

Roche believes that it is critical for patients and physicians to receive complete information to fully understand the results of “IDEAL,” so that treatment decisions can be based on sound scientific data.

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Please see below for additional information about the “IDEAL” trial, Roche and PEGASYS, including important safety information.

“IDEAL” Trial Design Issues

- Starting doses of ribavirin were different in the Peg-Intron and PEGASYS arms of the study
- The design calls for a more drastic ribavirin dose reduction for side effect management in most patients in the PEGASYS arm compared to patients in the Peg-Intron arms; in some cases, ribavirin dose reductions for patients in the PEGASYS arm were three times greater than for patients in the Peg-Intron arms. This is important because a substantial number of patients being treated for hepatitis C require their ribavirin dose to be reduced to manage side effects, and this could have an impact on the efficacy of the regimen
- The PEGASYS arm was not blinded, meaning that patients and physicians knew which treatment was being administered. Many comparative studies are blinded to ensure that bias does not compromise the results
- Erythropoietin (EPO) is a medication that is often given to treat ribavirin-related anemia and help patients maintain a higher ribavirin dose. However, physicians could only prescribe EPO after the first dose ribavirin reduction in the “IDEAL” trial. Since patients in the Peg-Intron arms generally had smaller ribavirin dose reductions, this introduces another potential bias and means those Peg-Intron patients were potentially able to maintain a higher dose of ribavirin compared to PEGASYS patients

About PEGASYS

PEGASYS was launched by Roche in 2002 and quickly became the leading treatment for patients with hepatitis C. It is indicated in combination with COPEGUS (ribavirin) for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not previously been treated with interferon alpha. Efficacy has been demonstrated in patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that are clinically stable (e.g., antiretroviral therapy not required or receiving stable antiretroviral therapy). In addition, PEGASYS in combination with COPEGUS is the first and only FDA-approved regimen for the treatment of chronic hepatitis C in patients coinfecting with hepatitis C and HIV. PEGASYS is the only pegylated interferon indicated for the treatment of adult patients with chronic hepatitis B (HBeAg positive and HBeAg negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and liver inflammation).

PEGASYS is dosed at 180mcg as a subcutaneous injection taken once a week. COPEGUS is available as a 200mg tablet, and is administered orally two times a day as a split dose. Roche has backed PEGASYS with the most extensive clinical research program ever undertaken in hepatitis C, with major studies initiated to advance treatment for hepatitis C patients with unmet needs, including patients co-infected with HIV and HCV, African Americans, patients with cirrhosis, and patients who have failed to respond to previous therapy.

Important Safety Information about PEGASYS

PEGASYS, alone or in combination with COPEGUS, is indicated for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class

A).

Alpha interferons, including PEGASYS (Peginterferon alfa-2a), may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping PEGASYS therapy (see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS and ADVERSE REACTIONS in complete product information).

Use with Ribavirin. Ribavirin, including COPEGUS, may cause birth defects and/or death of the fetus. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin causes hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen (see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS and ADVERSE REACTIONS in complete product information).

PEGASYS is contraindicated in patients with hypersensitivity to PEGASYS or any of its components, autoimmune hepatitis, and hepatic decompensation (Child-Pugh score greater than 6; class B and C) in cirrhotic CHC monoinfected patients before or during treatment. PEGASYS is also contraindicated in hepatic decompensation with Child-Pugh score greater than or equal to 6 in cirrhotic CHC patients coinfecting with HIV before or during treatment. PEGASYS is also contraindicated in neonates and infants because it contains benzyl alcohol. Benzyl alcohol is associated with an increased incidence of neurological and other complications in neonates and infants, which are sometimes fatal. PEGASYS and COPEGUS therapy is additionally contraindicated in patients with a hypersensitivity to COPEGUS or any of its components, in women who are pregnant, men whose female partners are pregnant, and patients with hemoglobinopathies (eg, thalassemia major, sickle-cell anemia).

COPEGUS THERAPY SHOULD NOT BE STARTED UNLESS A REPORT OF A NEGATIVE PREGNANCY TEST HAS BEEN OBTAINED IMMEDIATELY PRIOR TO INITIATION OF THERAPY. Women of childbearing potential and men must use two forms of effective contraception during treatment and during the 6 months after treatment has concluded. **Routine monthly pregnancy tests must be performed during this time.** If pregnancy should occur during treatment or during 6 months post-therapy, the patient must be advised of the significant teratogenic risk of COPEGUS therapy to the fetus. Healthcare providers and patients are strongly encouraged to immediately report any pregnancy in a patient or partner of a patient during treatment or during 6 months after treatment cessation to the Ribavirin Pregnancy Registry at 1-800-593-2214.

Chronic hepatitis C (CHC) patients with cirrhosis may be at risk of hepatic decompensation and death when treated with alpha interferons, including PEGASYS. During treatment, patients' clinical status and hepatic function should be closely monitored, and PEGASYS treatment should be immediately discontinued if decompensation (Child-Pugh score ³6) is observed.

The most common adverse events reported for PEGASYS and COPEGUS combination therapy observed in clinical trials were fatigue/asthenia (65%), headache (43%), pyrexia (41%), myalgia

(40%), irritability/anxiety/nervousness (33%), insomnia (30%), alopecia (28%), neutropenia (27%), nausea/vomiting (25%), rigors (25%), anorexia (24%), injection site reaction (23%), arthralgia (22%), depression (20%), pruritus (19%) and dermatitis (16%).

Serious adverse events in hepatitis C trials included neuropsychiatric disorders (homicidal ideation, suicidal ideation, suicide attempt, suicide, psychotic disorder and hallucinations), serious and severe bacterial infections (sepsis), bone marrow toxicity (cytopenia and rarely, aplastic anemia), cardiovascular disorders (hypertension, supraventricular arrhythmias and myocardial infarction), hypersensitivity (including anaphylaxis), endocrine disorders (including thyroid disorders and diabetes mellitus), autoimmune disorders (including idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, psoriasis, lupus, rheumatoid arthritis and interstitial nephritis), pulmonary disorders (dyspnea, pneumonia, bronchiolitis obliterans, interstitial pneumonitis and sarcoidosis), colitis (ulcerative and hemorrhagic/ischemic colitis), pancreatitis, and ophthalmologic disorders (decrease or loss of vision, retinopathy including macular edema and retinal thrombosis/hemorrhages, optic neuritis and papilledema). Adverse reactions reported during post-approval use of PEGASYS therapy, with and without ribavirin, include hearing impairment, hearing loss, serious skin reactions, including erythema multiforme major, and infections (bacterial, viral and fungal).

About Roche

Hoffmann-La Roche Inc. (Roche), based in Nutley, N.J., is the U.S. pharmaceuticals headquarters of the Roche Group, one of the world's leading research-oriented healthcare groups with core businesses in pharmaceuticals and diagnostics. For more than 100 years in the U.S., Roche has been committed to developing innovative products and services that address prevention, diagnosis and treatment of diseases, thus enhancing people's health and quality of life. An employer of choice, in 2007 Roche was named Top Company of the Year by Med Ad News, one of the Top 20 Employers (Science) and ranked the No. 1 Company to Sell For (Selling Power). In previous years, Roche has been named as a Top Company for Older Workers (AARP) and one of the Best Companies to Work For in America (Fortune). For additional information about the U.S. pharmaceuticals business, visit our websites:

<http://www.rocheusa.com> or www.roche.us.

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Drug Approved. Is Disease Real?

<http://news.aol.com>

By ALEX BERENSON
The New York Times

(Jan. 14) - Fibromyalgia is a real disease. Or so says Pfizer in a new television advertising

campaign for Lyrica, the first medicine approved to treat the pain condition, whose very existence is questioned by some doctors.

For patient advocacy groups and doctors who specialize in fibromyalgia, the Lyrica approval is a milestone. They say they hope Lyrica and two other drugs that may be approved this year will legitimize fibromyalgia, just as Prozac brought depression into the mainstream.

But other doctors — including the one who wrote the 1990 paper that defined fibromyalgia but who has since changed his mind — say that the disease does not exist and that Lyrica and the other drugs will be taken by millions of people who do not need them.

As diagnosed, fibromyalgia primarily affects middle-aged women and is characterized by chronic, widespread pain of unknown origin. Many of its sufferers are afflicted by other similarly nebulous conditions, like irritable bowel syndrome.

Because fibromyalgia patients typically do not respond to conventional painkillers like aspirin, drug makers are focusing on medicines like Lyrica that affect the brain and the perception of pain.

Advocacy groups and doctors who treat fibromyalgia estimate that 2 to 4 percent of adult Americans, as many as 10 million people, suffer from the disorder.

Those figures are sharply disputed by those doctors who do not consider fibromyalgia a medically recognizable illness and who say that diagnosing the condition actually worsens suffering by causing patients to obsess over aches that other people simply tolerate. Further, they warn that Lyrica's side effects, which include severe weight gain, dizziness and edema, are very real, even if fibromyalgia is not.

Despite the controversy, the American College of Rheumatology, the Food and Drug Administration and insurers recognize fibromyalgia as a diagnosable disease. And drug companies are aggressively pursuing fibromyalgia treatments, seeing the potential for a major new market.

Hoping to follow Pfizer's lead, two other big drug companies, Eli Lilly and Forest Laboratories, have asked the F.D.A. to let them market drugs for fibromyalgia. Approval for both is likely later this year, analysts say.

Worldwide sales of Lyrica, which is also used to treat diabetic nerve pain and seizures and which received F.D.A. approval in June for fibromyalgia, reached \$1.8 billion in 2007, up 50 percent from 2006. Analysts predict sales will rise an additional 30 percent this year, helped by consumer advertising.

In November, Pfizer began a television ad campaign for Lyrica that features a middle-aged woman who appears to be reading from her diary. "Today I struggled with my fibromyalgia; I had pain all over," she says, before turning to the camera and adding, "Fibromyalgia is a real, widespread pain condition."

Doctors who specialize in treating fibromyalgia say that the disorder is undertreated and that its sufferers have been stigmatized as chronic complainers. The new drugs will encourage doctors to treat fibromyalgia patients, said Dr. Dan Clauw, a professor of medicine at the University of Michigan who has consulted with Pfizer, Lilly and Forest.

