

## **HCV Advocate Weekly News Review**

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

*Alan Franciscus  
Editor-in-Chief*

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January 27<sup>th</sup>, 2007

## ***Waiting on the gift of life***

<http://www.journal-news.net>

By Crystal Schelle / Living staff writer

*A local man is hoping for a liver transplant.*

INWOOD — Mike Glascock, 54, can only be described as a strapping man in family photos.

He had played football in high school and for the past 31 years he was employed with Winchester and Western Railroad, working his way up to being roadmaster.

Now more than 10 years after he was diagnosed with hepatitis C, Mike is a shadow of his former self. The disease has attacked his body over the years and most recently it has started to attack the liver, which caused the years of muscle he worked so hard to pack on to drop away like it had never been there.

Sporting a 75th anniversary Redskins cap, Mike sits in his home living room that he shares with his wife, Judy, a special education aide at Musselman High School.

A routine workup for work had found the hep C and doctors informed him and Judy what the long-term effects could be. Mike says he appreciated his doctor being upfront about the disease. “They told me it was a chronic illness, not acute,” he says. “But I knew what could happen if it progressed.”

Judy says when Mike was diagnosed, treatments were started right away. “It was real hopeful,” she says.

For a time, his health was doing well, mostly because of how he had treated his body before the diagnosis. Mike says he doesn't drink or smoke. “I was in pretty good health,” he says.

But a liver biopsy had shown the disease had attacked his body. Without the proper use of his liver, Mike's weight dropped and his body filled with toxins. “The worst part is just feeling so weak all the time,” he says.

One of the scariest side effects is a form of eropothy [sic], which attacks the brain because of the toxins that fill up in the body. “It’s horrible. It’s this brain fog that just takes control of him,” Judy says.

She says the episodes can be scary for her; one instance she found him on the living room floor.

Mike, however, has no recollection of the episodes until he wakes up in the hospital. Once the amino acids build up in the body, Judy calls it “a domino effect.”

Because Judy is still working and Mike is home, they have formulated their own “test.” She says in the morning she’ll talk to him in the morning, call him again at lunch and when she first comes home. She says she’s been able to quickly realize when her husband’s in trouble and get him the help he needs.

The biggest sign, she says, is his change in personality. “Mike is the most easy-going person I know,” she says.

But once the eropothy sets in, Mike can be irritable. “It’s like I can’t even reach him,” she says.

Judy says since April 2004, Mike had been taken to the hospital 17 times – 15 times at Winchester Medical Center and twice at University of Virginia Hospital in Charlottesville, Va.

On top of caring for Mike, his father was living with the couple for nine years as he battled prostate cancer until he died earlier in 2007.

Medications, they say, can only help combat the hep C, but what it boils down to is that he needs a liver transplant.

Mike, who has always been the rock of the family, which includes three grown children from a previous marriage (Gabe, 29, Joe, 25, and Maryann, 23), is now depending on others to help him day to day. The worst part, he says, is that he can’t even get out and work on his yard, although he’s appreciative of his neighbor’s help.

“The fatigue’s the worst,” he says.

The truth is Mike is in a fight for his life. He needs a liver transplant and soon. He has two hopes, the first that his daughter might be a match so that she can be a “live donor.”

The relatively new procedure allows the donor to only have a portion of her liver removed and placed in the recipient. Even though early tests are favorable, Mike’s daughter still has to undergo a battery of tests. Items such as blood type and even size must be matched up against his daughter or any other potential donor.

At this point, it will take about three months before doctors give the OK for the donation. In addition to the blood work and other medical tests, his daughter has to undergo psychological tests to make sure that she is ready to donate a part of her liver.

Mike says at first he didn't even want her to try. "I'm a parent and I was worrying what could happen to her," he says.

After talking it over with her and finding out more information about the process Mike says he supports her decision. "She'll have 60 percent of her liver and still be able to live a complete life," he says.

Mike says she understands that even after three months there is no guarantee that his daughter will even be a match. And even if she does donate a portion of her liver that doesn't mean there isn't a chance that his body could reject the new piece of liver. The only saving grace if it fails is that Mike would have to be moved to the top of the donor list.

His other hope, Judy says, is that he can receive a full-sized liver that would be harvested from a deceased donor. Or someone can make a direct liver donation.

But even though his liver failure is noticeable, Mike is not at the top of the list. According to the Organ Procurement and Transplantation Network, as of Jan. 11, there are 17,413 in the United States who are waiting on a liver. So that means because Mike isn't at the top of the list, it will be a waiting game.

A God-fearing man, Mike says he has put whatever happens into His hands. That's why Judy and Mike are making plans for life post-liver transplant. They say they want to travel, especially to see their granddaughter, Lily, and spend some time together.

It's because of Mike's need for a new liver is the reason why the Glascocks have decided to share their story. Judy says they're hoping that by reading this story more people will be willing to check that box on their driver's license and, most importantly, talk with their family.

"My hope is that by telling our story that we'll be able to make people aware of organ donation," she says.

Judy says they have even inspired her 79-year-old aunt to make sure that she is an organ donor.

Mike says he knows he won't be able to donate any of the organs that have been affected by the Hep C, but he plans on checking the boxes on what he can donate.

Judy wants to make sure that maybe she'll be able to help another life. "I have checked that box," she says.

## **Fact Box**

### *Facts about organ donation:*

- People of all ages and medical histories can be a potential donor. A person's medical condition at the time of death will determine what organs and tissue can be donated.
- Organs and tissues that can be donated include: heart, kidney, lungs, pancreas, liver, intestines, corneas, skin, tendons, bone and heart valves.
- There is no national registry of organ donors. Even if you have indicated your wishes on

your drivers' license or a donor card, be sure you have told your family as they will be consulted before donation can take place.

- All major religions approve of organ and tissue donation and consider donation the greatest gift.
- An open-casket funeral is possible for organ and tissue donors.

information provided by the United Network for Organ Sharing, [www.unos.org](http://www.unos.org)

**For more information about being a donor visit:**

- Donate Life America at [www.donatelife.net](http://www.donatelife.net)
- National Marrow Donor Program at [www.marrow.org](http://www.marrow.org)
- American Red Cross (blood and tissue donation) at [www.redcross.org](http://www.redcross.org)
- The Organ Procurement and Transplantation Network at [www.optn.org](http://www.optn.org)
- U.S. Department of Health and Human Services Web site for Organ Donation at [www.organdonor.gov](http://www.organdonor.gov)

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## ***Patients at Risk for Liver Cancer Should Be Screened With Ultrasound: Presented at ASCO-GI***

<http://www.docguide.com>

By Ed Susman

ORLANDO, FL -- January 27, 2008 -- As the numbers of people in the United States who are at risk of hepatocellular cancer increase, more screening and surveillance of these at-risk populations are required, researchers say.

"For patients at high risk of hepatocellular cancer, screening and surveillance with ultrasound should be conducted every 6 months," said Eugene Schiff, MD, Leonard Miller Professor of Medicine, Chief, Division of Hepatology, and Director, Center for Liver Diseases, University of Miami School of Medicine, Miami, Florida.

In his plenary address here on January 26 at the American Society of Clinical Oncology's 2008 Gastrointestinal Cancers Symposium (ASCO-GI), Dr. Schiff said, "Hepatocellular carcinoma is becoming more common in patients with liver disease. Active hepatitis C virus infection with or without alcohol use accounts for most of the hepatocellular carcinoma in the United States."

The symposium is cosponsored by ASCO with the American Gastroenterological Association Institute, the American Society for Therapeutic Radiology and Oncology, and the Society for Surgical Oncology.

Dr. Schiff said that cases of liver cancer in the United States have increased 7-fold since 1998.

He added that the at-risk population includes the following groups:

- Patients infected with hepatitis C virus, especially if that patient has already developed signs of cirrhosis
- Patients infected with hepatitis B virus, even if the patient has no signs of cirrhosis and especially if that patient was born and raised in areas such as Africa and Asia, where hepatitis B virus is endemic
- Patients who consume large amounts of alcohol, which contributes to cirrhosis
- Patients who have other risk factors such as hemochromatosis or nonalcoholic fatty liver disease

Use of alpha fetoprotein (AFP) as a screening tool is controversial because it has a low positive predictive value and a very low negative predictive value, Dr. Schiff said. Patients with AFP levels higher than 200 ng/mL have about a 67% risk of having hepatocellular carcinoma, but only about 5% of patients with hepatocellular cancer are likely to have advanced disease.

While ultrasound can be utilized as a screening tool, computed tomography (CT) scans can be used to visualize more clearly the arterial system involved, and T2 magnetic resonance imaging (MRI) will also improve visualization of the tumor.

He said the use of CT and MRI are likely to help define tumors that are found with ultrasound, but are too expensive to be used as screening devices.

Dr. Schiff said liver biopsies for most patients are not necessary, especially if masses are seen in patients with a history of cirrhosis. Liver biopsies are also prone to cause hemorrhage.

*[Presentation title: Identifying High-Risk Populations for Hepatocellular Carcinoma: What Is the Standard for Screening? Plenary Address]*

## **Studies in the area of cancer reported from I. Borbath and co-researchers**

<http://www.newsrx.com>

*Hepatitis Weekly*

"Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death, and its incidence is increasing worldwide. Due to the known risk factors (mainly hepatitis B and C viruses), we believe there is a rationale for a chemopreventive approach to treat HCC," scientists writing in the journal *Cancer Science* report.

"Here, based on described in vitro data, we evaluated the preventive effects of **lanreotide**, a somatostatin analog, on the induction of early carcinogenic events. We monitored preneoplastic foci induced by a two-stage initiation/promotion model of hepatocarcinogenesis in male Wistar rats, using diethylnitrosamine and 2-acetylaminofluorene. Lanreotide was given starting the day after the first diethylnitrosamine injection. By quantitative morphometry, we showed that lanreotide significantly decreases the size of induced preneoplastic foci. Analysis of proliferation

and apoptosis assessed by immunohistochemistry, showed decreased proliferation and increased cell death in rats treated with lanreotide. As these events were associated with a significant decreased expression of the cell cycle regulator cyclin D1 and an increased expression of the cyclin-dependent kinase inhibitor p27(kip1) compared to the non-treated group, it is tempting to speculate that these factors are involved in the favorable effect of lanreotide," wrote I. Borbath and colleagues.

The researchers concluded: "Lanreotide significantly decreases early carcinogenic transformation in a two-step rat model. As lanreotide has a low toxicity profile, we believe it would be interesting to evaluate its effect in chemoprevention of HCC."

