

HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus
Editor-in-Chief*

Week Ending: October 27th 2007

In This Issue:

- [New Virus Drug Will Have To Shoot At Moving Targets](#)
- [Can-Fite liver cancer drug may regenerate liver](#)
- [Hepatitis C victims left in the dark for 5 years](#)
- [Hep C infection after test missed](#)
- [New drug improves condition of liver cancer patients](#)
- [Hepatitis B, liver cancer hit Asian community](#)
- [Forum On Use Of Safer Needles Kicks Off In Geneva](#)
- [R7128 Receives Fast Track Designation from the FDA for the Treatment of Chronic Hepatitis C Infection](#)
- [Ruling bloc eyes hepatitis treatment subsidies](#)
- [Study: MRI scan can predict liver fibrosis](#)
- [More Accurate Diagnosis of Some Liver Diseases Using Alpha-Fetoprotein \(AFP\) Levels: Presented at ASCP](#)
- [Weight-based Dosing of Ribavirin Improves Outcomes for Patients with Hepatitis C](#)
- [Flamel Cites Positive Drug Trial Data](#)
- [Look at the big picture, says Jason](#)
- [Hepatitis scandal sparks anger at Japan government](#)

October 20th, 2007

New Virus Drug Will Have To Shoot At Moving Targets

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

The reproduction of the deadly hepatitis B virus is dependent on the mobility of one of the virus's RNAs. This is shown by Katja Petzold and Jurgen Schleucher, Umea University, Sweden, in an article in the latest issue of the journal *Nucleic Acids Research*.

More than 300 million people all over the world are infected by hepatitis B virus (HBV), and there are 2 million deaths per year. The Umea researchers have studied the mobility of the virus's RNA, a property that is necessary for HBV to reproduce. Besides Jurgen Schleucher and Katja

Petzold, Karin Kidd-Ljunggren of Lund University in Sweden and Sybren Wijmenga of Nijmegen University in Holland are co-authors of the article.

The structures of proteins and nucleic acids are usually presented as still images. However, the molecules' functions or interactions with drugs are dependent on structural changes, and it is possible to reach only indirect conclusions about these on the basis of still images. Nuclear Magnetic Resonance (NMR) is the only technology that enables studies of movements in specific parts of molecules. With the aid of NMR, the relationship between the movement and function of molecules has been mapped for many proteins, but only for a few nucleic acids. This is unfortunate, especially because several new classes of RNA with regulatory functions have recently been discovered. This means that RNA is now regarded to an even greater extent as an active regulator of cellular events, not merely a passive messenger for information.

When new HBV particles are formed in infected cells, the virus must translate RNA to DNA, a process that is called reverse transcription. It starts with the virus enzyme reverse transcriptase binding to a strongly conserved RNA structure in the virus. The authors found that fully conserved nucleotides (the building blocks of RNA) in this RNA evince striking patterns of mobility. This indicates that these nucleotides in the free RNA temporarily visit the structures that they use in complexes with reverse transcriptases, and that their mobility facilitates binding. This means that drugs directed toward the hepatitis virus RNA need to bind to a moving target.

These detailed findings are based on the first application of a new NMR method that was developed at Umea University. The new method enables studies of movements in the bindings in the RNA molecule that give it its form. The method can also be used for complex bindings between drug candidates and proteins or nucleic acids in order to elucidate the stabilizing forces at the atomic level. Therefore, this can be a key tool in biotechnology and the discovery of new drugs. The research team is now moving on to computer simulations to produce images of the movements in an RNA.

VETENSKAPSRADET (THE SWEDISH RESEARCH COUNCIL)

Regeringstgatan 56

103 78 Stockholm

<http://www.vr.se>

October 21st, 2007

Can-Fite liver cancer drug may regenerate liver

<http://www.globes.co.il/>

Gali Weinreb and Globes correspondent

The company said it would be patenting the use of the drug for this purpose.

Drug development company Can-Fite BioPharma Ltd. (TASE:CFBI) has disclosed that its CF102 drug for viral hepatitis was found in preclinical trials (on animals) to be effective in promoting liver tissue regeneration, following partial hepatectomy. "This procedure is usually performed in patients with primary of metastatic liver cancer. No drugs are currently available to speed the regeneration process," said the company in its announcement.

Can-Fite also announced that it would begin Phase I safety trials in the first quarter of 2008. The company said it believes the market for drugs that promote liver regeneration consists primarily of patients with hepatitis B and C. "Out of 130 million patients with hepatitis C and 350 million patients with hepatitis B, 100 million patients are at high risk of for developing liver failure or liver cancer, and may need drugs that speed up the regeneration of their infected liver during the course of the disease," it noted.

October 22nd, 2007

Hepatitis C victims left in the dark for 5 years

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

THE ASAHI SHIMBUN

The health ministry for five years had documents that may have identified at least 165 people unknowingly exposed to the hepatitis C virus through tainted blood products--but did nothing to warn them, ministry officials said Monday.

The ministry set up a team Monday to investigate why ministry officials had denied the documents' existence for so long, and why it failed to alert the at-risk patients.

The ministry received the documents on 418 patients in 2002 from the former Mitsubishi Pharma Corp., now called Mitsubishi Tanabe Pharma.