“What’s going to happen with fibromyalgia is going to be the exact thing that happened to depression with Prozac,” Dr. Clauw said. “These are legitimate problems that need treatments.”

Dr. Clauw said that brain scans of people who have fibromyalgia reveal differences in the way they process pain, although the doctors acknowledge that they cannot determine who will report having fibromyalgia by looking at a scan.

Lynne Matallana, president of the National Fibromyalgia Association, a patients’ advocacy group that receives some of its financing from drug companies, said the new drugs would help people accept the existence of fibromyalgia. “The day that the F.D.A. approved a drug and we had a public service announcement, my pain became real to people,” Ms. Matallana said.

Ms. Matallana said she had suffered from fibromyalgia since 1993. At one point, the pain kept her bedridden for two years, she said. Today she still has pain, but a mix of drug and nondrug treatments — as well as support from her family and her desire to run the National Fibromyalgia Association — has enabled her to improve her health, she said. She declined to say whether she takes Lyrica.

“I just got to a point where I felt, I have pain but I’m going to have to figure out how to live with it,” she said. “I absolutely still have fibromyalgia.”

But doctors who are skeptical of fibromyalgia say vague complaints of chronic pain do not add up to a disease. No biological tests exist to diagnose fibromyalgia, and the condition cannot be linked to any environmental or biological causes.

The diagnosis of fibromyalgia itself worsens the condition by encouraging people to think of themselves as sick and catalog their pain, said Dr. Nortin Hadler, a rheumatologist and professor of medicine at the University of North Carolina who has written extensively about fibromyalgia.

“These people live under a cloud,” he said. “And the more they seem to be around the medical establishment, the sicker they get.”

Dr. Frederick Wolfe, the director of the National Databank for Rheumatic Diseases and the lead author of the 1990 paper that first defined the diagnostic guidelines for fibromyalgia, says he has become cynical and discouraged about the diagnosis. He now considers the condition a physical response to stress, depression, and economic and social anxiety.

“Some of us in those days thought that we had actually identified a disease, which this clearly is not,” Dr. Wolfe said. “To make people ill, to give them an illness, was the wrong thing.”

In general, fibromyalgia patients complain not just of chronic pain but of many other symptoms, Dr. Wolfe said. A survey of 2,500 fibromyalgia patients published in 2007 by the National

Fibromyalgia Association indicated that 63 percent reported suffering from back pain, 40 percent from chronic fatigue syndrome, and 30 percent from ringing in the ears, among other conditions. Many also reported that fibromyalgia interfered with their daily lives, with activities like walking or climbing stairs.

Most people “manage to get through life with some vicissitudes, but we adapt,” said Dr. George Ehrlich, a rheumatologist and an adjunct professor at the University of Pennsylvania. “People with fibromyalgia do not adapt.”

Both sides agree that people who are identified as having fibromyalgia do not get much relief from traditional pain medicines, whether anti-inflammatory drugs like ibuprofen — sold as Advil, among other brands — or prescription opiates like Vicodin. So drug companies have sought other ways to reduce pain.

Pfizer’s Lyrica, known generically as pregabalin, binds to receptors in the brain and spinal cord and seems to reduce activity in the central nervous system.

Exactly why and how Lyrica reduces pain is unclear. In clinical trials, patients taking the drug reported that their pain — whether from fibromyalgia, shingles or diabetic nerve damage — fell on average about 2 points on a 10-point scale, compared with 1 point for patients taking a placebo. About 30 percent of patients said their pain fell by at least half, compared with 15 percent taking placebos.

The F.D.A. reviewers who initially examined Pfizer’s application for Lyrica in 2004 for diabetic nerve pain found those results unimpressive, especially in comparison to Lyrica’s side effects. The reviewers recommended against approving the drug, citing its side effects.

In many patients, Lyrica causes weight gain and edema, or swelling, as well as dizziness and sleepiness. In 12-week trials, 9 percent of patients saw their weight rise more than 7 percent, and the weight gain appeared to continue over time. The potential for weight gain is a special concern because many fibromyalgia patients are already overweight: the average fibromyalgia patient in the 2007 survey reported weighing 180 pounds and standing 5 feet 4 inches.

But senior F.D.A. officials overruled the initial reviewers, noting that severe pain can be incapacitating. “While pregabalin does present a number of concerns related to its potential for toxicity, the overall risk-to-benefit ratio supports the approval of this product,” Dr. Bob Rappaport, the director of the F.D.A. division reviewing the drug, wrote in June 2004.

Pfizer began selling Lyrica in the United States in 2005. The next year the company asked for F.D.A. approval to market the drug as a fibromyalgia treatment. The F.D.A. granted that request in June 2007.

Pfizer has steadily ramped up consumer advertising of Lyrica. During the first nine months of 2007, it spent \$46 million on ads, compared with \$33 million in 2006, according to TNS Media Intelligence.

Dr. Steve Romano, a psychiatrist and a Pfizer vice president who oversees Lyrica, says the

company expects that Lyrica will be prescribed for fibromyalgia both by specialists like neurologists and by primary care doctors. As doctors see that the drug helps control pain, they will be more willing to use it, he said.

“When you help physicians to recognize the condition and you give them treatments that are well tolerated, you overcome their reluctance,” he said.

Both the Lilly and Forest drugs being proposed for fibromyalgia were originally developed as antidepressants, and both work by increasing levels of serotonin and norepinephrine, brain transmitters that affect mood. The Lilly drug, Cymbalta, is already available in the United States, while the Forest drug, milnacipran, is sold in many countries, though not the United States.

Dr. Amy Chappell, a medical fellow at Lilly, said that even though Cymbalta is an antidepressant, its effects on fibromyalgia pain are independent of its antidepressant effects. In clinical trials, she said, even fibromyalgia patients who are not depressed report relief from their pain on Cymbalta.

The overall efficacy of Cymbalta and milnacipran is similar to that of Lyrica. Analysts and the companies expect that the drugs will probably be used together.

“There’s definitely room for several drugs,” Dr. Chappell said.

But physicians who are opposed to the fibromyalgia diagnosis say the new drugs will probably do little for patients. Over time, fibromyalgia patients tend to cycle among many different painkillers, sleep medicines and antidepressants, using each for a while until its benefit fades, Dr. Wolfe said.

“The fundamental problem is that the improvement that you see, which is not really great in clinical trials, is not maintained,” Dr. Wolfe said.

Still, Dr. Wolfe expects the drugs will be widely used. The companies, he said, are “going to make a fortune.”

January 14th, 2007

Study Probes Why U.S. Blacks Wary of Medical Trials

<http://www.therapeuticsdaily.com/>

By Will Dunham, *Reuters Health*

WASHINGTON (Reuters) - Distrust of doctors and concern over being abused as human guinea pigs may explain why U.S. blacks have been less willing than whites to volunteer to take part in medical studies, researchers said on Monday.

Experts have known for decades that blacks are more reluctant than whites to take part in clinical trials, which are vital in testing the effectiveness of new treatment, prevention and diagnosis methods for various diseases.

But if a study of a new drug, for example, involves mostly white volunteers, there can be doubts

on whether its results are applicable to everyone.

Researchers at Johns Hopkins University in Baltimore went through the process of recruiting volunteers to take part in a mock clinical trial testing a pill to treat heart disease.

Their study involved 717 patients -- about a third black and the rest white -- at 13 medical clinics in Maryland. They found that blacks were about 40 percent less willing to participate in the mock clinical trial.

The researchers asked a series of questions to learn why people did or did not want to volunteer.

They found that 58 percent of blacks, compared to just 25 percent of whites, said they believed doctors use drugs to experiment on people without a patient's consent.

In addition, 25 percent of the blacks, compared to 15 percent of whites, expressed the belief their doctor would be willing to ask them to take part in a study even if the study might harm them. And 28 percent of blacks, compared to 22 percent of whites, said their doctors would be willing to expose them to unnecessary risks.

DISTRUST OF DOCTORS

"African American participants expressed markedly greater concerns about experiencing harm from participation in clinical trials and distrust toward medical researchers than white participants," the researchers wrote in the journal *Medicine*.

"These factors, in turn, appear to explain much of the resistance among African American persons to participate in clinical trials compared to white persons," they added.

Dr. Neil Powe, one of the Johns Hopkins researchers, said the reluctance of the blacks to volunteer may be a legacy of past abuses like the infamous Tuskegee syphilis experiment.

"That may have led to distrust of medical research, particularly by African Americans," Powe said in a telephone interview.

In that 40-year, government-sponsored experiment, hundreds of black men in Alabama with syphilis were brought into a study in which researchers withheld proper medical treatment in order to document what happens to men with untreated syphilis.

Some researchers have tried to better understand racial disparities in medicine, including the fact that blacks are more likely than whites to develop certain types of diseases as well as getting different treatment than whites.

Last week, other researchers reported that U.S. blacks continue to get inferior cancer treatment compared to whites. They looked at lung, breast, colon, rectal and prostate cancer, and found that black patients consistently were less likely than whites to receive the recommended types of treatment.

(Editing by Maggie Fox and Jackie Frank)

Three Rivers Pharmaceuticals(R), LLC Acquires Hepatitis C Drug Infergen(R) from Valeant Pharmaceuticals

<http://www.centredaily.com>

Three Rivers Pharmaceuticals

CRANBERRY TOWNSHIP, Pa., Jan. 14 — Three Rivers Pharmaceuticals, LLC finalized acquisition of the hepatitis C drug Infergen from Valeant Pharmaceuticals International (NYSE: VRX). Valeant is receiving \$91 million from Three Rivers for the procurement.

"Adding Infergen to our growing portfolio is very exciting," said Donald J. Kerrish, RPh, Three River's president and chief executive officer. "This purchase is only a beginning for Three Rivers' continuous strategy to increase its product offerings through product acquisition and internal product development of pharmaceutical therapies."

Infergen, or consensus interferon, is a bio-optimized, selective and highly potent type 1 interferon alpha originally developed by Amgen and launched in the United States in 1997. It is currently indicated as monotherapy for the treatment of adult patients suffering from chronic hepatitis C viral infections with compensated liver disease and is dosed three times per week.