Borbath and colleagues published their study in *Cancer Science* (Inhibition of early preneoplastic events in the rat liver by the somatostatin analog lanreotide. *Cancer Science*, 2007;98(12):1831-1839).

Additional information can be obtained by contacting I. Borbath, Clinic University St. Luc, Gastroenterology Laboratory, B-1200 Brussels, Belgium.

## ***Regular marijuana use increases risk of hepatitis C-related liver damage***

<http://www.eurekalert.org>

Bethesda, MD (Jan. 28, 2008) – Patients with chronic hepatitis C (HCV) infection should not use marijuana (cannabis) daily, according to a study published in *Clinical Gastroenterology and Hepatology*, the official journal of the American Gastroenterological Association (AGA) Institute. Researchers found that HCV patients who used cannabis daily were at significantly higher risk of moderate to severe liver fibrosis, or tissue scarring. Additionally, patients with moderate to heavy alcohol use combined with regular cannabis use experienced an even greater risk of liver fibrosis. The recommendation to avoid cannabis is especially important in patients who are coinfecting with HCV/HIV since the progression of fibrosis is already greater in these patients.

“Hepatitis C is a major public health concern and the number of patients developing complications of chronic disease is on the rise,” according to Norah Terrault, MD, MPH, from the University of California, San Francisco and lead investigator of the study. “It is essential that we identify risk factors that can be modified to prevent and/or lessen the progression of HCV to fibrosis, cirrhosis and even liver cancer. These complications of chronic HCV infection will significantly contribute to the overall burden of liver disease in the U.S. and will continue to increase in the next decade.”

This is the first study that evaluates the relationship between alcohol and cannabis use in patients with HCV and those coinfecting with HCV/HIV. It is of great importance to disease management that physicians understand the factors influencing HCV disease severity, especially those that are potentially modifiable. The use and abuse of both alcohol and marijuana together is not an uncommon behavior. Also, individuals who are moderate and heavy users of alcohol may use cannabis as a substitute to reduce their alcohol intake, especially after receiving a diagnosis like

HCV, which affects their liver.

Researchers found a significant association between daily versus non-daily cannabis use and moderate to severe fibrosis when reviewing this factor alone. Other factors contributing to increased fibrosis included age at enrollment, lifetime duration of alcohol use, lifetime duration of moderate to heavy alcohol use and necroinflammatory score (stage of fibrosis). In reviewing combined factors, there was a strong (nearly 7-fold higher risk) and independent relationship between daily cannabis use and moderate to severe fibrosis. Gender, race, body mass index, HCV viral load and genotype, HIV coinfection, source of HCV infection, and biopsy length were not significantly associated with moderate to severe fibrosis.

Of the 328 patients screened for the study, 204 patients were included in the analysis. The baseline characteristics of those included in the study were similar to those excluded with the exception of daily cannabis use (13.7 percent of those studied used cannabis daily versus 6.45 percent of those not included). Patients who used cannabis daily had a significantly lower body mass index than non-daily users (25.2 versus 26.4), were more likely to be using medically prescribed cannabis (57.1 percent versus 8.79 percent), and more likely to have HIV coinfection (39.3 percent versus 18.2 percent).

The prevalence of cannabis use amongst adults in the U.S. is estimated to be almost 4 percent. Regular use has increased in certain population subgroups, including those aged 18 to 29.

Hepatitis is an inflammation of the liver. Hepatitis C is the most common form of hepatitis and infects nearly 4 million people in the U.S., with an estimated 150,000 new cases diagnosed each year. While it can be spread through blood transfusions and contaminated needles, for a substantial number of patients, the cause is unknown. This form of viral hepatitis may lead to cirrhosis, or scarring, of the liver. Coinfection of hepatitis C in patients who are HIV positive is common; about one quarter of patients infected with HIV are infected with hepatitis C. The majority of these patients, 50 to 90 percent, were infected through injection drug use. Hepatitis C ranks with alcohol abuse as the most common cause of chronic liver disease and leads to about 1,000 liver transplants yearly in the U.S.

### **About the AGA Institute**

The American Gastroenterological Association (AGA) is dedicated to the mission of advancing the science and practice of gastroenterology. Founded in 1897, the AGA is one of the oldest medical-specialty societies in the United States. Comprised of two non-profit organizations—the AGA and the AGA Institute—our more than 16,000 members include physicians and scientists who research, diagnose and treat disorders of the gastrointestinal tract and liver. The AGA, a 501(c6) organization, administers all membership and public policy activities, while the AGA Institute, a 501(c3) organization, runs the organization's practice, research and educational programs. On a monthly basis, the AGA Institute publishes two highly respected journals, *Gastroenterology* and *Clinical Gastroenterology and Hepatology*. The organization's annual meeting is Digestive Disease Week®, which is held each May and is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. For more information, please visit [www.gastro.org](http://www.gastro.org).

About *Clinical Gastroenterology and Hepatology*

The mission of *Clinical Gastroenterology and Hepatology* is to provide readers with a broad spectrum of themes in clinical gastroenterology and hepatology. This monthly peer-reviewed journal includes original articles as well as scholarly reviews, with the goal that all articles published will be immediately relevant to the practice of gastroenterology and hepatology. For more information, visit [www.cghjournal.org](http://www.cghjournal.org).

## ***Ailing Souris man angry over news in tainted blood case***

<http://www.theguardian.pe.ca/>

NANCY WILLIS

*The Guardian*

*Dwayne Clements frustrated he has no compensation from Ottawa*

SOURIS — Dwayne Clements is weary — weary and just plain worn out.

Clements is a hemophiliac who contracted Hepatitis C in the 1990s as a result of improperly screened blood supplied by the Canadian Red Cross.

He, like over 5,000 other Canadians who believe they are innocent victims of a system gone bad, have waited for years for a promised financial settlement, and time is running out.

When he saw the news recently that all remaining criminal negligence charges causing bodily harm had been dropped against former Red Cross director Dr. Roger Perrault, Clements was stunned. Perrault was at the centre of the blood scandal in the 1980s.

“This is such an incredible slap in the face for all victims of this mess, and I am one of those victims,” he said.

“I am so angry that these people are just walking away, these individuals like Perrault and the Red Cross itself, which simply issued a public apology, closed down its blood division and changed the name to Canadian Blood Services.”

Clements, a husband and father of two little girls, is desperate for the promised compensation package, which is a decade in coming.

Since 2000 he has been unable to work. He used to be employed with provincial parks and made what he describes as “good money”, but over the last five years he has gone from \$2,000 a month to a disability pension of \$899.

“We have lost our house and we have a two-year-old and a seven-year-old to raise and I am at the point now where I just sold some bottles to buy this cup of coffee,” he said, holding the cup to his mouth.

What’s infuriating him and the thousands of other victims is that they are all still waiting for the federal government’s promised package deal.

“They keep changing the rules as they go along. Now we have to have more tests to prove where we fall from level one to six, and the responsibility is ours to trace back through all the paperwork.”

It has taken him eight years to follow the paper trail that will prove him eligible, and it has not been easy.

“Some provinces have a good tracking or traceback system but P.E.I. is not the best at keeping these records,” he said.

“All I want is the settlement of this claim. Get it done and over with. I may not live to see it but maybe my kids will. I’ll tell you I am just really worn out and fed up with the federal government.

“These guys like Perrault get off, the Red Cross simply apologizes on TV and they all walk away clean, while I can’t even get into a public swimming pool.”

**January 29<sup>th</sup>, 2007**

### ***Needed to death***

<http://www.chron.com>

*Texas needs to join the 49 states that offer drug addicts clean syringes to stop the spread of disease*

This month, three Christian activists were arrested in San Antonio as they handed out clean syringes to, according to police, a group of "known prostitutes and drug addicts" in exchange for their used drug needles. Now, for their efforts to stop the spread of AIDS and hepatitis, the activists, including an elderly man and woman, are facing a year in prison.

The incident makes a a mockery of clear thinking in this state when it comes to containing infectious disease among intravenous drug users, the people who love them and even their babies: Texas is the one state in the union in which it is illegal to run a needle exchange program of any kind, even though such programs have been shown to reduce the spread of HIV infection and hepatitis.

According to information maintained on the Web site of the Centers for Disease Control, as of 2004, about one-fifth of all HIV infection and almost all hepatitis C infection are the result of injecting drugs with used needles. These viruses are then transmitted further via unprotected sex and sharing of contaminated needles. Pregnant women can transmit these diseases to their babies at birth or by breast-feeding.

Congress has for the past 20 years prohibited the use of federal funds to support sterile needle distribution programs of any kind — even though the U.S. government spends billions per year on global AIDS prevention. So it is up to the states to take on this important, life-saving work.

Texas has at least started down this road. Last year, lawmakers approved a pilot needle exchange

program for Bexar County. Frustratingly, District Attorney Susan Reed is doing her best to thwart the effort. She made it plain to police and public health officials that her office will recognize no protection against criminal liability.

That stopped the pilot program cold. Now the county is awaiting an opinion on the matter from Texas Attorney General Greg Abbott.

Meanwhile, Bill Day, 73, Mary Casey, 67, and Melissa Lujan, 39, members of the nonprofit group Bexar Area Harm Reduction Coalition, first faced possession of drug paraphernalia charges, a Class C misdemeanor punishable by a fine of up to \$500 after their Jan. 5 arrest. Reed now says she'll prosecute them for distribution of paraphernalia, a Class A misdemeanor punishable by up to a year in jail and fines up to \$4,000.

That's an abusive use of her prosecutorial office. Reed might not care for needle exchange programs and all the good they can do in a community to reduce the spread of infectious disease. But overzealous prosecution of three people who clearly had no intention of profiting from the sale of drug paraphernalia is a gross misapplication of the law.

"These are enormously decent, charitable people, and what's happening with them smacks of persecution," Neel Lane, an attorney with Akin Gump Strauss Hauer & Feld, told the *San Antonio Express-News*. The prestigious law firm is defending the group at no cost.

Studies show that needle exchange programs are effective at controlling the spread of HIV and other blood-borne illnesses. And the programs provide intravenous drug users with access to HIV/AIDS counseling services and testing, substance abuse treatment and screening for tuberculosis, hepatitis and other infections.

The research also shows that, contrary to public perception, clean needle programs do not encourage drug use or trafficking. They save tax dollars that would otherwise go to treat people who become infected through sharing dirty needles.

Texas lawmakers should revisit this issue in the next legislative session. Texas needs a fully funded, statewide needle exchange program run by local public health officials. While they are at it, legislators should include in the bill clear language that protects clean needle providers from overly aggressive prosecutors.

