

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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In This Issue:

- [Artificial Liver Extends Lives](#)
- [Two transplants later, couple longs for home](#)
- [Merck to buy Schering-Plough for US\\$41.1-billion](#)
- [Human Genome hepatitis C drug disappoints, shares crash](#)
- [Infection control flaws found at most Nev. Clinics](#)
- [Scripps Research Team Identifies Key Molecules that Inhibit Viral Production](#)
- [16 patients have hepatitis in Army needle scare](#)
- [IHC cleared after carer catches hepatitis](#)
- [Public health warning issued over Mississauga tattoo parlour](#)
- [Ethnic Differences Found for Fatty Liver Disease and Insulin Resistance](#)
- [Hepatitis C increased risk for immune thrombocytopenic purpura](#)
- [FDA Approves Expanded Indication for Peginterferon-Based Combination Therapy for Chronic HCV](#)
- [VA Denies Hepatitis Results](#)
- [Roche and Genentech Reach a Friendly Agreement to Combine the Two Organizations and Create a Leader in Healthcare Innovation](#)
- [Vertex Pharmaceuticals Closes on Acquisition of ViroChem Pharma](#)
- [Anadys CEO says in late-stage partnership discussions](#)
- [Doctor fears needle disease outbreak](#)

Artificial Liver Extends Lives

<http://www.thedenverchannel.com>

BACKGROUND: Each year, more than 6,000 people undergo a liver transplant in the United States, says the Organ Procurement and Transplantation Network. Patients receive donor livers either from someone with a healthy liver who has recently died or a family member who donates part of his or her liver.

The Mayo Clinic says patients who qualify for liver transplants have failed to respond to other medical or surgical treatment for serious problems caused by a liver disorder; need a transplant to replace cancerous tumors of the liver or bile ducts like hepatocellular carcinoma and cholangiocarcinoma; or need a transplant to cure abnormalities in metabolism that threaten long-term health.

Some diseases that damage the liver to the extent that a patient might need a transplant include Hepatitis B and C, alcoholic liver disease, genetic high cholesterol and liver tumors if they are confined to the liver.

For patients who might otherwise die, a liver transplant is a life-saving operation. About 75 percent of patients survive three years or longer after a transplant, according to the National Institutes of Health.

Risks involved with liver transplants are most serious after surgery. These include a life-long need for immunosuppressive drugs -- which weaken the body's ability to fight off infections -- and transplant rejection. Transplant rejection happens when the body of a patient who has received an organ attacks that transplanted organ. Doctors try to prevent this by "typing" the organ to identify antigens it contains and make the new organ match the patient as closely as possible. However, since no two people are identical, no two people have identical organs.

A DANGEROUS GAP: While 6,000 liver transplants are performed every year, 27,000 die from liver disease. This is in part because it's hard to replace the functions of the liver without a transplant. Dialysis can provide good support for failed kidneys, various assistive devices can sustain a failed heart, but options like that aren't available for failed livers.

"The attempt to provide liver support has been far more challenging because most of those efforts were largely focused on trying to replace the filtering capabilities of the liver without replacing the synthetic functions, or the things that the liver cell makes that are also missing in the failing liver," Robert S. Brown, Jr., M.D., a liver disease and liver transplant specialist at New York-Presbyterian Hospital/Columbia in New York, N.Y., said.

A NEW SOLUTION: A new out-of-body artificial liver is addressing the problem by essentially doing what dialysis does for kidneys. A patient's plasma passes through the dialysis membrane in the machine. The plasma then filters through human liver cells. "That plasma then bathes these liver cells, and the liver cells perform their function and return purified and detoxified plasma to the patient," Dr. Brown said.

FOR MORE INFORMATION, PLEASE CONTACT:
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March 8, 2009

Two transplants later, couple longs for home

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

by Tom Shea

Phyllis Chretien laughs.

It's nice to hear her laugh, after all she has been through.

"No," I don't have a Southern accent.

Pause.

"Yet," she adds.

Phyllis and her husband Don of Springfield have been living in Jacksonville, Fla., since November 2007, almost 16 months.

The couple moved south because Don, 60, was on a liver transplant list at the Mayo Clinic in Jacksonville, leaving behind their jobs, family, friends and 16 Acres home.

Don was suffering from end-stage liver disease caused by hepatitis C.

The hope was that he might be able to undergo a transplant within four months.

"But," his stepson, Dennis Wassung says. "It is all about supply and demand. It is about matching donors and blood types. It can get complicated. It can test your patience." So Don and Phyllis waited and waited, in a rented partially furnished first-floor apartment, a five-minute drive from the hospital.

Phyllis' sons, Dennis and Dan, chipped in to purchase their parents the baseball cable package so Don could watch his beloved Red Sox and make Massachusetts and home feel not that far away.

On the Monday before Thanksgiving 2008, a little less than a year after they moved south, Don received his liver transplant.

The operation was considered a success. Recovery was steady and sure - until it wasn't in early January of this year.

"It started to become very obvious Don was going to need another transplant," Dennis says. "Fast."

On Feb. 2, Don underwent his second liver transplant in 39 days.

Recovery has been slower this time, but progress is being made.

Don was released from the hospital on Feb. 25.

Most days he has to return to the Mayo Clinic for various tests. He still takes more than 20 prescription medicines. He can walk, but spends much of the day navigating the world in a wheelchair.

Phyllis, everybody says, has been nothing short of heroic in supporting her husband of 23 years.

"If you are ever in need of serious medical care, the Mayo Clinic is the place to be," Phyllis says. "They are thorough, gracious, compassionate. I'm talking the doctors, nurses, and, the house cleaning crew. And Jacksonville has been wonderful. The people have been very friendly, except when they are driving."

She laughs again.

The best soul medicine for both, though, was last week when Dennis brought his two sons, Parker and Cooper, to visit.

"We can't get enough of them," Phyllis says. "Don out of hospital, making progress, the kids here. It was good to get some good news."