Important Safety Information

Physicians and patients can obtain additional prescribing information regarding Infergen, including the product's safety profile and the box warning for all interferon alphas regarding neuropsychiatric, autoimmune, ischemic and infectious disorders, by visiting www.infergen.com

About Three Rivers Pharmaceuticals

Three Rivers Pharmaceuticals is a privately held company headquartered in Cranberry Township, Pennsylvania and focuses on specialized therapies including hepatitis C therapies. Three Rivers is the first drug company to focus on the needs of the emerging specialty market. With its unique experience and understanding of the complex challenges of treating chronic, difficult diseases, Three Rivers is a valuable partner in the healthcare community.

The company's mission is to develop, manufacture, and market the highest quality branded and generic drug products for patients with serious diseases. Three Rivers Pharmaceuticals focuses on specialized therapies because of our extensive knowledge and experience in this area. More information about the company can be found at www.3riverspharma.com.

SOURCE Three Rivers Pharmaceuticals

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New York outpatient oversight among toughest

<http://www.newsday.com>

BY RIDGELY OCHS

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With a new law that took effect yesterday, New York's oversight of outpatient facilities - including pain-management practices such as Dr. Harvey Finkelstein's - will be among the toughest in the nation, advocates and health officials said.

But some said the law fails to address ways to ensure good infection control in all outpatient settings, an issue for Long Islanders in light of the state's recent notification of more than 10,000 of Finkelstein's patients after the Dix Hills doctor's reuse of syringes led to a transmission of hepatitis C in 2004.

Experts estimate that more than half of medical practice, including surgeries and invasive procedures such as colonoscopies, take place in offices and clinics. The state has about 2,000 of these facilities, which unlike hospitals, have not been required to be accredited.

The result has been little hard data on how well the practices operate and reports of botched surgeries and disease outbreaks such as in the Finkelstein case.

The new state law requires any ambulatory surgery center that uses moderate or heavy sedation to be accredited by one of three national groups or the doctor will lose his license. The centers also will be obligated to report adverse events, including patient deaths, or any other serious or life-threatening occurrence within 30 days.

The reporting requirement began yesterday; practices have until July 14, 2009, to become accredited. Podiatrists and dentists, regulated by the state Education Department, are not included. Neither are medical offices that use only light sedation, such as Valium.

Dr. John Morley, the state Health Department's medical director of the office of health systems management, said he believed the law will "make a major difference" in office-based surgery practices.

Others agreed.

"We probably have the best legislation for this kind of thing nationwide," said Dr. Bernard Rosof, senior vice president for corporate relations and health affairs at North Shore-LIJ Health System. In 1997, Rosof chaired a committee that developed guidelines on office-based surgery. Eight years later, he chaired the committee whose recommendations led to the law signed by Gov. Eliot Spitzer in July.

Twenty-six states have some legislation on outpatient surgery and New York's is the toughest, said Dr. Alan Gold, a Great Neck plastic surgeon. Gold is also president of the American Association for Accreditation of Ambulatory Surgery, one of the groups approved to accredit

these facilities. "This is the law with the most significant degree of enforcement attached to it," he said.

To be accredited every three years by Gold's group, which has 1,100 members nationwide, the applicant must comply with a booklet full of requirements - ranging from anesthesia to safety equipment to the office layout. In an announced visit, an inspector reviews procedures. A perfect score is required before accreditation is given, Gold said. After that, the group may periodically send in unannounced inspectors.

Arthur Levin, director of the Manhattan-based Center for Medical Consumers, called the law a "huge breakthrough."

But Levin and others concede that the law, based on sedation levels, may not be broad enough to include all outpatient facilities where invasive and potentially dangerous procedures are done.

Dr. Tom McKnight of Fremont, Neb., whose wife, Evelyn, was one of 99 people who contracted hepatitis C in 2002 at an outpatient cancer treatment clinic there - the largest such outbreak ever - called the New York law "a step towards reform." But because sedation wasn't used in the clinic, "the legislation would not have helped Evelyn or any other victims," he said.

And although accreditation would make a doctor like Finkelstein show he understands good infection control, it is not clear under the law whether his infecting a patient with hepatitis C would have been reported as an adverse event, said Health Department spokeswoman Claudia Hutton. That's because, she said, he didn't realize what was happening at the time. So far, 11 of Finkelstein's former patients have tested positive for hepatitis B and nine for hepatitis C, according to the Nassau County Department of Health. The state Health Department has said it is impossible to tell whether Finkelstein's office was the source.

Sen. Kemp Hannon (R-Garden City), chairman of the Senate Health Committee, said he and Health Commissioner Richard Daines have discussed trying to find ways to ensure good infection control.

"The current [law] utilizes major accrediting agencies to ensure good practices," he said. "The next question is: Can we use something akin to that for sanitary practices, short of having to inspect 20,000 private offices?"

New rules for outpatient centers

Signed into law by Gov. Eliot Spitzer last summer, a new public health law tightens oversight of outpatient medical facilities that provide office-based surgeries. Key elements of the law:

Physicians, physicians' assistants or specialists' assistants who work at such facilities must report "adverse events," just like those who work at hospitals. Adverse events include patient deaths or unplanned transfers to a hospital.

Starting on July 14, 2009, practices performing office-based surgery must be accredited by one of three national groups.

"Office-based surgery" is any invasive procedure performed outside of a hospital in which moderate sedation, deep sedation or general anesthesia is used.

The kinds of procedures covered include: gastrointestinal endoscopy; bronchoscopy; rhinoplasty; and breast augmentation or reduction.

Proteomic profiling shown more accurate than traditional biomarkers in identifying liver cancer

<http://www.eurekalert.org>

BOSTON – As the incidence of liver cancer continues to grow-- fueled in large part, by rising rates of hepatitis C infections – so too does the need for tests to help diagnose the disease at an earlier stage. A study appearing in the January 15 issue of *Clinical Cancer Research* demonstrates that a novel mass-spectrometry based form of proteomic profiling is more accurate than traditional biomarkers in distinguishing liver cancer patients from patients with hepatitis C liver cirrhosis, particularly with regard to identifying patients with small, curable tumors. Led by researchers at Beth Israel Deaconess Medical Center (BIDMC), the study could help lead to earlier diagnostic methods – and subsequent treatments -- for liver cancer.

“Proteomics represents a potentially powerful tool for the serologic recognition of protein profiles associated with cancer,” explains co-senior author Towia Libermann, PhD, Director of the Genomics Center at BIDMC and Associate Professor of Medicine at Harvard Medical School.

“Although this particular proteomics technology, **SELDI-TOF MS** [surface enhanced laser desorption/ionization time of flight mass spectrometry] had already proven capable of identifying liver cancer in some limited studies, this was the first time that the technology was compared side-by-side with the clinical standard biomarker in a cohort of patients at risk for developing the disease,” adds Liebermann, who is also Director of the Dana-Farber/Harvard Cancer Center Proteomics Core in the Division of Interdisciplinary Medicine and Biotechnology at BIDMC.

Over a single decade, the incidence of liver cancer (hepatocellular carcinoma) increased from 1.8 to 2.5 per 100,000 patients, in large part due to a rise in the spread of hepatitis C virus.

“Hepatitis C has become a tremendous public health problem,” explains co-senior author Nezam Afdhal, MD, Director of the Liver Center at BIDMC and Associate Professor of Medicine at Harvard Medical School. “And a significant number of hepatitis C-infected patients will go on to develop liver cirrhosis.” Cirrhosis results when healthy tissue is replaced by scar tissue, preventing the liver from properly functioning. Cirrhosis itself is responsible for more than 25,000 deaths each year. But, adds Afdhal, secondarily, cirrhosis greatly increases a person’s chances of developing liver cancer.

“Each year, cirrhosis patients have a two to five percent chance that their condition will escalate to cancer,” he explains. “And the problem is that, right now, there is no reliable means of detecting liver cancer at an early stage, when surgical treatment is an option. Typically by the

time the disease is discovered, the cancer has advanced and treatment options become much more limited.”

The best hope for early detection is cancer biomarkers, serum proteins found in altered amounts in blood or other body fluids. The current biomarker for liver cancer in clinical use is alpha fetoprotein (AFP). In many cases, patients with hepatitis C undergo routine monitoring for AFP levels as an indicator of whether tumors may have developed in their livers.

But, as Libermann explains, the AFP biomarker has a number of shortcomings, including false positives and false negatives. “AFP not only fails to detect many early tumors, but it also lacks specificity. Consequently, elevated AFP levels could be indicators of not only cancer, but also of other liver diseases or even benign conditions, while on the other hand, many patients with small tumors will test negative for AFP.”

The authors, therefore, decided to evaluate the sensitivity and specificity of SELDI-TOF MS for the detection of liver cancer and to compare its effectiveness with AFP.

Examining serum samples of 92 patients – including 51 patients with liver cirrhosis and 41 patients with liver cancer, and among the cancer patients, individuals with both large and small (less than 2 cm) tumors -- by SELDI-TOF mass spectrometry, the investigators were able to identify an 11-protein signature that accurately discriminated between the cirrhosis and cancer patients, first in a training set (made up of 26 cirrhosis and 20 liver cancer patients), and then again in an independent validation set (consisting of 25 cirrhosis and 19 liver cancer patients). The resulting diagnostic value – 74 percent sensitivity and 88 percent specificity – compared favorably with the diagnostic accuracy of AFP (73 percent sensitivity and 71 percent specificity) as well as with two other biomarkers currently in clinical development for liver cancer, AFP-L3 and PIVKA-IL.

“Most strikingly,” notes Libermann, “in patients with small tumors (less than 2 cm), where AFP identified only three, and AFP-L3 and PIVKA-II only one each, the 11-protein signature correctly identified seven of eight patients at this early stage of disease.

“Biomarkers play a major role in all aspects of personalized medicine, not only in early disease detection, but also in outcome prediction and evaluation of therapeutic responses,” he adds.

“This study provides strong evidence that serum contains early detection biomarkers and supports the notion that a combination of multiple biomarkers may prove more effective than individual biomarkers for diagnosis of liver cancer, as well as other cancers.”

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This study was funded by grants from the National Institutes of Health.

