

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Jan 10, 2009

Cadaver Livers with High Steatosis Do Poorer for HCV-Related Cirrhosis

<http://www.medpagetoday.com>

By Kristina Fiore, Staff Writer, *MedPage Today*

Reviewed by Robert Jasmer, MD;

Associate Clinical Professor of Medicine, University of California, San Francisco

CORDOBA, Spain, Jan. 9 -- Higher levels of hepatic steatosis in donor livers correspond to poorer outcomes for transplant patients with cirrhosis from hepatitis C virus infection, researchers here said.

Patient and graft survival significantly decreased with degree of steatosis (P=0.008 and P=0.012, respectively), Ruben Ciria, M.D., of Reina Sofia University Hospital here, and colleagues reported in the January issue of *Liver Transplantation*.

And HCV recurrence was earlier, more frequent, and more severe among these patients (P=0.042), the researchers said.

"Our results show a direct relationship between marginal donors, graft steatosis, and more frequent, more severe, and earlier viral recurrence after orthotopic liver transplantation for HCV-related cirrhosis," the researchers said.

They said that recent studies have shown survival rates among transplanted HCV cirrhosis patients have been falling. A number of factors could be contributing to this decline, they said, but these have not been widely studied.

One possible explanation is that the limited number of available liver donors has led to the increased use of marginal livers that don't meet optimal criteria.

So to assess the influence of donor graft steatosis on outcomes including patient survival, graft survival, and viral recurrence, the researchers analyzed 120 patients who had a liver transplant as a result of HCV cirrhosis from 1995 through 2005 at Reina Sofia University Hospital (62.5% male, mean age 51).

Donor steatosis was categorized as absent (0% to 10%), mild (11% to 30%), moderate (31% to

60%), or severe (>60%).

Patient survival significantly decreased with the degree of hepatic steatosis, the researchers said. Those who received a liver with steatosis levels lower than 30% had a survival rate of 66% at three years, compared with 47% for those who received a liver with steatosis levels of 30% or more (P=0.008).

Graft survival also decreased significantly with the degree of fatty content. For those transplanted with steatosis-free livers, survival at three years was 72%. Survival was 58% for those transplanted with mildly steatotic livers and 43% for those with moderate steatosis. Patients transplanted with severely steatotic livers had a survival rate of 42% at three years (P=0.012).

In a multivariate analysis, the only other statistically significant predictors of graft survival were cold ischemia time greater than 12 hours (P=0.0001) and donor age greater than 55 (P=0.048).

The researchers also found an increased risk of earlier and more frequent viral recurrence associated with donor graft steatosis (P=0.042).

The severity of viral recurrence was greater for patients who received more steatotic livers. For example, at 12 months, 40% of patients given a liver with steatosis of 30% or more had fibrosis scores higher than two, compared with 17% of patients given a liver with steatosis less than 30% (P=0.035).

The researchers compared these findings to 87 patients with end-stage alcoholic liver disease who had a liver transplant during the same time period.

Overall survival at 12 months for these patients given a liver with steatosis of 30% or more was 81%, compared with 63% for the hepatitis C transplant patients.

"These results clearly show the higher impact of donor steatosis on graft survival in [hepatitis C] recipients versus non-[hepatitis C] recipients," the researchers said.

They added that what constitutes a "marginal donor" is not the same for all transplant surgeons, so the definition of a marginal graft will continue to vary between centers "until reliable parameters are available for prospectively predicting early graft function."

They concluded that "further multicenter studies and a global consensus may be necessary to finally assess if the use of expanded criteria grafts is safe for HCV-positive recipients and if the organ allocation system needs to be changed for this cohort of patients."

In an accompanying editorial, Nevin Yilmaz, M.D., and Mitchell L. Shiffman, M.D., of Virginia Commonwealth in Richmond, said they were concerned with the study's conclusions.

They said there was not enough data on the patients with alcohol-induced cirrhosis to be sure the populations were comparable.

They were, however, "intrigued" by the finding that a combination of donor graft steatosis and a

prolongation in cold ischemic time was associated with severe reperfusion injury.

"We strongly suggest that cold ischemia time should be limited when the donor graft contains greater than 30% steatosis and that such grafts should be used only with caution for patients with chronic HCV infection."

Jan 11, 2009

Using Math To Understand Hep. C: Patterns Paint Picture Of Who Will Respond To Treatment

<http://www.sciencedaily.com>

ScienceDaily (Jan. 12, 2009) — Genetic patterns are like the tea leaves in the bottom of a cup for predicting which patients are likely to respond to medical therapy for life-threatening viruses such as hepatitis C, Saint Louis University researchers have discovered.

"We identified mathematical patterns, which are called 'covariance networks,' to analyze the sequence of proteins in the genes or 'genetic patterns' of hepatitis C virus in two groups of patients – those who responded to and those who resisted traditional therapy," said John Tavis, Ph.D., professor of molecular and microbiology at Saint Louis University and a lead author of the paper.

"What we found will allow a doctor to predict whether or not a medication will work in a patient."

Similar covariance network analysis could tell us more about other RNA viruses, such as HIV or influenza virus, Tavis said.

About 3.8 million Americans are infected with hepatitis C, which is spread by blood-to-blood contact and can cause advanced scarring – or cirrhosis – of the liver, and induce liver cancer or liver failure. Hepatitis C causes the deaths of between 10,000 and 12,000 Americans each year.

Patients with hepatitis C typically are treated with a 24- to 48-week course of two powerful drugs – pegylated interferon and ribavirin, Tavis said. The therapy, which can cause patients to "feel like they have a very bad case of the flu for a year," clears the virus from about half of the patients but fails in the others. Scientists are baffled as to why it works in some patients, but not others.

Interferon is part of the body's natural defenses against viruses, and it triggers multiple protective mechanisms. But the hepatitis C virus actively fights back against the effects triggered by interferon.

"The body's interferon responses and the virus' counter-responses are like evenly-matched boxers -- about half of the time during therapy the virus wins, and in about half of the time the body wins," Tavis said.

Tavis and his collaborators, Rajeev Aurora, Ph.D., and Maureen Donlin, Ph.D., used a mathematical model to draw a map of the viral genome of 94 hepatitis C patients who responded

and did not respond to standard therapy.

They found a complex web of amino acid interactions in the viral proteins that resembled an airline map, with amino acid hubs that linked to many other amino acids in much the way that certain cities are centers of activity for incoming and outgoing flights.

"The hubs may be valuable targets for new antiviral drugs," Tavis said.

The team also identified "subnetworks" that are always associated with the failure of therapy, which they believe are "biomarkers" that can help predict whether standard hepatitis C therapy will be effective.

He suggests scientists could design a test to see if the viruses infecting these patients have these genetic characteristics to determine whether or not standard hepatitis C therapy is likely to work.

"The side effects of the medicines to treat hepatitis C are terrible," Tavis said. "Why beat on a patient for a year if the treatment isn't going to work anyway?"

"On the other hand, if we know the medicine is likely to work, we can coax patients to stick with the therapy. It would help doctors to positively support their patients through trying times."

In addition, hepatitis C therapy is very expensive, with a course of treatment costing up to \$30,000. A custom test that determines whether a patient would benefit from the treatment could be developed for about \$100 per sample and given to patients before the standard treatment is prescribed, Tavis said.

"If the test shows the treatment won't work, physicians could counsel against interferon-based therapy, avoiding tens of thousands of dollars in expenses and painful side effects for the patient," Tavis said. "It's wasteful to spend millions of dollars on medicine that won't work."

These findings are published in the Dec. 22 early online issue of the *Journal of Clinical Investigation*.

Jan 12, 2009

Hep C inquiry chairman appointed

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

A chairman has been appointed to lead a public inquiry into the deaths of two people who contracted Hepatitis C through NHS blood products.

Lord Penrose will chair the probe into how Eileen O'Hara and Rev David Black contracted the virus while in NHS care.

It follows complaints by relatives of the victims over the length of time it has taken to start the inquiry.

The Scottish Government said the withdrawal of the original chair, judge Lady Cosgrove, had

led to the delay.

Health Secretary Nicola Sturgeon told the Scottish Parliament the inquiry will be known as the Penrose Inquiry.

She said: "I have every sympathy with those who have suffered or lost loved ones as a result of Hepatitis C or HIV infection through NHS treatment with blood or blood products.

"I hope the Penrose Inquiry can provide answers and the closure which I know they so desperately want.

"This inquiry will also ensure that all possible lessons are learned to prevent such a tragedy occurring again."

Examining documents

Lord Penrose and a fully-staffed inquiry team are in place. Lord Penrose has indicated he will begin by examining documents, which date back 20 years and, due to the volume involved, it is expected to take some time.

Mrs O'Hara and Mr Black died in 2003 after contracting Hepatitis C through blood transfusions or blood products supplied by the NHS.

Last February, Court of Session judge Lord Mackay ruled that their relatives had the right to expect a reasonably prompt inquiry into their deaths.