### ***Dr. Mehta: Hepatoma: Liver cancer -- new advances***

<http://www.suburbanchicagonews.com>

BY NILESH MEHTA M.D.

[drnileshdmehta@gmail.com](mailto:drnileshdmehta@gmail.com)

Mr. K is a 78-year-old patient who saw me almost two years ago for a second opinion. His symptoms included an unexpected 50-pound weight loss and abdominal pain. He took some over-the-counter pain medications without much relief.

A CT scan of his abdomen showed a tennis ball sized mass in the liver along with several smaller

grape sized masses in the liver as well. In addition, there were several enlarged lymph nodes around the liver. Biopsy of the liver revealed cancer called hepatocellular carcinoma.

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide, particularly in Southeast Asia, due to hepatitis B virus infection and aflatoxin B1 food contamination. The disease is linked to viral infection related to hepatitis B and C.

In the U.S., there are some 17,000 cases yearly compared to 137,000 cases in China. HCC is also seen in patients who have an iron overload state with a genetically acquired liver disease called hemochromatosis.

While some cancers can metastasize to the liver, HCC is a primary malignancy of the liver. Patients with HCC often have cirrhosis of the liver generally related to alcoholism. Males are far more likely to develop HCC compared to females. Generally, the survival rate following diagnosis is only six to 20 months.

One treatment option for patients with HCC includes surgical resection. While this could certainly be a very aggressive and effective approach, most patients are unable to undergo this treatment procedure due to underlying liver dysfunction. Other modalities of treatment utilized for this disease also include radiofrequency ablation, chemoembolization, chemotherapy and recently targeted drugs.

In May 2007, cancer researchers reported on a novel, oral anti-cancer drug called Nexavar which is the first approved non-chemotherapy treatment for HCC. Nexavar (Sorafenib) also is used to treat patients with advanced kidney cancer and acts by tricking the cancer cells and shutting off the blood supply to the tumor.

It makes patients with this lethal disease live longer by a few months. This option was discussed with Mr. K. He was quite steadfast in his decision: "Leave it alone, let me enjoy my life." It has been nearly two years since his diagnosis and he is doing quite well except for occasional and manageable abdominal pain.

Choice of treatment is not an absolute dogma coming from the doctor. It is a two-way street and patient input and desire are to be considered in this process. Mr. K knew from the beginning that he was not interested in any sort of treatment and wanted supportive care to keep him comfortable.

I must say that he has been achieving this goal quite successfully thus far. He has taken trips to Alaska and Las Vegas as a part of his "therapy." Physicians have to understand the patients' perspective of the treatment choices presented to them.

This reminded me of a quote from Abraham Lincoln: "And in the end, it's not the years in your life that count. It's the life in your years."

## **ASCO GI: HCV Infection Does Not Blunt Sorafenib Response in Liver Cancer**

<http://www.medpagetoday.com>

By Peggy Peck, Executive Editor, *MedPage Today*

Reviewed by Zalman S. Agus, MD; Emeritus Professor  
University of Pennsylvania School of Medicine.

ORLANDO, Jan. 28 -- Infection with hepatitis C did not affect response to **sorafenib (Nexavar)** used to treat liver cancer, researchers said here.

Overall survival and time to symptomatic progression among 93 HCV-positive patients treated with sorafenib mirrored results in hepatocellular carcinoma patients who were free of HCV, Luigi Bolondi, M.D., of the University of Bologna, told attendees at the Gastrointestinal Cancers Symposium.

The findings came from a post hoc analysis of data from the SHARP (Sorafenib HCC Assessment Randomized Protocol) trial.

Last year, the SHARP investigators reported that sorafenib (400 mg bid) increased median survival by 44% compared with placebo (see: ASCO: Sorafenib (Nexavar) Improves Survival in Primary Liver Cancer). But questions have been raised about the findings because less than a third of the 602 patients in the trial were HCV positive.

Hepatitis C virus is a key risk factor for HCC and accounts for 50 to 70% of cases in Europe and North America.

Dr. Bolondi's post hoc analysis was confined to 178 HCV-positive patients, of whom 93 were randomized to sorafenib.

In this group, median overall survival was 14 months in the sorafenib arm versus 7.9 months in the placebo group (HR 0.58, 95% CI 0.37 to 91).

Time to symptomatic progression was the same in both groups.

The median time to progression (measured by independent review and RECIST) was 7.59 months in the sorafenib arm versus 2.76 months in the controls (HR 0.44, 95% CI 0.25 to 0.76).

Disease control rate (complete response + partial response + stable disease) was 44% with sorafenib versus 31% for placebo.

Most frequent grade 3/4 adverse events were hand-foot skin reaction (12.9% with sorafenib versus 0% for placebo), diarrhea (10.8% versus 2.4%), hyperbilirubinemia (9.7% versus 2.4%), ascites (6.5% versus 9.4%), and fatigue (6.5% versus 8.2%).

Adverse events resulted in a dose reduction for sorafenib (32%) and placebo (8%).

Although the HCV data were encouraging, Alan Paul Venook, M.D., of the University of

California San Francisco, cautioned that the SHARP patients, irrespective of HCV status, might not reflect liver cancer patients as a whole.

"The study considered 900 patients and only randomized 602, and the patients who were randomized had extraordinary performance status," Dr. Venook said during his podium discussion of the paper. He compared the SHARP patients to the 1980 U.S. Olympic hockey team, which won a gold medal.

Dr. Bolondi agreed that more than half of all SHARP patients, including those who were HCV positive, had good performance status.

Dr. Venook's overall assessment of the sorafenib findings were mixed -- "the results, while landmark, are modest and more work needs to be done."

Sorafenib is approved for treatment of advanced kidney cancer.

**Disclosures:**

- The SHARP trial was funded by Bayer HealthCare and Onyx Pharmaceuticals.
- Dr. Bolondi disclosed financial support from Bayer.
- Dr. Venook disclosed research funding from Amgen, Genentech, GlaxoSmithKline, and Pfizer.

**January 29<sup>th</sup>, 2007**

***Home Diagnostic Kits Misleading Patients, UK***

<http://www.medicalnewstoday.com>

Home diagnostic tests sold over the internet are offering unsatisfactory product information which could be misleading consumers, warns a paper published in the *Journal of the Royal Society of Medicine*.

The authors<sup>1</sup> of the study evaluated the information provided on 168 websites marketing home diagnostic tests for conditions such as hepatitis C, HIV and prostate cancer. Their findings highlight the fact that many websites provide poor quality information to the general public, leading to the potential for misdiagnosis.

"Home diagnostic medical tests are part of a rapidly growing market of health-related products available for purchase on the internet," write the authors. "Despite their increasing popularity, there are concerns that inadequate, misleading or confusing advertisement can potentially result in inappropriate use of these tests and lead to false reassurance or unnecessary anxiety, which may have serious health consequences."

The authors looked at existing UK and international regulatory codes when assessing the quality of information accompanying the on-line marketing of home diagnostic tests.

Overall, 55.9% of the websites complied with less than half of the criteria suggested by the authors. Only one website complied with all of their criteria. Information on the accuracy of the

tests was found on 51.7%, with only 8.9% providing a scientific reference (an indication of the validity of the product and whether it had been researched prior to marketing).

The authors highlighted the fact that the majority of websites marketing home diagnostic tests provided information of inadequate quality, and often failed to demonstrate any evidence of official approval or certification. Instructions for use were only found in 57.9% of all websites. As little as a quarter of the tests included what action should be taken after obtaining the test result.

Dr Adrija Kumar Datta, one of the authors of the study, says "Not all diagnostic kits marketed on-line are reliable. In my personal experience, I have seen 'sperm test kits' for home use give incorrect results. A test result of 'poor sperm count' was proven wrong by retesting the same individual's semen twice in the hospital laboratory. That caused initial frustration and subsequent confusion to the person concerned."

He went on, "It is difficult to control internet marketing by national legislation; since this business is not restricted to any political boundary. The Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom and the Food and Drug Administration (FDA) in the United States, have started regulating the sale of 'over-the-counter' diagnostic kits within their own countries<sup>2</sup>. On-line marketing of these kits, including the publishing of product information on the net, however, remain beyond legal control."

Dr Adrija Kumar Datta concludes, "As our study showed, the available guidance is far from being implemented and followed across the globe. There needs to be ongoing auditing and quality assurance of any guidelines."

## References

1. Dr Adrija Datta, Dr Tara Selman, Dr Teresa Tang, Dr Khalid Khan
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'Quality of information accompanying on-line marketing of home diagnostic tests' is published in the January issue (Vol.101) of the *Journal of the Royal Society of Medicine*.

JRSM is the flagship journal of the Royal Society of Medicine. It has full editorial independence of the RSM. It has been published continuously since 1809. Its Editor is Dr Kamran Abbasi.

The January issue of the JRSM will be available free at <http://www.jrsm.org> shortly.

Founded in 1805, the Royal Society of Medicine is an independent organisation that promotes the exchange of knowledge, information and ideas in medical science and continued improvement in human health.

*Royal Society of Medicine*

## **Long-Term Hepatitis B Outlook Often Good**

[www.medscape.com](http://www.medscape.com)

NEW YORK (Reuters Health) Jan 18 - The majority of Caucasian patients with hepatitis B e antigen (HBeAg)-positive chronic hepatitis become inactive carriers over time, Italian researchers report.

In the January issue of *Gut*, Dr. Giovanna Fattovich of the University of Verona and colleagues note that studies conducted in Asian populations suggest high liver-associated morbidity and mortality in chronic hepatitis B patients, and thus further evaluation of the long-term outlook in Caucasians is required.

To do so, the researchers examined data on 70 patients with HBeAg-positive hepatitis B who were followed for a median of 25 years.

In all, 61 patients (87%) underwent spontaneous HBeAg seroconversion. During a median of 22.8 years after seroconversion, 40 (66%) became inactive carriers.

Liver-related deaths occurred in 11 patients, 5 due to hepatocellular carcinoma and 6 because of liver failure.

Overall, 50 patients were alive at the end of follow-up and the cumulative probability of survival was 90% at 10 years and 86% at 25 years. The 25-year probability of survival was 95% in inactive carriers, 50% in patients with HBeAg-negative hepatitis or HBeAg reversion, and 40% in those who were persistently HBeAg positive.

Summing up, Dr Fattovich told Reuters Health that "most patients with HBeAg seroconversion became inactive carriers with a very good prognosis."

The risk of liver-related mortality, she added, "is strongly related to sustained disease activity and an ongoing high level of hepatitis B virus replication, independently of HBeAg status."

*Gut* 2008;57:84-89.

