

HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus
Editor-in-Chief*

Week Ending: August 9, 2008

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Aug 1, 2008

Etidronate Reduces Fractures in Osteoporotic Women With Liver Disease

www.reuters.com

NEW YORK (Reuters Health) Aug 01 - In postmenopausal women with osteoporosis and chronic viral liver disease, treatment with etidronate is associated with lower fracture rates over the long term, according to a report in the July *Journal of Medical Virology*.

"Cyclic etidronate treatment reduces the appearance of bone fractures," Dr. Yasuji Arase from Toranomon Hospital in Tokyo told Reuters Health. "The survival rate after episodes of bone fracture was poor. About half of the postmenopausal women with osteoporosis died at the fifth year after the bone fracture."

Dr. Arase and colleagues studied 80 postmenopausal women with osteoporosis and chronic liver disease due to hepatitis B or C who received etidronate (cycles of 200 mg daily for 2 weeks, followed by 10 weeks without etidronate) and 400 matched controls who were not given drugs for their postmenopausal osteoporosis.

After a mean follow-up of 8 years, 4.9% of women in the etidronate group had bone fractures, compared with 13.8% of women in the control group, the authors report.

On multivariate analysis, treatment with cyclic etidronate therapy, age under 65 years, and serum albumin level of at least 3.5 g/dL were independently associated with a lower rate of bone fracture. These factors were also associated with significant decreases in the risk for vertebral fracture.

"Adverse side effects of bisphosphonate are gastritis, gastric ulcer, and gastric bleeding," Dr. Arase said, "and patients with chronic hepatitis or liver cirrhosis tend to have these side effects. However, there were no severe or moderate side effects with cyclical etidronate therapy."

"A serum albumin level of at least 3.5 g/dL and cyclic etidronate treatment reduce the development of bone fracture in postmenopausal women with osteoporosis and chronic liver disease," the authors conclude.

J Med Virol 2008;80:1302-1307.

Aug 4, 2008

Schering-Plough drug results pressure Vertex stock

<http://news.yahoo.com>

Schering-Plough Corp (SGP.N) said on Monday that results from a study of its experimental hepatitis C drug showed promising results, sending the shares of rival Vertex Pharmaceuticals Inc (VRTX.O) down nearly 11 percent.

Schering's drug, **boceprevir**, is the closest competitor to Vertex's experimental hepatitis C drug **telaprevir** and, although Vertex is further ahead in development, investors are closely watching the competitive landscape.

Analysts said data from the mid-stage boceprevir trial was better than expected in patients who have not received previous treatment and a reminder that Vertex, while still in the lead, has rivals nipping at its heels.

Schering-Plough's shares rose nearly 3 percent to \$20 in afternoon trading.

The company said interim analysis of a mid-stage trial showed that at 48 weeks, 74 percent of patients receiving boceprevir in combination with standard treatment had undetectable levels of the hepatitis C virus in their blood for a sustained period of time, compared with 38 percent of patients receiving standard treatment alone.

The results were achieved by first giving patients a four-week "lead-in" time where they received the standard current treatment alone.

The company also tested a group of patients who did not receive "lead-in" treatment. In those patients, 66 percent saw the virus eliminated from the blood-stream.

Analysts said the results were solid, but most held to their view that Vertex's drug holds the commercial advantage since telaprevir requires a shorter period of treatment and appears to be more effective in patients who have failed previous therapies.

"Our model assumes telaprevir will face increased competition one to two years after launch," said Geoffrey Meacham, an analyst at JP Morgan, in a research report. "However, we believe telaprevir's profile is superior."

Hepatitis C is a viral infection of the liver. An estimated 170 million people worldwide are chronically infected with the virus, according to the World Health Organization.

Schering-Plough said that in two 28-week groups of the study, 56 percent of patients who received the lead-in treatment had not experienced a return of their virus 24-weeks later, while 55 percent of patients who did not receive the lead-in treatment continued to be virus-free.

Vertex shares fell about 11 percent to \$29.01 in afternoon trading, while the shares of Schering-Plough rose some 3 percent to \$21.08 on the New York Stock Exchange.

(Reporting by Toni Clarke, editing by Dave Zimmerman and Andre Grenon)

Many U.S. adults with chronic illness are uninsured

www.reuters.com

By Anne Harding

NEW YORK (Reuters Health) - An estimated 11.4 million Americans with at least one chronic illness have no health insurance, new research published in the *Annals of Internal Medicine* shows.

These people are much less likely to have a regular place to get medical care, much less likely to have seen a doctor in the past year, and much more likely to use the emergency room than chronically ill people who are insured, Dr. Andrew P. Wilper and colleagues from Cambridge Health Alliance/Harvard Medical School in Cambridge, Massachusetts, found.

"Primary care doctors know that people who don't have access to health care due to health insurance suffer," Wilper, who is now with the University of Washington School of Medicine in Seattle, told Reuters Health. "We wanted to study that issue and bring public attention to it."

He and his colleagues analyzed data from the National Health and Nutritional Examination Survey for 1999-2004, which included 12,486 men and women 18 to 64 years old. Based on this nationally representative sample, they calculated that 16.1 percent of people with heart disease, 15.5 percent of those with high blood pressure, and 16.6 percent of diabetics are uninsured.

Among the uninsured, 22.6 percent had not visited a physician in the previous 12 months, compared to 16.2 percent of insured chronically ill people.

The corresponding percentages for those lacking a regular site receiving health care were 22.6 percent and 6.2 percent, and for those using the emergency room for regular care the numbers were 7.1 percent and 1.1 percent.