On Monday, Natsuki Hayama, president of Mitsubishi Tanabe Pharma, separately told health minister Yoichi Masuzoe that the company has found the names of 197 patients and initials for 170 patients who were exposed to hepatitis C infections through its tainted blood products.

The Ministry of Health, Labor and Welfare has instructed Mitsubishi Tanabe Pharma Corp. to notify people whose names or initials are contained on the documents and urge them to seek treatment.

Hayama told reporters the company had not informed the patients of their possible infection risk "to protect the patients' privacy."

However, he added his company now plans to set up a task force to quickly notify the patients.

Health ministry officials said patients were not informed because of confusion caused by personnel changes.

But the ministry's explanation so far on the issue has not been solid.

On Thursday, health ministry officials in a meeting with Minshuto (Democratic Party of Japan) Diet members denied the ministry possessed documents containing data that could identify at-risk patients.

On Friday, however, two documents were found in a ministry storage room that listed the full

names of two at-risk patients and initials for 116 others who received tainted blood, ministry officials said.

Ministry officials admitted for the first time on Saturday that as far back as 2002, it had the documents the former Mitsubishi Pharma Corp. had submitted.

On one document, all data that could help establish the identity of patients was blacked out. But on the other copy, nothing was blacked out.

In 2002, the ministry instructed Mitsubishi Pharma to provide data on patients who had developed hepatitis C and other side effects after being treated with fibrinogen, the tainted blood product provided by the company.

The documents found Friday contained partial information on 165 patients, such as full names, initials, names of medical institutions, names of doctors or other details that could help establish their identities, according to the ministry.

In three patients' cases, for example, only the names of medical institutions were entered.

Hayama told Masuzoe that of the 197 full names obtained by the company, addresses are listed for 40. In 27 cases, only the city, town or village is listed. In 12 cases, only the prefecture is listed.

Of the 170 patients listed by their initials, two had addresses, 13 had a city, town or village, and 10 a prefecture.

Kazutaka Nakazawa, director of the General Affairs Division at the ministry's Pharmaceutical and Food Safety Bureau, said, "The team probing the hepatitis problem at that time disbanded, and the person who is now in charge had no knowledge (the documents existed)."

Meanwhile, nine people in the ministry's documents may be plaintiffs in lawsuits pending against the government and drug companies over the tainted blood product infections, sources said.

Of the nine, two were not acknowledged by the government as receiving tainted blood products. One of the two may

Hep C infection after test missed

<http://www.smh.com.au/>

Annabel Stafford

A PATIENT has contracted Hepatitis C from an organ transplant after a test that would have detected the disease was not performed until after the operation.

The nucleic acid test (NAT) was not done before the transplant because it was not available after hours.

Had the test been done before the operation, the patient would not have had the transplant and would not have contracted Hepatitis C, a spokeswoman for NSW Health has admitted.

The name of the hospital where the incident occurred, and the exact time it happened, has not been revealed because these details could lead to identification of the organ donor - who died on the night in question - or the recipient.

But the incident, which occurred at a major Sydney teaching hospital in the past six months, has led to calls for NAT tests to be available 24 hours a day across the country.

NAT tests are generally used before organ transplants because they can more accurately pick up Hepatitis C and HIV than the antibody tests that are mandatory before any transplant.

In the wake of the incident NSW Health has committed to funding 24-hour-a-day availability for NAT testing, and the Australian Red Cross Blood Service, which provides the tests, is in the process of implementing the new service.

Australians Donate - the peak body for organ and tissue donation - has backed similar changes for the whole of Australia.

NAT testing is not mandatory.

In the case of the the patient who contracted Hepatitis C, a spokeswoman for the Red Cross Blood Service said the organisation had fulfilled all its responsibilities and that, in the end, the decision to go ahead was up to the doctors.

"NAT testing was undertaken according to our standard procedures and the results communicated to the treating physicians as soon as they were available," she said.

The NSW Deputy Chief Health Officer, Kerry Chant, said while a NAT test was performed in the case of the infected patient, "it was done on the routine run the next morning" rather than at the time.

Had the test been ordered immediately "it would have come back in time for the transplant", Dr Chant said.

She also admitted: "It would have changed the decision in this case if the testing had been done."

October 23rd, 2007

New drug improves condition of liver cancer patients

<http://www.manilastandardtoday.com>

By Neil Ray Ramos

As far as I can remember, the one thing I feared most as a kid was the belief that a big, bad liver-eating monster actually resided underneath my bed. It may sound funny now but darn it if it didn't used to give me many a sleepless night.

Though I eventually outgrew it all, the liver-eating monster is fast proving to be as real a menace in that it has actually been claiming lives across the globe.

No, this one doesn't go about lurking under children's beds inasmuch as it doesn't go about disguising itself in a huge, scary form. In fact, it goes about unconcernedly if not blatantly, that science has found a name for it.

Hepatocellular carcinoma, as primary liver cancer, is the most common form of liver cancer known to man. And it is indubitably deadly. In fact it has claimed approximately 600,000 people (about 13,000 Americans and 57,000 Europeans) in 2002 alone.

In Asia, liver cancer is the second most common cause of cancer-related deaths with a reported 396,000 deaths annually. Liver cancer is particularly common in China, Japan, Korea, Indonesia, Papua New Guinea and the Philippines.