In addition to Libermann and Afdhal, study coauthors include BIDMC investigators Noah Zinkin MD, and Franck Grall, PhD, (joint first authors), Killimanagalam Bhaskar, MD, Hasan Otu, PhD, Dimitrios Spentzos, MD, Brett Kalmowitz, MD, Meghan Wells, Manuel Guerrero, BSc, and John Asara, PhD.

Beth Israel Deaconess Medical Center is a patient care, teaching and research affiliate of Harvard

Medical School and consistently ranks among the top four in National Institutes of Health funding among independent hospitals nationwide. BIDMC is clinically affiliated with the Joslin Diabetes Center and is a research partner of Dana-Farber/Harvard Cancer Center. BIDMC is the official hospital of the Boston Red Sox. For more information, visit www.bidmc.harvard.edu.

Basic accord ends hepatitis C legal fights

<http://www.japantimes.co.jp/>

Kyodo News

Victims, Fukuda Get Together

The protracted legal battle waged by people who contracted hepatitis C through tainted blood products finally ended Tuesday with the signing of a basic accord by the government and lawyers representing the plaintiffs, setting the stage for lawsuits across Japan to be settled out of court.

The basic agreement is based on a law enacted Friday to offer blanket relief to people who became infected with the liver illness through contaminated blood products, including fibrinogen, that were administered to stop bleeding.

Pending suits at five district courts and five high courts will go into settlement procedures based on the accord.

Upon signing the agreement, Health, Labor and Welfare Minister Yoichi Masuzoe told the plaintiffs, "I sincerely apologize to the victims and their families as the state failed to prevent the damage from spreading."

Michiko Yamaguchi, the leader of the plaintiffs, responded: "We have finally reached this point, but there still remain many hepatitis sufferers who will not benefit from the aid. I hope the government will seek a full explanation for the hepatitis disaster and will take preventive measures."

After the signing, the plaintiffs met Prime Minister Yasuo Fukuda at his official residence.

During the meeting, Fukuda reiterated his apology and said, "I have reinforced my thoughts that a recurrence of drug-induced suffering must be prevented."

While welcoming the agreement, Yamaguchi reminded the prime minister that the government did not taken any action until the victims acted first.

"Please make this the last case," she said.

Fukuda later said at a news conference that he was happy because the patients "really looked bright" while stressing the importance of disclosing information on the risks of new medicine, although he did not elaborate.

The basic agreement will require the government to accept responsibility and offer its apologies, pay subsidies to the victims and set up a third-party panel to re-examine the infection problem. The health ministry will also hold regular meetings with the patients.

The courts will determine who is eligible for the settlement, and will make comprehensive judgments concerning people whose medical treatment records have already been disposed of by hospitals by accepting as evidence such documents as surgery records, medication instructions and statements by doctors and nurses.

The victims will receive compensation ranging from ¥12 million to ¥40 million each depending on the severity of their conditions. The number of patients entitled to the relief is likely to total around 1,000.

The lawsuits were filed starting in October 2002 by people who were administered with the blood-clotting agents during operations or childbirth from around 1970 to the early 1990s. The combined number of plaintiffs currently stands at around 200. It has been reported that some 10,000 people were infected by tainted blood products.

Lessening the Burden of Hepatitis B Virus Infection and Liver Cancer Among Asian and Pacific Islander Americans

<http://www.newswise.com>

Newswise — Fremont, CA: A research scientist at the Northern California Cancer Center, a leading, independent, population-based research organization, has recently collaborated with colleagues at the Asian Liver Center at Stanford University on two papers that demonstrate the effectiveness of culturally aligned interventions that may help reduce the disproportionate burden of chronic HBV infection and liver cancer among Asian/Pacific Islander Americans.

“Our studies show that community-based organizations, health care professionals, researchers, and the general public can work together to increase awareness and prevention of chronic HBV infection and liver cancer in the Asian and Pacific Islander community,” explained Ellen Chang, Sc.D. of the Northern California Cancer Center. “HBV testing is the key: anyone who is chronically infected with HBV should be regularly screened for early liver cancer, while anyone who is unprotected can receive a vaccine that will protect them against HBV.”

Asian Americans are proportionally the fastest growing racial group in the US and the majority are immigrants from eastern or southeastern Asia – areas with a high prevalence of chronic hepatitis B virus (HBV) infection and, consequently, high incidence of liver cancer. In these regions, the prevalence of chronic HBV infection is over 10%, compared with less than 0.5% in the US. As a result, the incidence of liver cancer among Asian/Pacific Islander Americans is over three times that of non-Hispanic White Americans.

“This work is vitally important because detection of this infection allows for routine liver cancer screening in the high-risk chronically infected population, as well as treatment using effective antiviral therapies to decrease the risk of progression to cirrhosis and liver cancer,” continued Chang. “Despite the major public health impact of liver disease, Asian/Pacific Islander American

communities have low levels of awareness and knowledge regarding HBV and liver cancer. Poor HBV-related knowledge is a barrier to the prevention, diagnosis, and management of this chronic infection. And, because chronic HBV infection usually causes no symptoms, many people who are infected don't even know they have it."

The first paper, "Building partnerships with traditional Chinese medicine practitioners to increase hepatitis B awareness and prevention" (published in *The Journal of Alternative and Complementary Medicine*), details the results of the Annual Hepatitis B Prevention and Education Symposium, conducted for traditional Chinese medicine providers and acupuncturists in California. This culturally targeted intervention developed partnerships between non-western and western health care providers to prevent chronic HBV infection and death from liver cancer among Asians and Pacific Islanders. For four years, 2004 through 2007, the organizers partnered with professional, academic and community-based groups to organize the full-day educational symposium. Over 1,000 participants attended the four symposia combined; most were born in Asia, and the majority of their patients were also Asian/Pacific Islander Americans. The symposium activities included educational lectures and games, presentation of a physician's guide to HBV management, and case studies. After attending the symposium the participants' percentage of correct answers to knowledge-based questions about hepatitis B virus infection rose from below 60% to above 75%.

The second paper, "The Jade Ribbon Campaign: A model program for community outreach and education to prevent liver cancer in Asian Americans" (published in the *Journal of Immigrant and Minority Health*), describes a culturally targeted, community-based outreach program that provided free HBV screening and education to 476 Chinese Americans living in the San Francisco Bay Area. The results of the screening showed a 13% prevalence of chronic HBV infection among the participants, whereas only 8% showed evidence of prior vaccination against the infection. Participants reported low preventive action against chronic HBV infection and liver cancer before the clinic, but after one year, 67% of those with chronic HBV infection had consulted a physician for liver screening, and 78% of all participants had encouraged family members to be tested for HBV. These results demonstrate that HBV screening, when supplemented with tailored recommendations for clinical follow-up, can lead patients to seek appropriate medical management of chronic HBV infection and screening for early detection of liver cancer.

Quick Facts about Hepatitis B virus infection:

Symptoms:

There are no symptoms of chronic HBV infection, so that's why people have to get tested. Essentially, every Asian/Pacific Islander American-- particular those born in Asia or the Pacific Islands, or those with parents born there-- should get tested.

The Vaccine:

The vaccine consists of three shots (0 months, 1-2 months, and 6 months). Getting vaccinated prevents future HBV infection.

Transmission:

HBV is transmitted through blood, not casual contact with infected individuals. The primary

routes of HBV transmission are 1) from mother to newborn at birth, 2) sexual intercourse, 3) other contact with infected blood, e.g., through shared toothbrushes or razors, but NOT through contaminated food, contaminated water, kissing, or casual contact. The greatest risk of chronic infection is at birth and during infancy/childhood/early adulthood.

The Northern California Cancer Center recommends:

- 1) Get tested for HBV infection
- 2) If you are unprotected, get vaccinated against HBV
- 3) If you are chronically infected, visit a doctor to get screened for liver cancer
- 4) Tell your friends and family members about HBV and liver cancer, and encourage them to get tested for HBV
- 5) Ask your health care provider whether he or she tests all Asian/Pacific Islander patients, especially the foreign-born, for HBV

About the Northern California Cancer Center:

The Northern California Cancer Center (www.nccc.org) is a nationally recognized leader in understanding the causes and prevention of cancer and in improving the quality of life for individuals living with cancer. The organization has been working with scientists, educators, patients, clinicians, and community leaders since 1974. NCCC is a 501(c) 3 nonprofit with 170 employees and a \$15 million operating budget.

January 16th, 2007

GB Virus C May Reduce Severity of HCV-Related Liver Disease in HIV Patients

www.medscape.com

By Will Boggs, MD

NEW YORK (Reuters Health) Jan 09 - In patients coinfecting with HIV and hepatitis C virus (HCV), the presence of GB virus C (GBV-C) is associated with a reduction in liver disease severity, according to a report in the December issue of *Gastroenterology*.

"GBV-C was associated with a significant reduction in HCV-related liver disease in the setting of HCV/HIV co-infection," Dr. Mark D. Berzsenyi from Alfred Hospital, Prahran, Victoria, Australia told Reuters Health. "If the mechanism can clearly be identified and reproduced in vitro, perhaps in the future this could form the basis of a new therapeutic approach."

Dr. Berzsenyi and colleagues assessed the influence of GBV-C infection on liver disease in 158 patients coinfecting with HCV and HIV.

There were no significant differences in HIV viral load, frequency of AIDS diagnosis, or time from HIV diagnosis to AIDS between patients with GBV-C and without GBV-C, the authors report, but CD4 counts were insignificantly higher in the active GBV-C group.

Active GBV-C viremia was associated with significant reductions in cirrhosis and decompensated cirrhosis, the report indicates, as was persistent infection with GBV-C RNA.

Along with greater CD4 count at follow-up, active GBV-C viremia was significantly associated with compensated/decompensated cirrhosis-free survival, the researchers note, but there was no association between active GBV-C and liver-related death or overall survival.

"GBV-C is thought to lead to upregulation of T-helper 1 cytokines and down-regulation of T-helper 2 cytokines, leading to an immunologic profile that is associated with an improved outcome for HIV/AIDS," the investigators say.

"Further work is planned to prospectively confirm this study with a multi-centered study," Dr. Berzsenyi said. "As well, we are currently looking at the mechanism of action and intend to expand on this work. Part of this work would be looking at the effect of GBV-C in the setting of HCV/HIV infected patients being considered for combination therapy."