After the researchers adjusted for age, gender and race or ethnicity, they found that the chronically ill uninsured patients were four to six times more likely than sick patients with insurance to have these access problems.

People with chronic illnesses who don't receive regular medical care run the risk of "catastrophic consequences," Wilper said.

For example, individuals whose diabetes isn't under control may wind up on dialysis for the rest of their lives, or need to have a limb amputated. Improving access to care could "prolong their life and prevent disabling complications and a lot of needless suffering," he added.

In an editorial accompanying Wilper's study, Dr. Marshall H. Chin of the University of Chicago writes, "Health care insurance reform is necessary for good care for chronic disease." However, he adds, it won't be enough until efforts are made to tackle disparities in health care.

Wilper noted that while both US presidential candidates are talking about health care reform, neither has a plan that will solve the issue of inadequate access to health care among chronically ill Americans. "Regardless of who wins the presidential election, for example, we won't see the problem that we defined here go away."

SOURCE: Annals of Internal Medicine, August 5, 2008

Top-Line Results of Boceprevir Phase II Study Showed High Rate of Sustained Response (SVR) in Genotype 1 Treatment-Naive Hepatitis C Patients

<http://pharmalive.com/>

74 percent of patients achieved SVR 12 with 48-week boceprevir-based combination therapy

KENILWORTH, N.J., August 04, 2008 /PRNewswire-FirstCall/ -- Schering-Plough Corporation today reported top-line results from a planned interim analysis of a Phase II study of boceprevir, its investigational oral hepatitis C protease inhibitor. The analysis showed a high rate of sustained virologic response (SVR) in patients receiving boceprevir-based combination therapy in this study of 595 treatment-naive patients with chronic hepatitis C virus (HCV) genotype 1.

In a 48-week treatment regimen, the SVR rate at 12 weeks after the end of treatment (SVR 12) was 74 percent (ITT) in patients who received 4 weeks of PEGINTRON(TM) (peginterferon alfa-2b) and REBETOL(R) (ribavirin, USP) prior to the addition of boceprevir (800 mg TID) (P/R lead-in), compared to 38 percent for patients in the control group receiving 48-weeks of PEGINTRON and REBETOL alone.(1-3)

Patients in the study who received 48-weeks of boceprevir in combination with PEGINTRON and REBETOL from the beginning of treatment (no P/R lead-in) achieved 66 percent SVR 12.

In the two 28-week boceprevir arms of the study, SVR at 24 weeks after the end of treatment (SVR 24) was 56 percent and 55 percent for patients in the lead-in and no lead-in arms, respectively.

Importantly, for patients who received the PEGINTRON and REBETOL lead in and had rapid virologic response (RVR), defined as undetectable virus (HCV-RNA) in plasma after 4 weeks of boceprevir treatment, SVR (ITT) was 82 percent in the 28-week regimen and 92 percent in the 48 week regimen.

"These top-line results with boceprevir are very exciting, especially given that genotype 1 is the most common and hardest to treat form of hepatitis C," said Paul Kwo, M.D., associate professor of medicine and medical director, liver transplantation, Department of Medicine, Division of Gastroenterology/Hepatology, , Indianapolis, and lead investigator of the study. "Boceprevir was well tolerated by patients in this study, including those who received 48 weeks of boceprevir in the longer duration treatment arms."

Safety data from the study showed that the most common adverse events reported in the boceprevir arms were fatigue, anemia, nausea and headache. No increase in skin adverse events (rash or pruritus) beyond what was seen in the PEGINTRON and REBETOL control arm was observed. Treatment discontinuations due to adverse events were between 9 and 19 percent for patients in the boceprevir arms, compared to 8 percent for the control arm.

In the study, known as HCV SPRINT-1 (HCV Serine Protease Inhibitor Therapy-1), boceprevir (800 mg TID) was evaluated in three treatment regimens: 4 weeks of PEGINTRON (1.5 mcg/kg once weekly) and REBETOL (800-1400 mg daily based on patient weight) therapy followed by the addition of boceprevir to the combination for 24 or 44 weeks (totaling 28 or 48 weeks of treatment); boceprevir in combination with PEGINTRON and REBETOL at the doses described above for 28 or 48 weeks; and boceprevir in combination with PEGINTRON and low-dose REBETOL (400-1000 mg daily) for 48 weeks, compared to a control of PEGINTRON (1.5 mcg/kg once weekly) and REBETOL (800-1400 mg daily based on patient weight) alone for 48 weeks (an approved treatment regimen). The primary endpoint of the study is SVR after 24 weeks of follow up (SVR 24). This is an ongoing study and SVR 24 rates are not yet available for patients in the 48-week boceprevir arms or the 48-week control arm of the study.

Sustained Virologic Response (ITT)*

Treatment Arm	All patients
No P/R Lead-in 28 Weeks	55% (59/107)
P/R Lead-in 28 Weeks	56% (58/103)
No P/R Lead-in 48 Weeks	66% (68/103)
P/R Lead-in 48 Weeks	74% (76/103)
P/R Control 48 Weeks	38% (39/104)

- *P/R Lead-in equals PEGINTRON and REBETOL for 4 weeks prior to the addition of boceprevir*
- *P/R Control equals PEGINTRON and REBETOL alone for 48 weeks*
- *SVR 12 for 48 week arms; SVR 24 for 28 week arms(1-3)*

"These top-line results further validate this novel treatment paradigm and the design of our pivotal Phase III studies of boceprevir, one in treatment-naïve patients and one in patients who had failed prior treatment, in which all patients will receive 4 weeks of PEGINTRON and REBETOL prior to the addition of boceprevir," said Thomas P. Koestler, Ph.D., executive vice president and president of Schering-Plough Research Institute. "Additionally, this strategy has the potential to reduce the likelihood of the development of resistance by identifying patients who are responders to interferon and ribavirin prior to their receiving a protease inhibitor."