Don worked as a salesman for a building supply company. Phyllis was a popular manicurist at Allure Nail Salon on Springfield's Dickinson Street. They were happily middle class. Texas Roadhouse people for their weekly treat.

Now they have bills and debts as high as the Alps.

"We never thought something like this could happen to us," Phyllis says. "No one ever does."

Dennis adds: "They aren't the kind of people who would ask for help. They are used to helping."

He and his brother have started a fund drive to help Don and Phyllis with COBRA medical insurance premiums, and prescription co-pays.

"Through the National Transplant Assistance Fund (NTAF) we've opened an account in Don's honor," Dennis says. "The NTAF is non-profit, tax-exempt organization, and donations are tax-deductible. If you'd like to help go to www.transplantfund.org and enter Chretien in the find a patient website box. Given the current economic climate, our family sincerely appreciates any and all contributions."

"People have been so nice," Phyllis says. "I miss Springfield. I miss my friends. My job. The fact my grandchildren are only a car ride away. The only thing I haven't missed has been two winters. But I'm looking forward to next year's. Everybody home and happy. Our life back."

March 9, 2009

Merck to buy Schering-Plough for US\$41.1-billion

<http://www.financialpost.com>

NEW YORK - Merck & Co Inc. said on Monday that it would acquire Schering-Plough Corp for \$41.1-billion, uniting the makers of cholesterol drugs Zetia and Vytorin, in the second megadeal for Big Pharma in weeks.

The two New Jersey-based drugmakers, which announced significant job cuts last fall, have been striving to become more efficient amid setbacks to Vytorin and Zetia, whose combined fourth-quarter sales slumped 26 percent.

Under the agreement, Schering-Plough shareholders will receive 0.5767 shares of Merck and \$10.50 in cash for each of their shares. Each Merck share will automatically become a share of the combined company.

Merck Chief Executive Richard Clark will lead the combined company.

The Merck/Schering-Plough marriage follows on the heels of the \$68 billion Pfizer purchase of Wyeth, another New Jersey-based pharmaceutical company. It finally consummates a deal that has been speculated upon for years, given the marketing partnerships and cost savings opportunities between Merck and Schering-Plough.

Human Genome hepatitis C drug disappoints, shares crash

www.reuters.com

By Jennifer Robin Raj

BANGALORE (Reuters) - Human Genome Sciences' (HGSIO) drug to treat chronic hepatitis C met the main goal in a late-stage trial, but failed to show numerically better efficacy compared to standard-of-care, raising questions about the drug's adoption and sending shares crashing to an all-time low.

Analysts had expected the trial to meet its main goal of non-inferiority compared to Pegasys, but they had also said that the trial must show numerically better sustained virologic response (SVR) rates to convince the market of the drug's commercial viability.

In the trial, named ACHIEVE 1, patients were either given the drug Albuferon every two weeks or standard-of-care Pegasys once weekly and the company said the rate of SVR among the two groups "was comparable."

"This means that you have a drug that is statistically comparable but for the vast majority of prescribers who have used Pegasys for ever, they are not going to change their prescribing trends based on this data," said Piper Jaffray analyst Edward Tenthoff.

The current standard of care for hepatitis C is antiviral ribavirin in combination with an interferon. Human Genome's Albuferon, which is a type of interferon, was also being studied in

combination with ribavirin.

Interferons currently in the market are Roche's (ROG.VX) Pegasys and Schering-Plough Corp's (SGP.N) PegIntron. Interferon treatment is hard to tolerate and can cause flu-like symptoms.

Patients on the arm receiving 900 micrograms of albuferon had SVR rates of 48.2 percent, while patients on the Pegasys arm achieved SVR rates of 51.0 percent.

Patients originally randomized to receive 1,200 micrograms of albuferon had SVR rates of 47.3 percent.

"SVR rate is the key prescribing criteria (for physicians). With a numerically inferior SVR rate, Albuferon will have difficulty unseating market leader Pegasys," said Tenthoff, who downgraded the stock to "neutral."

Albuferon's sole benefit is less frequent dosing but the trial did not show the quality of life benefits observed in prior studies, Tenthoff said and cut his price target on the stock to \$1.70 from \$6.

Higher rate of pulmonary adverse events and discontinuations in the albuferon arm may limit its ability to take market share from Pegasys, said Leerink Swann's Joseph Schwartz.

The company also has \$404 million in convertible debt due in 2011 and 2012.

"We project Human Genome has sufficient cash to reach Albuferon approval next year. However, we believe the debt will remain an overhang and negatively impacts our cash flow projection," Piper's Tenthoff added.

Human Genome is developing Albuferon in partnership with Swiss drugmaker Novartis (NOVN.VX) under an agreement signed in June 2006.

The company expects to file for marketing approvals globally in the fall of 2009.

Shares of Human Genome, which touched an all-time low of 80 cents, recovered some losses to trade at 95 cents in midday trade on Nasdaq.

(Editing by Himani Sarkar)

March 10, 2009

Infection control flaws found at most Nev. Clinics

<http://www.mercurynews.com>

The Associated Press

LAS VEGAS—A state health investigation found 25 of 49 outpatient surgical centers in Nevada had infection control deficiencies similar to those blamed for an outbreak of hepatitis C last year in Las Vegas.

A draft report found inappropriate use of single-use items such as syringes accounted for nearly one-third of infection-control problems identified in fiscal 2008, and that sterilization and disinfection issues accounted for almost half.

Marla McDade Williams, chief of the state's Bureau of Health Care Quality and Compliance, called it a concern that regulations weren't being followed. She said stepped-up inspections by staff surveyors would reinforce the regulations for ambulatory surgical centers.

"We want them to know far more frequently that there are state standards that they must adhere to," Williams said.