"Future studies on the effect of GBV-C on HCV-related pathogenesis should include examination of the effect of GBV-C on cohorts with HCV-related and other forms of liver disease, and in HIV-infected and uninfected cohorts," Dr. Jack Stapleton from The University of Iowa and Iowa City VA Medical Center writes in a related editorial.

"This will allow determination as to whether the effect is restricted to HIV-infected people, and if this result is specific for HCV-induced hepatic injury," he explains.

Gastroenterology 2007;133:1821-1830,2042-2045.

Ribosomal S-6 Kinase Mediates Development of Liver Fibrosis

www.medscape.com

By Will Boggs, MD

NEW YORK (Reuters Health) Jan 08 - The ribosomal S-6 kinase (RSK)-C/EBP-beta phosphorylation pathway is critical for the development of liver fibrosis, according to a report in the December 26th *PLoS*.

"We are working in collaboration with other groups to develop small molecules active in this pathway," Dr. Martina Buck from University of California, San Diego, California told Reuters Health. "There is hope to cure hepatic fibrosis through the development of this and similar technologies."

Dr. Buck and Dr. Mario Chojkier used a mouse model of liver injury and fibrosis to investigate the role of RSK and phosphorylation of C/EBP-beta on Thr217 in hepatic stellate cells (HSC) in the development of liver fibrosis.

All mice with wild-type C/EBP-beta (having Thr217) developed severe liver fibrosis after exposure to carbon tetrachloride, the authors report, while mice with C/EBP-beta bearing Ala217 instead of Thr217 had minimal or no fibrosis.

Blocking phosphorylation of C/EBP-beta-Thr217 by inhibiting RSK activity also decreased the fibrotic response of the liver to chronic injury.

Mice expressing the RSK-inhibitory transgene (C/EBP-beta-Ala217) proved to be resistant to hepatotoxin-induced liver inflammation and HSC activation and proliferation.

Moreover, the investigators say, a C/EBP-beta-Ala217 peptide able to permeate cells stimulated cell death in hepatotoxin-induced activation of HSC and inhibited progression and stimulated regression of hepatotoxin-induced liver fibrosis.

Activated HSC in biopsies of human liver fibrosis showed increased expression of active RSK and C/EBP-beta Thr266 (the human equivalent of Thr217), the researchers note.

"This study suggests that blocking RSK activity inhibits fibrogenesis directly by inducing HSC apoptosis, and indirectly, by reducing liver injury and inflammation," the authors conclude. "We speculate that these findings may facilitate the development of small molecules potentially useful in the prevention and treatment of liver fibrosis."

PLoS 2007;2:e1372.

Living Donor Liver Transplant Yields Better Survival Than Deceased Donor

www.medscape.com

By David Douglas

NEW YORK (Reuters Health) Jan 07 - Compared to waiting for a deceased donor, use of liver from a living donor leads to reduced mortality, according to investigators.

"Our study confirms that the practice of living donor liver transplantation provides considerable reduction in risk of pre-transplant death to liver transplant candidates," lead researcher Dr. Carl Berg told Reuters Health.

Dr. Berg, of the University of Virginia, Charlottesville and colleagues analyzed data on 807 potential living donor recipients. They report their findings in the December issue of *Gastroenterology*.

After a median follow-up of 4.4 years, 638 had undergone liver transplant -- 389 from a living donor and 249 from a deceased donor. Ninety-nine died without transplantation and 70 were awaiting transplantation at last follow-up.

Compared to those with a deceased donor, recipients from a living donor had an adjusted mortality hazard ratio of 0.56.

In addition, the researchers determined that as centers performed more than 20 living transplants and hence gained greater expertise, the mortality hazard ratio fell to 0.35.

This reduction in transplant candidate mortality, write the investigators, "must be balanced against the risks undertaken by the living donors themselves." One report indicated that as many as 38% of donors may experience complications.

Nevertheless, concluded Dr. Berg, "the quantification of this risk reduction may now allow families to more concretely balance the benefits to the living donor liver transplant recipient with the theoretical risks to the living donor."

Gastroenterology 2007;133:1806-1813.

Percutaneous Radiofrequency Ablation Effective for Small Liver Tumors

www.medscape.com

NEW YORK (Reuters Health) Jan 03 - Radiofrequency ablation (RFA) of small hepatocellular carcinoma (HCC) is as effective when delivered percutaneously as with a surgical approach, but with lower morbidity, according to a report in the December issue of the *Archives of Surgery*.

However, surgical RFA may be preferable for larger tumors.

RFA has been shown to be 85% to 95% effective in ablating HCC 3 cm or less in diameter, the authors explain, but it remains unclear whether the percutaneous or surgical approach should be favored.

Dr. Muhammad Rizwan Khan and colleagues from The University of Hong Kong, Pokfulam, compared the outcome of RFA with the percutaneous approach or the surgical approach in 155 patients with small HCC (3 cm or less) and 73 patients with medium HCC (3.1-5 cm).

For patients with small HCC, postprocedural hepatic function was significantly worse, postoperative complications were more common, intensive care admission was higher, and overall hospital stay was longer in the surgical group, the authors report.

For patients with medium HCC, though, hepatic function, intensive care admission, and complications after RFA were comparable in the two groups. Overall hospital stay was longer in the surgical group.

Complete tumor ablation was achieved in 95% of patients with small HCC in both the percutaneous and surgical groups, the report indicates, and there was no significant difference in the development of recurrence after a mean follow-up of 19 months (36% and 41%, respectively).

Similarly, the complete tumor ablation rates of medium HCC were comparable among patients treated with percutaneous RFA (95%) and surgical RFA (92%), but there was an insignificant trend to higher recurrence rates and distant metastases with percutaneous RFA.

One-year and 3-year overall and disease-free survival rates did not differ between the two groups of patients with small HCC, the investigators say, but both survival rates were worse for patients with medium HCC treated with percutaneous RFA than for those treated with surgical RFA.

"Our study suggests that the percutaneous route is the preferred approach for RFA for small

HCC," the authors conclude. "For medium HCC, the surgical approach seems to achieve better tumor control and overall survival and may be the preferred approach if the patient can safely tolerate the procedure."

Arch Surg 2007;142:1136-1143.

Acute inflammatory demyelinating polyneuropathy associated with pegylated interferon alpha 2a therapy for chronic hepatitis C virus infection.

<http://www.peerview-institute.org>

The combination of pegylated interferon (Peg-IFN) and ribavirin is the standard of care for chronic hepatitis C virus (HCV) infection treatment. In general, common side effects related to this combination therapy are mild and are very well tolerated. However, peripheral neuropathy including demyelinating polyneuropathy related to Peg-IFN is extremely rare. We present the first case of an acute inflammatory demyelinating polyneuropathy (AIDP) associated with Peg-IFN-alpha 2a (Pegasys) after 16 wk of a combination therapy with Pegasys and ribavirin in a 65-year-old woman with chronic HCV infection. She developed tingling, numbness, and weakness of her upper and lower extremities and was hospitalized for acute neurological deficits. Her clinical course, neurological findings, an electromyogram (EMG), nerve conduction studies (NCS), muscle biopsy, and a sural nerve biopsy were all consistent with AIDP likely related to Pegasys use. The patient recovered completely with the use of intravenous immunoglobulin (IVIG) including physical therapy and neurological rehabilitation. It is very important that gastroenterologists and/or hepatologists recognize this rare neurological complication related to Peg-IFN treatment very early, since it requires a prompt discontinuation of therapy including an immediate referral to a neurologist for the confirmation of diagnosis, management, and the prevention of long-term neurological deficits.

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World J Gastroenterol. 2008 Jan 14;14(2):318-21.

Dept. of Health: Manhasset doc reused syringes

<http://www.newsday.com>

BY RIDGELY OCHS

ridgely.ochs@newsday.com

A Manhasset doctor is sending letters to 36 of his patients after the doctor reused syringes when he gave them flu shots last fall, the state Department of Health said Tuesday.

The state began investigating the practice of Dr. E. Jacob Simhaee, an obstetrician-gynecologist, in December after a complaint was filed with the Nassau County Department of Health.

The state's release of information yesterday contrasts sharply with its handling of the case of Dr. Harvey Finkelstein. It waited three years before telling the public last fall that the Dix Hills doctor had reused syringes, which resulted in transmission of hepatitis C.

"It's amazing that in this amount of time, they conducted an investigation and made a notification," said Mary Curtis, Nassau's deputy executive of health and human services. "The state and Nassau County did a great job. We've really learned from the past."

But state Sen. Kemp Hannon (R-Garden City) said a second such case perhaps warrants legislative action. "We're going to have to look into the prohibition of multiple-use vials or limiting the use of syringes to single-use syringes," he said.

As with Finkelstein, the department determined that Simhaee used a single syringe, which held up to six doses of flu vaccine, on multiple patients. Infection-control procedures require that a new syringe be used for each patient.

No diseases have been transmitted, the state said, and it said Simhaee has cooperated fully. Simhaee's patients who received the flu shot between September and December are being urged to be tested for hepatitis C, hepatitis B and HIV, and to be revaccinated against the flu.

State health department spokeswoman Claudia Hutton said yesterday's announcement reflects health commissioner Richard Daines' "concern that the public be alerted more swiftly when there is a public health issue."

More than 10,000 of Finkelstein's patients were notified that they could have been at risk and should be tested. As of Tuesday, 13 Finkelstein patients have tested positive for hepatitis B and nine for hepatitis C. The state has said it is impossible to determine whether Finkelstein's office was the source of infections.

Hutton said Simhaee was contacting the patients by phone and letter. She said the health department composed the letter, but the doctor asked to sign it.

Simhaee declined to comment Tuesday. "This is a very highly respected doctor who has been cooperating in every way with state and county officials and will continue to do so," said his attorney, Craig Schaum of Garden City.

Simhaee graduated in 1982 from the Albert Einstein School of Medicine at Yeshiva University in the Bronx, according to the state health department Web site. He did his graduate medical education at Maimonides Medical Center in the Bronx in obstetrics and gynecology, and is board certified in obstetrics and gynecology.