The rationale for this novel treatment regimen is based on the fact that both PEGINTRON and REBETOL reach steady-state concentrations by week 4, so patients have the protease inhibitor added at a time when the backbone drug levels have been optimized. In addition, the patient's immune system will have been activated and primed by PEGINTRON at the time that boceprevir is added to the regimen. This approach may minimize the period of time when there is a "functional monotherapy" with a direct antiviral, potentially reducing the likelihood for the development of resistance.

The HCV SPRINT-1 study was conducted at sites across the United States, Canada and Europe. Overall, 77 percent of the 595 patients in the study were enrolled in the United States. African-Americans represent 16 percent of the patients enrolled and 7 percent of patients in the study are cirrhotic.

Results from the HCV SPRINT-1 study will be submitted for presentation at a major medical conference later this year.

About Boceprevir Phase III Studies

The boceprevir Phase III studies are expected to begin enrolling patients this summer. For more information about the Phase III study of boceprevir in treatment-naïve patients, known as HCV SPRINT-2, and the Phase III study in patients who failed prior treatment, known as HCV RESPOND-2, please visit www.clinicaltrials.gov, search term boceprevir.

Endnotes:

- (1) SVR, the protocol specified primary efficacy endpoint, is defined as achievement of undetectable HCV-RNA at 24 weeks after the end of treatment. Per protocol, if a patient does not have a 24-week post-treatment assessment, the patient's 12-week post-treatment assessment will be utilized.
- (2) SVR 12 is defined as undetectable HCV-RNA in plasma at 12 weeks after the end of treatment. The protocol specified primary efficacy endpoint of the HCV SPRINT-1 study is SVR as defined above.
- (3) Intention-To-Treat (ITT) analysis includes any patient who has taken at least one dose of any study drug.

Aug 5, 2008

Pharmasset Reports Preliminary Results of a 4-week Combination Study of R7128 for the Treatment of Chronic Hepatitis C

<http://biz.yahoo.com>

- 88% of patients achieve undetectable HCV RNA levels following 4 weeks of treatment with R7128 1000mg BID with Pegasys(R) plus Copegus(R) –

- Safety and tolerability comparable to placebo administered with Pegasys plus Copegus -

PRINCETON, N.J., Aug. 5 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS - News) announces the preliminary results of the third cohort of a 4-week Phase 1 clinical trial evaluating **R7128** 1000mg twice daily (BID) in combination with the standard of care (SOC), Pegasys® (pegylated interferon) plus Copegus® (ribavirin), in 31 treatment-naïve patients chronically infected with hepatitis C virus (HCV) genotype 1. R7128, a prodrug of PSI-6130, is a nucleoside analogue polymerase inhibitor of HCV that is being developed in collaboration with Roche.

As previously reported for Cohorts 1 and 2 of this study, R7128 has demonstrated potent short-term antiviral activity and was generally safe and well tolerated at doses of 500mg and 1500mg administered for 28 days in combination with SOC. In Cohort 3, a new formulation of R7128 1000mg BID was administered in combination with SOC. Of the 31 patients enrolled, 25 patients received R7128 1000mg BID and 6 received placebo. 88% (22 of 25) patients receiving R7128 1000mg BID with SOC for 4 weeks achieved undetectable HCV RNA levels (<15 IU/mL). This high rate of Rapid Virologic Response (RVR) compares favorably with the 85% RVR demonstrated earlier this year with R7128 1500mg BID in combination with SOC. Based on these results, R7128 1000mg BID will be among the doses carried forward into Phase 2b studies, which we expect to be submitted to the FDA this Fall.

The preliminary safety and tolerability of R7128 1000mg BID with SOC was comparable to placebo with SOC in Cohort 3. One patient was discontinued from the study at day 7 for noncompliance with the protocol. One SAE of suicidal ideation was reported in a patient with significant psychiatric history (including prior suicide attempts) who was two weeks beyond the 28 days of dosing with R7128 and remaining on SOC.

Dr. Michelle Berrey, Pharmasset's Chief Medical Officer, stated, "This result indicates that it is unnecessary to carry the 1500 mg dose forward, since the 1000mg dose may provide a greater margin of safety over longer treatment periods without sacrificing efficacy. Even at the dose of 500mg, R7128 in combination with SOC has demonstrated a greater percentage of RVR compared to SOC alone, which provides flexibility in selecting doses for future clinical studies."

R7128 4-week Combination Study Overview

The 4-week Phase 1 combination clinical trial was a multiple center, observer-blinded, randomized and placebo-controlled study that was conducted in 81 treatment-naive patients chronically infected with HCV genotype 1. The primary objective was to assess the safety, tolerability, pharmacokinetics and antiviral activity of R7128 in the clinically-relevant setting of combination therapy for chronic HCV infection. Cohort 1 administered R7128 500mg BID, Cohort 2 administered R7128 1500mg BID, and Cohort 3 administered an intermediate dose of 1000mg BID, all given in combination with pegylated interferon and ribavirin for 28 days. All subjects then went on to receive a total of 48 weeks of the standard-of-care regimen. In Cohort 4, Patients with HCV genotypes 2 and 3 who did not achieve a SVR with previous interferon-based therapy were administered R7128 1500mg BID in combination with SOC for 4 weeks, and subsequently treated with an additional 20 weeks of SOC. Results from this cohort will be reported at a later date.

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. Results from an oral single ascending dose study of PSI-6130 in 24 healthy male volunteers showed that PSI-6130 was generally well tolerated with no serious adverse events in doses up to 3000 mg.