He said: "Since the deaths of Mrs O'Hara and Mr Black, both the lord advocate and the Scottish ministers have acted in a manner incompatible with the European Convention of Human Rights of the deceased."

Lord Mackay quoted article two of the convention, which states that "everyone's right to life shall be protected by law".

He quashed the lord advocate's decision not to hold Fatal Accident Inquiries into the deaths and also referred to ministers' refusal at the time to hold a full public inquiry into the general issue of infections through NHS blood products.

After this ruling, Health Secretary Nicola Sturgeon said she would honour an SNP manifesto promise to hold a public inquiry into how NHS patients were infected during the 1970s and 1980s.

Lady Cosgrove was originally appointed to head the inquiry, but she stepped down due to personal reasons.

Mrs O'Hara and Mr Black were among more than 4,000 people who became infected with the virus during the 1980s, before effective screening.

The Scottish National Blood Transfusion Service did not introduce any Hep C screening test for blood donations until 1991.

Lord Penrose also led an inquiry into the collapse of mutual life insurer Equitable Life, which reported in 2004.

Frank Maguire, the lawyer representing both families, criticised the proposed powers of the inquiry and said they were considering further legal action to force the creation of a joint Scottish/UK inquiry.

Mr Maguire said the Penrose Inquiry would have "no power to require the evidence of witnesses from UK departments, including the Department of Health nor will it have power to require them to produce all and any relevant documents".

He added: "That means the families have absolutely no assurance that the inquiry will have the powers it requires to get at the truth."

Mr Maguire went on: "We believe the family's rights under Article 2 of the European Convention on Human Rights would only properly be respected with an inquiry set up jointly between the Scottish Government and the UK Government."

InterMune Up Despite So-So Hep C Data

<http://www.thestreet.com>

Adam Feuerstein

SAN FRANCISCO -- InterMune(ITMN Quote - Cramer on ITMN - Stock Picks) has moved forward with development of a new hepatitis C drug, dubbed **ITMN-191**, on the premise that it will be more potent and more convenient to administer than a similar drug from Vertex Pharmaceuticals(VRTX Quote - Cramer on VRTX - Stock Picks).

But new data released Monday morning on ITMN-191 doesn't completely live up to that billing.

A 600 mg dose of ITMN-191 given twice daily and combined with the current standard of care therapy for hepatitis C reduced the amount of virus below detectable levels in 13% of patients treated for 14 days.

Using a less stringent measure of efficacy, 75% of these patients had no detectable virus in their system. InterMune reported the new data on ITMN-191 ahead of the start Monday of the J.P. Morgan Healthcare Conference.

InterMune said it was pleased with the data and that the company and partner Roche plan to move ahead with new ITMN-191 studies in the second quarter. However, Wall Street's biotech investors never evaluate hepatitis C drugs in a vacuum, and in this case, Monday's ITMN-191 data doesn't stack up very well against Vertex's telaprevir.

In a similar 14-day "triple combination" study done in 2006 by Vertex, 25% of telaprevir patients had undetectable levels of virus in their system. That number jumped to 92% when using a less stringent measure of efficacy.

Now, patients in the Vertex study had to take telaprevir every 8 hours, or three times a day,

which is less convenient than the twice-daily dosing for InterMune's ITMN-191. If InterMune wins on convenience, Vertex still appears ahead on potency.

The study reported Monday by InterMune also treated groups of patients with a three-times-daily dose of ITMN-191 for 14 days. In the best of these groups, 57% of patients treated with ITMN-191 and standard of care had undetectable levels of the hepatitis C virus in their system under the most stringent measures.

These data on ITMN-191 top the performance of Vertex's telaprevir, however, InterMune and Roche will have a hard time pushing ahead with a three-times-daily dose of ITMN-191 because they are well behind Vertex in the race to get new hepatitis C drugs approved.

Vertex announced Monday morning that it has already completed enrollment in two pivotal phase III studies of telaprevir in treatment-naïve patients, with data expected in 2010. InterMune and Roche, on the other hand, are still planning phase II studies to start next quarter.

Furthermore, other hepatitis C competitors such as Schering-Plough(SGP Quote - Cramer on SGP - Stock Picks), Johnson & Johnson(JNJ Quote - Cramer on JNJ - Stock Picks), Boehringer Ingelheim are also ahead of InterMune, with some of these drugs dosed once a day.

InterMune shares closed up 4.8% to \$9.40 in Monday.

Pharmasset and Roche Obtain FDA Consent to Start a Phase 2b Study With R7128 in Treatment Naïve HCV Patients

<http://www.pharmalive.com>

PRINCETON, N.J., Jan. 12 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (NASDAQ:VRUS) announced today that they and their development partner, Roche, have agreed with the FDA on the final design for a phase 2b trial with R7128, a nucleoside inhibitor of hepatitis C (HCV), slated to initiate in the first quarter of this year.

"We are pleased that R7128 is advancing into a large phase 2b trial," stated Michelle Berrey, MD, MPH, Pharmasset's Chief Medical Officer. "R7128 is the most advanced nucleoside polymerase inhibitor in development and we believe this class of drug brings a number of advantages to HCV-infected patients. R7128's higher barrier to resistance and activity across multiple viral genotypes, as well as the promising short-term safety and tolerability, may bring patients a new option for therapy. We look for this trial to better define the optimal treatment duration with R7128 in combination with the standard of care."

The phase 2b trial is anticipated to enroll about 400 treatment naïve, genotype-1 or genotype 4 HCV-infected patients. The trial will evaluate the dose and duration of treatment of R7128 in combination with Pegasys(R) plus Copegus(R). The primary efficacy endpoint of the trial will be the proportion of patients that achieve a sustained virologic response (SVR), defined as undetectable (measured by Roche TaqMan assay) HCV RNA 24 weeks after completion of treatment. Patients will be enrolled into one of 5 arms:

- 24 weeks of total treatment, with R7128 500mg bid in combination with pegylated

interferon and ribavirin for 12 weeks, followed by 12 weeks of pegylated interferon and ribavirin

- 24 weeks of total treatment, with R7128 1000mg bid in combination with pegylated interferon and ribavirin for 12 weeks, followed by 12 weeks of pegylated interferon and ribavirin
- 24 weeks of total treatment, with R7128 1000mg bid in combination with pegylated interferon and ribavirin for 8 weeks, followed by a further 16 weeks of pegylated interferon and ribavirin
- 48 weeks of total treatment, with R7128 1000mg bid in combination with pegylated interferon and ribavirin for 12 weeks, followed by a further 36 weeks of pegylated interferon and ribavirin.
- A control arm with pegylated interferon and ribavirin for 48 weeks.

Patients in the 24 week arms will discontinue treatment at week 24 if they achieved a rapid virological response (RVR), defined as undetectable level of HCV RNA at week 4 ("RVR-guided"). Patients that do not achieve an RVR will continue on the standard of care until week 48.

According to the current study design, patients will be enrolled as two cohorts, with randomization of the second larger cohort being initiated based on 12 week safety data of the first cohort.

During 2009, we expect to provide updates on the progress of the trial.

About R7128

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a cytidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. R7128 has shown in vitro activity against all of the most common HCV genotypes (1, 2, 3 and 4).

In a 4-week Phase 1 combination study that was conducted in 81 treatment-naive patients chronically infected with HCV genotype 1, R7128 demonstrated significant short-term antiviral activity with safety and tolerability comparable to placebo with SOC. Results from the 500mg, 1500mg and 1000mg dose cohorts (cohorts 1, 2 and 3) in 81 treatment-naive patients infected with HCV genotype 1 indicated:

- Results with R7128 500mg bid, 1000mg bid and 1500mg bid with SOC achieved a mean 3.8 log₁₀ IU/mL (30% RVR, 6 of 20), 5.0 log₁₀ IU/mL (88% RVR, 22 of 25) and 5.1 log₁₀ IU/mL (85% RVR, 17 of 20) decrease in HCV RNA, respectively. Results with placebo with SOC indicated patients achieved a mean 2.9 log₁₀ IU/mL decrease in HCV RNA and 18.75% (3 of 16) patients achieved RVR (<15 IU/ml).

In a harder to treat, non-responder, genotype 2 and 3 HCV patient population treated for 4 weeks:

- Results with R7128 1500mg bid with SOC led to 90% of patients achieving an RVR (<15 IU/ml) compared to 60% in the standard of care arm.

In November 2008, Pharmasset, Roche and InterMune initiated the INFORM-1 trial to investigate the combination of R7128 with InterMune's R7227 (ITMN-191), a protease inhibitor in HCV patients in the absence of pegylated interferon and ribavirin. Patients will receive a maximum of 14 days of combination treatment, followed by Pegasys(R) plus Copegus(R) for a further 46 weeks. The aim of the study is to investigate the safety and antiviral activity of the combination.

About Pharmasset

Pharmasset is a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Pharmasset's primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America and Europe. Clevudine is already approved for HBV in South Korea and marketed by Bukwang Pharmaceuticals in South Korea under the brand name Levovir. R7128, an oral treatment for chronic HCV infection, has completed a 4-week clinical trial in combination with Pegasys(R) plus Copegus(R) through a strategic collaboration with Roche. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.