## **Return of vicious circle of HCV infection?**

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

Masago Minami, *Yomiuri Shimbun* Senior Writer

The government may have passed its law offering assistance to those infected with the hepatitis C virus through tainted blood products, but it still needs to map out comprehensive measures for helping about 2 million HCV patients infected by other means.

On Jan. 17, the day after enactment of the blanket relief law, the Health, Labor and Welfare Ministry distributed copies of a government bulletin listing medical institutions across the nation

believed to have used the blood product fibrinogen, which was administered to stop bleeding and was in some cases tainted with the virus.

The bulletin called on people who might have been infected to have medical checkups.

Since then, the ministry and public bodies offering counseling services have been inundated with phone calls seeking help.

Last year, when the ministry had decided to hold a meeting of experts to map out measures to cope with the HCV infections, it was hit by the furor surrounding a list it had ignored of 418 people believed to have been infected through tainted blood products. Because of this, the planned meeting was never held.

There are about 500,000 people currently suffering from liver inflammation, liver cirrhosis and liver cancer after being infected with the hepatitis C virus.

The treatment of HCV is similar to that of hepatitis virus B, but the route by which people are infected with HCV and the time span before its symptoms come to light are completely different.

HCV was discovered in 1988, 20 years after the discovery of HBV. By that time it had already spread all around the world. While treatment has improved, a vaccine has yet to be developed.

A rapid increase in the number of people dying from liver cancer in Japan around 1975 is said to have been related to HCV infection.

HCV infection has several characteristics. Infection rates differ greatly according to location and age group. In northern Kyushu, Hiroshima and Osaka, the number of cases is relatively high.

Meanwhile, people aged 50 or older, are far more likely to be infected. In fact, the infection rate goes up in tandem with the generation, with a low infection rate among those under 40 even in areas in which infection is rampant.

In the late 1990s, the infection rate among intravenous drug addicts was more than 60 percent.

While HCV is said to be one ten-thousandth the strength of HBV in terms of infectiousness, about 70 percent of patients exposed to the virus become carriers.

Without its carriers showing symptoms for between 10 and 20 years, the virus can suddenly develop into liver cirrhosis or liver cancer. This is why HCV is so frightening.

Hiroshi Yoshizawa, a professor at Hiroshima University's Faculty of Medicine specializing in medical hygiene, has been studying hepatitis viruses since the 1970s.

Based on his expertise and epidemiological research factoring in postwar social conditions, Yoshizawa believes that the strengthening of the Narcotics Control Law in the 1950s had a major impact. Drug addicts switched from taking drugs in pill form to intravenous injections. As they tended to share unsterilized syringes among themselves, this led to a large rise in carriers among

them. This development eventually triggered an explosive increase in hepatitis infection, according to Yoshizawa.

Some addicts also sold their blood. They would often have to inject themselves with iron supplements to recover from anemia caused by regularly drawing blood. This also helped increase the number of virus carriers, spreading the reach of infection ever wider.

Even otherwise healthy people are highly prone to infection if they are involved in medical procedures--such as blood transfusions or injections--or getting tattoos or undergoing folk remedies that might cause bleeding. This is another factor that can result in a vicious circle of infection involving the whole of society.

The Japan Red Cross Society established a blood donation system in 1968 after it was discovered that a U.S. Ambassador to Japan, Edwin Reischauer, had been infected with hepatitis through a blood transfusion he was administered following a bizarre incident in which he was stabbed in 1964.

In the 1970s, improvements in the medical environment meant medical equipment was disposed of after use, while hygiene levels throughout society improved, significantly reducing the number of hepatitis infections through blood transfusions and ordinary infections.

However, the thorough disposal of syringes only became a requirement in 1988, so it cannot be denied that the government was slow in taking necessary measures.

Furthermore, it was not until 1992 that it became possible to completely remove the virus from donated blood by measuring the presence of HCV antibodies.

It therefore took nearly half a century to put an end to the vicious circle of infection.

"The HCV carrier rate declines with each generation, revealing the changes that took place in Japanese society during the 50 years after the war," Yoshizawa said. "Taken from the opposite angle, though, there are still carriers who are a potential source of infection. Deteriorating social conditions could restart the vicious circle."

His remark is not a groundless warning.

For example, there are about 30,000 people undergo dialysis treatment every year. According to the Japanese Society for Dialysis Therapy, 19.5 percent of dialysis patients across the nation are infected with HCV and the number of new HCV patients increases 3.6 percent per year, making dialysis patients the group in which infections are rising quickest in the country at the moment.

At the end of last year, patients undergoing cardiac examinations at a hospital in Kanagawa Prefecture were found to have been infected with HCV. It transpired that a device used to monitor blood pressure may have caused the infection as it was repeatedly used on a variety of patients.

With medical services deteriorating, there could be a new explosion in HCV infections. All

people must therefore be taught about the risks of possible infection.

The number of infected people and the cause of those infections stemming from postwar social conditions have made the virus a national disease.

The government should immediately come up with comprehensive measures, including the establishment of the best possible medical system, to prevent further infections and to treat HCV patients.

## ***Insulin resistance means a poorer response to anti-HCV therapy in HIV/HCV coinfecting patients***

[www.aidsmap.com](http://www.aidsmap.com)

Michael Carter

HIV-positive patients coinfecting with hepatitis C virus who have insulin resistance have a poor response to anti-hepatitis C therapy, according to a small Italian study published in the February 1st edition of the *Journal of Acquired Immune Deficiency Syndromes*. The investigators suggest that diagnosing and correcting insulin resistance in coinfecting patients before initiating therapy for hepatitis C could lead to better treatment outcomes.

Treatment with anti-HIV therapy has been associated with an increased risk of insulin resistance, glucose intolerance and type-2 diabetes. It has been suggested that protease inhibitors may have a significant role in the development of these side-effects, although traditional risk factors may also be important.

There is a relationship between infection with hepatitis C virus and an increased risk of insulin resistance. The presence of insulin resistance has been associated with poorer six month response to anti-hepatitis C treatment with pegylated interferon and ribavirin in patients monoinfected with hepatitis C.

Coinfection with hepatitis C is common in HIV-positive patients, and although insulin resistance occurs with greater frequency in coinfecting than hepatitis C-monoinfected patients, its effect on the outcome of anti-hepatitis C therapy in coinfecting patients is poorly understood.

Investigators therefore undertook a study to see if there was a relationship between insulin resistance and early response to anti-hepatitis C treatment in HIV/hepatitis C coinfection. An early response to hepatitis C therapy – an undetectable hepatitis C viral load after three months of treatment – is a good indication of the likely long-term success of such treatment.

The study involved 29 patients who received anti-hepatitis C therapy from January 2006. All were men and the median age was 43 years. Insulin resistance was present in ten patients (35%).

After three months of anti-hepatitis C therapy median ALT and AST levels fell significantly in both patients with insulin resistance ( $p < 0.01$ ) and those without insulin resistance ( $p < 0.01$ ).

But despite these improvements in liver function, the investigators noted that there insulin

resistance appeared to have a significant effect on the chances of achieving both an early and rapid virological response to treatment (undetectable hepatitis C viral load after a month of therapy).

A rapid response to therapy was achieved by eight of the patients without insulin resistance but one of the patients with insulin resistance.

Furthermore, of the 19 patients without insulin resistance, 16 had an undetectable hepatitis C viral load after three months of therapy with pegylated interferon and ribavirin. However, none of the ten patients with insulin resistance had an early virological response.

“In the present study, including only HIV/hepatitis C virus-infected subjects, we found that subjects without insulin resistance at baseline are more likely to reach rapid virological response and an early virological response than others...the presence of insulin resistance does not allow for the achievement of a rapid virological response and an early virological response”, write the investigators.

The investigators recommend that coinfecting patients should always be monitored for the presence of insulin resistance before anti-hepatitis C therapy is initiated. They add, “the correction of insulin resistance, and the consequent recovery of insulin sensitivity, could improve early virological response in the HIV/hepatitis C-coinfecting population treated with pegylated interferon and ribavirin.”

## **Reference**

Bongiovanni M et al. Insulin resistance affects early virologic response in HIV-infected subjects treated for hepatitis C infection. *J Acquir Immune Defic Syndr* 47: 258 – 259, 2008.

## ***Judge's ignorance of AIDS draws fire***

<http://www.thestar.com>

Tracey Tyler

Legal Affairs Reporter

*Witness with HIV forced to wear a mask in court, groups complain*

An Ontario judge is at the centre of a misconduct investigation after insisting a witness who is HIV-positive and has Hepatitis C don a mask while testifying in his courtroom.

Three groups have complained to the Ontario Judicial Council about the conduct of Barrie judge Justice Jon-Jo Douglas, who later moved the case to a bigger courtroom in order to create more distance between the witness and the bench.

The judge refused to accept Crown counsel Karen McCleave's entreaties there was no need for such measures.

"The HIV virus will live in a dried state for year after year after year and only needs moisture to reactivate itself," Douglas insisted, according to a transcript of the Nov. 23 trial proceedings.

"This is outlandish," Bluma Brenner, an assistant professor at the McGill AIDS Clinic at McGill University in Montreal, said yesterday. A drop of human immunodeficiency virus drying on the floor "would be inactivated within 20 minutes," Brenner said in an interview.

But Douglas, a former Crown attorney appointed to the Ontario Court of Justice 10 years ago, was not prepared to continue the trial until he was satisfied "the safety and integrity of this courtroom" was protected.

"I mean, he speaks within two feet of me with two serious infectious diseases," Douglas told McCleave. "Either you mask your witness and/or move us to another courtroom or we do not proceed."

At one point, court staff returned after a recess wearing rubber gloves and placed documents touched by the witness in plastic bags.

Douglas, who continues to preside in Barrie, declined to speak with the *Star* yesterday.

In their Jan. 17 letter of complaint, the Canadian HIV/AIDS Legal Network and the HIV and AIDS Legal Clinic (Ontario) say Douglas's response to the witness, a complainant in a sexual assault case, reveals "shockingly discriminatory thinking" and is a "particularly extreme example of unacceptable conduct by a judicial officer."

The organizations say the case also raises questions about the extent to which judges are informed about HIV/AIDS and related human rights issues.

Their complaints target not only Douglas, but two courts – his own and the Superior Court of Justice, for failing to clearly condemn the behaviour.

The Crown applied to the Superior Court of Justice to have Douglas removed from the case for creating an appearance of bias. But Justice Margaret Eberhard declined, saying while his approach may have been wrong, Douglas had jurisdiction to take the steps he felt necessary to ensure courtroom safety.