Symptoms of primary liver cancer include weight loss (for no known reason and without trying to lose weight); continuing lack of desire for food; feeling of fullness even after a small meal; swelling in the area of the stomach; ongoing stomach pain; skin and eyes becomes yellow-green in color (jaundice); and becoming even sicker with the onslaught of chronic hepatitis or cirrhosis.

At risk are those suffering from on-going (chronic) infection with hepatitis B virus and/or hepatitis C virus; and cirrhosis (widespread disruption of normal liver structure by fibrosis and the formation of regenerative nodules that is caused by various chronic progressive conditions affecting the liver).

Also at risk are those with family history of liver diseases; those with long-term exposure to aflatoxins; tobacco use; and long-term use of anabolic steroids.

As it is, there are four standard treatments used to treat liver cancer. And that is if the cancer is found at an early stage and the rest of the liver is still healthy. These include cryosurgery (to freeze and destroy abnormal tissue); partial hepatectomy, or a removal of the part of the liver where cancer is found; total hepatectomy and liver transplant; and radio frequency ablation, in which a special probe with tiny electrodes is used to kill cancer cells.

But that's not all folks. Now, Bayer Schering Pharma is offering renewed hope for patients via Sorafenib (Nexavar), an oral multi-kinase inhibitor that targets both the tumor cell and tumor vasculature.

According to Dr. Luis Abola, medical director of BSP, the company has undertaken a robust program of clinical trials throughout Asia-Pacific countries to support the potential of the kidney cancer therapy Sorafenib in the treatment of primary liver cancer.

“Sorafenib, which is actually currently licensed for the treatment of kidney cancer, is found, through the studies, to significantly improve overall survival in patients with HCC, or primary liver cancer. It is in fact, the first product to succeed in improving overall survival after 30 years of research and over 100 randomized controlled trials,” he said.

Results of these trials were presented recently to the media by Dr. Antonio Villalon, a prominent figure in oncology.

In the pre-clinical models, Sorafenib (Nexavar) prove itself able in targeting members of two classes of kinases that are involved in cell proliferation (growth) and angiogenesis (blood supply)—two important processes that enable cancer growth. Another good thing is that Sorafenib (Nexavar) has been found to be generally well-tolerated with manageable side-effects.

“But as of this writing, Sorafenib has yet be approved for the treatment of HCC,” said Dr. Abola adding that additional measures are being studied with regards to its effects.

“Once approved for the treatment of primary liver cancer, Sorafenib will yet be another significant medical breakthrough; this is good news especially for patients suffering from this devastating disease.”

Hepatitis B, liver cancer hit Asian community

<http://www.contracostatimes.com>

By Kristina Peterson
MEDIANEWS STAFF

Groups announce program to help increase early detection

Hans Wang felt no different than normal when a routine blood test in May revealed that he had liver cancer.

Even though the 44-year-old Cupertino resident had been getting annual blood tests, the tumor on his liver was already five centimeters wide -- just small enough that doctors could surgically remove it, he said.

But Wang, now a cancer survivor, is unusual among local Asian-Americans. Many are not screened for chronic hepatitis B or liver cancer despite their heightened susceptibility to the diseases.

On Thursday, the Asian Liver Center at Stanford University and the American Cancer Society California Chinese Unit unveiled a new outreach program aimed at increasing early liver cancer detection rates in the region's Asian population.

"There is no effective chemotherapy to treat liver cancer," Dr. Samuel So, director of the Asian Liver Center, said Thursday. "The only way of improving chances of liver cancer survival rates is early detection."

Asian-Americans are nearly three times as likely to develop liver cancer than other ethnicities largely because of the prevalence of chronic hepatitis B virus in their community, So said. San Francisco has the highest liver cancer rate of any city in the country because of its large Asian population, he said.

The virus that causes hepatitis B is spread through contact with infected blood or other bodily fluids of people who have hepatitis B. Pregnant women who are infected with hepatitis B can pass the virus to their babies.

Because 69 percent of Asians living in the United States are foreign-born, according to U.S. Census data, most of those with chronic hepatitis B were infected outside the country, often from dirty medical supplies used in doctor's offices, So said. Those born in the United States most often contract the disease from their mothers, he added.

Almost 10 percent of Asians living in the United States have chronic hepatitis B, compared to 0.1 percent of Caucasians, So said. And those infected with chronic hepatitis B have a 25 percent chance of developing liver cancer, according to a paper released this year by So, Steven Lin and Ellen Chang of the Asian Liver Center.

Most alarmingly, in a survey of 3,163 Bay Area Asian-Americans screened for hepatitis B, half to two-thirds of those with the disease were unaware they were infected, according to the paper.

May Sung, vice president of the American Cancer Society's California Division, said language barriers, lack of access to health care and cultural taboos all contribute to Asian-Americans not getting screened for hepatitis B and for liver cancer on a regular basis.

Wang said that without the blood tests, he would never have suspected he had cancer.

"I didn't feel anything different," he said. Wang only began getting annual tests after his mother died of liver cancer in 2000.

So said the majority of his patients with early liver cancer have no symptoms and as a result often come to his clinic too late for help. Last week, So saw a recently diagnosed patient who has only three to four months to live.

"Week after week, I see people dying from a disease they should not be dying from," said So, adding that liver cancer most often strikes people ages 35 to 65, "in the prime of their life."