Source: Pharmasset, Inc.

Vertex Outlines 2009 Business Priorities: Registration Programs in Hepatitis C and Cystic Fibrosis; Balanced Investment to Maintain Financial Strength

<http://www.businesswire.com>

- Broad telaprevir registration program for treatment-naïve and treatment-failure HCV patients nears enrollment completion -

SAN FRANCISCO--(BUSINESS WIRE)--Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today provided an update on the Company's clinical development programs and announced 2009 business priorities in conjunction with the 27th Annual J.P. Morgan Healthcare Conference in San Francisco. The Company also provided an update on its cash position and outlined its strategy for maintaining financial strength in 2009. Joshua Boger, Ph.D., President and Chief Executive Officer of Vertex, will discuss recent progress and provide an overview of Vertex's 2009 objectives as part of a live webcast presentation, which will be available on Vertex's website, www.vrtx.com, on Tuesday, January 13 at 1:30 p.m. PT (4:30 p.m. ET).

“Our industry’s greatest successes - of which there are many - resulted from transformational products that improved patients’ lives and delivered real value to the health care system,” said Dr. Boger. “The companies that tackled the most serious unmet medical needs, such as HIV, cancer and cardiovascular disease, are today the companies that are the anchors of the biotechnology industry. At Vertex, we target nothing less than some of the world’s most

devastating diseases. Today we have two major medicines in clinical development for hepatitis C and cystic fibrosis that we believe have the potential to drive major advances in the treatment of these diseases.

“In clinical trials to date, telaprevir has demonstrated an unprecedented ability to improve outcomes for both treatment-naïve and treatment-failure patients chronically infected with the hepatitis C virus,” continued Dr. Boger. “Enrollment is expected to be complete by the end of the first quarter for telaprevir’s broad registration program, positioning Vertex to potentially be first to market with a highly differentiated direct acting therapy for patients with HCV.

“Beyond HCV, Vertex is finalizing the design of a registration program for VX-770 in patients with cystic fibrosis. By targeting the underlying defect in CF, VX-770 has shown the potential in early clinical trials to increase lung function in patients with the G551D mutation and enhance the function of the defective protein responsible for this disease. We look forward to commencing the registration program for VX-770, which will be focused on adult and pediatric patients with the G551D mutation.”

Broad Clinical Development Program for Telaprevir

ADVANCE and ILLUMINATE trials in treatment-naïve patients fully enrolled

Vertex today announced that the ILLUMINATE clinical trial is fully enrolled. Together with the ADVANCE clinical trial, which was fully enrolled in October 2008, Vertex has enrolled more than 1,500 genotype 1 treatment-naïve HCV patients as part of the Company’s broad registration program for telaprevir:

ADVANCE: Vertex and Tibotec completed enrollment in October 2008 in the global 3-arm pivotal Phase 3 ADVANCE trial that is focused on 24-week telaprevir-based response-guided regimens in genotype 1 treatment-naïve HCV patients. In the ADVANCE trial, telaprevir is being dosed for 8 or 12 weeks. All patients are expected to have completed 8 or 12 weeks of dosing with telaprevir or placebo by the end of January 2009. Vertex expects to have sustained viral response (SVR) data from the ADVANCE trial in the first half of 2010. The ADVANCE trial enrolled approximately 1,050 patients.

ILLUMINATE: Vertex today announced that the Company has completed enrollment in the global 2-arm ILLUMINATE trial that will include evaluation of 24-week and 48-week telaprevir-based regimens in genotype 1 treatment-naïve HCV patients. In the ILLUMINATE trial, telaprevir is being dosed for 12 weeks. The Company expects to have SVR data from the ILLUMINATE trial in the first half of 2010, which will supplement SVR data obtained from the pivotal Phase 3 ADVANCE trial. The ILLUMINATE trial enrolled approximately 500 patients.

Differentiated profile in treatment-failure patients

Full enrollment of approximately 650 patients in the global 3-arm pivotal Phase 3 REALIZE clinical trial is expected in the first quarter of 2009. This trial is focused on 48-week telaprevir-based regimens in genotype 1 HCV patients who failed to achieve SVR with prior treatment of pegylated interferon (peg-IFN) and ribavirin (RBV). The REALIZE trial is expected to enroll relapser, partial responder and the most difficult to treat null responder patients who are well-

documented with respect to their prior response to HCV therapy. In the REALIZE trial, telaprevir is being dosed for 12 weeks.

Vertex presented interim clinical data, including safety information, from the Phase 2 PROVE 3 trial in November 2008 at AASLD. The data showed a 52% SVR12 rate in treatment-failure HCV patients, with a 24-week telaprevir-based treatment regimen. All patients in PROVE 3 completed dosing in the second quarter of 2008. Vertex expects to present final SVR data from the telaprevir and control arms of PROVE 3 at a medical meeting in the first half of 2009.

Vertex exploring utility of telaprevir in other patient populations and dosing regimens

Interim results presented in November 2008 from the ongoing, Phase 2, open-label, randomized C208 study examining a twice-daily (q12h) telaprevir dosing regimen versus a three-times-daily (q8h) regimen in combination with RBV and peg-IFN-alfa-2a (PEGASYYS®) or peg-IFN-alfa-2b (PEGINTRON™) in treatment-naïve genotype 1 HCV patients, including safety information from the study, support the potential for twice-daily dosing of telaprevir. Tibotec expects to present additional data from this trial, including SVR data for patients who completed dosing and have been followed 24 weeks post-treatment, at a medical meeting in 2009.

Vertex and Tibotec plan to discuss a proposed HIV/HCV co-infection program with the U.S. FDA and European health authorities in the coming months.

HCV portfolio strategy advancing

Vertex is also developing VX-500 and VX-813, additional HCV protease inhibitors that are currently in Phase 1 clinical development. Vertex expects to have safety, pharmacokinetic and viral kinetic data for VX-500 from Phase 1 studies in the first quarter of 2009.

The combination of telaprevir with other novel specifically targeted antiviral therapies for HCV (STAT-C) is a key business priority for Vertex in 2009. The Company continues to evaluate other STAT-C agents as they advance in clinical development.

Vertex collaborator initiates Phase 3 clinical development in Japan

Vertex today announced that its collaborator Mitsubishi Tanabe Pharma Corporation has initiated Phase 3 clinical development of telaprevir that is designed to include evaluation of 24-week telaprevir-based regimens in approximately 300 genotype 1 treatment-naïve and treatment-failure HCV patients in Japan. In Phase 3 studies of telaprevir being conducted by Mitsubishi, telaprevir is being dosed for 12 weeks in combination with peg-IFN-alfa-2b (PEGINTRON™) and RBV. Mitsubishi expects to have SVR data from its Phase 3 clinical trials of telaprevir in mid-2011.

Human Genome Sciences Announces Initiation of Phase 2b Trial of Albuferon(R) Dosed Monthly in Chronic Hepatitis C

<http://news.prnewswire.com>

- Trial conducted by Novartis to evaluate safety and efficacy of Albuferon administered every four weeks in combination with ribavirin in patients with genotypes 2 and 3 hepatitis C -

ROCKVILLE, Md., Jan. 12 /PRNewswire-FirstCall/ -- Human Genome Sciences, Inc. (Nasdaq: HGS) today announced that Novartis has initiated dosing in a Phase 2b trial that will evaluate the safety and efficacy of Albuferon(R) (albinterferon alfa-2b) administered monthly in combination with ribavirin in treatment-naive patients with genotypes 2 and 3 chronic hepatitis C. Albuferon is being developed by HGS and Novartis under an exclusive worldwide co-development and commercialization agreement entered into in June 2006.

"Patients undergoing treatment for chronic hepatitis C often find it challenging to participate in normal daily activities, especially in the days following dose administration," said Stephen Pianko, M.D., F.R.A.C.P., Ph.D., Monash University, Melbourne, Australia. "Pegylated interferons, the current standard of care, require administration once every week. Albinterferon alfa-2b dosed every four weeks with a total of six injections could offer an important treatment option, if it demonstrates comparable safety and efficacy vs. peginterferon alfa-2a dosed weekly with a total of 24 injections."

In December 2008, HGS announced that Albuferon met its primary endpoint of non-inferiority to peginterferon alfa-2a (Pegasys) in ACHIEVE 2/3, a Phase 3 clinical trial of Albuferon in combination with ribavirin in treatment-naive patients with genotypes 2 and 3 chronic hepatitis C. In these patients, the Phase 3 study showed that 900-mcg Albuferon administered every two weeks had efficacy comparable to peginterferon alfa-2a, with comparable rates of severe and/or serious adverse events and discontinuations due to adverse events.

"Hepatitis C is the most common chronic blood-borne infection in the developed world, and there continues to be a significant need for more effective and better tolerated treatments," said Mani Subramanian, M.D., Ph.D., Executive Director, Clinical Research - Infectious Diseases, HGS. "Only an estimated 40% of U.S. patients diagnosed with chronic hepatitis C have undertaken treatment to date - in part due to the side effects associated with interferon injections, which are currently required on a weekly basis. A monthly dosing schedule with Albuferon may well result in more patients choosing to be treated."