Ontario's Criminal Lawyers Association has also lodged a complaint with the judicial council. The lawyers' group contends Douglas did not bring a judicial temperament to trial proceedings and treated a witness differently on the basis of irrelevant personal characteristics. Contacted yesterday, association president Frank Addario declined to discuss the allegations. The complaints are being investigated by a judicial council subcommittee, which will determine if a public inquiry into Douglas's fitness to remain on the bench is warranted.

Meanwhile, Douglas hastily resigned from the board of Stevenson Memorial Hospital in Alliston on Jan. 14, just over a month after he was appointed.

The controversy surrounding the witness began on Nov. 23, during the trial of a man charged with sexually assaulting a fellow inmate at the provincial jail in Penetanguishene.

The alleged victim testified he was HIV-positive and had Hepatitis C, but didn't inform his

alleged attacker because he was traumatized. "I could be ... shanked," said the man, whose identity is shielded by a publication ban.

According to a trial transcript, during the lunch break, Douglas bumped into defence lawyer Angela McLeod and voiced concern the witness had been allowed to testify without the court being informed of his health status.

When court resumed, Douglas raised the issue with McCleave, the Crown attorney as well. "I am frankly shocked that in this day and age we were not advised," he said.

McCleave replied she knew of no issues arising from the witness being in the courtroom or touching "a couple of pieces of paper" that were introduced as evidence.

That's when Douglas offered his view that HIV will live "for year after year after year" in a dried state.

McCleave explained that she wasn't prepared to ask the witness to wear a mask in court when he faces no such requirement in the community. There were also practical problems with the judge's request, she suggested – the court reporter might not be able to accurately record his testimony.

Douglas refused the Crown's request to grant a mistrial, declined to recuse himself from the case and refused to consider granting bail to the accused, Lee Wilde, when it became clear the trial would have to be adjourned until the judge's concerns were addressed.

A new trial will begin Feb. 14.

An official with the National Judicial Institute in Ottawa, which has developed educational programs for judges, said while the curriculum addresses "emerging social issues," there's no course specifically addressing HIV/AIDS – though one is being planned. It should be up and running within "a couple of years," she said.

### ***Ex-addict warns over virus***

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

A FORMER drug addict who turned around his life only to discover he had caught a life-threatening disease is today urging people in Suffolk to get tested for the virus.

Tom Spark, of Chillesford, near Woodbridge, discovered he was infected with hepatitis C in 2001.

Since then his life has been plagued by tiredness as well as gruelling and painful treatments which tried, and failed, to combat the disease which damages the liver.

Now Mr Spark is adding his voice to a Department of Health campaign to encourage people in Suffolk to get tested for hepatitis C as many people who have it are unaware as it can take years for any symptoms to show.

Those at risk include people who had blood transfusions before September 1991, injected drugs using shared equipment, or had an unsafe tattoo.

To highlight the campaign there will be an exhibition of portraits of people with the blood-borne virus at Ipswich's Buttermarket shopping centre today and tomorrow.

Mr Spark, 47, said: "When I found out I had hepatitis C I was devastated. I thought I had been lucky and escaped HIV and other diseases you can get if you use drugs, but I was wrong, it had caught up with me and it was a massive blow.

"It means I get really tired. Some days it feels like I'm wading through treacle. It is very depressing to think that you are so ill."

Despite various treatment Mr Spark, who has a nine-year-old son, knows his only option in the future may be a transplant if his liver does stop working.

He added: "I used drugs back in the seventies and eighties and managed to come clean in 1988 and it is very upsetting that something from so long ago is having such an affect on me now."

For more information about hepatitis C call the confidential information line on 0800 451451 or visit [www.hepc.nhs.uk](http://www.hepc.nhs.uk) .

## ***Rise in Number of Hepatitis Infections***

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

*The number of people with hepatitis C has risen sharply in the past year.*

In North Lincolnshire the number of people registered with the disease rose from 24 in 2006 to 41 in 2007. Hepatitis is swelling or inflammation of the liver. Contracted through contact with infected blood, and less commonly through other bodily fluids, it can cause long-lasting infection and lead to liver disease.

A campaign, launched in 2004 by the NHS and aimed at healthcare professionals and the public, saw visits to the NHS website and hepatitis C information line more than double and it is believed this is one reason for the surge in numbers.

A spokeswoman for the Health Protection Agency (HPA) in North Lincolnshire, which released the new figures, said: "There has been an increase of hepatitis C cases in North Lincolnshire since the millennium.

"But we have to remember figures represent the number of cases which have been diagnosed, so people may have had the disease for a while and not realised.

"So what the figures reflect are more people coming forward for testing as a result of campaigning work to raise awareness.

"This probably accounts for the discrepancy in figures for North Lincolnshire between 2006 and 2007."

Statistics for North Lincolnshire however, buck national trends.

While 2006 statistics for North Lincolnshire were lower than the 40 cases recorded in 2005 and the increased number in 2007, nationally, the number of newly-diagnosed cases of hepatitis C infection rose to 8,346 in 2006 - 10 per cent higher than in 2005.

Professor Pete Borriello, Director of the HPA's Centre for Infections, said although campaigns had proved a success, further work was still needed.

"The improved public awareness we are seeing for hepatitis C represents a marked change to the position we were in just a few years ago," he said.

Professor Borriello added: "There is no room for complacency. Despite the increase in awareness and diagnosis of hepatitis C, there is still some considerable way to go if the burden of this infection is to be reduced in the future."

Dr Helen Harris, a hepatitis C expert from the HPA, said: "Injecting drug use remains the single most important risk factor for acquisition of hepatitis C infection, estimated to be responsible for more than 90 per cent of all newly-acquired infections. If someone has ever shared equipment for injecting drugs - even if it was a long time ago, and even if they only did it once - they can be at risk from hepatitis C."

Celebrities have been diagnosed with the disease over the years, including Anita Roddick, founder of the Body Shop, who died last September after suffering a brain haemorrhage.

The campaigner and fundraiser contracted the illness from a blood transfusion in the 1970s. Other people who have had hepatitis C include model and actress Pamela Anderson and former vocalist with ZZ Top, Dusty Hill.

### ***Health commissioner wants ban on multidose vials***

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

By Ridgely Ochs

[ridgely.ochs@newsday.com](mailto:ridgely.ochs@newsday.com)

State Health Commissioner Richard Daines Wednesday called on the U.S. Food and Drug Administration to eliminate the manufacture and distribution of medications in multidose vials, the source of hepatitis C transmission by Dr. Harvey Finkelstein of Dix Hills.

Even as he made the recommendation, Daines, speaking at Hofstra University Wednesday, acknowledged it was not now entirely feasible because some medicines need to be administered using the multidose vials. Said Daines: "You go in with a goal even though there may be exceptions."

Daines, one of nine doctors and health officials at a discussion on infection control headed by state Sen. Kemp Hannon (R-Garden City), chairman of the Senate Health Committee, said doctors must at times use multidose vials to deliver the right dose.

However, he said that "engineering out" the possibility of human error is the best way to ensure infection control. Both needles and syringes are supposed to be used only once. But if they are not, eliminating multidose vials would get rid of a possible source of contamination.

The health department came under fire in November after it was revealed that because of legal delays and complicated lab tests, it had waited three years before telling the public that Finkelstein had reused syringes in multidose vials. At least one case of hepatitis C resulted.

On Jan. 15, the state also announced that a Manhasset obstetrician-gynecologist, Dr. E. Jacob Simhaee, had reused syringes in a multidose vial when giving patients flu vaccine. Thirty-six patients were notified; no disease transmission has been reported.

In a letter dated three days later and also signed by New York City's health commissioner, Dr. Thomas Frieden, Daines said that despite "numerous guidelines and recommendations," some doctors continue to misuse needles and syringes, leading to contamination of multidose vials.

Daines maintained that New York is the only state that requires infection prevention training every four years as well as strict infection control requirements in hospitals and office-based surgeries. Nevertheless, he listed five hepatitis C and hepatitis B outbreaks caused by poor infection control in the state since 2001.

The FDA is reviewing the letter, a spokesman said.

Hannon said because eliminating use of multidose vials may not be possible, he favored encouraging development of a syringe that cannot be reused. There are several models to prevent reuse, but Hannon said they can be altered and reused. He said state research money could perhaps be allocated to develop such a syringe.

### ***Double-dose hepatitis B revaccination has good results in HIV-positive patients not responding to standard vaccine***

[www.aidsmap.com](http://www.aidsmap.com)

Michael Carter

Use of a double-dose of hepatitis B virus vaccine in HIV-positive patients who did not respond to standard vaccination has a 50% success rate, according to a Dutch study published in the January 15th edition of the **Journal of Infectious Diseases**.

HIV and hepatitis B are transmitted in similar ways, and it is estimated that approximately 6% - 10% of HIV-positive gay men are infected with hepatitis B virus. Patients infected with HIV and hepatitis B virus are often said to be coinfecting. High rates of HIV/hepatitis B coinfection are also present in HIV-positive patients in many resource-limited countries.

Antiretroviral therapy can mean a longer, healthier life for HIV-positive patients, but since effective anti-HIV treatment became available, liver disease caused by hepatitis B and hepatitis C virus has become a major cause of illness and death in people with HIV. It is estimated that individuals coinfecting with HIV and hepatitis B virus have an eight-fold increased risk of death compared to individuals who are only infected with HIV.

Patients who are coinfecting with HIV and hepatitis B are also less likely to clear hepatitis B surface antigen and hepatitis B e antigen, have a higher rate of hepatitis B replication and therefore have an increased risk of passing on hepatitis B to others. Coinfecting patients also have a greater risk of progression to cirrhosis and of experiencing flare-ups of hepatitis.

Preventing hepatitis B in HIV-positive patients is therefore a priority. A vaccine against the virus exists and it is recommended that all HIV-positive patients should receive this. However, compared to individuals with a strong immune system, HIV-positive patients have a poor response to hepatitis B vaccination with only 40% - 76% developing protective antibodies against the infection.

All asymptomatic HIV-positive patients in the Netherlands are provided with hepatitis B vaccination consisting of three 10 µg doses of HBvaxPro. These are provided by intramuscular injection. But approximately 50% of patients do not develop a protective level of antibodies against the infection.

To try and achieve a higher rate of response investigators revaccinated 144 non-responders at monthly intervals with double the recommended dose of the vaccine.

Most of the patients (108, 75%) were men and the mean age was 43 years. At the time of revaccination, 96 patients (67%) were receiving antiretroviral therapy and 89 patients (62%) had an undetectable HIV viral load. Median nadir (lowest ever) CD4 cell count was 204 cells/mm<sup>3</sup> and at the time the first course of hepatitis B vaccination was offered, median CD4 cell count was 360 cells/mm<sup>3</sup>. Median CD4 cell count was similar when revaccination was provided.