R7128 demonstrated potent, dose-dependent antiviral activity across four prior treatment-failure patient cohorts (n=40) receiving 750 mg or 1500 mg administered either once-daily or twice-daily for 14 days as monotherapy. The greatest mean decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg twice-daily, the highest dose of R7128 administered in the study. These patients demonstrated a mean 2.7 log₁₀IU/mL (>99%) decrease in HCV RNA. There was no evidence of the development of viral resistance in any dose cohort after 14 days of dosing.

In a 4-week Phase 1 combination study that was conducted in 50 treatment-naive patients chronically infected with HCV genotype 1, R7128 demonstrated potent short-term antiviral activity and was generally safe and well tolerated. Eighty-five percent (85%) of patients receiving R7128 1500mg twice-daily with SOC for 4 weeks achieved undetectable HCV RNA levels with safety and tolerability comparable to placebo with SOC. Thirty percent (30%) of patients receiving R7128 500mg twice-daily with SOC for 4 weeks achieved undetectable HCV

RNA levels with safety and tolerability comparable to placebo with SOC. Ten percent (10%) of patients receiving placebo with SOC for 4 weeks achieved undetectable HCV RNA levels.

About Hepatitis C

Hepatitis C is a blood-borne infectious disease of the liver and is a leading cause of chronic liver disease and liver transplants. The WHO estimates that nearly 180 million people worldwide, or approximately 3% of the world's population, are infected with hepatitis C virus (HCV). The CDC has reported that almost four million people in the United States have been infected with HCV, of whom 2.7 million are chronically infected.

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, is in a Phase 1 clinical trial in combination with Pegasys® plus Copegus® 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.

Dynavax and Merck & Co., Inc. Announce Phase 3 Trial with Investigational Hepatitis B Vaccine (HEPLISAV(TM)) Met its Primary Endpoint

<http://biz.yahoo.com>

BERKELEY, Calif. & WHITEHOUSE STATION, N.J.--(BUSINESS WIRE)--Dynavax Technologies Corporation (Nasdaq:DVAX - News) and Merck & Co., Inc. announced today top-line immunogenicity results from a Phase 3 clinical trial comparing HEPLISAV™, an investigational hepatitis B virus (HBV) vaccine, to a currently marketed HBV vaccine, Engerix-B® (1). The study achieved its primary endpoint. HEPLISAV is being jointly developed by Dynavax and Merck for use in adults and in patients with end stage renal disease.

This study, called PHAST (Phase 3 Heparin Short-regimen Trial), evaluated a two-dose regimen of HEPLISAV administered at 0 and 1 month compared to a three-dose regimen of Engerix-B® administered at 0, 1 and 6 months. The primary endpoint was the proportion of subjects who developed protective antibodies to hepatitis B after administration. In PHAST, 95.1 percent of subjects who received two doses of HEPLISAV (n=1,819) developed protective antibodies to hepatitis B when measured at 12 weeks versus 81.1 percent of subjects who received three doses of Engerix-B® (n=608) when measured at 28 weeks. The multi-center study evaluated 2,427 subjects from 11 to 55 years of age in Canada and Germany. Results of additional analyses from this trial will be presented in the future.

As previously disclosed, the U.S. Food and Drug Administration (FDA) placed a clinical hold on the two Investigational New Drug (IND) Applications for HEPLISAV that is still in effect. In issuing the clinical hold, the FDA requested a review of clinical and preclinical safety data for HEPLISAV. Additionally, the FDA requested all available information about a single case of Wegener's granulomatosis reported in this Phase 3 trial.

HEPLISAV is based on Dynavax's proprietary immunostimulatory sequence (ISS) that specifically targets Toll-Like Receptor 9 (TLR9) to stimulate an innate immune response. HEPLISAV combines ISS with HBV surface antigen (HBsAg) and is designed to enhance the speed of protection.

Webcast Today

Dynavax will webcast a discussion of the HEPLISAV Phase 3 data along with the company's second quarter 2008 financial results on Tuesday, August 5, 2008 at 4:30 p.m. Eastern Daylight Time / 1:30 p.m. Pacific Daylight Time. The webcast can be accessed on Dynavax's website at <http://investors.dynavax.com/events.cfm>. A telephonic replay of the discussion will be available through August 19, 2008 by dialing 1-888-203-1112, access code: 4643391. International callers can dial 1-719-457-0820, access code: 4643391.

Aug 6, 2008

Revolutionary Technique Could Reduce Lifelong Drugs For Transplant Patients

<http://www.sciencedaily.com>

ScienceDaily (Aug. 6, 2008) — Researchers have developed a ground-breaking procedure that could avoid the need for transplant patients to spend the rest of their lives taking a cocktail of drugs to stop their system from rejecting their new organ, according to a series of papers in the August issue of *Transplant International*.

The team, led by Professor Fred Fandrich from the University of Schleswig-Holstein in Kiel, Germany, has developed a technique based on tailor-made regulatory cells.

This involves taking infection-fighting white cells from the blood of the transplant recipient and subjecting them to a highly complex procedure involving cells taken from the living or deceased donor. The tailor-made cells are then administered back to the patient.

In the two clinical trials described in *Transplant International* this was done in two ways, either after the transplant, as an addition to the traditional drug therapy to stop the patient's immune system rejecting the kidney, or before the transplant surgery was carried out.

“Until now the only option for transplant patients has been to take a cocktail of drugs for the rest of their lives” explains lead author Dr James A Hutchinson from the University's Division of Transplantation Medicine and Biotechnology.