About the Design of the Phase 2b Monthly Dosing Trial

This Phase 2b trial is a randomized, open-label, multi-center, active-controlled, adaptive-design dose-ranging study to evaluate the safety and efficacy of albinterferon alfa-2b administered every four weeks plus daily ribavirin in treatment-naive patients with genotypes 2 and 3 chronic hepatitis C. Approximately 375 patients will be randomized in a 4:4:4:3 ratio into four treatment groups, including three that will receive albinterferon alfa-2b administered once every four weeks (900 mcg, 1200 mcg or 1500 mcg), in addition to the active-control group, which will receive peginterferon alfa-2a at the standard 180-mcg dose once every week. All patients in the study will receive 800-mg daily oral ribavirin. The total duration of treatment will be 24 weeks. The primary efficacy endpoint is sustained virologic response (SVR) at Week 48 (24 weeks following the end of treatment).

About Albinterferon Alfa-2b (Albuferon)

Albinterferon alfa-2b is a novel, longer-acting form of interferon alfa that was created using the proprietary HGS albumin-fusion technology. Human albumin is the most prevalent naturally occurring blood protein in the human circulatory system, persisting in circulation in the body for approximately 19 days. Research has shown that genetic fusion of therapeutic proteins to human albumin decreases clearance and prolongs the half-life of the therapeutic proteins. Albuferon

results from the genetic fusion of human albumin and interferon alfa.

Albuferon is being developed by HGS and Novartis for the treatment of chronic hepatitis C under an exclusive worldwide co-development and commercialization agreement entered into in June 2006. HGS and Novartis will co-commercialize Albuferon in the United States and will share clinical development costs, U.S. commercialization costs and U.S. profits equally. Novartis will be responsible for commercialization in the rest of the world and will pay HGS a royalty on those sales. Clinical development, commercial milestone and other payments to HGS could total as much as \$507.5 million, including \$132.5 million received to date.

SOURCE Human Genome Sciences, Inc.

Injection practices exposed at least 60,000 to hepatitis

<http://www.newsday.com>

BY RIDGELY OCHS | ridgely.ochs@newsday.com

Unsafe injection practices such as those of Dr. Harvey Finkelstein have exposed at least 60,000 patients to hepatitis B and hepatitis C in the past decade, according to the federal Centers for Disease Control and Prevention.

Calling it "a wider and growing problem," the CDC documented 33 outbreaks in the United States that resulted in 448 people getting hepatitis B or C from doctors' offices or clinics from 1998 to 2008.

In all the outbreaks, the infections were caused by "failure of health care personnel to adhere to fundamental principles of infection control," the authors said in the review published last Tuesday in the *Annals of Internal Medicine*.

The cases ranged from Finkelstein, a Plainview pain management doctor who in 2004 was observed reusing syringes in multidose vials, causing at least one transmission of hepatitis C, to a Nevada endoscopy clinic where poor anesthesia practices last year put 40,000 at risk for the virus.

Evelyn McKnight said she was surprised the CDC's numbers were so low. McKnight, a Fremont, Neb., audiologist, was one of 99 patients who got hepatitis C in 2004. She contracted the virus at a Nebraska oncology clinic where she was being treated for breast cancer.

"I would have thought the number was closer to 100,000," said McKnight, who has since started HONORreform, a foundation that has worked closely with the CDC to promote good infection control.

The CDC report reflects the tip of the iceberg, the authors acknowledged. That's in part because health care has shifted from hospitals, where standard infection control practices - such as not reusing needles or syringes - are regulated, to doctors' offices and clinics, where they may not be, chief author Nicola Thompson said.

"Outpatient settings often do not have the same type of focus on prevention and infection

control," she said. "There's been a lack of oversight."

Hepatitis C is the most common chronic blood-borne viral infection in the United States, according to the CDC; about 3.2 million Americans have a lifelong, chronic infection. About 1.4 million Americans have a chronic hepatitis B infection. Both can lead to liver disease and death.

Seven of the 33 outbreaks - including the Finkelstein case - occurred in New York. Claudia Hutton, a spokeswoman for the state Department of Health, said that reflects New York's better oversight, not sloppier health care workers.

"We have more data, better surveillance and better investigations," Hutton said.

Thompson agreed, praising New York's surveillance and investigations compared with many other states.

But the department came under fire for its handling of the Finkelstein case. It took almost three years before the state began informing patients of his practices. Since then, the state has initiated changes to prompt and speed up investigations. It also has passed a law requiring ambulatory surgery centers - including practices like Finkelstein's - to be accredited like hospitals.

Bristol-Myers to develop new hepatitis C drug

<http://www.nj.com>

by Staff and wire

Bristol-Myers Squibb signed a \$1.12 billion deal yesterday with the biotech company ZymoGenetics to develop a hepatitis C drug based on a new type of interferon, a powerful immune-system stimulant.

Bristol-Myers will pay ZymoGenetics \$85 million in cash for the rights to develop the Seattle company's **PEG-Interferon lambda**, which is already in early-stage human studies.

The agreement requires Bristol-Myers to pay its new partner a license fee of \$20 million this year, followed by payments that could total just over \$1 billion if a series of milestones are reached, according to the companies.

The two companies will test the drug jointly in the United States and Europe and share the expenses of the studies. ZymoGenetics will continue the ongoing early-stage studies and then advance the drug into more advanced testing.

ZymoGenetics will have an option to jointly sell and share in product profits from U.S. sales, and will receive royalties from Bristol-Myers on foreign sales, according to the terms of the deal.

Interferon is a substance that stimulates the immune system to fight invading diseases. It has been used to treat hepatitis C, a viral infection of the liver, as well as some forms of cancer.

The collaboration between Bristol-Myers and ZymoGenetics will focus on a new, type-3 interferon with a technology, called pegylation, which is designed to keep the drug active in the

body for as long as possible, something now standard for advanced hepatitis C treatments. The companies said their compound targets a different cell receptor than existing interferon treatments. If the compound is successfully developed, it could result in patients receiving more targeted therapy, which would treat the disease more effectively.

Bristol-Myers, which has a large presence in New Jersey although its headquarters is located in New York City, does not currently have a hepatitis C medicine among its products. The company has three other prospective treatments for the disease in development, according to a company spokeswoman.

Nearly 170 million people worldwide are infected with hepatitis C, a virus transmitted by blood that damages the liver and is difficult to treat. Among people with chronic hepatitis C infection, 1 percent to 5 percent develop liver cancer, and others may need a liver transplant.

As part of its agreement with Bristol-Myers, ZymoGenetics would get up to \$430 million if it reaches certain milestones for development and approval of PEG-Interferon lambda for treating hepatitis C. It could also receive up to \$287 million for development and regulatory approvals of drugs to treat other conditions, and up to \$285 million for meeting certain sales goals.

Jan 13, 2009

How Do Couples Cope When One Partner Has a Chronic Illness?

www.medscape.com

Colin T. Son

The Internet has played an important role in creating an informed and empowered patient population. Blogs, for example, are oases where patients can exchange information and experiences.

One particular patient blog, *In Sickness and In Health*, has a unique focus. The blog's author, Barbara Kivowitz, wants readers to understand that chronic illness is rarely, if ever, faced alone. Rather, it touches the lives of everyone around the patient, especially a significant other. She should know, as she has gone through it personally. Ms. Kivowitz recently described the difficulties that couples often face in dealing with chronic illness and shared her advice, based on her own experience, for dealing with those issues.

Colin Son: Dealing with illness as a couple is one of the main topics in your blog. What do you think is the single most important piece of advice that you can give to a couple dealing with a chronic disease?

Barbara Kivowitz: Surprisingly, the topic of couples and illness is one that has not received much study or attention.

When you're in a relationship and serious illness hits one partner, both lives are dislocated. The changes are profound ones. Illness becomes the uninvited third party in the relationship and inserts itself into some very tender places: into the image partners have of each other, into the activities and routines that the relationship depends on, into the kitchen, and into the bedroom. Doctors, drugs, hospitals, and healers become part of the substance of the relationship. Illness

gets to make decisions that once belonged to the couple -- decisions about work, travel, finances, and family. Pain and exhaustion take precedence over desires and chores. What was once a relationship of equals often becomes one of caregiver and patient.

The question that is central to my quest is: How can a couple achieve a new kind of balance, one that accommodates the reality of the illness but also maintains a balanced partnership?

The key is communication.

The most important advice I can give couples dealing with illness is to talk to each other openly and honestly about your experience of the illness. Talk about your feelings and ask for what you need and what you don't want from your partner. Too often, without communication, the well partner comes to see the ill partner as not trying hard enough, and the ill partner comes to see the well partner as just not understanding. This can foster resentment and distance. Communicating recreates the connections that brought the couple together in the first place and builds a stronger foundation for both people to stand on to deal with the illness together.