The division, formerly known as Licensure and Certification, has 34 surveyors and 14 supervisors who do inspections of nursing homes, ambulatory surgery clinics, group homes and hospitals. Williams said adding 11 surveyors would allow inspections of all 1,100 state-licensed facilities every 18 months.

She said money for more surveyors could come from increased licensing fees collected from the facilities.

Williams said that in the past, state surveyors spent 70 percent of their time with facilities such as nursing homes that the federal Centers for Medicare and Medicaid Services pay Nevada to certify and inspect.

The report, issued Friday, didn't identify which surgical centers not connected to the hepatitis outbreak investigation had deficiencies.

Nevada State Health Division spokeswoman Martha Framsted said that by summer, all health care surveys will be posted on a Web site for the public to examine.

Health officials advised some 50,000 Las Vegas-area patients in February 2008 to get tested for exposure to hepatitis C, after inspectors reported finding doctors and nurses had been reusing syringes and vials of anesthesia at two now-closed outpatient endoscopy centers.

The effort represented the largest patient notification in U.S. history

Nine people were found to have contracted the debilitating and incurable liver virus, and health authorities identified another 105 cases of hepatitis C that may have been linked to the clinics.

The public health crisis has spawned more than 100 lawsuits, and several bills are now under consideration by the Nevada Legislature.

Information from: *Las Vegas Review-Journal*, <http://www.lvrj.com>

Scripps Research Team Identifies Key Molecules that Inhibit Viral Production

<http://www.allamericanpatriots.com>

Discovery May Aid in the Development of Anti-Hepatitis C Virus Drugs

JUPITER, FL, March 9, 2009—A team from The Scripps Research Institute has found a way to inhibit viral production of the Hepatitis C virus (HCV). The advance has the potential to accelerate future research on the virus life cycle and to aid in the development of novel HCV drugs.

The research, led by Professor Donny Strosberg of Scripps Florida, was published on March 4, 2009, in the *Journal of General Virology's* advance, online edition, *Papers in Press*.

In the new study, Strosberg and his colleagues describe peptides (molecules of two or more amino acids) derived from the core protein of hepatitis C. The team found that these peptides inhibit not only dimerization of the core protein (the joining of two identical subunits), but also production of the actual virus itself.

"We went for the simplest solution, taking a peptide from core to see if we could block the interaction," Strosberg said, "and it did."

The Problem with Hepatitis C

With over 170 million people infected worldwide by HCV, new therapeutic strategies for HCV—a blood-borne disease that affects the liver—are urgently needed.

But one of the critical problems in developing drugs for HCV is that it mutates at such prodigious rates. An RNA virus like hepatitis C can mutate at a rate estimated as high as one million times that of DNA viruses; in contrast, DNA viruses contain an enzyme (polymerase) that acts as something of a proof reader to ensure that newly transcribed DNA strands are the same as the original, helping to reduce mutations.

"In one sense, the ongoing issue with hepatitis C is that there are still so very few drugs to treat the virus and very few tools to study it," Strosberg said. "We set out to develop new tools and to identify a new target – core, the capsid protein. By targeting the interactions of core with itself or other proteins, we could reduce the problem of rapid mutation not only because the core protein mutates significantly less, but also because mutations that would affect the interface between core and itself or other proteins would often be more likely to deactivate the virus, in contrast to mutations in viral enzymes which often lead to increased resistance to drugs."

Recent efforts to develop therapeutic strategies against HCV have concentrated on designing inhibitors that target several of the 10 HCV proteins that comprise the virus, including mostly the non-structural proteins. However, as the study points out, the one HCV structural protein that has not been targeted yet is the core protein, the one responsible for assembly and packaging of the HCV RNA genome.

The Core of the Matter

Core, the most conserved protein among all HCV genotypes, plays several essential roles in the viral cycle in the host cell; studies have suggested that these core-core or core-other protein interactions can modulate various functions including signaling, apoptosis or programmed cell death, lipid metabolism, and gene transcription.

The core protein is particularly important in the assembly of the hepatitis C nucleocapsid, an essential step in the formation of infectious viral particles; the nucleocapsid is the viral genome protected by a protein coat—the capsid. This core protein plays an essential role in the HCV cycle during assembly and release of the infectious virus, as well as disassembly of viral particles upon entering host cells.

Looking closely at the core interaction with itself, Strosberg developed several novel quantitative assays or tests for monitoring these protein-protein interactions with the specific goal of identifying inhibitors of the core dimerization, which would block virus production.

"People have been dreaming about inhibiting protein-protein interactions, as a new El Dorado for finding novel drug targets," says Strosberg, "but few conclusive studies have emerged, except in the virus-host area."

Inhibition of HCV Production

The new research, however, led to the discovery of two peptides that inhibited HCV production by 68 percent and 63 percent, respectively; a third related peptide showed 50 percent inhibition. When added to HCV-infected cells, each of the three peptides blocked release but not replication of infectious virus; viral RNA levels were reduced by seven fold. Strosberg notes that the efficacy of small molecules like these can often be improved over initial levels.

"After we'd finished our work, we learned that Frank Chisari—one of the leading experts on HCV who works at Scripps Research in La Jolla—had been looking at similar peptides using a very different approach," said Strosberg. "One of his peptides was the same as ours—it also inhibited virus production. It's an incredible coincidence and a confirmation of our study."

The first author of the study, "Peptide Inhibitors of Hepatitis C Core Oligomerization and Virus Production," is Smitha Kota, a member of the Strosberg laboratory at The Scripps Research Institute's Florida campus. Other authors include Carlos Coito, and Guillaume Mousseau of The Scripps Research Institute and J-P Lavergne of the Institut de Biologie et Chimie des Protéines of the CNRS at the University of Lyon, France. See <http://vir.sgmjournals.org/cgi/content/abstract/vir.0.008565-0v1>.

The study was supported by The Scripps Research Institute and The Factor Foundation (Florida).