“These drugs can cause severe side effects and cannot always prevent the slow destructive process of chronic rejection which often leads to the failure of the transplanted organ.

“That is why our use of transplant acceptance-inducing cells (TAICs) in kidney transplant patients is such an exciting development, as it could eventually offer patients who have had transplant surgery a much higher quality of life, free from complex drug regimes.

“Although our use of TAICs is still in the preliminary stages, the results of our clinical trials on 17 kidney transplant patients are promising.”

During stage one of the clinical trials 12 patients received kidneys from deceased donors and were given the TAICs in addition to the traditional drug therapy used to prevent organ rejection. Nine men and three women aged between 30 and 61 took part in the trial.

Ten of the 12 patients were weaned off conventional immunosuppression drugs over a period of eight weeks, starting in the fourth week after transplantation. Medical staff were then able to wean six of them down to low-dose tacrolimus monotherapy, which is a much less intrusive drug regime with fewer side effects.

“We concluded that although the stage one trial showed that TAIC therapy was both safe and clinically practicable, the trial was unable to provide evidence that postoperative TAIC administration has a beneficial effect” says Dr Hutchinson.

Stage two comprised five patients who were transplanted with kidneys from live donors and received TAICs before their surgery was carried out.

Four men and one woman aged between 39 and 59 took part in the trial. Two received a kidney from their brother, one from his daughter and two from a spouse.

One patient was able to go eight months without any immunosuppression drugs and a further three were successfully weaned from a conventional immunosuppression regime to low-dose tacrolimus monotherapy.

“Although our stage two clinical trial did not provide conclusive evidence of a beneficial effect of pre-operative TAICs treatment, the results were encouraging” says Dr Hutchinson.

“They suggest that TAICs promote a physical state that might allow us to minimise the drugs we use to stop the patient’s immune system from rejecting their new organ.”

None of the patients in either trial experienced acute or delayed adverse events as the result of the TAIC infusion.

“Our research clearly shows that infusing TAICs into patients before they have a kidney transplant, or after the procedure has been carried out, is a practical and safe clinical option.

“Although this procedure is still being developed and refined, it poses an exciting possibility for clinicians and patients alike.”

Four papers on the research are included in the August issue of *Transplant International* – the results of the first and second clinical trials, a detailed case study of a living-donor kidney

transplant and an expert commentary by Professor Lucienne Chatenoud from Universite Paris Descartes.

Adapted from materials provided by Wiley - Blackwell, via AlphaGalileo.

Vertex on the Verge of Victory

<http://www.fool.com>

By Brian Lawler

Last week, Vertex Pharmaceuticals (Nasdaq: VRTX) concluded one of the most important quarters in its history, with the announcement of its second-quarter financial results. Like the vast majority of biotech drugmakers, Vertex's financials proved less crucial than the clinical trial results from the drugmaker's pipeline.

During the quarter, we all got a better glimpse of the excellent data for Vertex's second large phase 2 study of its lead drug, **telaprevir**, in hepatitis C genotype 1 patients. The study, called PROVE-2, should signal to all investors that Vertex and partner Johnson & Johnson (NYSE: JNJ) have a compound with very high odds of eventually gaining marketing approval worldwide.

Unfortunately, we also found out in the second quarter that Vertex (in the U.S.) and Johnson & Johnson (in Europe) likely won't be filing marketing applications to get telaprevir onto the market until after their phase 3 studies in newly diagnosed hepatitis C patients are completed in 2010. Add some necessary time to collect all the data and submit the drug for regulatory review, and telaprevir most likely won't be on the market for newly diagnosed hepatitis C patients in the U.S. or Europe until the first half of 2011.

Today, Vertex's main rival in hepatitis C treatments, Schering-Plough (NYSE: SGP), announced excellent new phase 2 data for its competing compound, **boceprevir**. In response, Vertex shares fell 10%. I've always argued that telaprevir will face stiffer-than-expected competition from drugmakers like Schering, Gilead Sciences (Nasdaq: GILD), Novartis (NYSE: NVS), and Roche. In addition, other compounds in early development from drugmakers like InterMune (Nasdaq: ITMN) and Pharmasset (Nasdaq: VRUS) look similarly promising.

With so many top hepatitis C drugmakers pouring large amounts of resources into their own (or partnered) antiviral drug programs, telaprevir will inevitably face direct competition in the future. Nonetheless, telaprevir has produced the most robust data by far, in the largest number of patients, of all the hepatitis C compounds currently in testing.

Investors can't ask for much more than a near-certain approval for a drugmaker's lead candidate. Vertex and its strong telaprevir data almost definitely provided this in the second quarter. As long as no major safety issues pop up in phase 3 tests, we should see telaprevir start producing sales and royalty revenue for Vertex no later than 2011.

Aug 7, 2008

Hep C activist dies at 54

<http://www.canada.com>

Craig Pearson, The Windsor Star

Feds denied Pillon-Trudeau hepatitis C compensation weeks before her death Sunday

As a nurse and hepatitis C activist, Janice Pillon-Trudeau spent a lifetime helping others, but in the end could not help herself.

Pillon-Trudeau died Sunday at 54 of complications from hepatitis C -- which she contracted through tainted blood -- only seven weeks after the federal government deemed her not sick enough to collect any of the \$1 billion earmarked for people who contracted hepatitis C from the blood system.

"She was strong right to the end," her husband Henry (Hank) Trudeau said at the couple's home on Wednesday. "She wrote some stuff recently while she was in hospital. She was preparing herself."

Trudeau said his wife died Sunday morning at home from an apparent heart attack.

Pillon-Trudeau helped found the the Essex County group which fought for government hepatitis C compensation. She later received \$10,000 from the Red Cross, which supplied the contaminated blood, and \$25,000 from the Ontario government.