Reach Kristina Peterson at kpeterson@dailynewsgroup.com .

Forum On Use Of Safer Needles Kicks Off In Geneva

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

Press Release: United Nations

With an estimated 6 billion injections given every year with syringes or needles that are reused without sterilization, the United Nations health agency has gathered together global experts to explore ways to promote the use of safer needles, which in turn can prevent the spread of viruses such as Hepatitis.

The annual meeting of the Safe Injection Global Network (SIGN), which kicked off at WHO's headquarters in Geneva, brings together UN agencies, donors, experts, countries and industry.

Over the next three days, participants will examine how best to encourage countries and procurement agencies to purchase the safest needles, how to encourage manufacturers to lower the price of such products, and how to boost countries' local manufacturing capacity.

WHO estimates that 40 per cent of all injections given in developing countries - and up to 70 per cent in some countries - are with needles or syringes that are reused without sterilization.

While the agency has been advising countries to use needles with safety features, most cannot afford these new technologies. Less sophisticated needles cost about \$0.03, while more advanced, safer ones are about \$0.15.

"The new technologies should be available to developing countries, where injections are used more and where the risk of infection transmission is greater," Dr. Howard Zucker, WHO's Assistant Director-General for Health Technology and Pharmaceuticals, stated.

According to WHO, unsafe injections and needle stick injuries suffered by health-care workers together cause 33 per cent of new Hepatitis B infections and 2 million new cases of Hepatitis C in the world each year. Unsafe injections in health-care settings also account for an estimated 5 per cent of new HIV cases worldwide.

The use of syringes with features that prevent reuse and needle stick injuries would avert about 1.3 million global deaths per year by preventing infections and the epidemics caused by their spread, WHO estimates.

To promote safer injections, the agency will discuss with manufacturers possible ways to lower the price of safer injection devices, as well as promote interaction between local manufacturers and the two umbrella organizations for injection device manufacturers - the International Association for Safe Injection Technology and the European Medical Technology Industry Association.

October 24th, 2007

R7128 Receives Fast Track Designation from the FDA for the Treatment of Chronic Hepatitis C Infection

<http://www.genengnews.com>

PRNEWswire

PRINCETON, N.J., Oct. 24 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS) has received fast track designation from the U.S. Food and Drug Administration (FDA) for **R7128** for the treatment of chronic hepatitis C virus (HCV) infection. R7128 is a prodrug of PSI-6130, an oral cytidine nucleoside analog polymerase inhibitor of HCV that is being developed through Pharmasset's collaboration with Roche. Pharmasset is currently enrolling a 28-day Phase 1 clinical trial to evaluate R7128 in combination with Pegasys(R) (pegylated interferon) plus Copegus(R) (ribavirin) in treatment-naive patients chronically infected with hepatitis C virus (HCV) genotype 1. Please see www.clinicaltrials.gov or e-mail clinicaltrials@pharmasset.com for more information.

Under the FDA Modernization Act of 1997, fast track designation may facilitate the development and expedite the review of a drug candidate that is intended for the treatment of a serious life-threatening condition and demonstrates the potential to address an unmet medical need for such a condition. R7128 was granted the fast track designation primarily due to the need for HCV treatments with novel mechanisms of action, oral administration, different resistance profiles and improved safety and efficacy over the existing standard of care for both treatment-naive and treatment-experienced patients.

"The FDA's fast track designation for R7128 acknowledges the urgent need for new HCV drugs," stated Dr. Michelle Berrey, Pharmasset's Vice President, Clinical Development & Chief Medical Officer. "Currently, there are no HCV polymerase inhibitors approved for the treatment of chronic HCV infection. We continue to work closely with our HCV partner, Roche, and the FDA on the development and regulatory review of R7128, which has demonstrated compelling antiviral activity and has been generally well-tolerated in clinical trials to date."

About Pharmasset

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

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in the Americas and Europe. Clevudine is already approved for HBV in South Korea and marketed by Bukwang Pharmaceuticals in South Korea under the brand name Levovir. R7128, an oral treatment for chronic HCV infection, is enrolling a 28-day Phase 1 clinical trial in combination with Pegasys(R) and Copegus(R) through a strategic collaboration with Roche. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.

About R7128

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a pyrimidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. Results from an oral single ascending dose study of PSI-6130 in 24 healthy male volunteers showed that PSI-6130 was generally well tolerated with no serious adverse events in doses up to 3000 mg.

R7128 Phase 1 Study Overview

The Phase 1 clinical trial is a multiple center, observer-blinded, randomized and placebo-controlled study to investigate the pharmacokinetics, pharmacodynamics, safety, tolerability and food effect of R7128 in healthy volunteers and in patients chronically infected with HCV genotype 1. This adaptive Phase 1 study is comprised of three parts:

Part 1 is a single ascending dose study of R7128 conducted in 46 healthy volunteers. The primary objective of Part 1 is to assess the safety, tolerability and pharmacokinetics of R7128 following single ascending doses under fasting conditions. The secondary objective of Part 1 is

to explore the effect of food on the pharmacokinetics of R7128. Results from the single ascending dose portion of the study indicated that all doses of R7128 studied (500 mg to 9000 mg) were generally safe and well-tolerated. All patients completed the study, and none experienced gastrointestinal adverse events or serious adverse events during the study. No hematological or laboratory abnormalities of clinical significance were noted.