Colin Son: Can you tell us a little of your own story? What brought you online as a patient?

Barbara Kivowitz: Prior to the onset of my pain condition, I had been a business consultant, writer, and psychotherapist. Richard and I loved adventure and had taken a year off to travel around the world. All of our vacations were built around hiking and mountain climbing. Illness upended our world and left us floundering.

Like many other sufferers, I went from specialist to specialist to find a diagnosis and treatment approach that could offer me a livable life. Richard became my anchor point. His scientific mind and problem-solving skills often helped me find a path out of my confusion and fear. His kindness and love could, at times, lift me above my pain. He took on all the household responsibilities I could no longer do. And, while he was doing all of this for me, he was living in his own hell, the hell of having a wife who was slipping away to illness.

The couple relationship is an additional casualty when illness hits, but it can also be a vessel for healing. I began blogging about couples and illness because I found little on the Internet about this topic and wanted to share my experiences and learn how other couples cope with illness. I have learned from and been moved by the stories of despair and of renewal that I have heard from readers of my blog.

Colin Son: How has your time as a psychotherapist shaped your experience with your illness?

Barbara Kivowitz: There's nothing like the real thing. As a psychotherapist, I worked with patients who had physical and mental illness. I even worked with victims of political violence and with a hospice program. I helped my patients grieve, cope, find resources in themselves and in their communities, and rebuild. But it wasn't until I got whacked with my own illness that I truly understood how violating, grievous, and burdensome illness is, to the patient and the partner.

Colin Son: What are some posts that highlight the relationship between patients and their significant others?

Barbara Kivowitz: I did a series on How To Have the Hard Conversations, which I hope readers found helpful. My favorite hope post is about An Unexpected Conversation in a Waiting Room. One of the most amazing stories I heard and wrote about is A Story About Alzheimer's: Paul and Mary, about how one couple coped.

Colin Son: Any final thoughts?

Barbara Kivowitz: When couples face serious illness it is grievous, but it is also an opportunity to learn how to be with each other on deeper levels. Before illness, the couple can cruise along adapting to circumstances in the moment. After illness, the couple needs to be more intentional and candid. But the effort made to build new habits, to assess responsibilities and lifestyle, to communicate with authenticity, and to become more conscious about adapting to changing circumstances will strengthen the relationship in ways that reach far beyond the illness.

On January 13, 2009, Barbara Kivowitz will host Grand Rounds, the weekly collection of favorite posts submitted by medical bloggers. This weekly blog carnival gives you a chance to sample many different blogs while also getting to know the host blogger.

Antidepressants ease fibromyalgia pain: study

www.reuters.com

LONDON (Reuters) - Antidepressants appear to relieve pain, sleep disturbances and other symptoms of fibromyalgia, a debilitating and painful ailment with no known cure, German researchers said on Tuesday.

A range of antidepressants look to improve quality of life for people with the condition that affects up to an estimated 6 percent of people in North America and Europe, they added.

"Fibromyalgia syndrome is also associated with high direct and indirect disease-related costs," Winfried Hauser of Klinikum Saarbrücken in Germany and colleagues wrote in the *Journal of the American Medical Association*.

"Effective treatment of fibromyalgia syndrome is therefore necessary for medical and economic reasons."

The condition mainly strikes women and can cause severe pain and tenderness in muscles, ligaments and tendons. Shoulder and neck pain is common but some people with the ailment also have problems sleeping, and suffer anxiety and depression.

Doctors usually prescribe exercise and relaxation techniques, painkillers or sometimes a low-dose antidepressant to treat the symptoms.

Pregabalin, a drug that calms nerve cells, gained U.S. regulatory approval last year to treat the condition. It is sold as Lyrica by Pfizer Inc.

Hauser and colleagues analyzed 18 previously published studies involving 1,427 participants and found strong evidence antidepressants led to improved symptoms and quality of life.

Older tricyclic and tetracyclic antidepressants seemed to have a large effect in easing pain, fatigue and sleep disturbances while selective serotonin reuptake inhibitors (SSRIs) such as Prozac had smaller effect for pain relief.

Prozac was initially introduced by U.S. drugmaker Eli Lilly and Co in 1987 and is now off patent and widely available generically as fluoxetine.

A newer class of treatments called serotonin and noradrenaline reuptake inhibitors (SNRIs) were linked to a reduction of pain, sleep disturbances and depressed mood, and monoamine oxidase inhibitors appeared to help reduce pain.

While the analysis suggests antidepressants may help, the researchers said doctors should closely monitor people using them because there is a lack of evidence about their long-term impact.

"Their effects should be re-evaluated at regular intervals to determine whether benefits outweigh adverse effects," the researchers wrote.

(Reporting by Michael Kahn; editing by Tim Pearce)

New Phase of National Hepatitis C Awareness Campaign Launched for GPs

<http://www.pharmiweb.com>

Department of Health

The Department of Health is gearing up to launch a hepatitis C public health campaign to improve detection and diagnosis among the 100,000 people in England who are thought to be unaware they have the infection.

The campaign will get underway at the start of next month with radio and press advertising to remind the public of life experiences that could have exposed them to infection.

GPs will be encouraged to support the campaign by offering information and testing for patients in at risk groups.

The campaign coincides with the 20th anniversary of the virus being identified and follows a recent letter from the Chief Medical Officer and Chief Nursing Officers to Primary Care Trusts on improving the detection and diagnosis of hepatitis C in primary care.

Many people who have hepatitis C do not show symptoms for many years and may have normal liver function tests. Over time, hepatitis C can cause serious liver damage (cirrhosis, primary liver cancer or liver failure), which can be prevented by effective drug therapy.

The Department is calling on GPs to be extra vigilant and consider testing for the virus in patients in at risk groups such as those who may have injected drugs in the past, even if only once or twice or a long time ago, or those who may have had a tattoo or piercing with unsterile equipment.

In the lead up to the campaign, a number of information resources are being made available for health professionals, including on NHS Choices, a quick reference guide for primary care and a new patient information leaflet.

Professor Steve Field, Chairman of the Royal College of General Practitioners said: "We are pleased to see the launch of a new phase of the Department of Health's campaign to raise awareness of hepatitis C amongst GPs and the public. GPs play an important role in detection and diagnosis of hepatitis C and we want this to continue. It is important to make sure that healthcare professionals are aware of the transmission routes, and diagnosis and treatment of the virus, so that patients at risk are identified at the earliest possible opportunity and can be treated effectively."

For more information:

<http://www.nhs.uk/hepc>

Hepatitis C may increase pancreatic cancer risk

<http://www.eurekalert.org>

New study shows that infection with hepatitis C virus increases risk for a highly fatal cancer of the biliary tree

A new study shows that infection with hepatitis C virus (HCV) increases a person's risk for a highly fatal cancer of the biliary tree, the bile carrying pathway between the liver and pancreas. This finding is in the January issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD). The article is also available online at Wiley Interscience (www.interscience.wiley.com).

More than 4 million Americans are infected with HCV, which causes chronic hepatitis, cirrhosis and liver cancer. However, the associations between the virus and other potentially-related cancers are less clear.

To better understand the associations between HCV and these cancers, researchers led by Hashem El-Serag of Baylor College of Medicine, conducted a retrospective cohort study of more than 718,000 U.S. veterans who were treated at Veterans Affairs medical facilities between October 1, 1988 and September 30, 2004. Among them, 146,394 were infected with HCV and 572,293 were not. Uninfected subjects were matched to infected ones by sex, age and type and date of visit.

The researchers followed the subjects for an average of 2.3 years to determine the incidence these cancers. They found that "risk for biliary tree cancer in the HCV-infected cohort, although low (4 per 100,000 person-years), was more than double that in the HCV-uninfected cohort."

The study is the first to formally examine the association between HCV and pancreatic cancer. It is also the first time a significant association has been detected between HCV and this type of cancer in a large cohort study. The findings may lead to greater examination of rare malignancies.

Article:

"Risk of Hepatobiliary and Pancreatic Cancers Following Hepatitis C Virus Infection: A Population-based Study of U.S. Veterans." El-Serag, Hashem; Engels, Eric; Landgren, Ola; Henderson, Louise; Chiao, Elizabeth; Amaratunge, Harshinie; Giordano, Thomas. *Hepatology* ; January 2009.

Idenix Pharmaceuticals Initiates Proof-of-Concept Study Of IDX184 For The Treatment Of Hepatitis C Virus (HCV)

<http://www.medicalnewstoday.com>

Idenix Pharmaceuticals, Inc. (Nasdaq: IDIX), a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral and other infectious diseases, today announced that it has initiated a proof-of-concept study of IDX184, a liver-targeted nucleotide prodrug candidate for the treatment of HCV under an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA). The study is evaluating IDX184 in treatment-naive hepatitis C genotype-1 infected patients.