Hepatitis C Cases Alarm Bosnian Doctors

<http://www.balkaninsight.com>

Nidzara Ahmetasevic in Sarajevo

More than a decade after the end of the Bosnian war, there are increasing concerns about a rise in Hepatitis C cases, many of them caused by medical treatment of those injured in the conflict.

More than 50,000 people are estimated to be infected with the Hepatitis C virus in Bosnia and Herzegovina but doctors fear that number could be much higher. They say many patients may have been subjected to unsafe practices when they received blood transfusions or other medical treatment during the 1992-95 Bosnian war.

Testing blood samples for Hepatitis C has been standard practice in most developed regions of the world since 1990. It has been routine in the Herzegovina region in southern Bosnia since 1993, but in many other parts of country, blood has only been commonly screened for Hepatitis C since the end of the war.

Experts are concerned that in many cases, blood used for transfusions was not tested for the virus.

For example, data from hospitals in the city of Zenica show that out of the 63 patients treated for Hepatitis C infections in 2003, 90% had sustained injuries during the war.

Because the virus has a long incubation period, there could be a sudden increase in cases of the disease, many years after the war ended.

In December 2007, the Ministry for Veterans in the Sarajevo canton (one of the 10 cantons that make up the Bosnian Federation, one of the two autonomous entities, along with the Serb Republic) initiated a programme allowing all residents injured during the war, to be tested for viruses.

Hajrudin Ibrahimovic, a deputy in the Sarajevo canton, told Balkan Insight that since December 20, 2007, out of 460 war veterans tested for Hepatitis C, 32 were found infected with the disease.

“In Sarajevo canton, we have more than 10,000 veterans who were treated during the war in hospitals. We would like to test all of them. The final goal is to find out how many are infected so they can be treated. Sarajevo canton's Ministry of Health will pay for the whole treatment. We are expecting a huge number of such cases”, said Ibrahimovic.

Doctor Suzana Arapcic, from the Clinical Centre University in Sarajevo also warns of a high prevalence of cases.

“I do not have exact number at the moment but I can say that we have discovered many people with this virus. Of the 16 and 17 people we are able to test per week, one or two are found to be infected', she said.

Doctor Arapcic suggests that while some of those infected were drug addicts, a high proportion

of those testing positive for Hepatitis C had received wartime medical treatment.

'During the war, doctors tried hard to get everything sterilised and made safe for patients. But we are well aware that some patients were infected through blood transfusions or with unclean surgical instruments', she said.

Doctors and government ministers caution that given the nature of the virus, it is difficult to say who was infected and when.

Every person who comes for testing at Sarajevo canton's hospitals is asked about their medical history, and whether they received medical treatment during the war. But more research will need to be carried out to establish the link between infections and the war.

“We ask doctors to ask patients as many questions as is possible, and we hope that the answers could provide us with some clues. For example, let's say we have ten people infected with the virus, all of them say they were wounded during the war, in the same period of time, and they received treatment, that will give us a clearer picture”, explains Ibrahimovic.

Doctor Jelena Ravlija, from the HIV and Hepatitis Centre in Bosnia's southern city of Mostar, told Balkan Insight that a study conducted in 2006 showed that there had been an increase in Hepatitis C infections. However she added the research did not investigate a link with wartime medical treatment.

“We have to do a thorough study on this problem and to explore a possible correlation. But I have to be very honest, even then, it will be hard to establish a link”, suggests Ravlija.

The answer may lie with the Institute of Transfusions which has offices across the country. But specialists have so far refused to comment.

Research from Europe shows that most of the people who are infected with the virus do not even know they have the disease. World Health Organisation, WHO, figures from 2006 show that Hepatitis C kills around 500,000 people a year.

The organisation's office in Sarajevo claims the people most vulnerable to the disease are those who received medical treatment during the war.

The WHO together with several other organisations, is calling for initiatives like the one in Sarajevo canton, to be introduced across Bosnia, with all individuals encouraged to be screened for Hepatitis C.

But this mammoth task is compounded even further by the fact that the number of people who received wartime medical treatment, or were indeed injured in the war, remains unknown.

Nidzara Ahmetasevic is a regular Balkan Insight contributor. Balkan Insight is BIRN's online publication.

Outpatient clinic had its own hepatitis outbreak

<http://www.therapeuticsdaily.com>

Newsday (Melville, NY) (KRT)

Jan. 15--Evelyn McKnight's tale could be a TV medical drama.

The Fremont, Neb., audiologist was fighting a recurrence of breast cancer in 2002 when she learned she had hepatitis C.

She was confounded. She had none of the virus' usual risk factors: drug use, multiple sex partners, tattoos.

Then her husband, Tom, a family physician, noticed that four of his patients also had been diagnosed with hepatitis C. Around the same time, a nearby doctor noticed that two of his patients had it, too.

What they all had in common was going to the same outpatient cancer treatment center in Fremont.

Nebraska and federal investigators determined that the nurse responsible for medication infusions at the center routinely employed the same syringe to draw blood and then to draw catheter-flushing solution used for multiple patients.

It was syringe reuse in multiple vials that led to transmission of hepatitis C by Dix Hills physician Dr. Harvey Finkelstein, a case the McKnights have closely followed as they work to make syringe reuse and infection control a national issue.

Tom McKnight confronted the charismatic and beloved head of the cancer center, Dr. Tahir Javed, about the cases shortly after his wife's diagnosis. Days later, Javed left for his native Pakistan, telling McKnight that his mother there had suffered a stroke.

He left behind 99 patients with hepatitis C -- the nation's largest such outbreak. At least one person died.

Evelyn McKnight, along with 88 others, sued the cancer center. The nurse was fired and the cancer center closed by October. McKnight is using her settlement money to start a foundation called HONOR for Reform. Her goal is to make all outpatient centers meet the same infection-control standards required of hospitals.

Javed, in the meantime, lost his license to practice medicine in Nebraska and New York but became the health minister of Punjab province. A March 9, 2006, article by the Pakistan Press International Information Services noted that he was a speaker at a seminar on the hazards of reusing syringes.

Attention: Extra-hepatic manifestation of hepatitis C virus infection

<http://www.eurekalert.org>

In 1994, the team of Tchernev and Petrova from Alexandrovska Hospital in Sofia examined a female patient with liver cirrhosis caused by chronic Hepatitis C virus (HCV). They were intrigued by the patient's many extra-hepatic manifestations -- vascular lesions on the lower limbs, acute pain in the joints, intense tingling of the fingers, and extreme labor-impairing fatigue. They were also intrigued by the presence of cryoglobulins in the patient's blood. Two years later, the patient developed enlarged lymph nodes on the neck. When one of the nodes was histologically tested, the patient was found to have lymphoma.

This case spurred the interest of the investigators in the extra-hepatic manifestations and complications of HCV infection, and for over a decade they studied the links between HCV infection, cryoglobulinemia, and lymphoma.

A research article published on December 28, 2007 in the *World Journal of Gastroenterology* addresses this problem. In a study of 136 Bulgarian patients with HCV, the team of Tchernev and Petrova found 76.5% of the patients had extra-hepatic manifestations. Common manifestations were fatigue (59.6%), renal impairment (25%), type 2 diabetes (22.8%), paresthesia (19.9%), arthralgia (18.4%), and purpura predominantly of the lower limbs (17.6%). Over 37% of the patients had cryoglobulins, and 8.8% had B-cell lymphoma.

The study found positive links between the presence of extra-hepatic manifestations and age, female gender, duration of the infection, infection by transfusion of blood and blood products, and extensive liver fibrosis. Therefore, elderly women with chronic HCV and advanced liver fibrosis, who were infected by transfusion during childbirth, are at the highest risk of developing extra-hepatic manifestations of HCV infection.

The study also showed most extra-hepatic manifestations of HCV infection are associated with the presence of cryoglobulins. In particular, the risks of developing B-cell non-Hodgkin lymphoma are much higher in cryoglobulin-positive than in cryoglobulin-negative patients. In the study, 17.6% of cryoglobulin-positive patients had lymphoma, whereas only 3.5% of cryoglobulin-negative patients did.

Given the prevalence of HCV around the world, it is important for physicians to recognize the extra-hepatic signs and symptoms of HCV infection. Patients who exhibit such manifestations should be tested for HCV infection. This can lead to prompt diagnosis and effective treatment of the infection before the development of cryoglobulinemia, when treatment gives poor results or is ineffective.

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1 Reference: Stefanova-Petrova DV, Tzvetanska AH, Naumova EJ, Mihailova AP, Hadjiev EA, Dikova RP, Vukov MI, Tchernev KG. Chronic hepatitis C virus infection: Prevalence of extrahepatic manifestations and association with cryoglobulinemia in Bulgarian patients. *World J Gastroenterol* 2007; 13(48): 6518-6528

<http://www.wjgnet.com/1007-9327/13/6518.asp>

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Vertex Shares Rise After Upgrade

<http://biz.yahoo.com>

Vertex Pharmaceuticals Shares Rise As Banc of America Upgrades on Hepatitis Drug Potential

NEW YORK (AP) -- Shares of biotechnology company Vertex Pharmaceuticals Inc. rose Wednesday after Banc of America Securities upgraded the stock, citing a positive forecast for the hepatitis C drug candidate telaprevir.

Shares rose 97 cents, or 4.3 percent, to \$23.70 Wednesday. The stock has traded between \$20.71 and \$41.42 over the last 52 weeks.

Banc of America analyst William Q. Sargent upgraded the stock to "Buy" from "Neutral" and raised the price target to \$34 from \$29, citing increased confidence that upcoming study results will drive shares higher.

The company's key drug candidate is telaprevir. Positive results from a midstage study could be released in the second quarter, according to the analyst. Sargent also expects the Food and Drug Administration to approve late-stage studies for the drug candidate.

"Telaprevir's market leadership may be under-appreciated," he said, in a note to investors, adding that recent discounts to Vertex shares have created a buying opportunity for investors.

Cambridge, Mass.-based Vertex faces competition from Schering-Plough Corp., which is conducting midstage studies on its hepatitis C drug candidate boceprvir. Results are expected later this year. InterMune Inc., meanwhile, is still in the early stages of development for its experimental drug ITMN-191.