Source: The Scripps Research Institute

16 patients have hepatitis in Army needle scare

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

By Alicia A. Caldwell - The Associated Press

EL PASO, Texas — Army officials say 16 patients exposed to a mismanaged insulin needle program have tested positive for hepatitis B or C.

The William Beaumont Army Medical Center patients were among more than 2,000 diabetics who may have been exposed to blood-borne illnesses between August 2007 and January 2009 because of the program that systematically gave multiple patients injections from the same

insulin pen.

Officials at the Army hospital at Fort Bliss have said it's unclear if the patients contracted hepatitis from the injections

IHC cleared after carer catches hepatitis

<http://www.nzherald.co.nz>

By Andrew Koubaridis

The IHC is not to blame for one of its staff catching hepatitis B from a woman she was caring for because it accepted her word she had been immunised, a court has ruled.

The worker, who has name suppression, was providing live-in care for an intellectually disabled Hawkes Bay woman with hepatitis B. The woman was unsteady on her feet and twice fell on the carer with her teeth breaking the carer's skin.

After both injuries the carer sought medical help and was tested for hepatitis B. She said she had been immunised years earlier when she began working as a carer but the test showed that she was not immune to the disease

and the doctor did not tell her. After the second injury the doctor did not refer to the blood test or give her medication to prevent her developing the disease and she was diagnosed with hepatitis B soon after. She suffered kidney and liver failure and eventually needed a liver transplant.

The Department of Labour took the case to court because it believed the woman suffered "serious harm" which Idea Services had failed to take "practicable" steps to prevent.

It said that Idea Services - the IHC's community services provider - should have screened for hepatitis B.

But in a ruling in the Hastings District Court in November, Judge Geoff Rea said it was not practicable for an employer to demand a blood test to prove immunity. He was satisfied the carer had received enough training and Idea Services had done everything that could be realistically expected.

He said the carer claimed to be fully immunised even though she had only one of the three vaccinations needed.

He was "quite sure" the carer thought she was immune because he doubted she would have played "Russian roulette" with her health.

However, all that could be done was to "strongly recommend" screening and Judge Rea found that Idea Services had done that on "many occasions".

Philippa Sellens of IHC New Zealand said a conviction would have had "serious implications" for a number of sectors, not just disability but aged care, corrections and healthcare.

Public health warning issued over Mississauga tattoo parlour

<http://www.cbc.ca>

Public health officials are urging customers of a Mississauga, Ont., tattoo and piercing parlour over the last four years to get blood tests over concerns as many as 3,000 clients may have been exposed to hepatitis B, hepatitis C and HIV.

People who received tattoos or piercings at Moonshin Tattoo between March 2005 and February 2009 may have been exposed to equipment that was not adequately sterilized, said Dr. Eileen de Villa, associate medical officer of health for Peel Region.

De Villa said a health inspection of the facility last month, the first since 2005, determined that the studio did not have appropriate records to show it had sent samples from its sterilizer to be approved by an independent lab.

But she classified the risk to clients as "very low."

She said public health officials don't have the resources to conduct yearly inspections of such businesses, a standard set by the provincial Health Ministry.

"There has been a shortage of resources, particularly from the province, which has impacted the level of service that we would like to provide," de Villa told CBC News.

"At the end of the day, the onus is on the operators."

Store 'free to operate'

Since the February inspection, the shop has met all required standards for documentation and is "free to operate," de Villa added.

"They were asked to meet certain standards and they have done so," she said.

Public health officials are calling clients directly from a list provided by the studio to advise them and discuss testing, she said.

Those who received tattoos or body piercings at the studio should take the following precautions until blood tests rule out possible infections:

- Use a condom during sexual activity.
- Avoid sharing clippers, razors, toothbrushes, needles and other personal items.
- Postpone blood donations.

The shop's website says safety is its "No. 1 concern" and states that tools and equipment for tattooing "have been properly sterilized and kept in a sterile condition."

Calls placed by CBC News to the studio, which is regularly closed on Tuesdays, were not answered. The shop's voicemail system was full.

Ethnic Differences Found for Fatty Liver Disease and Insulin Resistance

www.medscape.com

Laurie Barclay, MD

February 28, 2009 — Ethnic differences have been found for nonalcoholic fatty liver disease (NAFLD) and insulin resistance, according to the results of the largest population-based study of this topic to date, reported in the March issue of *Hepatology*.

"[NAFLD] is a spectrum of disorders defined by abnormal accumulation of triglyceride in liver," write Richard Guerrero, from the University of Texas Southwestern Medical Center at Dallas, and colleagues. "We have previously shown that Hispanics were at greater risk for nonalcoholic fatty liver disease than were African-Americans despite a similar prevalence of risk factors between these groups."

The goal of this study was to assess the contribution of body fat distribution to the differing prevalence of hepatic steatosis in 3 major US ethnic groups: black, Hispanic, and white. Proton magnetic resonance spectroscopy, dual-energy x-ray absorptiometry, and multislice abdominal magnetic resonance imaging were performed in a study cohort of 2170 participants.

Compared with Hispanics and whites, blacks had less intraperitoneal (IP) fat and more lower extremity fat, despite controlling for age and total adiposity. After controlling for total, abdominal subcutaneous, and lower extremity adiposity, these groups still differed in hepatic triglyceride content (HTGC). Controlling for IP fat nearly abolished the differences in HTGC, however, which suggests that IP and liver fat are closely related independent of ethnicity.

Although blacks had lower levels of IP and liver fat, prevalence of insulin resistance in this group was similar to that in Hispanics, in whom levels of IP and liver fat were highest. After controlling for IP fat, blacks had the highest insulin levels and homeostasis model assessment values and the lowest serum triglyceride levels.

"IP fat is linked to HTGC, irrespective of ethnicity," the study authors write. "The differing prevalence of hepatic steatosis between these groups was associated with similar differences in visceral adiposity. The metabolic response to obesity and insulin resistance differs in African-Americans when compared to either Hispanics or Caucasians: African-Americans appear to be more resistant to both the accretion of triglyceride in the abdominal visceral compartment (adipose tissue and liver) and hypertriglyceridemia associated with insulin resistance."