"Believe me, there's not much left over when you have hepatitis C, but some dreams," said Trudeau, shortly before visitation began for his wife. "These people counted on the money for some dreams."

Last summer, Prime Minister Stephen Harper announced that Ottawa would pay almost \$1 billion to Canadians infected with hepatitis C from the blood system before 1986 or after 1990. The government had already paid more than \$1 billion to people who were infected from the blood system between 1986 and 1990, when the government knew a blood screening system existed but did not use it.

The government has paid more than \$100 million of the most recent award, according to a Public Health Agency of Canada press release.

"The Courts determined that Crawford Class Action Services would administer the settlement agreement for Pre-1986/Post-1990 hepatitis C compensation at arm's length from the government," Philippe Brideau, Public Health Agency of Canada spokesman, wrote in an e-mail. "Consequently, the Minister of Health may not intervene in the court-approved standard operating procedures and protocols that Crawford Class Action Services uses in making its decisions on whether to approve or reject applications."

Brideau, who cannot by law comment on individual cases, said Crawford Class Action Services has approved far more cases than it has declined. He said most declined cases were due to insufficient evidence of infection through transfusion.

"The government waits and waits and waits so long that they have one person less off the bill," Trudeau said. "It might not be that way, but it seems like that."

Trudeau said his wife was told about seven weeks ago that a test indicated her liver showed no sign of sclerosis -- a devastating effect of hepatitis C -- so she would not be eligible for any federal government compensation.

"Before she passed away, Janice was really upset with the hepatitis C compensation people," Trudeau recalled. "She said, 'The damn government killed me.'

"The people who give the cash award said, 'You're fine now. You get nothing.' It was just like a bullet through the heart."

Trudeau said his wife, with whom he had sons Nicholas and Douglas and grandchildren Elijah and Logan, suffered from the effects of hepatitis for perhaps two decades. She likely contracted the disease in 1976, he said, when she received a transfusion while giving birth, though she might have become infected in the 1980s through a needle prick at the former Grace Hospital, where she worked as a nurse.

He said she lost her teeth and had her hips replaced because of lost bone density, had liver problems, struggled with serious weight fluctuations and difficult breathing, and suffered emotional troubles because of her two-decade-plus battle with hepatitis.

Nevertheless, Trudeau said his wife will be remembered not just as an activist, but as someone who helped others -- on and off the job.

"She took care of people," said Trudeau, choking up with emotion. "She helped patients who weren't hers. She had kids around all the time. She was concerned with other people. She was everything she should have been."

Reuse of blood-check devices widespread

www.japantimes.co.jp

Kyodo News

A government survey has found that 13,408 hospitals, clinics and other institutions violated a health ministry ban and reused blood-check devices for drawing a small amount of blood from fingertips, putting patients at risk of hepatitis and other infections.

While no health problems have been reported due to the practice, which is employed to measure blood-sugar counts and other data for diabetics, the Health, Labor and Welfare Ministry is urging people who may have been affected to contact the relevant institutions.

The nationwide survey was conducted by the ministry following the revelation in May that a clinic in Shimane Prefecture was using needles for drawing blood on multiple patients.

The health ministry issued a ban on the reuse of such blood-check devices in March 2006 following reports of hepatitis infections in Britain. But in Shimane Prefecture, for instance, the prefectural government did not thoroughly communicate the ban to individual institutions.

In the survey, three institutions were found to have reused needles, while the others reused a cap at the tip of the device that encloses the needle. The ministry said that because the cap does not come into contact with blood, it should not pose a high risk of hepatitis or other infections.

The total comprises 3,291 hospitals, 8,458 clinics, 844 nursing-care institutions for old people, 532 other institutions, including caregiver facilities for elderly people with special needs, and 283 institutions for training health-care personnel.

Reuse was acknowledged at 65 percent of the hospitals that provided the blood-check service and 48 percent of the clinics, according to the ministry.

The Education, Culture, Sports, Science and Technology Ministry also said Wednesday that such reuse was found at 137 universities that have medicine faculties and high schools that offer courses for training nurses. Tokushima University's faculty of dentistry was one such institution that reused needles, the ministry said.

Court Date Set for First Hep C Case

<http://www.lasvegasnow.com>

The courts have been flooded with lawsuits and now the first trial has been scheduled against the Endoscopy Center of Southern Nevada.

The first patient shown to be infected in the hepatitis outbreak will have his day in court next year. It's a case that could set a precedent for hundreds of others treated at the clinics that used dangerous injection practices.

The word came down late Wednesday -- the first of what could be many trials in this unprecedented case will take place a year from October.

The victim says justice must be served. "I was the first one that set the stage. They did not know anything," said Michael Washington.

Washington never imagined a routine visit to a doctor's office would give him a potentially deadly disease, "He said, 'Good morning, I'm Dr. Desai. I'm here to do the exam.' and then everything proceeded."

Tests by the Centers for Disease Control indicate Washington was the first patient infected at the Endoscopy Center of Southern Nevada. His life changed after his July 25, 2007 appointment.

After losing about 40 pounds, Washington was shocked and in fear, "I became very upset, and I guess with my wife's help, I kind of calmed down and realized that we just have to accept that fact and live with it."

Michael's wife of nearly 30 years, Josephine, is a retired nurse and can't understand how Dr. Dipak Desai could run a practice of dangerous medicine, "I was angry really, truly angry,

because it was so unnecessary. That's nursing 101 -- medicine 101. You're taught certain things on how to handle a syringe, not reusing syringes."