Part 2 is a multiple ascending dose study of R7128 conducted in 40 patients chronically-infected with HCV genotype 1 who previously failed interferon therapy. The primary objective of Part 2 is to assess the safety, tolerability and pharmacokinetics of R7128 after once-daily (QD) or twice-daily (BID) dosing for 14 days. The secondary objective is to assess antiviral activity by measuring the change in HCV RNA. Preliminary data from the multiple ascending dose portion of the study indicated that R7128 demonstrated potent, dose-dependent antiviral activity in four patient cohorts receiving 750 mg or 1500 mg administered either once-daily or twice-daily for 14 days as monotherapy. Patients receiving 1500 mg BID demonstrated a mean 2.7 log₁₀ IU/mL (>99%) decrease in HCV RNA. There was no evidence of viral rebound in any dose cohort during the 14 days of dosing. R7128 was generally safe and well tolerated. There were no serious adverse events, no adverse events requiring dose modification, no dose-related gastrointestinal adverse events and no clinically significant changes in hematologic or other laboratory parameters.

Part 3 is a multi-center, observer-blinded, within-cohort randomized, placebo-controlled study being conducted in up to 75 treatment-naïve patients with genotype 1 hepatitis C virus. The primary objective is to assess the safety, tolerability and pharmacokinetics of R7128 in combination with Pegasys plus Copegus. The secondary objective of Part 3 is to evaluate the short-term change in HCV RNA. The study will include two to three oral doses of R7128 (500 mg to 1500 mg) that are being administered twice-daily with Pegasys plus Copegus for 28 days.

Pegasys(R) and Copegus(R) are registered trademarks of Roche.

About Hepatitis C

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

Contact

Alan Roemer, Vice President
Investor Relations & Corporate Communications
alan.roemer@pharmasset.com
Office: (609) 613-4125

Forward-Looking Statements

Pharmasset "Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: Statements in this press release regarding our business that are not historical facts are "forward-looking statements" that involve risks and uncertainties, including without limitation the risk that the FDA withdraws the R7128 fast track designation, the risk that the FDA does not expedite the

review or approval of any application for R7128, the risk that adverse events could cause the cessation of the Phase 1 study and/or our development of R7128, the risk that our collaboration with Roche will not continue or will not be successful, the risk that the on-going or anticipated clinical trials for any one or more of our product candidates will not be successful or will not provide meaningful data and the risk that any one or more of our product candidates will not be successfully developed and commercialized. For a discussion of these risks and uncertainties, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section of our Quarterly Report on Form 10-Q for the quarter ended June 30, 2007 filed with the Securities and Exchange Commission entitled "Risk Factors" and discussions of potential risks and uncertainties in our subsequent filings with the Securities and Exchange Commission.

SOURCE Pharmasset, Inc.

Ruling bloc eyes hepatitis treatment subsidies

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

The Yomiuri Shimbun

The ruling coalition parties are planning to submit a bill to the current Diet session that will provide a subsidy for patients undergoing hepatitis therapy, among other measures to combat the disease, it has been learned.

The basic bill drafted by lawmakers includes a comprehensive suite of measures aimed at prevention, treatment and research into hepatitis. It also stipulates financial support for patients suffering from hepatitis and the setting up of "hub" hospitals specializing in the disease, according to sources.

The Liberal Democratic Party and New Komeito are likely to demand that the state establish basic guidelines for the prevention and treatment of hepatitis, they said.

The Democratic Party of Japan has already submitted an emergency bill on hepatitis to the Diet, providing financial support for hepatitis B and C patients undergoing interferon treatment.

Under the DPJ proposal, such patients would pay about 10,000 yen a month toward their interferon treatment, which costs about 80,000 yen a month, with the state to finance the rest.

The ruling parties plan to map out a set of concrete measures at a project team looking into the amount of subsidy needed to help hepatitis patients, the sources said.

According to the Health, Labor and Welfare Ministry, an estimated 3.5 million people across the nation are suffering from hepatitis B and C.

Among these, about 10,000 developed hepatitis C after being administered with hepatitis-tainted blood products.

The ruling coalition's basic bill stresses the importance of taking comprehensive

countermeasures, pointing out that "while a great number of people are infected with hepatitis, the disease will become chronic if patients let the disease proceed without treatment."

The parties incorporated in the bill measures they believe the government should take--including financial support for patients undergoing hepatitis therapy, developing hepatitis specialists and rapid approval of new medicines for the treatment of the disease.

It also includes the need to set up a system to collect and provide information about hepatitis, the sources said.

To map out the hepatitis guidelines, they also plan to launch a council at the ministry to promote countermeasures against hepatitis, with participants to include hepatitis patients, their families and specialists.

While lawsuits over tainted blood products have often been brought, the ruling coalition decided to include provisions in the basic bill specifying the legal responsibility of the state, local governments and medical doctors.

Initially, the ruling coalition parties believed that providing for hepatitis care could be done by adjusting budgetary allocations, and without introducing new legislation.

Study: MRI scan can predict liver fibrosis

<http://social.moldova.org/>

A U.S. study has determined moderate to severe chronic liver disease can be predicted with the use of a type of magnetic resonance imaging.