Revaccination was successful in 74 of the 144 patients, a response rate of 51%. Median hepatitis B antibody titers were 107.9 iu/l in these patients, well above the protective threshold of 10 iu/l.

Female patients were found to have a significantly better response rate ( $p = 0.03$ ). A response was also more likely in patients under 40 years, irrespective of their HIV viral load. For patients aged 40 and above, revaccination was significantly more likely to be successful in patients with an undetectable HIV viral load ( $p = 0.005$ ).

“To our knowledge, this is the first study describing the results of double-dose hepatitis B virus rechallenge vaccination at monthly intervals in HIV-infected patients not responding to their initial vaccination,” write the investigators, “we revaccinated 144 patients who had failed to have an antibody response after standard vaccination and found a 50.7% response rate.”

The investigators conclude that such a response rate shows that their strategy of double-dose revaccination was justified and call for further prospective studies.

## Reference

De Vries-Sluijs TEMS et al. A prospective open study of the efficacy of high-dose recombinant hepatitis B rechallenge vaccination in HIV-infected patients. *J Infect Dis* 197: 292 – 294, 2008.

January 31<sup>st</sup>, 2007

## ***Blind River man waits for new liver***

<http://www.elliottlakestandard.ca>

Posted By SHANNON QUESNEL

When Bill and Edith Hendry found out the former had liver problems it was they, not the doctors, who got them started on the long road to an organ transplant.

The couple says the lesson is that people need to look after themselves and not rely on others to provide all the answers. In many cases, patients need to help their doctors so they can help them.

Most doctors are overworked and even a simple instruction, such as fill out a transplant form, could escape their notice.

Edith says, “You have to be on top.

“When he has blood work... one doctor sometimes does not get the report of another.”

The Hendrys keep all the records in a large binder and take it with them for appointments.

“It helps them,” she says.

Since this process began the Hendrys have much to be thankful for, not the least of which is their own initiative.

Then there is the person who offered to donate part of her own liver. If the donor passes the right medical tests Bill could be looking at a new and healthy organ. Until that time however, Bill has to wait.

And friends have raised funds to offset expensive trips to Toronto and Dr. Mark Bradford of Blind River has been with them from day one.

## **Mysterious fatigue**

Bill’s health problems started in 1985, when he was working with a car dealership in Toronto. He and Edith met 10 years earlier.

Bill found himself becoming tired, for no reason.

“(I had) very severe fatigue, to the point they had to put me on a medical pension.

“They didn’t know what it was. They thought I had maybe cirrhosis.”

Cirrhosis is the result of a liver disease.

A consequence of cirrhosis is the replacement of healthy liver tissue by scar tissue, which can lead to a partial or complete loss of liver function.

Edith says at the time the doctors told Bill he only had two years to live.

“It wasn’t until 1991 that they found out that it was... hepatitis C.

“And I was told at that time it eventually could turn to cancer.”

### **Virus exposure**

Bill says he does not know where or when he contracted the infectious, viral disease.

There are many ways, from sharing of needles, toothbrushes and razors to being exposed to hepatitis-C infected blood while on the job.

Medical and dental personnel, firefighters and paramedics can be exposed to the virus through exposure to blood through accidental needle punctures or blood spatter to the eyes or open wounds.

Bill figures he might have been exposed while later working at a Salvation Army correctional house in Toronto.

If a person has a cut on their palm and grabs a blood-covered object, like a bloody shirt that can be enough to get an infection.

He says he might have also been infected when he was a child.

“It could have been a possibility when I had a blood transfusion as a kid.”

Bill moved to Blind River in 1992.

“(Toronto) was getting pretty ritzy. Rents were going up and food was going up.”

### **Coming north**

Blind River proved a cheaper place to live and promised a slower pace of life.

The couple had an idea that since Bill was on a medical pension and was not tied down by a job there would be more time for leisure activities.

Even with Bill’s fatigue problems that was not the case.

“We got up here and Bill never stopped,” says Edith.

“He kept doing things. Anybody who was building something he was out there helping.”

Later, he upgraded his hockey training education and became a trainer for the Blind River Beavers.

It was not to last.

Bill got more and more tired and soon found himself unable to fulfill the role of a junior 'A' hockey trainer.

He did not leave hockey however and became a trainer for the Blind River Badgers midget team.

The cancer that the doctors suspected Bill had started to take more of a toll on him. He had to give up being a trainer altogether.

He was officially diagnosed with cancer, in the form of several liver tumours, in November.

The former hockey trainer was given a poor prognosis that without treatment he could be dead in less than a year.

### **Bad news**

Edith says it was scary to hear such news.

"I was surprised. I knew someday he could get cancer.

"Everything was happening so fast. I still couldn't really grasp it until we got to Toronto," she says, for more medical tests.

Bill asked himself, "What could I do about it?"

"We did a lot of praying. We had a lot of other people praying for us. It's out of our hands."

Bill has seen a lot of doctors since they first suspected he had cancer. In the past year alone, he saw 17 physicians.

One of them mentioned Bill should get a transplant. That was the first and last thing the doctors said about new organs.

Edith says the doctors kept talking about treatments and tests, but there was no more talk about transplants.

She decided to get the ball rolling.

"I phoned Toronto and talked to the (transplant) co-ordinator and said, 'Does Bill have to be free of cancer before he is put on a transplant list.' She said, 'No.'

"I said, 'What does he have to do to get on the transplant list?'

She said, she could send a form.

“I think if we hadn’t said anything it might not really have gone anywhere.”

### **Initiative pays off**

Bill might have been left with less hope than he has right now.

Filling out the form was the start of a long process.

Bill had to see cardiologists, liver and cancer doctors as well as social workers.

This meant multiple, costly trips for tests in Sudbury and Toronto.

Bill did not pass one test and that could have ended his chances for a new liver.

He had a blockage near his heart. To qualify for a transplant doctors had to insert a stent. This device expands and pushes the blockage against the artery walls, allowing blood to flow more smoothly.

With the blockage corrected, Bill had a chance to receive a new liver.

He does not know where he is on the transplant list. He says there is no list.

“There is no number.”

Who gets a new liver is determined by blood type, tissue type and the condition of the receiving patient.

Bill lucked out with the blood. He has type O blood, the most common.

And with the blockage corrected Bill now follows the rules of the waiting game.

The couple has to be ready to leave at a moment’s notice.

When the call comes that a liver is available for Bill, he will go to the Blind River District Health Centre and he and Edith will be flown to Toronto.

Bill will have to wait in Toronto before and after the surgery.

Edith says staying in Toronto is expensive. The couple felt blessed when a friend living in Toronto offered her apartment while there.

“We are Christian and we believe God is watching over us. So many things have worked out like this for us.”

This includes a Blind River bake sale, which raised about \$900 for the couple’s travel cost and Jackie Emery. This friend of the Hendrys lives on a farm in Massey and offered a portion of her liver for Bill.

Doctors said Bill could either get a whole new liver or a partial one from a live donor.

Bill's new partial liver would quickly grow to full size after insertion. Emery's reduced liver would also grow back to its original size.

Bill says this experience has changed him.

"I appreciate when I see the flowers come up now, believe it or not. And I hate flowers," he says with a laugh.

The 64-year-old was an active person, whether he was working for a pay cheque or helping somebody out.

His health problems meant he had to stop much of his activities.

He says he will be back on the ice if things work out.

"I am pretty sure if I have this operation and I recover I will probably be behind the bench next season.

"The Guy upstairs still has work for me to do," says Bill.

"And when I look at it that way, I don't feel alone in this sickness."

## ***MIGENIX to Add 600mg Daily Celgosivir Dose to Phase II Viral Kinetics Study***

<http://www.bctechnology.com>

Thursday, January 31, 2008

Vancouver, BC, January 31, 2008--(T-Net)--MIGENIX Inc. (TSX: MGI, OTC: MGIFF), a clinical-stage developer of drugs for infectious diseases, will add a 600mg **celgosivir** combination therapy arm to its currently enrolling Phase II viral kinetics study in hepatitis C virus ("HCV") treatment-naive patients. The protocol amendment to this study has received Health Canada and Institutional Review Board (IRB) approvals. The purpose of this new treatment arm is to assess 600mg celgosivir (an oral alpha glucosidase I inhibitor) for tolerability, pharmacokinetics and viral kinetics when combined with the standard of care drugs, pegylated interferon plus ribavirin, as compared to the standard of care drugs alone and to 400mg celgosivir plus the standard of care for up to 12 weeks of therapy.

AnnKatrin Petersen, M.D., VP Clinical Development for MIGENIX commented, "The favorable tolerability experienced to date with 400mg per day of celgosivir in triple combination with pegylated interferon plus ribavirin, along with the clinically significant benefit demonstrated in our previous non-responder study, gives us confidence that increasing the dose to 600mg per day in combination therapy is an important development step for the optimization and advancement of celgosivir."

The currently enrolling Phase II viral kinetics study is a 12-week randomized, active-controlled study initially planned to enroll up to 20 patients in two treatment arms: (i) celgosivir (400mg once daily) plus peginterferon alfa-2b plus ribavirin ("PRC"); and (ii) peginterferon alfa-2b plus ribavirin ("PR"). Tolerability, pharmacokinetics and viral kinetics are being evaluated in the trial. The approved protocol amendment allows for the addition of a 600mg once daily dosing arm and the flexibility to increase the total number of patients in the study up to 50. With 15 patients enrolled to date, it is planned that approximately six additional patients will be enrolled, all in the new 600 mg arm. Results from the study are expected to be reported in the third calendar quarter 2008.

Jim DeMesa, M.D., President and CEO of MIGENIX added, "With results from this study expected in the third quarter 2008, we now have another near-term clinical milestone. Additional key clinical milestones include Omigard Phase III results for preventing catheter-related infections (CLIRS study) expected by our partner, Cadence Pharmaceuticals, in the second half of 2008 (enrollment to be completed in the second quarter) and Cutanea Life Sciences, our partner in the CLS001 rosecea product, planning to advance CLS001 to Phase III."

### **About Celgosivir (MX-3253)**

Celgosivir, an oral inhibitor of alpha-glucosidase I, is currently the only anti-HCV drug in clinical development which acts on host-directed glycosylation. In preclinical studies, celgosivir has shown in vitro synergy with various interferons on the market or in development including Pegasys, PEG-Intron, Infergen, Alferon and IFN-omega (with or without ribavirin) and other drugs in development for the treatment of HCV (e.g. polymerase inhibitors) and therefore could have the potential to be included as part of many combination therapeutic approaches to improve efficacy in future anti-HCV therapies.