Based on data already available for telaprevir, Sargent said, the drug should be able to clear hepatitis virus more effectively than current treatments, and may even receive a quicker review process by the Food and Drug Administration. Despite that possibility, he shifted expectations for approval to early 2011 from late 2010.

Elsewhere, on Tuesday Robert W. Baird analyst Thomas Russo initiated coverage on Vertex with a "Neutral" rating and \$25 price target, saying telaprevir has multi-billion dollar potential and will be adopted quickly if approved.

Analysts expect Vertex to provide an update on its late-stage study design for telaprevir Feb. 11.

Lazard Capital Markets analyst Terence Flynn reaffirmed a "Sell" rating with a \$16 price target for Vertex while touting a "Buy" rating and \$30 price target for InterMune.

He said telaprevir's launch will most likely occur after 2010, and initial details show the late-stage study design could be more cumbersome than initially expected. InterMune, meanwhile, will likely successfully develop a twice-daily dosing schedule for ITMN-191, he said. The company has been working on both twice-daily and three-times per day dosing.

Shares of Brisbane, Calif.-based InterMune rose 37 cents, or 2 percent, to \$19.09, while shares of Kenilworth, N.J.-based Schering-Plough fell 29 cents, 1.2 percent, to \$23.49.

What is the more suitable for early detection of low abundant lamivudine-resistant mutants?

<http://www.physorg.com>

Lamivudine is an effective antiviral agent for treatment of patients with chronic hepatitis B and advanced liver diseases. However, long-term lamivudine monotherapy leads to the emergence of lamivudine-resistant hepatitis B virus (HBV) mutants in some patients chronically infected with HBV. Sensitive methods for early detection of lamivudine-resistant mutants will help physicians make clinical decisions in treating patients with HBV infection.

To date, many assays have been used for detection of lamivudine-resistant mutants in patients with Hepatitis B. Differences in sensitivity, specificity, cost, and time required, exist in these methods. Real-time PCR is able to quantitatively detect a small portion of resistant mutants in HBV populations and ligase detection reaction (LDR) is a newly developed method for detection of low abundant mutants in the background of wild-type HBV. However, there are no studies which have compared the clinical performance of the two methods.

A research article to be published on January 7 in the *World Journal of Gastroenterology* (volume 14, issue 1) addresses this question. It compared LDR and real-time PCR for detection of low abundant YMDD mutations in mixed plasmids and serum samples from 52 lamivudine treated patients. Time required and reagent cost for both assays were evaluated. The research was conducted carefully by an experienced team of investigators.

The article suggested both methods are sensitive and inexpensive for detection of YMDD mutation; but LDR is more sensitive than real-time PCR. The results obtained with both methods were completely concordant in all serum samples. LDR was able to detect as low as 0.01% (100 copies/mL) of YIDD plasmid, while real-time PCR only detected 0.1% (1000 copies/mL) of YIDD plasmid in the background of YMDD plasmid. In addition, the cost of LDR is slightly lower than that of real-time PCR.

However, real-time PCR is much more rapid and requires less manual work than LDR. The total assay time for LDR and real-time PCR was 4.5 and 2.5 h, respectively. Another advantage of the real-time PCR method is it is able to calculate the ratio of mutants to total virus in samples. This will be useful in clinical studies on the dynamics of resistant mutants during lamivudine therapy.

Source: World Journal of Gastroenterology

Liver-gender disruption makes men more vulnerable to liver cancer

<http://www.thaindian.com>

Washington , Jan 16 (ANI): In a study of mice, researchers at the Massachusetts Institute of Technology, have discovered that the cause behind men's susceptibility to liver cancer is the initiation of an unpredictable gene profile termed liver-gender disruption.

They said that there's a fundamental difference in the way males and females respond to chronic liver disease at the genetic level, and this makes men more prone to liver cancer.

The study was led by Arlin Rogers, an MIT experimental pathologist, and a principal research scientist in MIT's Division of Comparative Medicine.

This is the first genome-wide study that helps explain why there is such a gender effect in a cancer of a nonreproductive organ, where you wouldn't expect to see one, he said

Men develop liver cancer at twice the rate of women in the United States and in Asia , the rate for men can be eight or 10 times that for women. Liver cancer is the fifth most common cancer in the world and the third-biggest killer.

It's an epidemic waiting to happen, said Rogers .

According to the researchers, Male and female livers are inherently different mainly due to the differences arising during puberty when male livers are exposed to periodic bursts of growth hormone, thereby prompting male livers to express different genes than female livers. This explains why men and women react differently to certain antibiotics and other medications.

Mice also have higher liver cancer rates among males and thus the researchers infected the mice with *Helicobacter hepaticus*, which produces the same hepatitis symptoms characteristic of human hepatitis B and C.

Healthy males and females both in humans and mice, can respond to acute toxins and other stresses. However, the male liver is not very well equipped to cope with the chronic inflammation triggered by certain infectious agents.

Thus on developing chronic hepatitis some masculine liver genes were upregulated and others were turned off in male mice. Some feminine genes were also reactivated at the same time. This resulted in an unpredictable gene profile termed liver-gender disruption.

There's no rhyme or reason to it. There's just a complete scrambling of masculine and feminine genes, said Rogers .

On mapping the sex-specific genes, intimate associations with inflammatory pathways were found. In males with chronic hepatitis, some gender-specific genes were overexpressed and others underexpressed, the liver was unable to maintain normal metabolic function and cancer emerged in a significant number of the animals.

It was suggested that adult females are less susceptible to liver-gender disruption as there is no requirement for the active signaling needed to maintain a masculine gene profile.

Rogers said that due to the female liver following the default developmental pathway, a greater disturbance is needed to initiate the cancer process.

The scientists hoped that castrating male mice at one year of age when they had chronic hepatitis, but not cancer, would have a protective effect. Some mice were also given a powerful androgen to examine whether it would promote tumors.

None of the treatments had any effect, indicating that male sex hormones like testosterone do not promote liver cancer in adults directly.

These results may have implications in cancers of other organs, such as the stomach and colon, also associated with chronic inflammation and are more common in men.

The study appeared last month in the journal Cancer Research. (ANI)

January 17th, 2007

Number of Hepatitis Cases Climbs in Southern West Virginia

<http://www.statejournal.com/>

Story by Jessica Lilly

Officials say it's because of a rise in IV drug users in the region.

BECKLEY -- Hepatitis is on the rise in southern West Virginia according to health experts.

Officials say there is a link between the amount of IV drug users and the disease.

Brian Bell is an epidemiologist.

He says the number of hepatitis B cases reported is on the rise.

In 2002 there were 9 cases reported, in 2006 there were 42.

Those numbers are expected to continue to climb.

Bell says the number of cases is rising because there are more needle-drug users in the area, and because there are improved methods for monitoring the illness.

He says Hepatitis B is treatable.

There is a vaccine for Hepatitis B, but there is no vaccine for Hepatitis C.

Kathy Armentrout is the associate director at FMRS Health Systems. The clinic offers group and individual counseling for recovering addicts. Armentrout says there has also been an increase in

the number of people coming for counseling that are addicted to an IV drug or shooting up, [m]any of them are dealing with Hepatitis B.

Health experts say Hepatitis B is more contagious than HIV because the virus can survive outside of the body for a month. FMRS helps low income people in need of help.

For more information you can call them at 256-7100.

January 18th, 2007

Innogenetics says US court confirms Abbott infringed Hepatitis C virus patent

<http://www.forbes.com>

BRUSSELS (Thomson Financial) - Innogenetics said the United States Court of Appeals for the Federal Circuit last night confirmed the US District Court's finding that Abbott Laboratories infringed the biopharmaceutical group's patented Hepatitis C virus genotyping technology.

The Federal Circuit also upheld the jury's finding that Abbott pay Innogenetics damages for infringement and sanctions for making a 'baseless claim against Innogenetics', estimated to total approximately 10 mln usd.

Innogenetics sued Abbott in 2005.

simon.zekaria@thomson.com

Treatment of Hepatitis C Reduces Incidence of Non-Hodgkin's Lymphoma

<http://professional.cancerconsultants.com/>

Researchers from Japan have reported that viral elimination in hepatitis C virus (HCV) infected patients reduces the incidence of non-Hodgkin's lymphoma (NHL). The details of this study appeared in the December, 2007 issue of the *American Journal of Medicine*.

Hepatitis C affects approximately 170 million individuals worldwide. Following acute infection, the virus persists in many patients and a minority of patients develop chronic disease. Chronic hepatitis can progress slowly over many decades to chronic active hepatitis and cirrhosis, ultimately leading to end-stage liver disease or hepatocellular carcinoma. Studies from other countries, but not from the United States, have also shown an increased incidence of NHL in patients with HCV infection. Some researches suspect that this correlation can only be observed in populations where HCV is highly prevalent.

The current study was carried in 501 patients with HCV infection who had never received interferon and 2,708 patients who had received interferon. These authors reported that by one year, 0.6% of untreated patients had developed NHL which by 5 years had increased to 2.3% and

by 10 years to 2.6%. In contrast, there were no cases at 5, 10 and 15 years for the 1,048 patients with HCV infection who had sustained virologic response. The remaining patients who were treated and had persistent viral infection had an incidence of NHL of 0.4% at the fifth year, 1.5% at the tenth year and 2.6% at the fifteenth year.

Comments:

These data support the concept that treating HCV infection aggressively can reduce the incidence of NHL.

Reference:

Kawamura Y, Ikeda K, Arase Y, et al. Viral elimination reduces incidence of malignant lymphoma in patients with hepatitis C. *The American Journal of Medicine*. 2007;12:1034-1041.

The Good Times Roll for Pharmasset

<http://www.fool.com/>

Brian Lawler

The award for best announcement from a development-stage drugmaker at the JPMorgan health-care conference goes to ... Pharmasset (Nasdaq: VRUS)! Since last week's conference, when the company announced results from a phase 1b study of its hepatitis C virus (HCV) compound, shares of Pharmasset have more than doubled.

With so much other pharma news and earnings guidance out there, I didn't have time to cover the data Pharmasset announced in conjunction with JPM last week. But the clinical trial results that Pharmasset released for its potential HCV polymerase inhibitor, **R7128**, were nothing short of excellent.