The researchers at New York University Medical Center said the diffusion-weighted MRI scans appear promising, although further study is needed.

"Due to the increased incidence of chronic hepatitis in the United States, particularly hepatitis C, there is a strong need for non-invasive methods to replace or supplement liver biopsy, which is relatively invasive and limited by interobserver variability and sampling error," said Dr. Bachir Taouli, lead author of the research.

"At this point, this is an experimental method that needs to be tested in a larger series," said Taouli. "However, diffusion imaging does show potential for decreasing the number of biopsies and decreasing the number of antifibrogenic drug trials."

The study appears in the October issue of the *American Journal of Roentgenology*.

More Accurate Diagnosis of Some Liver Diseases Using Alpha-Fetoprotein (AFP) Levels: Presented at ASCP

<http://www.docguide.com>

By Lexa W. Lee

NEW ORLEANS, LA -- October 23, 2007 -- Serum alpha-fetoprotein (AFP) levels above 700 ng/dL appear to be diagnostic of hepatocellular carcinoma (HCC), researchers reported here at the American Society of Clinical Pathologists (ASCP) Annual Meeting.

The current literature cites a range of AFP values from above 20 ng/dL to 400 mg/dL as being associated with HCC; levels above that are reported as being diagnostic of HCC. The findings of a new study trying to establish a more accurate range for HCC screening were presented.

To establish a more accurate range of AFP values for HCC screening, Todd LeLeux, MD, Resident Pathologist, Michael E. DeBakey VA Medical Center, Houston, Texas, United States, and colleagues performed a retrospective chart review of patients who had been tested for AFP at their institution in the previous 5 years.

Out of the total sample of 2,538 patients, the researchers identified 101 patients diagnosed with HCC who were then divided into three groups, based on their AFP values. Patient records were reviewed for tissue confirmation, clinical findings, X-rays, and follow-up.

Within the three groups, 18 patients had AFP < 20 ng/dL, 29 had AFP from 20-400 ng/dL, and 54 had AFP > 400 ng/dL. Diagnosis was made by clinical presentation, radiography of the liver, and AFP values, for the most part.

Incidence of hepatitis C virus infection (HCV) and alcoholic cirrhosis (ETOH) varied with AFP values (49% HCV, 44% ETOH in < 20 ng/dL; 85% HCV, 10% ETOH in 20-400 ng/dL; 98% HCV, 5% ETOH in > 400 ng/dL). The diagnosis of HCC was made by FNA, liver biopsy, or radiography. There were eight cases of metastatic carcinomas and one germ cell tumour. Only AFP values > 700 ng/dL were indicative of HCC, in the absence of a germ cell tumour.

In patients with AFP values between 400 and 700 ng/dL, five did not have HCC. These had nonalcoholic steatohepatitis (NASH), hepatorenal syndrome, and interferon therapy. The patients without HCC who had AFP values > 100 ng/dL had alcoholic hepatitis, liver failure, cirrhosis, and interferon therapy.

Values of AFP can be increased by factors such as cirrhosis, interferon therapy, alcoholic hepatitis, nonalcoholic steatohepatitis, hepatorenal syndrome, germ cell tumours, and metastatic carcinomas.

The study findings showed that values > 400 ng/dL are suggestive but not diagnostic of HCC, the researchers said. In patients with HCC, AFP values < 20 ng/dL have a strong correlation to ETOH alone. Values > 20 ng/dL are associated with HCV, with or without ETOH.

Dr. LeLeux said, "We concluded that AFP values > 700 ng/dL were diagnostic of HCC in a sample of patients dominated by men with HCV-related liver disease. Lower values cannot be

used to make a definitive diagnosis of HCC without radiography or biopsy."

[Presentation title: Screening AFP Levels in Hepatitis and ETOH Abuse in Patients in the US: What Is a Diagnostic or Suggestive Value? Poster 46]

October 25th, 2007

Weight-based Dosing Of Ribavirin Improves Outcomes For Patients With Hepatitis C

<http://www.sciencedaily.com>

ScienceDaily (Oct. 26, 2007) — Patients with hepatitis C treated with combination therapy of pegylated interferon and ribavirin had better outcomes when taking a weight-based dosage of ribavirin compared to a flat dosage. This treatment technique also improved the response rates of African American patients, whose outcomes have lagged behind those of Caucasian patients. These findings are in the October issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD).

Combination therapy of pegylated interferon and ribavirin is the standard of care for patients with chronic hepatitis C, allowing more than half to achieve a sustained viral response. However, previous studies have suggested that a weight-based dose of ribavirin might lead to even better results. To examine this possibility, researchers, led by Ira Jacobson of Cornell University, conducted a large, multi-center, randomized, prospective, open-label study between December 2000 and June 2005.

They enrolled 5,027 patients with hepatitis C from more than 200 centers around the country. All participants were 18 to 70 years old, weighed less than 125 kg, had detectable HCV RNA in their blood, and had never been treated for it. They were randomly assigned to receive interferon and a flat dose of ribavirin (800 mg/day), or interferon and a weight-based dose of ribavirin, which started at 800 mg/day for patients weighing under 65 kg, and increased by 200 mg/day for up to each additional 20 kg of weight up to a maximum dose of 1400 mg. Those with HCV genotype 2 or 3, which is more responsive to interferon-based therapy, also tested treatment durations of 24 and 48 weeks. Each patient was followed up for 24 weeks after treatment.