"We are very pleased with the progress that we have made in our hepatitis C discovery program in 2008, having successfully advanced IDX184 from IND to a proof-of-concept study, while simultaneously advancing two additional HCV discovery programs into IND-enabling preclinical studies," said Jean-Pierre Sommadossi, Ph.D., chief executive officer of Idenix. "As we work to finalize a partnership for our lead HIV drug candidate, our goal in 2009 is to become the first biopharmaceutical company with innovative drugs from three major classes of direct-acting hepatitis C antivirals in clinical development."

The proof-of-concept trial in HCV-infected patients is being conducted at multiple centers around the world. The trial design is a phase I/II, double-blind, placebo-controlled, dose-escalation study to evaluate the safety and antiviral activity of IDX184 in treatment-naive adult patients infected with chronic hepatitis C. The study will evaluate four doses of IDX184, ranging from 25 to 100 mg once-per-day, administered for three days. Each cohort of the study will evaluate ten patients randomized eight to IDX184 and two to placebo.

About IDX184

IDX184 is a once-daily, oral nucleotide prodrug candidate based on Idenix's proprietary liver-targeting technology. This technology enables the delivery of high levels of nucleoside triphosphate in the liver, potentially maximizing drug efficacy and limiting systemic side effects. In HCV genotype-1 infected chimpanzees, once-daily oral administration of 10 mg/kg/day of IDX184 produced a mean viral load reduction of 2.3 log₁₀ after four days of dosing. In a phase I study in healthy volunteers evaluating doses ranging from 5 to 100 mg/day, IDX184 was safe and well-tolerated; the most common adverse event reported in this study was dizziness and it was more frequently reported in subjects receiving placebo.

About Idenix

Idenix Pharmaceuticals, Inc., headquartered in Cambridge, Massachusetts, is a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral and other

infectious diseases. Idenix's current focus is on the treatment of infections caused by hepatitis C virus and HIV. For further information about Idenix, please refer to <http://www.idenix.com>.

Jan 14, 2009

Neoplastic Seeding After RF Ablation Tied to Liver Tumor Differentiation

www.medscape.com

NEW YORK (Reuters Health) Jan 07 - The extent of poor tumor differentiation is a risk factor for neoplastic seeding in patients who undergo radiofrequency (RF) ablation for hepatocellular carcinoma, Japanese researchers report in the December issue of the *American Journal of Gastroenterology*.

Senior investigator Dr. Masao Omata and colleagues at the University of Tokyo note that the reported rate of seeding in such patients may reach as high as 12.5%.

However, Dr. Omata told Reuters Health that this "seeding rate is too high...because the rate in subsequent studies, including ours, is 1 to 2%."

The investigators came to this conclusion after studying data on 1031 patients who underwent 1845 treatments of RF ablation. Over a median follow-up 35.3 months, 33 patients showed evidence of neoplastic seeding.

This amounted to an incidence of 3.2% per patient or 1.8% per treatment. Twenty-one of the cases occurred on the line of previous RF ablation needle insertion.

The median time until detection was 15.2 months and cumulative 1-year survival after detection was 86%, which declined to 47% after 2 years.

On multivariate logistic regression analysis, the team found that only the degree of poor differentiation was associated with the risk of neoplastic seeding. Surrogate markers for poor differentiation were larger tumors and elevated tumor marker levels.

In these circumstances, the researchers conclude that the indications for RF ablation "should be carefully considered."

Am J Gastroenterol 2008;103:3057-3062.

NIH Issues Guidelines on Hepatitis B Management

www.medscape.com

Laurie Barclay, MD

January 8, 2008 — The National Institutes of Health (NIH) have issued a consensus development conference statement on management of hepatitis B virus (HBV) infection and have published the new guidelines in the January 20 print issue of the *Annals of Internal*

Medicine.

"Hepatitis B is a major cause of liver disease worldwide, ranking as a substantial cause of cirrhosis and hepatocellular carcinoma," write Michael F. Sorrell, MD, from University of Nebraska Medical Center in Omaha, and colleagues. "The development and use of a vaccine for...HBV has resulted in a substantial decline in the number of new cases of acute hepatitis B among children, adolescents, and adults in the United States. However, this success has not yet been duplicated worldwide, and both acute and chronic HBV infection continue to represent important global health problems."

This NIH statement was prepared by independent panels of health professionals and public representatives based on a systematic review of the literature contracted by the Agency for Healthcare Research and Quality as well as on presentations, conferences, and other communication with pertinent experts and among panel members.

Issues addressed by this statement included the current burden of HBV infection, the natural history of HBV, benefits and risks of currently available treatments of HBV infection, which persons with HBV infection should be treated, available measures to monitor treatment and evaluate outcomes, and the most pressing needs and opportunities for future research on HBV infection.

The major goals of anti-HBV therapy are to prevent disease progression, specifically development of cirrhosis and liver failure, and to prevent the development of hepatocellular carcinoma and reduce mortality rates.

In the United States, 7 drugs are currently approved for treatment of adults with chronic HBV infection: interferon-alpha; pegylated interferon-alpha; and the nucleoside or nucleotide analogues lamivudine, adefovir dipivoxil, entecavir, telbivudine, and tenofovir disoproxil fumarate. For children with HBV infection, only interferon-alpha and lamivudine have been approved.

These 7 drugs have been shown in short-term randomized controlled trials to improve intermediate disease markers such as HBV DNA level, loss or seroconversion of hepatitis B surface antigen (HBsAg), liver enzyme tests, and liver histologic features. However, evidence is limited regarding their effects on important long-term clinical outcomes such as overall mortality rate, liver-specific mortality rate, or development of hepatocellular carcinoma, because the outcomes often do not occur for many years after infection with HBV.

Interferon use has a defined, self-limited course (16 - 48 weeks) and is not associated with the development of antiviral resistance, whereas treatment with nucleoside or nucleotide analogues can be long term, are often indefinite in duration, and may promote emergence of resistance. All approved treatments decrease HBV DNA levels, but the amount of decrease is greater, and the time to decrease is shorter with nucleoside or nucleotide analogues vs interferon.

Interferon is given by subcutaneous injection and may cause systemic symptoms of headache, nausea, flu-like symptoms, depression, and some hematologic abnormalities. In contrast, nucleoside and nucleotide analogues are given orally and may be used safely in patients who have not responded to interferon therapy. If treatment with nucleoside and nucleotide analogues

is stopped prematurely, however, there may be resurgence of HBV DNA levels or reactivation of hepatitis. Some nucleoside and nucleotide analogues may cause renal toxicity, myopathy, and/or mitochondrial toxicity.

Treatment with nucleoside and nucleotide analogues is indicated for patients with rapidly deteriorating liver function and for those with decompensated cirrhosis complicated by ascites, hepatic encephalopathy, or hemorrhage from portal hypertension. Because of the risk for hepatic failure, interferons are contraindicated in this group.

Patients with compensated cirrhosis should also be treated because they are at increased risk for clinically significant complications. Patients with HBV infection who receive immunosuppressive or cancer chemotherapy for other medical conditions are at high risk for exacerbation of hepatitis, and they should therefore be treated with antiviral therapy before starting immunosuppressive or cancer chemotherapy.

"The evidence available at this time does not permit concrete recommendations regarding selection of a particular therapeutic course," the statement authors write. "Health care providers should discuss the risks and benefits of treatment options with patients to arrive at the best possible decisions."

In persons with chronic HBV infection, persistently elevated HBV DNA and alanine aminotransferase (ALT) levels in the blood are the most important predictors of cirrhosis or hepatocellular carcinoma. In addition, other risk factors include HBV genotype C infection, male sex, older age, family history positive for hepatocellular carcinoma, and coinfection with hepatitis C virus or HIV.

Various monitoring strategies have been proposed, but there is no clear evidence allowing selection of a single best approach. The loss of HBsAg may be the best marker because it reflects immunity to HBV, lowered risk for development of cirrhosis and hepatocellular carcinoma, and better survival rates, but such seroconversion seldom occurs in response to treatment.

Elevated HBV DNA level appears to predict development of cirrhosis and hepatocellular carcinoma, and suppression of HBV DNA has been associated with improvement of ALT levels and improved histologic features. However, it is not as clear whether treatment-induced decreases in HBV DNA levels are associated with improved clinical outcomes.

"From the time of initial diagnosis, optimal management of HBV infection requires a lifetime of routine monitoring, even when patients are asymptomatic," the statement authors write. "We wish to emphasize that provider and patient education are key to ensuring ongoing adherence with routine disease and treatment response monitoring and with therapy."

The statement identifies the most important research needs as defining the natural history of the disease with representative prospective cohort studies; and determining the effects of available treatments on clinical health outcomes in large, randomized controlled trials of monotherapy and combined therapies, including placebo-controlled trials.

Routine screening for HBV infection is recommended for newly arrived immigrants to the United States from countries where the prevalence of HBV infection exceeds 2%. Although the

screening test should not be used to prohibit immigration, it should provide public health data on the burden of disease in immigrant populations and improve provision of medical and public health services for infected patients and their families.

The accompanying review of available studies indicates that "evidence was insufficient to assess treatment effect on clinical outcomes or determine whether inconsistent improvements in selected intermediate measures are reliable surrogates. Future research is needed to provide evidence-based recommendations about optimal antiviral therapy in adults with chronic hepatitis B infection."