In a 50-person phase 1 study, in combination treatment with Roche's Pegasys, the highest dosage of R7128 was able to lower the amount of HCV to undetectable levels in 85% of genotype 1 patients after four weeks. (Genotype 1 is the most common subtype of HCV in North America.) Compare these results to the 79% of patients that Vertex Pharmaceuticals' (Nasdaq: VRTX) telaprevir was able to bring down to undetectable levels after four weeks in its Prove 1 study -- as well as the data that other drugs, like ViroPharma's (Nasdaq: VPHM) HCV compound, have produced -- and you can see that Pharmasset has a very exciting drug candidate on its hands with R7128.

Four weeks of testing is usually too early for any derailing safety signals to pop up, and Pharmasset did note that there were no serious adverse events during the study. We'll have to wait until the data is presented at a scientific conference for more details on the safety and efficacy data, though.

The thousand-dollar question for investors is: With shares of Pharmasset up another 17% yesterday, are they still a value, or have they reached excessively optimistic, overvalued levels? If R7128 were the leading nucleoside polymerase inhibitor on the block, then I'd have no qualms about Pharmasset's \$720 million market capitalization, but R7128 isn't even Roche's top hepatitis C polymerase inhibitor. That distinction goes to Roche's internally developed R1626, which

produced undetectable levels of HCV in 81% of patients after four weeks in a phase 2a study that that was similar to Pharmasset's.

Roche has worldwide rights to Pharmasset's R7128, with Pharmasset retaining certain co-promotion rights in the United States. If Roche gets into the enviable position of having two top HCV polymerase inhibitors, it will undoubtedly hamper sales of R7128, unless the drug differentiates itself in its safety or efficacy profile from R1626. Surely, Roche wouldn't do anything to breach its collaboration agreement with Pharmasset, but it's not hard to figure out that Roche would prefer to take in 100% of revenue from its own drug, rather than having to give up revenue to Pharmasset.

With \$70 million in the bank at the end of September, and its share price bolstered by these recent trial results, Pharmasset will likely face a dilutive financing to bulk up its balance sheet in the coming weeks or months.

The risk that R7128 will be eclipsed by a drug from its own partner is definitely worth watching out for. But Pharmasset does have other valuable pipeline assets, and it doesn't deserve to be struck with the "overvalued" label yet, considering the price the market is awarding to exciting new anti-hepatitis C molecules.

Philippines orders Novartis to pull anti-arthritis drug

<http://www.therapeuticsdaily.com/>

MANILA, Jan 18, 2008 (AFP) - Philippine health regulators on Friday ordered Swiss pharmaceutical giant Novartis to pull the painkiller Lumiracoxib from the market amid fears the drug could cause liver damage.

The health department's Bureau of Food and Drugs ordered Novartis Healthcare Philippines Inc. to "immediately initiate a product recall and cease and desist from further importing, distributing, or selling **Lumiracoxib (Prexige)**" tablets.

A bureau advisory said it has "determined that the risks of Lumiracoxib-containing medicines are greater than their benefits," citing "reports of cases from abroad concerning potential serious liver-related side effects."

The anti-inflammatory drug is used to treat symptoms of osteoarthritis and dysmenorrhea as well as in dental and orthopaedic surgery, the bureau said.

"Patients who are using Lumiracoxib (Prexige) are advised to stop taking the drug and to immediately consult their physicians for information regarding their alternative treatments," the advisory added.

A spokeswoman for bureau director Leticia Gutierrez told AFP: "Novartis is in the process of recalling the drug from its distribution outlets."

She added that the bureau had no data on the number of people using the drug in the country and

there were no reports of any patients showing the same symptoms as those reported in other countries.

Novartis announced in November that Prexige had been suspended from sale and marketing in Britain and Germany amid fears it can cause liver damage.

Austria, Australia and Canada have taken similar steps, while Prexige has not been approved for sale in the United States.

cgm/kw/dan Health-Philippines-drug-Novartis

Sen. Brown Requests Probe of FDA's Fast-Track Drug Approvals

<http://www.therapeuticsdaily.com/>

Sen. Sherrod Brown (D-OH) wants Congress' research arm to take a close look at FDA's program that grants "Fast Track" status to certain drug applications, the Cleveland Plain Dealer reported Jan. 10. According to the newspaper, Brown has asked the Congressional Research Service to investigate whether Fast Track is fulfilling its goal of getting important drugs to patients who need them, or simply bolstering drug makers' profits.

According to the Plain Dealer, companies' stock prices rise an average 10 percent when they announce that FDA has granted one of their applications Fast Track status.

Fast Track was created in the 1997 FDA Modernization Act, with help from Sen. Edward Kennedy (D-MA).

Brown sits on the Senate health committee.

January 18th, 2007

Hemophiliac Society says tainted blood victims will be inflamed by dropped charges

<http://www.570news.com>

Gregory Bonnell

THE CANADIAN PRESS

HAMILTON - All remaining charges in the tainted blood scandal against Dr. Roger Perrault, former director of the Canadian Red Cross, were dropped Friday after the prosecution found there was no likelihood of conviction.

Six nuisance charges against Perrault, who was at the centre of the blood scandal of the 1980s, remained after he was acquitted in October 2007 of criminal negligence causing bodily harm.

The Superior Court judge at that time said the allegations against Perrault were not only unsupported, they were disproved.

On Friday, Crown prosecutor John Pearson said a review of the remaining charges against Perrault had been conducted and as a result "we have concluded that there no longer remains a reasonable prospect of conviction in this case."

More than 1,000 people were infected with HIV after receiving tainted blood products and another 20,000 people contracted hepatitis C in one of the biggest public health scandals in Canadian history.

After Friday's decision, Perrault's lawyer, Eddie Greenspan, said his client should never have been charged.

"Not every tragedy requires a scapegoat," Greenspan said.

"Dr. Perrault should have never been named for the tainted blood crisis."

John Playter, of the Canadian Hemophiliac Society, said he was extremely disappointed in the Crown's decision to withdraw the charges.

He said the decision would only inflame the passions of the victims and encourage them to look even harder for scapegoats.

"There are a lot of people out there that are hurting as a result of what happened," Playter said.

"They are going to walk away from this very confused, very upset with a lot of questions and it's going to generate a lot of anger.

"People can say the system has failed them once again."

Perrault was stoic both in court and outside and did not offer any words of reaction.

The common nuisance charges stemmed from an allegation he endangered the public for failing to properly screen donors, implement testing for blood-borne viruses and warn the public of danger regarding both hepatitis C and HIV.

Plan in works to cover uninsured

<http://www.charleston.net>

By Jill Coley (Contact)

The Post and Courier

Diane West's uninsured brother, William West, was hospitalized a week ago, suffering complications from a life-threatening inflammation of the pancreas. The 50-year-old, who also had hepatitis C and diabetes, died early Thursday.

Now, Diane West and her sisters are gathering in Cross to mourn. When it comes time to pay his medical expenses, they will throw up their hands, she said.

"I guess they're billing, but I don't know," said West, a resident of Moncks Corner.

Tri-county area hospitals provided more than \$68 million in services that patients couldn't pay for during 2006, the South Carolina Hospital Association estimated. Statewide, the amount topped \$660 million.

More than half of that cost was shifted to insured residents and employers who provide insurance. In 2005, the average American family paid \$922 more per year in premiums to help cover the care provided to the uninsured, the hospital association said.

In a matter of weeks, the Covering Carolina Collaborative is expected to unveil its plan to cover the uninsured. The collaborative — comprising the state hospital association, S.C. Medical Association, S.C. Chamber of Commerce and S.C. Managed Care Alliance, an insurer's group — has met since early 2007.

The plan will address affordable health care coverage by using different approaches depending on the population, said hospital association spokeswoman Patti Smoake.

"For people at a certain level, market options do not help," Smoake said. "Some can't afford any premiums." Solutions expected to be mentioned in the plan include expanding Medicaid and tax credits.

At a glance

Sixteen percent of South Carolinians, or 667,000 people, went without health insurance from 2004 through 2006, according to a U.S. Census Bureau report. The state ranks above the national average of 15.3 percent of the population, or 45 million.

Carolyn Thiedke represents South Carolinians for Universal Health Care, a group that favors a single-payer system, similar to those in Canada and France.

"One of the reasons our health care system is so expensive is this really complex insurance system," Thiedke said. "Any proposal that tries to work within that system will ultimately fail." Plans that call for vouchers and tax credits continue to work within the private insurance system, she said.

South Carolinians for Universal Health Care, which is seeking nonprofit status, is creating a plan to present to the Legislature in the next year and a half, Thiedke said.

"Right now in South Carolina, your health is your individual responsibility," said Lynn Bailey, a Columbia-based health care economist affiliated with the universal health care group. "You've got to figure out how to take care of and how to pay for it."

More than 115,000 of those without health coverage in the state are children, records show. The third edition of the Uninsured Children in the South, a report released this month from University of South Carolina's Southern Institute on Children and Families, found that 46 percent of the nation's uninsured children reside in the South.

Institute President Nicole Ravenell said she would welcome an expansion of coverage. The Legislature voted last year to increase the eligibility level for the State Children's Health Insurance Program from 150 percent to 200 percent of the federal poverty level. But the expansion has yet to be enacted.

Still, a lot can be done under current rules, she said. Reducing barriers to applying for assistance and educating people about what's available can help. "In South Carolina, there's very little outreach of enrolling in programs. Our goal is to make eligible people get enrolled."

West said her brother didn't have the best work history and struggled with alcoholism, but, she asked, is that a reason he should go without a safety net?

Before his death, the family worried how they would pay for the \$400-a-month medicine to keep him alive. "Everyone should have access to health care. I truly believe that, especially in this country," she said. "I thought we heard all this before. I thought we figured this out."

If you go

South Carolinians for Universal Health Care will meet at 10 a.m. Saturday at Circular Congregational Church, 150 Meeting St.

The group is interested in finding solutions for the increasing number of people without health coverage.

For more information call Carolyn Thiedke at 883-9583.

Reach Jill Coley at 937-5719 or jcoley@postandcourier.com.