Study limitations include inability to determine whether visceral fat causes the development of hepatic steatosis or is simply a marker of an underlying metabolic derangement contributing to excess liver fat.

"Many of the derangements in lipid metabolism typically associated with insulin resistance were not present in African-Americans," the study authors conclude. "A possible explanation for these findings is that the insulin-resistant phenotype is: (1) a function of the organ contributing primarily to reduced insulin sensitivity and/or (2) a function of the ability to expand subcutaneous adipose tissue in response to overnutrition. Further study is needed to establish the basis for this insulin resistance paradox."

The Donald W. Reynolds Cardiovascular Clinical Research Center at Dallas, supported by the National Institutes of Health grants, supported this study. The study authors have disclosed no relevant financial relationships.

Hepatology. 2009;49:791-801.

March 11, 2009

Hepatitis C increased risk for immune thrombocytopenic purpura

<http://www.hemonctoday.com>

by Leah Lawrence

Patients with hepatitis C may be at an increased risk for developing immune thrombocytopenic purpura, according to a study conducted among U.S. veterans. The treatment of hepatitis C with interferon alfa may also increase the risk of ITP as well as autoimmune hemolytic anemia, according to the study's findings.

Several small single-institution studies have previously linked hepatitis C to the development of autoimmune cytopenias. In this study, researchers examined a large cohort of 120,691 U.S. veterans infected with hepatitis C and compared them with 454,905 matched uninfected veterans. Mean follow-up was 2.5 years.

At the end of follow-up, there were 296 cases of ITP and 90 cases of autoimmune hemolytic anemia. The overall incidence rate of ITP was higher in veterans infected with hepatitis C compared with uninfected veterans (30.2 vs. 18.5 per 100,000 person years). Incidence of autoimmune hemolytic anemia was also higher among infected veterans compared with uninfected veterans (11.4 vs. 5.0 per 100,000 person years).

Infection with hepatitis C was associated with an increased risk for both ITP (HR=1.8; 95% CI, 1.4-2.3) and autoimmune hemolytic anemia (HR=2.8; 95% CI 1.8-2.4).

Researchers found that the development of autoimmune hemolytic anemia was associated with hepatitis C treatment and not the disease itself. Patients treated for hepatitis C had a HR of 11.6 for developing autoimmune hemolytic anemia (95% CI, 7.0-19.3).

However, both hepatitis C (HR=1.7; 95% CI, 1.3-2.2) and treatment for hepatitis C with interferon alfa (HR=2.4; 95% CI 1.5-3.7) were independently associated with an increased risk for ITP. by Leah Lawrence

Arch Intern Med. 2009;169:357-363

March 12, 2009

FDA Approves Expanded Indication for Peginterferon-Based Combination Therapy for Chronic HCV

www.medscape.com

Laurie Barclay, MD

March 12, 2009 — Schering-Plough Corporation announced yesterday that the US Food and Drug Administration (FDA) has approved an expanded indication for peginterferon-based combination therapy for chronic hepatitis C virus (HCV) infection. Peginterferon alfa-2b (PegIntron) and ribavirin, USP (Rebetol) combination therapy is no longer restricted to treatment-naive patients and may be used to treat chronic HCV infection in patients 3 years of age and older with compensated liver disease.

"With the FDA approval of Pegintron and Rebetol combination therapy for this new indication, U.S. physicians now have a treatment option that offers a second chance for success to certain patients who failed prior therapy," Robert J. Spiegel, MD, chief medical officer and senior vice president, Schering-Plough Research Institute, said in a news release.

In the United States, this pegylated interferon combination therapy is now the first and only such therapy available that is not restricted to treatment-naive patients, offering an important therapeutic option for selected patients refractory to previous HCV treatment. The numbers of such patients are increasing and currently exceed 100,000 patients.

Factors associated with lower probability of success from retreatment after failing a course of therapy include previous nonresponse, previous use of pegylated interferon, significant bridging fibrosis or cirrhosis, and infection with HCV genotype 1.

"Based on a patient's treatment history, physicians can identify which patients may be right for retreatment with Pegintron combination therapy and may have the best chance to achieve a sustained response," Eugene R. Schiff, MD, director of the Center for Liver Diseases, University of Miami Miller School of Medicine, Florida, and a lead investigator for the pivotal clinical trial, said in a news release. "Conversely, patients with certain treatment characteristics who are unlikely to respond to this regimen can be advised accordingly."

FDA approval of the expanded indication was based on findings from 1 of the clinical trials in Evaluation of PEG-INTRON in Control of Hepatitis C Cirrhosis study (EPIC3), in which achievement of undetectable HCV RNA at treatment week 12 strongly predicted sustained virologic response (SVR).

"Patients with undetectable virus at week 12 have a better chance for success and can be motivated to continue treatment, and those patients who fail to achieve an early response can have their therapy stopped with confidence, thus avoiding unnecessary treatment and potential adverse events," Dr. Schiff said.

In this noncomparative trial, 2293 adults with moderate to severe fibrosis or cirrhosis who failed previous treatment for at least 12 weeks with combination interferon alfa/ribavirin received peginterferon alfa-2b (1.5 µg/kg once weekly) plus weight-adjusted ribavirin (800 – 1400 mg daily). Prior nonresponders (who had detectable levels of HCV RNA after ≥12 weeks of treatment) and prior relapsers (who did not have detectable levels of HCV RNA at the end of treatment and later relapsed) were included.

Response rate, defined as undetectable HCV RNA at 24 weeks posttreatment, was 22% overall. At treatment week 12, 64% of patients did not achieve undetectable HCV RNA and were offered enrollment into long-term treatment trials. Among patients with undetectable HCV RNA at

treatment week 12, those infected with HCV genotype 1 had an SVR rate of 48% vs 70% for those with HCV genotype 2 or 3. For all HCV genotypes, patients with higher fibrosis scores were less likely to achieve SVR.