Ed Bernstein represents Washington in a trial that will be closely watched, "It's going to engage what the elements of damages are for subsequent cases. Mr. Washington has a very, very significant case."

For now Washington is waiting for his day in court, "Let's get it finished. That's the way I feel."

To make matters worse, treatment is not an option for Washington because of his diabetes and glaucoma. The trial begins October 19, 2009.

Through all the testing that's been done, there have been nine confirmed cases. Eight at the Endoscopy Center on Shadow Lane, including Mr. Washington, and one at the Desert Shadow clinic on Burnham.

Metabasis Therapeutics Announces Collaboration with Roche to Develop Liver-Targeted Compounds for the Treatment of Hepatitis C

<http://www.centredaily.com>

SAN DIEGO — Metabasis Therapeutics, Inc. (Nasdaq:MBRX) announced today that it has entered into a two-year research collaboration agreement with Roche to apply Metabasis' **HepDirect(R)** liver-targeting technology to Roche's proprietary lead nucleosides in order to develop new treatments for hepatitis C virus (HCV).

Under the terms of the agreement, Roche will provide a \$10 million upfront payment. In the event a development candidate is identified, Roche will assume development responsibility, and Metabasis will be eligible to receive up to \$193 million in additional payments upon achievement of predetermined preclinical and clinical development events, as well as regulatory and commercialization events for each product. For any marketed products that result from the collaboration, Roche will retain full commercial rights and pay Metabasis a royalty on net sales.

Dr. Mark Erion, Metabasis' chief scientific officer and executive vice president of research and development, stated, "The HepDirect technology has shown significant promise in delivering the activated form of certain antiviral nucleosides to the liver and therefore has the potential to both enhance the antiviral activity of these nucleosides, as well as to lower the effective dose. A partnership with Roche enables Metabasis and Roche to combine their respective strengths in liver-targeting and hepatitis C research with the hope that this combination will lead to a drug candidate for HCV in the near future."

"We are very pleased to form this alliance with Roche, a global healthcare company that is a leader in the discovery and development of drugs and tests for HCV," commented Dr. Ed Baracchini, senior vice president of business development for Metabasis Therapeutics.

"Evidence of the ability of our HepDirect technology to target drugs to the liver has been seen with the three internally-generated product candidates that we have put in the clinic that employ this technology. As evidenced by this collaboration, the HepDirect technology platform has garnered considerable attention within the pharmaceutical industry over the past several years.

This collaboration is just one of several business development initiatives that we are currently pursuing with respect to Metabasis' many assets."

About Metabasis (www.mbasis.com):

Metabasis is a biopharmaceutical company using its proprietary technologies, scientific expertise and unique capabilities for targeting the liver and liver pathways. The Company has established a broad pipeline of product candidates and advanced research programs targeting large markets with significant unmet needs. Metabasis' core area of focus is on the discovery and development of drug candidates to treat metabolic diseases such as hyperlipidemia and diabetes, among others. Although not a core focus of the Company, Metabasis has also discovered and developed drug candidates indicated for the treatment of liver diseases such as hepatitis and primary liver cancer, which it now intends to license or partner. All product candidates were developed internally using proprietary technologies.

Aug 8, 2008

"Found" needles pose low infection risk for kids

www.reuters.com

By Joene Hendry

NEW YORK (Reuters Health) - Children who are accidentally stuck with an improperly discarded needle or syringe appear to be at low risk for acquiring hepatitis or HIV, new research suggests.

In a study published in the journal *Pediatrics*, Canadian researchers found that of 274 children with needlestick injuries, none became infected with HIV or the hepatitis B or C viruses.

Nevertheless, parents should immediately seek medical advice whenever a child is stuck by a potentially contaminated needle, say Dr. Caroline Quach and her colleagues.

To insure efficacy, "most prophylactic (preventive) measures need to be given early after the injury," Quach, from Montreal Children's Hospital and McGill University, told Reuters Health.

For their study, Quach and her colleagues assessed the risk of infection among 274 children who'd been stuck by a potentially contaminated needle and were seen over a 19-year period at two major pediatric hospitals in Montreal.

The children, most of whom received therapies to prevent infection, were followed for six months. This is the longest period of time over which someone could develop antibodies against the viruses in question and therefore show they were infected, Quach explained.

After six months the investigators found no hepatitis B, hepatitis C or HIV infections among the children they were able to test.

Children frequently find discarded needles in "safe" areas such as parks and around home, Quach said. Children may pick up these needles and intentionally stick themselves "not realizing there is a potential health threat associated to a needlestick injury," she noted.

The children in her study were 8 years old, on average, and in most cases had been stuck by a discarded needle found in the street or a park. About 65 percent of the children intentionally picked up the needle.

The number of needlestick injuries followed and treated in this study "is large enough to comfort us in the low risk of transmission of infections," Quach said.

Still, she and her colleagues say, children may need to be better educated about the dangers of discarded needles.

SOURCE: Pediatrics, August 2008.

MASSARO: Mr. Practical learned faith while waiting

<http://www.rockymountainnews.com>

By Gary Massaro, *Rocky Mountain News*

Cliff Wilson's organ transplant put him through the grinder.

But now he's counting his blessings, instead of the days he has left to live.

Wilson, 53, used to be Mr. Practical, the guy who logically figured out solutions to his problems.

Then his liver went bad - cirrhosis and hepatitis C, which he thinks he picked up on shore leave when he was in the Navy. He thinks it was from an unsanitary razor a barber shaved him with.

Doctors diagnosed him in 1985, saying he'd eventually need a new liver.

"That's when I stopped drinking and tried to live a nice, clean healthy life, which is coincidentally the year I got married," Wilson said.