The statement authors and review authors have disclosed no relevant financial relationships.

Ann Intern Med. 2009;150:104-110, 111-124.

PEGASYS® Proven Effective as Hepatitis C Treatment for Latino Patients, According to Article in The New England Journal of Medicine

www.roche.com

- Largest Prospective Study Demonstrates Treatment Success, and Highlights Potential Factors that Affect Health Outcomes, in Latino Population Suffering from Chronic Hepatitis C -

NUTLEY, N.J., January 14, 2009 – Results from the LATINO study, the largest study conducted to-date in Latino patients with the hepatitis C virus (HCV), were published today in *The New England Journal of Medicine* (NEJM). This Roche study demonstrated that HCV can be successfully treated among Latino patients, a patient population that is historically difficult to treat. The study, “Peginterferon Alfa-2a and Ribavirin in Latino and Non-Latino Whites with Hepatitis C,” was conducted to better understand how previously untreated Latino patients with HCV genotype 1, the most difficult-to-treat genotype, responded to treatment with PEGASYS® (peginterferon alfa-2a) plus COPEGUS® (ribavirin) as compared to non-Latino whites.

“We know that the hepatitis C virus affects Latino patients differently than non-Latino patients, but there was little data available to support what we have seen clinically. The LATINO data are important because, for the first time, a large-scale study was conducted that focused on Latino patients, providing insight into this growing population,” said Maribel Rodriguez-Torres, M.D., of the Fundación de Investigación de Diego in Puerto Rico. “We hope that this landmark LATINO study will be the beginning of more clinical trials with greater numbers of Latino patients, which will help address the unmet medical need of this population.”

The data showed that Latino patients achieved sustained virological response (SVR) at a lower rate than non-Latino whites, and demonstrated that there were differences in predictors of SVR between the two patient populations. The results of this study add to a growing body of evidence of differences in treatment responses among ethnic groups and underscore the need to optimize treatment strategies in order to improve the rate of SVR among Latino patients infected with HCV genotype 1.

“As leaders in hepatology, we are proud to have conducted the largest prospective study of the Latino population with hepatitis C,” said Dr. Lars Birgeron, Head of Global Medical Affairs, Roche. “We look forward to further investigating unmet medical needs and providing future treatment options, for Latinos and other hard-to-treat populations, through our clinical research program.”

These findings point to an important public health issue, since Latinos, the fastest-growing minority population in the United States, have a higher prevalence of HCV and more rapid fibrosis progression than non-Latino whites, and a mortality rate of nearly twice that of non-Latino whites. The predicted expansion of the number of Latinos in the United States suggests that the prevalence of HCV infection will increase. These factors are likely to contribute to the already increasing rates of morbidity and mortality among Latinos due to liver disease.

The LATINO study, a prospective, multicenter, open-label, nonrandomized trial, was designed to compare the efficacy of PEGASYS plus COPEGUS in 269 Latino whites and 300 non-Latino whites infected with HCV genotype 1 who had not been previously treated. The primary endpoint of the study was SVR. All patients, between the ages of 18 and 65, were treated with PEGASYS 180 mcg/wk plus COPEGUS 1,000 or 1,200 mg/day for 48 weeks. Patients were then followed through 72 weeks. Latinos were required to have two generations of Latino ancestry with Spanish as a primary language, and non-white Latinos were excluded.

The results from LATINO showed that 34 percent (90/269) of the Latino patients achieved SVR when treated with PEGASYS plus COPEGUS. In comparison, 49 percent (148/300) of patients in the non-Latino group achieved SVR, a difference of 16 percent, highlighting that Latino patients with HCV are more difficult to treat. SVR was defined as undetectable HCV RNA 24 weeks after the end of treatment. Combination therapy with PEGASYS plus COPEGUS was generally well tolerated, with similar rates of withdrawals between the groups for serious adverse events, with fatigue, fever and flu-like symptoms being the most common adverse events.

These results contribute to a growing body of evidence that PEGASYS provides a successful outcome for many patients with HCV. PEGASYS has consistently demonstrated efficacy in a broad range of patient types, even those with poor prognostic factors, including African Americans and patients co-infected with HIV. Two independent, investigator-initiated, single-center Italian studies with PEGASYS have shown reproducible efficacy in HCV patients with genotype 1 and 4 compared to peginterferon alfa-2b. In genotypes 1 and 4 – the most difficult-to-treat patient group – 55 percent of patients taking PEGASYS achieved SVR, compared to 40 percent of patients in the peginterferon alfa-2b group. Results of another study found significantly higher SVR rates in patients treated with PEGASYS and ribavirin compared to those treated with peginterferon alfa-2b and ribavirin (66 percent vs. 54 percent). The difference was sustained in patients with the most difficult to treat forms of the virus, those infected with genotypes 1 or 4 (48 percent vs. 32 percent).

As the current foundation of HCV treatment, PEGASYS is the pegylated interferon therapy of choice for most HCV antiviral agents in development. These collaborations position Roche as a leader in the next evolution of HCV treatment, and the LATINO study underscores Roche’s role as a pioneer in the advancement of understanding HCV.

Hep C scandal

<http://www.irishtimes.com>

There is something deeply disturbing about a decision by the Director of Public Prosecutions (DPP) to drop all charges in the last remaining case involving the infection of women with hepatitis C. Nobody will now be prosecuted for the injuries and deaths visited on more than 1,000 people by contaminated blood products over a period of 15 years. This public failure is part of a pattern whereby prominent individuals charged with serious offences have not been tried as a result of a culture of official apathy, excessive delays and legal challenges.

It has taken more than 10 years and a succession of legal actions to reach this unsatisfactory conclusion. No wonder the surviving women who were infected by hepatitis C are angry. We should be angry too. Without accountability in public life, dangerous practices, inadequate services and political corruption will persist. At this time of economic transition, the opportunity for root and branch reform of our administrative and legal structures must be taken.

A public outcry forced the then government to appoint Mr Justice Finlay to investigate the supply of contaminated blood products by the Blood Transfusion Service Board (BTSB) in 1997. He found three employees had been primarily responsible for the failure. A subsequent – and extensive – Garda investigation resulted in a detailed file being sent to the DPP in 1999. No action was taken until 2003, when two surviving BTSB employees were eventually charged with causing seven women to become infected with hepatitis C. Separately, the Law Reform Commission recommended – without effect – that those in charge of organisations responsible for death should be charged with a new offence of corporate killing.

The extraordinary delay in the DPP's office was later categorised by a High Court judge as "blameworthy". And it was used by the two defendants in a series of legal challenges, along with the death of witnesses, as reason to abort their trials. But the court ruled, following the death of one defendant in 2006, that the public right to have a trial on a serious charge outweighed such considerations. That judgment has now been effectively overturned by the DPP's decision to drop all charges against the remaining defendant. Justice delayed has amounted to justice denied. And while nobody believes the BTSB officials behaved maliciously, they failed in their duty. As politicians, public servants and senior executives continue to evade their responsibilities, a new approach is required.

Hepatitis C action plan 'delayed'

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

An action plan drawn up to tackle the growing threat posed by hepatitis C in Wales is three years behind schedule, according to a group of MPs.

A parliamentary report claims the Welsh Assembly Government has drafted the plan, originally due in 2006, but has failed to publish it.

The Hepatitis C Trust accused ministers in Wales of "ignoring" sufferers.

The assembly government said Health Minister Edwina Hart was expected to publish the plan

shortly.

Hepatitis is an inflammation of the liver and hepatitis C is one of several viruses that can cause the illness.

Research from the University of Southampton estimates there are as many as 466,000 infected people in the UK, with 12,000 in Wales.

But the all party parliamentary hepatology group said there were "vastly inconsistent approaches in how hepatitis C is being tackled across the UK".

Its report shows Scotland is leading England and Wales in its response to the public health challenge and it has drawn up a two-phase action plan.

However, the Blood Borne Viral Hepatitis Action Plan for Wales, tackling both hepatitis B and C, has been drafted but not published or put out for consultation, said the MPs.

"Our report shows there's so much more that needs to be done to tackle hepatitis C in England and Wales," said Bob Laxton MP, co-chair of the all party parliamentary hepatology group.

"Scotland is leading the way and we must quickly follow otherwise we will continue to see more and more unnecessary deaths from hepatitis C."

'Little progress'

Charles Gore, chief executive of The Hepatitis C Trust, said the assembly government could not be allowed to continue postponing publication of its action plan any longer.

"Years have gone by with very little progress while the death toll just keeps growing - why are patients in Wales being ignored?" he added.

The assembly government said it was committed to meeting the challenge of blood-borne viral hepatitis.

A spokesman said: "A significant amount of work has been undertaken in the development of an action plan.

"A draft plan, prepared by the National Public Health Service (NPHS), was submitted to assembly government officials for consideration.

"The process for setting budget allocations for 2009-10 and beyond is currently underway and the costs and timetable for implementing the plan is being considered in that process."