Regardless of HCV genotype, the recommended treatment duration with peginterferon alfa-2b combination therapy is 48 weeks. Retreated patients with detectable HCV RNA at week 12 or 24 are highly unlikely to achieve SVR, and discontinuing treatment should therefore be considered.

Adverse events associated with peginterferon alfa-2b and ribavirin as retreatment are similar to those reported during clinical trials of treatment-naïve patients. Interferon alfa therapy requires close monitoring with periodic clinical and laboratory evaluations, because it may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.

Ribavirin may cause birth defects and fetal death, so pregnancy must be avoided in female patients and in female partners of male patients. Ribavirin also causes hemolytic anemia and should be considered a potential carcinogen.

VA Denies Hepatitis Results

www.wsmv.com

Reported By Demetria Kalodimos

At Least 6 Colonoscopy Patients Test Positive

MURFREESBORO, Tenn. -- A lawsuit could be coming at the Veterans Administration for what might be thousands of risky colonoscopies performed at the York Hospital in Murfreesboro.

Video: Positive Hepatitis Results Denied By VA

The Channel 4 I-Team has learned of at least a half-dozen patients who had the procedure there and have tested positive for hepatitis. Yet, the VA is on record saying there are no positive results.

It's been almost three months since the problem was discovered: an incorrect valve on a colonoscopy machine that posed the potential for bacteria to flow out of one patient and into the next.

"We know there were two patients potentially exposed," said Dr. Walter Smalley, of York's gastroenterology division.

But since then, two patients have grown to more than 6,000. In fact, every veteran who had a colonoscopy over the past five years, doctors said, could have been exposed to hepatitis B or C or even HIV.

Wednesday, a Nashville law firm began running an Internet ad, looking for vets who have had the procedure and are worried. The lawyers don't know how many patients they may find. But in documents obtained by Channel 4 News, it is clear that VA doctors are worried about breaking

the news to patients.

Last month, one physician wrote to others, "Already I have received positive results for Hepatitis B and C and do not wish to convey this to the patients over the phone, and I am not doing it."

A second doctor wrote, "I also have three critical ... results that are positive already."

Yet another health professional said, "Some of my patients are coming in and getting positives for Hep. C. ... One in particular was neg (sic) in 2007."

But the VA, which has refused to grant an interview on the matter, paints a different picture, saying, "As of Feb. 25, 2009, there have been no positive results reported for any of the patients that have been tested."

Doctors said the difficult part of this puzzle will be to determine whether patients who do turn up with hepatitis might have had it all along.

Regardless, attorneys said, there has been medical damage done.

"We need to get that information from the VA, and we need to probably subpoena that information," said Mike Sheppard.

No lawsuit has been filed yet; the firm is simply wanting to talk with vets who are concerned.

Roche and Genentech Reach a Friendly Agreement to Combine the Two Organizations and Create a Leader in Healthcare Innovation

<http://www.foxbusiness.com>

*BASEL and SOUTH SAN FRANCISCO, March 12, 2009 /PRNewswire-FirstCall via COMTEX/ -
----- Research and early development to operate as an independent center; South San Francisco site to become headquarters of combined U.S. commercial operations; Genentech's unique culture to be maintained*

-- Innovation will be enhanced through a diversity of research approaches and sharing of IP, technologies, partnerships and other key assets

-- Transaction expected to be EPS accretive in the first year after closing

Roche (SWX: ROG.VX; RO.S) and Genentech (NYSE: DNA: 94.0101, 0.0851, 0.09%) announced today that they signed a merger agreement under which Roche will acquire the outstanding publicly held interest in Genentech for US\$95.00 per share in cash, or a total payment of approximately US\$46.8 billion to equity holders of Genentech other than Roche. The special committee of Genentech's Board of Directors has approved the agreement and recommends that Genentech shareholders tender their shares in Roche's tender offer.

Dr. Charles Sanders, Chairman of the Special Committee of Genentech's Board of Directors, said: "We believe this is a fair offer for Genentech shareholders, and the Committee is pleased to



come to a successful conclusion of this process. We look forward to working with Roche to complete the transaction as expeditiously as possible."

Franz B. Humer, Chairman of the Roche Group, said: "We are very pleased that we have reached an agreement with Genentech and secured a positive recommendation from the special committee. As stated previously, an agreed transaction offers clear and important advantages for the shareholders of both companies. I am delighted that the intensive negotiations have led to a successful conclusion. Working together, we aim to close the transaction quickly, thus removing uncertainty for employees and allowing us to focus even more intently on innovation and long-term projects. We have tremendous respect for our colleagues at Genentech and look forward to working with them to further accelerate our search for solutions to unmet medical needs."

Arthur D. Levinson, Ph.D., chairman and chief executive of Genentech, said: "We have had a highly successful partnership with Roche for more than 18 years, and we intend to pursue our shared goal of discovering medications for serious and life-threatening conditions. We look forward to working with our partners at Roche to ensure a smooth transition once the transaction is complete and to continue our mission of serving patients."

Severin Schwan, CEO of the Roche Group, said: "Roche and Genentech saw the potential of a pharma-biotechnology partnership early on and we are now in an enviable position to expand on the success of our longstanding relationship, which has been a source of immense value for patients, employees and shareholders of both companies. We are excited about working with our colleagues at Genentech and look forward to partnering with them to develop a plan for the successful combination of the two companies."

Roche will amend its existing tender offer to reflect the increased price and eliminate the financing and certain other conditions to the offer. The tender offer remains subject to the condition that a majority of the public shareholders tender their shares. If the tender offer is completed, Roche will promptly consummate a second-step merger in which all remaining public shareholders will, without the need for further action by any public shareholder, receive \$95.00 per share for their shares. Roche and Genentech have also amended their affiliation agreement to permit all shareholders to receive the same increased price in the tender offer and the merger. The expiration date for the offer is March 25, 2009. As of the close of business on March 11, 2009, approximately 2.9 million shares have been tendered pursuant to the offer.