Then he went on the transplant list. He waited. And waited.

"I was on the waiting list seven years," he said. "Knowing you had a disease that was going to kill you, not knowing the timing of the transplant - it got to the point that I was ready to just live as long as I could."

Over the years, he had several phone calls from the hospital: Hurry in. There's a liver available. Need to test for a match. Sorry, no match.

In April, doctors called - there was a liver. It was a match.

While convalescing at home, Wilson wasn't feeling well. So his wife, Debra, took him to the hospital.

Pneumonia had set in, along with two rare viruses.

"I was down there in the hospital close to two months before they found out what was wrong and could find the right antibiotic," he said.

Wilson pitched his story because "maybe somebody would be interested in a story where everything didn't go as planned."

He wants to encourage others on a waiting list to not give up.

"People who need a transplant think their life's over. It doesn't have to be that way. I waited seven years for a transplant. Those weren't happy years."

He said he gave up his job as a sales executive for an electronics company, a business he got into after leaving his native Connecticut and studying philosophy at Hofstra University on Long Island.

He said he has lost 130 pounds. And his belly aches from all the pushing that docs did on his insides. But a bad day now is better than any other day pre-transplant.

Wilson signed up to be an organ donor. He encouraged others to do the same. But doctors told him he can't be a donor for fear of passing on hepatitis C to someone else.

"One day, I'll be reinfected and my liver will be reinfected. It'll probably take 20 years for that to happen. I'll be in my 70s, and who cares by then?"

He had a checkup Thursday.

"Every time these doctors see me, they refer to me as their walking miracle," he said.

He is thinking of his future, now that it looks like he'll have one.

"I've been working part time as a preacher," he said. "My hope is, now that I've been given a second chance, to finish my graduate degree in theology and become a full-time preacher."

massarog@RockyMountainNews.com or 303-954-5271

High prevalence of hepatitis C in Dutch HIV-positive gay men

www.aidsmap.com

Roger Pebody

The prevalence of hepatitis C infection among HIV-positive gay men attending a large Amsterdam sexual health clinic is 18% and rising, reported Anouk Urbanus at the XVII International AIDS Conference in Mexico City on August 7th.

Anonymous surveys were conducted at the clinic in May 2007, November 2007 and April 2008. A total of 3125 people took part in the survey, but almost four-fifths were heterosexual men and women, amongst whom hepatitis C prevalence was low at 0.3%. Moreover, prevalence was also low among HIV-negative gay men at 0.4% (2 of 532 men).

However among HIV-positive gay men, 18% had hepatitis C (28 of 157 men). Comparing the results between the three surveys, prevalence rose from 15% to 17% and then to 21%. Just under a third of these men were unaware of their infection.

In multivariate analysis, hepatitis C infection in gay men was associated with being HIV-positive (OR: 38.4), fisting (OR 15.0) and injecting drug use (15.5). However it is important to note that only 18% of the co-infected gay men reported injecting drug use.

The question and answer session at the conference highlighted continued confusion and doubt among delegates surrounding the risk factors for hepatitis C infection, although numerous studies have identified an association with fisting. Moreover Kevin Fenton of the US Centers for Disease Control, the chair of the session, intervened to question the limited public health response to the outbreaks of hepatitis C in Europe. He noted that outbreaks of syphilis and LGV had been given a more concerted and aggressive response, and called for a greater sense of urgency.

Reference

Urbanus A. HCV is emerging as an STI among HIV-infected MSM: a threat to the MSM community? XVII International AIDS Conference, Mexico City, abstract THPDC203, August 7 2008.

Early treatment is key to combating hepatitis C virus

<http://www.eurekalert.org>

Researchers publish research results in online edition of Journal of Virology

Montreal, August 8, 2008 - Canadian researchers have shown that patients who receive early treatment for Hepatitis C virus (HCV) within the first months following an infection, develop a rapid poly-functional immune response against HCV similar to when infection is eradicated spontaneously, according to a new study published in the *Journal of Virology*. Therefore, early treatment can restore immune response against HCV and help eliminate the virus rapidly. This new discovery of the mechanisms of viral eradication could contribute to the development of new treatments.

About a quarter of infected individuals eradicate the infection spontaneously, without treatment. Led by Dr. Naglaa Shoukry and Dr. Julie Bruneau, affiliated to both the Research Centre of the Université de Montréal Hospital Centre and the Université de Montréal, as well as with researchers from the Institut national de la santé et de la recherche scientifique (Montréal branch), the study found that early treatment restores a rapid poly-functional immune response, characterized by the simultaneous production of multiple antiviral mediators.

HCV is transmitted through infected blood. Although a quarter of infected patients can eradicate the infection spontaneously, the majority develop persistent infection, a major cause of cirrhosis and cancer of the liver. The only approved treatment for HCV is an anti-viral drug known as pegylated interferon alpha. This drug is successful in only half of cases when administered during chronic infection. Success rates among those treated early after infection are significantly higher or around 90%.

In North America alone, most new HCV infections occur among intravenous drug users (IDUs), a vulnerable population that is often undiagnosed and untreated. In the study, researchers followed a group of IDUs at high risk of HCV infection before and immediately after exposure to HCV. Their findings clearly show the importance of early diagnosis and treatment of HCV – particularly in marginalized populations such as IDUs and aboriginal populations.

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The study, published in the *Journal of Virology*, was funded by Canadian Institutes of Health Research and the Fonds de la recherche en santé du Québec. The study abstract is available online at: jvi.asm.org/cgi/content/abstract/JVI.01083-08v1

About Research Centre of Université de Montréal Hospital Centre Research Centre:
chumtl.qc.ca/research-centre.fr.html