'A sustained viral response was achieved by significantly more patients who received a weight-based dose (44.2 percent) than fixed dose (40.5 percent) ribavirin,' the authors report. 'Overall, response rates decreased as weight increased when a fixed dose was used but remained unaltered with a weight-based dose.' Discontinuation rates and reported adverse events did not differ significantly between the two treatment schemes, and relapse rates were lower for patients who had received weight-based dosing. The researchers also found that 48 weeks of treatment offered no additional benefit compared to 24 weeks for patients with genotypes 2 or 3.

Another group of researchers from the same study, also lead by Jacobson, used the study data to understand the impact of weight-based ribavirin with peginterferon alfa-2b in African American patients with HCV genotype 1. Genotype 1 is the hardest to treat, and it afflicts African Americans disproportionately.

Three hundred eighty seven African American patients with genotype 1 were included in the analysis: of those weighing 65 kg or more, and therefore receiving different doses of ribavirin in each arm, 188 had received flat-dose ribavirin, and 174 had received weight-based dosing. Significantly fewer patients in the flat-dose group (10 percent) attained a sustained virological response, compared to 21 percent in the flat-dose group. Relapse rates were 30 percent and 22 percent, respectively.

'An unexpected finding of our study was the increase in efficacy with an increase in ribavirin dose in heavier patients,' the authors report. That is, sustained viral response rates increased as body weight increased, suggesting that 'ribavirin distribution may be more complex than realized and body weight may only approximate the marker for size required to dose RBV consistently,' the authors say.

In conclusion, weight-based dosing of ribavirin offered a significant advantage in efficacy of treatment for African American patients, however, the rate of sustained viral response in this population remains low. 'Further studies are needed to elucidate the fundamental basis for the impaired responsiveness in this population,' they say.

In an accompanying editorial, Steven-Huy Han, MD and Jason Smith, PharmD of Los Angeles, report that this study adds significantly to our understanding of interferon therapy in African American patients. It will change the approach to ribavirin dosing and will benefit a difficult-to-treat population.

They suggest that the larger question of whether true weight-based dosing of ribavirin is superior to the currently approved standard dosing schemes still awaits head-to-head studies to answer. 'At the minimum,' they conclude, 'the traditional notion that ribavirin dosage should be fixed has now been sidelined by the idea that we should tailor ribavirin dosing to our patients.'

Article: 'Peginterferon alfa-2b and Weight-Based or Flat-Dose Ribavirin in Chronic Hepatitis C Patients: A Randomized Trial.' Jacobson, Ira; Brown, Robert; Freilich, Bradley; Afdhal, Nezam; Kwo, Paul; Santoro, John; Becker, Scott; Wakil, Ed; Pound, David; Godofsky, Eliot; Strauss, Robert; Bernstein, David; Flamm, Steven; Pauley, Mary Pat; Griffel, Louis; Brass, Clifford A. Hepatology; October 2007; (DOI: 10.1002/hep.21932).

Adapted from materials provided by John Wiley & Sons, Inc.

Flamel Cites Positive Drug Trial Data

<http://biz.yahoo.com>

Flamel Cites Positive Trial Data for Its Hepatitis C Drug Candidate

NEW YORK (AP) -- Flamel Technologies SA Thursday cited positive preliminary data from a clinical trial comparing its long-acting hepatitis C treatment to an already marketed drug, sending the biopharmaceutical company's shares soaring.

Shares of French drug developer Flamel jumped \$1.36, or 14.5 percent, to \$10.76 in afternoon

trading. Over the past year, the stock traded between \$7.90 and \$37.42.

The trial compared the safety, tolerability and long-acting activity of the drug, **Interferon-alpha-XL**, with Schering-Plough Corp.'s ViraferonPeg, in patients with chronic hepatitis C virus infection. The trial included three groups of 12 to 14 patients.

Flamel said IFN-alpha-XL is designed to act longer with a higher tolerability than approved interferon regimens, referring to substances that have been shown to help fight hepatitis C.

Data showed a "statistically significant" reduction in viral load for the group of patients who received the higher of two doses of IFN-alpha-XL compared with similar patients who received the standard dose ViraferonPeg, also called PegIntron in the U.S., according to Flamel.

Flamel also noted a "marked reduction" in side effects for patients given its treatment compared with those on PegIntron.

Side effects for both drugs included fever, flu-like symptoms, headache and white blood count abnormalities.

In 2006, Schering-Plough's PegIntron booked \$837 million in sales.

Flamel said it is seeking a licensing partner for its product.

Shares of Kenilworth, N.J.-based Schering-Plough rose 15 cents to \$30.08 in afternoon trading.

October 26th, 2007

Look at the big picture, says Jason

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

By Kathie Griffiths

Former drug addict Jason Creswell wants people in Bradford to face up to the risks of Hepatitis C.

The 37-year-old is taking part in a Government campaign to raise awareness of the blood-borne virus.

He was in the city-centre this week to unveil a larger-than-life exhibition of portraits in Bank Street featuring people with Hepatitis C - including him.