Results announced in April 2007 from a Phase II study demonstrated a clinically significant benefit when celgosivir was added to the standard of care in non-responder patients. Interim results from the first 10 patients in the current viral kinetics study who had completed 4-weeks of therapy were reported in December 2007. Detailed analysis of data from these two studies, and an extension protocol designed to provide expanded access to the non-responder patients, provided the rationale for increasing the dose of celgosivir from 400mg per day to 600mg per day in combination therapy as the next step for the optimization and advancement of celgosivir.

### **About HCV**

HCV, the most common chronic blood-borne infection in the United States, causes inflammation of the liver and may progress to more serious complications such as cirrhosis of the liver, liver cancer and death. Approximately 2.7 million people in the United States are chronically infected with HCV, and the Centers for Disease Control and Prevention (CDC) estimates that by the year 2010, the number of deaths attributed annually to HCV could surpass that due to HIV/AIDS in the US. Worldwide, the World Health Organization estimates that 170 million individuals have chronic HCV infection, with 3 to 4 million new infections each year.

Therapy for HCV currently employs a drug combination approach, which is anticipated to continue in the future. The current standard of care for treatment-naïve chronic hepatitis C is pegylated interferon combined with ribavirin (PR), which fails to provide a satisfactory outcome for approximately 50% of patients infected with HCV genotype 1 (the most prevalent genotype

in North America).

### **About MIGENIX**

MIGENIX is committed to advancing therapy, improving health, and enriching life by developing and commercializing drugs primarily in the area of infectious diseases. The Company's clinical programs include drug candidates for the treatment of chronic hepatitis C infections (Phase II and preclinical), the prevention of catheter-related infections (Phase III) and the treatment of dermatological diseases (Phase II). MIGENIX is headquartered in Vancouver, British Columbia, Canada with US operations in San Diego, California. Additional information can be found at [www.migenix.com](http://www.migenix.com).

### **FORWARD-LOOKING STATEMENTS**

This news release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995, and forward-looking information within the meaning of applicable securities laws in Canada, (collectively referred to as "forward-looking statements"). Statements, other than statements of historical fact, are forward-looking statements and include, without limitation, statements regarding our strategy, future operations, timing and completion of clinical trials, prospects, plans and objectives of management. The words "anticipates", "believes", "budgets", "could", "estimates", "expects", "forecasts", "intends", "may", "might", "plans", "projects", "schedule", "should", "will", "would" and similar expressions are often intended to identify forward-looking statements, which include underlying assumptions, although not all forward-looking statements contain these identifying words. By their nature, forward-looking statements involve numerous assumptions, known and unknown risks and uncertainties, both general and specific, that contribute to the possibility that the predictions, forecasts, projections and other things contemplated by the forward-looking statements will not occur.

Although our management believes that the expectations represented by such forward-looking statements are reasonable, there is significant risk that the forward-looking statements may not be achieved, and the underlying assumptions thereto will not prove to be accurate. Forward-looking statements in this news release include, but are not limited to, statements concerning our expectations for: increasing the celgosivir dose to 600mg being an important development step for the optimization and advancement of celgosivir; our plans to add approximately six patients at 600mg dose in the celgosivir Phase II viral kinetics study and having results from the study in the third quarter 2008; Cadence Pharmaceuticals completing enrollment in the CLIRS trial in the second quarter of 2008, with results available in the second half of 2008; and Cutanea Life Sciences' plans to advance omiganan for the treatment of rosacea to Phase III clinical development.

With respect to the forward-looking statements contained in this news release, we have made numerous assumptions regarding, among other things: our ability to enroll approximately six patients at the 600mg dose in the celgosivir Phase II viral kinetics study and having results from the study in the third quarter of 2008; Cadence's ability to enroll sufficient patients to complete the Omigard CLIRS trial; the adequacy of the CLIRS trial design to generate data that are deemed sufficient by regulatory authorities to support potential regulatory filings, including an NDA, for Omigard; Cutanea's ability to manage, fund and advance omiganan for dermatological applications into Phase III, the adequacy of Cutanea's Phase II results for regulatory authorities

to support advancing to Phase III; our ability to manage licensing opportunities; and our ability to initiate, fund and complete non-clinical studies, clinical studies, manufacturing and all ancillary activities within our expected timelines.

Actual results or events could differ materially from the plans, intentions and expectations expressed or implied in any forward-looking statements, including the underlying assumptions thereto, as a result of numerous risks, uncertainties and other factors including: dependence on corporate collaborations; potential delays; uncertainties related to early stage of technology and product development; uncertainties as to the requirement that a drug be found to be safe and effective after extensive clinical trials and the possibility that the results of such trials, if completed, will not establish the safety or efficacy of our products; uncertainties as to future expense levels and the possibility of unanticipated costs or expenses or cost overruns; the possibility that opportunities will arise that require more cash than presently anticipated and other uncertainties related to predictions of future cash requirements; and other risks and uncertainties which may not be described herein. Certain of these factors and other factors are described in detail in the Company's Annual Information Form and Annual Report on Form 20-F for and other filings with the Canadian securities regulatory authorities and the U.S. Securities & Exchange Commission.

Forward-looking statements are based on our current expectations and MIGENIX assumes no obligations to update such information to reflect later events or developments.

The Toronto Stock Exchange has not reviewed and does not accept responsibility for the adequacy or accuracy of this release.

#### **For further information**

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### ***Molecules may predict cancer survival***

<http://it.moldova.org>

U.S. scientists said tiny molecules that help cells regulate which proteins they make might one day help physicians predict liver cancer patient survival.

The Ohio State University-led study compared levels of molecules called **microRNA** in tumor and adjacent non-tumor cells from liver cancer patients, most of whom also had hepatitis and cirrhosis.

The study found patients with poor disease-free survival had low overall levels of 19 specific microRNAs, compared with those showing better survival after 16 years of follow-up.

The findings must be verified in larger groups of patients, but they suggest that we might improve survival in some liver cancer cases by adding back those microRNAs as a drug, said Associate Professor Thomas Schmittgen, the study's principal investigator.

However, Schmittgen added, that possibility would require years of additional laboratory and pre-clinical research.

The work that included researchers at the Mayo Clinic and the University of Oklahoma Health Sciences Center is published in the Jan. 15 issue of the journal **Clinical Cancer Research**.

***Vertex's lead drug telaprevir for the treatment of Hepatitis C will have to be monitored for the potential emergence of drug resistance, physicians say***

<http://www.ft.com>

By Kimberly Ha in New York

Vertex's lead drug **telaprevir**, for the treatment of Hepatitis C (HCV) will have to be monitored for the emergence of drug resistance, physicians told Pharmawire, due to the drug's potency.

When asked whether drug resistance will be an issue with telaprevir, and a class effect of protease inhibitors, Dr John Alam, Vertex's chief medical officer, said finding ways of minimizing resistance will be true for every company developing a polymerase and protease inhibitor.

Vertex remains focused on identifying a dose and duration of telaprevir-based treatment that will minimize the likelihood of drug resistance. "We did see resistance very early, when the drug was given by itself, in lower doses," he said.

Dr Eduardo Martins, Vice President of Clinical Development at Dynavax Technologies, a company that develops products to prevent infectious diseases, believed that Vertex "took a big risk that others didn't," as the potency seen with Vertex's drug was "quite remarkable."

Martins added that one of the concerns is the potential of inducing a super drug resistant virus, as it is so potent. However, the data so far suggests the majority of patients who received telaprevir have a sustained viral response, he said.

Alam explained that 7% of patients reported viral breakthrough in the US-based PROVE-1 trial, versus 2% in the European study. "Most of [the resistance] happens very early in treatment, within first 2-3 weeks. In order to prevent further resistance, the patients are taken off treatment. About 5% of patients will get screened out very early on, so the impact of resistance will be minimized," he explained.

Romark Laboratories, a private Florida-based biotech, may emerge as a potential "wild card" in the HCV developmental landscape, with a drug that does not seem to show the same levels of drug resistance as it is in an entirely different class.

"Drug resistance is very important," said Marc Ayers, CEO of Romark Laboratories. Romark's drug candidate **Alinia** (nitazoxanide), does not induce drug resistance in the same way as these new protease and polymerase inhibitors.

Dr Ned Snyder, chief of Clinical Gastroenterology and Hepatology at University of Texas Medical Branch, added that Alinia is a completely different drug and a "little bit of a wild card." However the drug is currently marketed and sports a safe side-effect profile. In Genotype 4 patients, the drug reported an impressive 79% SVR rate in interferon-naive patients.

With direct acting antivirals, such as protease inhibitors, SVR rates are reported very high earlier on in the course of treatment, but the rate drops off as the treatment progresses, due to side-effects and drug resistance and viral breakthrough between week-4 and week-12, Ayers explained.

Another potential concern is the rash that is reported in certain patients undergoing telaprevir treatment, which has been reported in previous trials. This may affect patient compliance, physicians have noted.

Amy Martin-Holohan, an HIV specialist pharmacist at Medco, explained that with certain HIV drugs, patients who missed "only a few doses" became resistant to the virus. Patients are required to take at least 95% of the scheduled doses at the scheduled time to prevent drug resistance. She highlighted Merck's recently approved integrase inhibitor Isentress, as an example. With HIV, the prevalence of drug resistance is between 6%-16%, she added.

"Vertex just announced their Phase III and they're looking to try the triple combination of the addition [of telaprevir] just for a short period of time," said Claire Steers, a spokesperson for Switzerland-based Roche.

In partnership with InterMune, Roche is currently developing a Phase Ib protease inhibitor **ITMN-191** (R7227). The drug is currently undergoing multiple-ascending-dose studies for the consideration as potential monotherapy. Roche is also developing polymerase inhibitor candidates.

Steers agreed that drug resistance may be an issue with protease inhibitors. "Polymerase inhibitors are attractive compounds as they have a much lower incidence of resistance than protease inhibitors," she added.

Reimbursement and pricing will also have to be taken into consideration, as many patients on Hepatitis C treatment have to take an additional EPO product to treat anemia that is encountered due to the side-effect of ribavirin.

However, the main issue remains whether or not Vertex can sustain the current SVR rates previously reported in Phase II trials.

Dr Roger Pomerantz, president of Tibotec Research and Development, who previously chaired the FDA panel for anti-virals, said the main goal is the decrease the treatment time patients are on interferon and ribavirin. He said that there is "no ulterior motive" than to drive down the treatment timeframe, and the shorter treatment duration was not because of the potential issue of drug resistance.