Strong benefits for both Genentech and Roche

The combined company will be the seventh largest U.S. pharmaceuticals company in terms of market share. It will generate approximately US\$17 billion in annual revenues and will employ around 17,500 employees in the U.S. pharmaceuticals business alone, including a combined sales force of approximately 3,000 people.

Research and early development will operate as an independent center within Roche from its existing campus in South San Francisco, retaining its talent and approach to discovering and progressing new molecules. Roche's Pharma commercial operations in the U.S. will be moved from Nutley, New Jersey to Genentech's site in South San Francisco. The combined company's U.S. commercial operations in pharmaceuticals will operate under the Genentech name, leveraging the strong brand value of Genentech in the U.S. market. The existing U.S. sales organizations of both companies will be maintained, resulting in a very strong presence in

several specialty areas.

The transaction will provide the opportunity to simplify the structure of the combined organization and maximize the benefits of enhanced scale. Roche has already begun to wind down operations at its Palo Alto facility and will relocate the site's Virology research and development activities to South San Francisco. Roche's Palo Alto Inflammation group is in the process of becoming part of Roche's Nutley research and development organization. Genentech's Late Stage Development and Manufacturing operations will be combined with the global operations of Roche, achieving substantial scale benefits, operational synergies and cost avoidance. Roche's manufacturing operations in Nutley will be closed and support functions, such as informatics and finance, will be consolidated with those of Genentech.

Financial Information

Roche expects the combination to generate annual pre-tax cost synergies of approximately US\$750 to \$850 million. Synergies will be largely driven by reducing complexity and eliminating duplicative functions and processes in areas like late stage development, manufacturing, corporate administration and support functions. Savings resulting from this combination will enable the new company to increase and better focus its investment in innovation.

The transaction is expected to be accretive to Roche's earnings per share in the first year after closing. The combined company will generate substantial free cash flow that will enable it to rapidly reduce acquisition-related debt, invest in further product launches and retain strategic flexibility.

Additional information about the transaction, including the offering documents, is available at www.transactioninfo.com/roche/.

Genentech's recommendation to stockholders on Schedule 14D-9 to accept Roche's offer will be made available today on Genentech's website, www.genentech.com, and via EDGAR on the SEC's website, www.sec.gov, and will be mailed to Genentech stockholders.

Greenhill & Co. is acting as financial advisor to Roche and Davis Polk & Wardwell is acting as legal counsel. The Special Committee is represented by Goldman, Sachs & Co. and Latham & Watkins LLP. Genentech is represented by Wilson Sonsini Goodrich & Rosati.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, and is a market leader in virology. It is also active in other major therapeutic areas such as autoimmune diseases, inflammatory and metabolic disorders and diseases of the central nervous system. In 2008 sales by the Pharmaceuticals Division totaled 36.0 billion Swiss francs, and the Diagnostics Division posted sales of 9.7 billion francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested nearly 9 billion Swiss francs in R&D in 2008.

Worldwide, the Group employs about 80,000 people. Additional information is available on the Internet at www.roche.com.

About Genentech

Founded more than 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with significant unmet medical needs. The company has headquarters in South San Francisco, California and is listed on the New York Stock Exchange under the symbol DNA. For additional information about the company, please visit <http://www.gene.com>.

Vertex Pharmaceuticals Closes on Acquisition of ViroChem Pharma

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

-Purchase Price \$100 Million and 10.7 Million Shares-

-Vertex Acquires Two HCV Polymerase Inhibitors in Deal-

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX), completed its acquisition today of ViroChem Pharma Inc., a privately-held company with two investigational HCV polymerase inhibitors in clinical development. ViroChem shareholders received \$100 million in cash and approximately 10.7 million shares of Vertex common stock. The shares issued in this transaction are expected to be available for resale upon filing of the registration statement.

The acquisition advances Vertex's strategy to pursue novel combinations of Specifically Targeted Antiviral Therapies for hepatitis C (STAT-Cs) in the treatment of HCV infection. Vertex now owns worldwide rights to the ViroChem HCV drug development portfolio, including VCH-222 and VCH-759, which have demonstrated substantial reductions in plasma HCV RNA when dosed as single agents and have been well tolerated in early clinical studies to date. Vertex expects to begin clinical evaluation of novel combination regimens of its HCV protease inhibitor telaprevir, currently in Phase 3 clinical development, in the second half of 2009.

About Vertex

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical companies. Vertex's product pipeline is focused on viral diseases, cystic fibrosis, inflammation, autoimmune diseases, cancer, and pain. Vertex co-discovered the HIV protease inhibitor, Lexiva, with GlaxoSmithKline.

Lexiva is a registered trademark of the GlaxoSmithKline group of companies.

Vertex's press releases are available at www.vrtx.com.

Anadys CEO says in late-stage partnership discussions

<http://www.guardian.co.uk>

By Toni Clarke

**Says thinks its drug is ahead of VCH-222*

**Suggests Anadys worth more than ViroChem*

BOSTON, March 13 (Reuters) - Anadys Pharmaceuticals Inc said drugmakers are lining up to examine, and potentially acquire, its experimental hepatitis C treatment.

"We're in fairly advanced discussions," said Steve Worland, the company's chief executive, in an interview on Friday. "Five companies have conducted formal due diligence, and we have a couple more scheduled."

Worland said the company is wrapping up an important set of drug data that will be available by the end of March, giving all potential acquirers or licensing partners the opportunity to assess it on a level playing field.

Anadys's lead product, known as **ANA598**, is a non-nucleoside polymerase inhibitor that the company is preparing for mid-stage, or Phase II, clinical trials.