There is no vaccine to protect against hepatitis C, which is usually transmitted through blood-to-blood contact, but there is effective treatment available.

According to the MPs' report, if left undiagnosed and untreated, the future burden of hepatitis C on the NHS in the UK could reach up to £8bn during the next 30 years.

Metabolic Syndrome Raises Liver Cirrhosis Risk in Patients with Hepatitis B

www.medscape.com

NEW YORK (Reuters Health) Jan 14 - The results of a study published in the January issue of the journal *Gut* suggest that metabolic syndrome is an independent risk factor for liver cirrhosis in patients with chronic hepatitis B.

"Metabolic syndrome is associated with non-alcoholic steatohepatitis and cryptogenic cirrhosis," Dr. H-Y Chan and colleagues from the Chinese University of Hong Kong write. "Whether metabolic syndrome affects the severity of chronic hepatitis B is unclear."

The researchers examined the prevalence of metabolic syndrome in patients with chronic hepatitis B, and assessed the relationship between viral factors, metabolic syndrome, and the risk of liver cirrhosis. Patients with chronic hepatitis B were prospectively recruited from primary care and hospital clinics. Liver stiffness measurement was performed using transient elastography to diagnose early cirrhosis.

A total of 1466 patients (mean age 46 years) with reliable liver stiffness measurements were included in the analysis. The subjects had a mean body mass index of 23.

Of the 1466 patients, 188 (13%) had metabolic syndrome. A subgroup of 167 patients underwent liver biopsy and 134 (80%) of these patients had adequate samples for histological assessment. Histological liver cirrhosis was found in 32 of 134 subjects (24%) with adequate liver biopsy.

Overall, 38% of patients with metabolic syndrome had histological liver cirrhosis, compared with 11% of those without metabolic syndrome ($p < 0.001$).

Results of multivariate logistic regression analysis demonstrated that metabolic syndrome remained an independent factor associated with probable cirrhosis (odds ratio 1.7).

The ORs for development of probable cirrhosis correlated with an increasing number of components of metabolic syndrome. In patients with one, two, three, four, or five components of metabolic syndrome, the ORs of probable cirrhosis increased proportionally at 1.4, 2.6, 4.1, 4.0, and 5.5, respectively.

"The underlying mechanism of the progression of fibrosis in relation to metabolic syndrome could be a direct stimulation of liver stellate cells by hyperinsulinemia and hyperglycemia, resulting in increased production of the connective tissue growth factor and subsequent accumulation of extracellular matrix," Dr. Chan's team suggests. "One possible hypothesis would be insulin resistance as the major driving force for liver fibrosis progression."

Gut 2009;58:111-117.

Manhattan Dialysis Center Notifies Patients Of Possible Exposure To Infections

<http://www.emaxhealth.com>

A Manhattan dialysis center is notifying patients after the facility identified, and a State Department of Health (DOH) investigation confirmed, one patient who contracted hepatitis C after undergoing dialysis there.

Approximately 170 patients of the Upper Manhattan Dialysis Center of Beth Israel Medical Center at 2465-67 Broadway in Manhattan are being notified in person or by mail that they may have been exposed to hepatitis C and possibly other bloodborne viruses while being treated at the facility.

"This situation is an example of infection prevention guidelines in action: frequent testing can quickly identify a problem. Steps can be taken right away to correct possible problems, and patients can be notified and tested," said Health Commissioner Richard F. Daines, M.D. He commended the facility on the completeness of testing and response. Patients who receive care at Upper Manhattan Dialysis Center are routinely screened for hepatitis B and C, both bloodborne viruses.

The transmission was identified after routine testing conducted by the facility identified a patient who became infected with hepatitis C while receiving treatment at the facility. DOH's investigation concluded that transmission had occurred at the dialysis center. The facility and DOH each conducted a thorough investigation that included an assessment of infection control procedures by a panel of independent experts. Neither assessment found major deficiencies, and the facility incorporated all of the experts' recommendations immediately.

DOH is recommending that only patients who were dialyzed at the Upper Manhattan Dialysis Center since February 2007 be tested promptly. Information packets are in the process of being delivered to all at-risk patients. Letters advise patients to get tested for the hepatitis C virus, hepatitis B virus, and human immunodeficiency virus (HIV). Testing can be done through the facility. There is no evidence at this time that any patient has contracted hepatitis B or HIV at the facility.

Hepatitis C is a liver disease caused by the hepatitis C virus and is spread by contact with the blood of an infected person. It is estimated that 1.6 percent of the population of New York State has been infected with hepatitis C.

By: New York Department Of Health - Thu, 01/15/2009 - 14:29

30 test positive for infection after High Prairie syringe scare

www.cbc.ca

Statistics may reflect prevalence in general population, official says

Thirty out of approximately 1,000 former endoscopy and dental surgery patients of the High

Prairie Health Complex have tested positive for hepatitis B, hepatitis C or HIV, health officials in High Prairie told CBC News on Wednesday.

The tests were ordered last fall after it was revealed single-use syringes had been reused at the health complex to inject medication into intravenous lines for years.

Final numbers are not in yet, and the statistics could simply be a reflection of the prevalence of these infections in the general population, according to Alberta's acting chief medical officer of health, Dr. Gerry Predy.

"These infections they're looking for ... hepatitis B and C and HIV, are relatively common. So if you're going to test hundreds of people, you will get some positives," he said.

The number of people who tested positive for each disease has not been released.

In November, the health region announced it would offer blood tests to 1,381 former patients who may have been at risk of infection.

It is still not clear whether those who tested positive were infected because of a health-care procedure, and Predy said determining that may be difficult.

"Once they find somebody who got an infection, they will ... look at that person's experience, risk factors and see if there might be any other explanations," he said.

"It's a pretty involved process to do all these analyses."

A preliminary report on the individuals who have been tested is expected by the end of the month, Predy said.

Health officials have insisted the risk of infection from the reuse of the single-use syringes is very low.

However, the practice was stopped in High Prairie as soon as it was discovered.

Panel considers cannabis for more uses

<http://www.krqe.com>

Reporter: Crystal Gutierrez

Web Producer: Devon Armijo

ALBUQUERQUE (KRQE) - Post traumatic stress disorder, nerve pain and Hepatitis C could soon be added to the list of ailments treated by medical marijuana in New Mexico.

On Thursday, petitioners asked a medical group to recommend the use of medical marijuana for several other ailments.

Medical marijuana became legal in New Mexico in July 2007.

There are currently seven qualifying conditions for acceptance to smoke marijuana in the state.

The petitions were heard by an out of state medical group.

So far four of the 17 ailments petitioned Thursday will be placed on a recommendation list that will go to the secretary of health for approval.

Many of the petitioners said that the recommendations are step in the right direction.

"It helps her cope and it gives her relief from pain. And how could we deny that for anyone with something as safe as medical marijuana," medical marijuana supporter Stephen Hunt said.

The panel has tabled some ailments including chronic pain. They said some of the tabled ailments need to be further researched.

The use of medical marijuana to treat depression was denied by the panel.

206 people in New Mexico have been granted medical marijuana licenses since the law took effect in 2007.

FDA okays new drug to treat fibromyalgia

<http://www.sciam.com>

The U.S. Food and Drug Administration (FDA) has approved a new med to treat fibromyalgia, a mysterious disease characterized by chronic widespread pain, fatigue, sleep disturbances and depression.

The agency yesterday gave its nod to **Savella** (milnacipran HCL), a type of antidepressant known as a dual selective serotonin and norepinephrine reuptake inhibitor (SSNRI), according to drug makers New York City-based Forest Laboratories and Cypress Bioscience in San Diego. SSNRIs work by making it easier for neurons (nerve cells) in the brain to use the neurotransmitters serotonin and norepinephrine to send signals to one another. Both of these neurotransmitters are known to play a key role in regulating pain and mood.

Until now, only two drugs were available for treating fibromyalgia: Cymbalta made by Eli Lilly (an antidepressant and painkiller), and Pfizer's Lyrica, an Rx designed to control seizures and pain. The drugmakers said in a statement that Savella is expected to be available in U.S. pharmacies by March 2009.

According to the American College of Rheumatology, as many as 12 million people in the U.S. (4 percent of the population) suffer from fibromyalgia. The cause of this puzzling ailment is unknown, but scientists suspect genetic factors and chronic stress may be involved.

The FDA nod comes just days after a study appeared in JAMA The Journal of the American Medical Association that found that Savella and several other drugs traditionally used as antidepressants reduced some of the symptoms of fibromyalgia.

Milnacipran is approved for use as an antidepressant (called Ixel and Toledomin) in several European, Asian, and South American countries.

"It's definitely a step in the right direction, but it's not the final answer," says Rae Marie Gleason, Executive Director of the National Fibromyalgia Association, a nonprofit based in Anaheim, Calif. Gleason says that neither Savella, nor the other two drugs currently FDA-approved, work for all patients or eliminate all symptoms. Researchers should continue studying, she says "combination treatments [that integrate medication with exercise and counseling] and other medicines that might come on board."