"We're very excited about telaprevir. It's not clear that one drug will be the answer. There may

be combination drugs,” said Pomerantz. Tibotec is also currently partnered with Vertex on the development of telaprevir.

Jarrold Dalton, a biostatistician with the Cleveland Clinic Foundation said that there will be comparative “statistical noise” between Phase II and Phase III trials as the drug will be tested in a larger and more diverse patient population.

When asked whether the transition to Phase III trials may lead the 61-67% SVR rates seen in Vertex’s Phase II trials to drop even lower in Phase III trials, Dalton said Phase II trials generally have more exclusion criteria than Phase III trials, which results in less patient-to-patient variability in the measured outcome.

Idenix Pharmaceuticals’ Director of Biostatistics, Bruce Belanger, explained that Phase II trials allow companies to learn which patients will do well on therapy. In Phase III trials, companies want to have a wider scope as possible to have applicability in the real world setting, which will add extra variation.

“The goal of Phase II trials is to demonstrate potential efficacy of a drug in a select group of patients, or patients where the investigator believes there to be the highest potential for efficacy,” Dalton added.

Patient enrollment for Phase III trials is expected in March 2008.

Vertex has a current market cap of USD 2.68bn.

## ***Glaxo, Sanofi Charged in France Over Hepatitis Vaccine***

<http://www.therapeuticsdaily.com>

Agence France-Presse English Wire

PARIS, Feb 1, 2008 (AFP) - Two drug companies are facing charges in France over a hepatitis B vaccine blamed for the death of a 28-year-old woman in 1998 and which caused serious side effects among 1,300 patients.

Smithkline Beecham, now GlaxoSmithKline GSK, and Pasteur Merieux MSD-Aventis Pasteur, now Sanofi Pasteur MSD, are accused of aggravated deceit for failing to disclose the possible side effects from the vaccine, justice officials said Thursday.

Pasteur MSD is also charged with involuntary homicide in the 1998 death of Nathalie Desainquentin, who allegedly contracted multiple sclerosis from the vaccine.

More than 20 million French people were vaccinated against hepatitis B from 1994 to 1998.

Lawyer Bernard Fau representing Desainquentin's family and other victims expressed satisfaction with the decision to press charges, saying "this supports our theory that the recommended use of the vaccination was not in line with the real risks".

France's former rightwing government had launched a national vaccination campaign against hepatitis B, which can infect the liver, in 1994 and suspended it in 1998 after several lawsuits were lodged.

A total of 29 victims have filed suit including five who claim the vaccine caused the death of a family member.

In 2005, a court threw out a suit for endangering lives against former health ministers Jean-Francois Mattei, Bernard Kouchner and Philippe Douste-Blazy over the vaccination campaign.

GSK and Pasteur MSD have repeatedly denied any wrongdoing.

pr/cml/mjs

*France-health-hepatitis-pharma-justice*

## ***Non-Invasive Ways to Assess Liver Disease***

<http://www.interscience.wiley.com/journal/hepatology>

*Studies test alternatives to liver biopsy*

Two new studies examine non-invasive ways to determine liver fibrosis and cirrhosis. An enhanced version of the Original European Liver Fibrosis panel was found to have good diagnostic accuracy for fibrosis in patients with non-alcoholic fatty liver disease. Conversely, transient elastography was unreliable for detecting cirrhosis in patients with acute liver damage. The studies are published in the February issue of *Hepatology*, a journal by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD). The articles are also available online at Wiley Interscience (<http://www.interscience.wiley.com/journal/hepatology>).

Liver biopsy is the undisputed best way to assess liver fibrosis or cirrhosis; however, it is an invasive procedure that can cause rare, but potentially life threatening complications. Researchers have been seeking less invasive ways to diagnose liver disease, developing and testing clinical tools, like the Original European Liver Fibrosis Panel and transient elastography.

Researchers led by William Rosenberg in the United Kingdom, sought to validate the Original European Liver Fibrosis panel and consider a simplification that removed age as a factor yielding the Enhanced Liver Panel. They also tested the diagnostic performance of the ELF panel with the addition of the following simple markers: age, BMI, presence of diabetes/impaired fasting glucose, AST/ALT ratio, platelets, and albumin.

They recruited 196 patients with non-alcoholic fatty liver disease from two separate centers and tested the diagnostic accuracy of the new panels. They found that the Enhanced Liver Fibrosis panel detected severe fibrosis, moderate fibrosis and no fibrosis at AUCs of .90, .82, and .76 respectively. The diagnostic accuracy of the ELF panel plus simple markers was .98, .93 and .84 respectively. They report that using either panel could eliminate the need for liver biopsy in

diagnosing severe fibrosis in more than 80 percent of cases.

“The ELF panel has good diagnostic accuracy in an independent validation cohort of patients with NAFLD,” the authors conclude. “The addition of established simple markers augments the diagnostic performance across different stages of fibrosis, which will potentially allow superior stratification of patients with NAFLD for emerging therapeutic strategies.”

Meanwhile, researchers in Germany led by Abdurrahman Sagir used transient elastography—Fibroscan (FS)—to measure liver stiffness in 20 patients presenting with acute hepatitis. In 15 (75 percent) of the patients, the test showed liver stiffness values that suggested cirrhosis. However, none of these patients showed any signs of cirrhosis in a physical exam, on ultrasound, or in liver histology.

“Liver stiffness measurement by FS in patients with acute liver damage overestimate the real stage of fibrosis and may erroneously suggest the presence of liver cirrhosis,” the authors report. The stiffness may relate to hepatocyte swelling, cholestasis, or infiltrates of inflammatory cells in the inflamed liver, they suggest.

“FS results need to be interpreted with caution in patients with acute liver damage and high values of liver stiffness do not predict the simultaneous presence of cirrhosis in these patients,” they conclude.

Both studies offer new information on the ability of non-invasive methods to diagnose liver disease, though further studies are needed to advance our understanding of these diagnostic tools.

**Article:** “Non-invasive markers of fibrosis in non-alcoholic fatty liver disease: validating the European Liver Fibrosis panel and exploring simple markers.” Guha, Indra Neil; Parkes, Julie; Roderick, Paul; Chattopadhyay, Dipanker; Cross, Richard; Harris, Scott; Kaye, Philip; Burt, Alastair; Ryder, Steve; Aithal, Guruprasad; Day, Christopher; Rosenberg, William. *Hepatology*; February 2008.

**Article:** “Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage.” Sagir, Abdurrahman; Erhardt, Andreas; Schmitt, Marcus; Haussinger, Dieter. *Hepatology*; February 2008.

## ***Silymarin Does Not Affect Virus Activity or ALT Levels in Patients with HCV***

<http://www.interscience.wiley.com/journal/hepatology>

In a survey of patients with chronic hepatitis C who participated in a National Institute of Diabetes and Digestive and Kidney Diseases-sponsored long-term treatment trial for patients who had failed to respond previously to antiviral therapy, approximately 40% acknowledged to interviewers at the time of enrollment that they were currently using or had in the recent past used herbal products for health purposes. This information was somewhat surprising because these were patients with advanced liver disease who were clearly committed to conventional antiviral treatment for chronic hepatitis C, having been so treated previously, some on more than

one occasion, but because they had failed to respond, were now willing to accept treatment again with pegylated interferon for another 3 and a half years. Among those who were or had used alternative therapies, silymarin (milk thistle) was the product of choice either on its own or together with other herbal products, representing 72% of all the herbals taken.

These findings are in the February issue of *Hepatology*, a journal published by Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD). The article was also available online at Wiley Interscience (<http://www.interscience.wiley.com/journal/hepatology>).

These results do not come from a rigorous scientific study because the products used were self-administered by the patients who entered the trial and no information was obtained on the duration or dose of the herbal taken. Still, in comparing users with non-users, while no difference was found for blood ALT or HCV levels between the two groups, the herbal users did report somewhat fewer symptoms and a better quality of life.

The current recommended treatment for patients with HCV infection is combination therapy with pegylated interferon and ribavirin. However, it leads to a sustained virological response in only a third to a half of all patients with the predominant form of the infection in the U.S., namely genotype 1, and it can cause unpleasant and sometimes serious side effects. The NIH study, referred to as the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C) Trial, was designed, therefore, to treat persons with advanced chronic hepatitis C who had failed previous antiviral therapy with the hope that the long-term treatment would reduce progression of the chronic liver disease even if it did not affect the virus itself. The reason for interviewing enrollees in the trial was to determine the extent of use of alternative therapies in this committed group, since the popularity of herbal products has increased in the U.S., many HCV patients choosing to supplement, or even replace, the standard treatment with herbals. Silymarin (milk thistle extract) has been the most popular option for people with liver disease. Although it is the most frequent product utilized, silymarin has not been rigorously studied using accepted scientific approaches, and therefore such studies are clearly required and warranted.

For the present survey, researchers interviewed all HALT-C participants on past and current use of all prescription and non-prescription drugs, including herbal medications, dietary supplements and other botanical products. Of 1145 study participants, 56 percent said that they had never used herbal products, while 23 percent were using them currently, some 60 different varieties. Silymarin was by far the most common. Usage was higher among men, among non-Hispanic whites, and among the more highly educated. Interestingly, the researchers also found geographic disparities in silymarin usage. It was most popular in Colorado, Michigan and Southern California and least popular in Maryland and Massachusetts.

In comparing the clinical data of silymarin users and non-users, the researchers found that “the levels of HCV RNA were not significantly different between silymarin users and non-users,” indicating no effect on virus activity. Similarly, the product did not alter serum ALT levels, indicating no effect on hepatic inflammation. However, after adjusting for covariates, the data showed that silymarin users reported less fatigue, nausea, liver pain, anorexia, muscle and joint pain and better general health than non-users.

The better scores in a small number of symptoms among silymarin users compared to non-users are insufficient to support the value of this alternative therapy, the authors conclude. Compelling information can come only if a scientifically valid study is performed. “Currently in progress, therefore, is a properly designed prospective, randomized, controlled trial in which a fully characterized, purified and standardized silymarin formulation is being evaluated,” they report. This trial is supported by the National Center for Complementary and Alternative Medicine (NCCAM) and by NIDDK, NIH.

**Article:** Herbal Product Use by Persons Enrolled in the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (Halt-C) Trial. Seeff, Leonard; Curto, Teresa; Szabo, Gyongyi; Everson, Gregory; Bonkovsky, Herbert; Dienstag, Jules; Shiffman, Mitchell; Lindsay, Karen; Lok, Anna; Di Bisceglie, Adrian, Lee, William; Ghany, Marc. Hepatology February, 2008.