Many pharmaceutical companies are seeking to develop specifically targeted antiviral therapies for hepatitis C. Vertex Pharmaceuticals Inc is leading the charge with a protease inhibitor known as telaprevir that it hopes will cut current 48-week treatment time for the disease in half.

Earlier this month, Vertex acquired Canadian drugmaker ViroChem Pharma Inc in a deal valued at about \$375 million in cash and stock. ViroChem's lead product is a polymerase inhibitor known as VCH-222. It is in the early stages of development.

Protease and polymerase inhibitors block proteins the hepatitis C virus needs to replicate. Many experts believe the two classes of drug can complement each other when combined.

The race is on not only to develop leading drugs in each class, but to be first with a strong combination product.

Worland said the value of the ViroChem deal represents an important benchmark for valuing Anadys, which currently has a market value of \$170 million. He declined to place a value on the company but said ANA598 was more advanced than VCH-222 and "it would make logical sense" for Anadys to be more highly valued than ViroChem.

At first glance, however, ViroChem's drug appears to eliminate the virus more effectively than ANA598. Worland said ANA598 eliminated roughly 99.4 percent of the virus within 72 hours while VCH-222 eliminated 99.9 percent of the virus.

"They are both extremely potent and the difference is not necessarily a measure of how they will

work in combination," he said.

Vertex believes it will be first to the market with a treatment that combines its protease inhibitor telaprevir with polymerase inhibitor VCH-222 because telaprevir is the most advanced protease inhibitor in development. The company argues that the FDA would be more likely to approve a combination faster if it were familiar with one part of it.

Telaprevir is currently being tested in combination with standard hepatitis C treatments pegylated-interferon and ribavirin.

Anadys argues that the speed of approval for a combination product will depend not on the stage of development of the most advanced part of the combination, but on the "trailing part."

Worland said he believes ANA598 is more advanced than VCH-222, and assuming Anadys partnered with a company having a more advanced drug, its combination would be approved faster than a Vertex combination.

"The Food and Drug Administration has been fairly clear about what they want to see," Worland said. "Both products need to clear certain hurdles and we believe we will clear them before VCH-222."

Worland declined to identify which companies have conducted due diligence, but the list could include the combined Merck & Co Inc and Schering-Plough Corp, whose protease inhibitor boceprevir is slightly behind telaprevir in development; and Johnson & Johnson, which has rights to telaprevir outside the United States and Japan. J&J has a second-generation protease inhibitor in development.

Roche Holding AG is also a big player in hepatitis C. Other interested companies could include Pfizer Inc, Gilead Sciences Inc and Bristol-Myers Squibb Co.

Anadys closed 2008 with \$27.9 million in cash and expects to end the first quarter of this year with \$20 million.

In afternoon trading, Anadys shares were off 38 cents or 6.4 percent to \$5.60 on Nasdaq. (Reporting by Toni Clarke, editing by Gerald E. McCormick)

Doctor fears needle disease outbreak

<http://mnsi.com/>

Tim Edwards

Northern News Services

SOMBA K'E/YELLOWKNIFE - Intravenous crack cocaine, a huge factor in the HIV and hepatitis C outbreaks in Vancouver over the last few decades, is becoming a growing problem in Yellowknife, according to one emergency room doctor.

Dr. David Pontin took a break from his job as an emergency room physician to do an interview

about the health problems intravenous crack cocaine poses to our community

Dr. David Pontin, a physician at Stanton Territorial Hospital, said he is beginning to see IV crack-related cases of hepatitis C in the ER.

In a letter addressed to the territorial government, Pontin wrote: "We have a situation here that is akin to kindling waiting for a flame. Our homeless population is highly addicted already and the introduction of IV crack use is the flame that will cause an explosion of HIV and hepatitis C." Crack cocaine in smoking form has given rise to hepatitis C and HIV problems in the past due to unsafe sex practised while on the drug. But melted down and injected, crack cocaine really kicks the spread of these diseases into high gear, he said.

"A hardcore heroin addict might inject twice a day. A hardcore IV crack user might inject twice an hour," said Pontin. "The chances of spreading illnesses like HIV or hepatitis C through dirty syringes explodes."

Dr. Pontin worked for many years at a downtown Vancouver hospital and saw the monumental problem the city faced with drug addiction and communicable disease.

Upon moving here a few years ago, he saw a strikingly similar demographic. The downtown homeless population accounts for the majority of the ER visits to Stanton, he said, and most of those visits stem from drug or alcohol problems.

"It may be an early alarm bell," said Pontin. "But it's an alarm bell nonetheless, and we need to take this very seriously."

He said if nothing is done now, the costs to the public may be high. Not only is the prevalence of communicable disease a huge risk to public health, but if the diseases are improperly treated, problems like multi-drug-resistant HIV arise.

What Vancouver has implemented in order to curb the rocketing rates of syringe-spread disease is a "syringe exchange program," and the highly-controversial and experimental Insite - a supervised facility where drug users can come and ingest their previously acquired substances in the safest manner possible. The cornerstone of an addictions management program, according to Pontin, is having a needle exchange program in place to curb the spread and then talking to the addicts about getting off the drugs with things like detox programs and long-term treatment programs.

"First of all, before all that, it's a cultural kind of change (that needs to take place)," said Pontin.

"We're moving farther and farther away from this idea that addicts are criminals, but if you look at addiction as a health problem - as a chronic health problem - it is the most treatable and curable of all health problems."

The situation is getting dire, and serious action needs to be taken before this problem has a chance to get worse, said Pontin.

Dr. Cindy Orlaw, the NWT's chief medical officer, said she only recently became aware of

intravenous needle use in the city but that doesn't mean it's something that should be taken for granted.

"It's a drug you don't experiment with, because if you do crack cocaine once you're addicted forever and you'll never get that high again," said Orlaw, adding that people try crack cocaine intravenously in an attempt to reach a high they used to get by smoking it.

"It does not do that," said Orlaw.