He said: "It's a bit weird seeing my face three metres big but if it gets people's attention, then it's well worth it. Some people know about Hep C but a lot don't understand it at all."

Jason, who kicked his 17-year habit to get clean and re-build his life, is now ten weeks into treatment to rid the virus from his system. Doctors warned him he would need a new liver and was at risk of cancer unless he got help.

He said: "I'd had tests and knew I'd got the virus when I was still on drugs but chose to ignore it because of my lifestyle. I've been clean for five years now and in the bigger picture of things, 12 months of treatment is nothing compared to getting my health back."

Jason, who now works with the Caleb drugs and alcohol recovery programme in Bradford that helped him kick his own habit, said: "I hope people will look at the portraits and get information from the stand and it will help them make a decision if they need to get tested or not, rather than just pretend it's not happening."

"There's a lot of ignorance around Hep C but I hope all this will help clear up a few things and make a difference. Even my own clients at Caleb who probably know more about it than most people don't get the facts right all the time."

"They still think you can get it through drinking from mugs and that kind of thing so we really need an exhibition like this to put things straight."

The Face It exhibition is touring 30 venues in the UK.

Jason said: "It's working so far, my virus count is much lower, I've got more energy and I'm sleeping better. Hopefully at the end of it the Hep C will have gone."

With a new baby on the way and already two children to care for Jason added: "Everything is looking brighter."

About 200,000 people in England have chronic hepatitis C infection. In Bradford there are 3,000 to 6,000, says Hepatitis C specialist nurse Lucy Fenton of the Bradford Royal Infirmary.

Hepatitis C is passed on mainly by contact with the blood of someone who has the virus and you cannot be vaccinated against it. Call the helpline on 0800 451451 or visit www.hepc.nhs.uk.

Hepatitis scandal sparks anger at Japan government

<http://www.reuters.com>

By Linda Sieg

TOKYO, Oct 26 (Reuters) - Eriko Fukuda was an active young woman of 20 when she was told she had contracted potentially deadly hepatitis C after being treated with a tainted blood product as an infant and needed costly and grueling treatment.

This week, she was outraged when Japanese health ministry officials admitted to possessing data that would have helped them to identify and warn hundreds of similarly afflicted patients years ago, before their illnesses worsened.

"It is unforgivable that people who did no wrong were forced into bitter lives, robbed of their dreams, their families, their health and their life, and left in tears," wrote the 26-year-old Fukuda -- one of more than 170 plaintiffs who have sued the Japanese government and drug makers -- on her blog.

The affair, which coincides with a separate scandal at the defence ministry, has embarrassed Prime Minister Yasuo Fukuda's month-old government, forcing him to apologise and pledge remedies after what critics say were decades of official neglect.

"Although the (health) ministry had a list of people suspected of having contracted hepatitis from blood products, they ignored the list and did not do anything about it for many years," the prime minister said in his weekly email magazine.

"Hearing the bitter voices of these people, I feel desperately sorry ... and I am fully aware of my own responsibility," he added.

The scandal has given fresh ammunition to resurgent opposition parties, which control parliament's upper house and are pushing for an early election for the powerful lower chamber.

"The only way to root out the structural causes of such scandals is to have a change in government," opposition Democratic Party lawmaker Tetsuro Fukuyama, who has been grilling the government over the issue, told Reuters in an interview.

Critics say the affair, which has dominated the media this week, is a disturbing rerun of coverups that led to nearly 2,000 haemophiliacs being exposed to the human immunodeficiency virus (HIV) in the early 1980s.

About 10,000 people have been estimated to have contracted hepatitis C from tainted coagulants.

LESSONS UNLEARNED

"Despite the fact that health officials are supposed to protect people's lives, they have more respect for companies," Takashi Kato, a lawyer for a group of 13 plaintiffs whose case is now before the Osaka High Court, told Reuters.

"That is the biggest problem, and it was the same in the case of those infected with HIV from tainted blood products."

Most of the cases have been linked to the coagulant fibrinogen, used to stop haemorrhaging during childbirth or surgery and sold in Japan even after being withdrawn in the United States in 1977.

The government issued warnings after eight women who had received fibrinogen were found to have contracted hepatitis C in 1988, and use of the product was virtually banned in 1998.

In 2002, media said, a drug maker gave the health ministry a list of 418 patients who had been exposed to the tainted product, but officials took no action to warn individuals.

Only in 2004 did the government publish the names of hospitals that had used the coagulant.

Last week, Health Minister Yoichi Masuzoe said the ministry had no data to identify individual patients. Just days later, he was stunned when officials said they had found documents

identifying more than 100 patients by name or initials in a dusty storeroom.

The drug company said it had originally submitted names or initials of nearly 370 people, according to media reports.

"The lesson from the HIV scandal is that the facts have to be made public as soon as possible. Instead, they tried to hide things and avoid responsibility," Democratic Party executive Naoto Kan told reporters this week. As health minister in 1996, Kan played a key role in exposing the HIV scandal.

The government now appears keen to settle the lawsuits, currently before several higher courts, and the ruling coalition is scurrying to draft a law to assist hepatitis patients.

But critics say the delay has cost victims their health and in some instances their lives.

"Hepatitis gets worse, becoming chronic and leading to cirrhosis and liver cancer," lawyer Kato said.

"By covering things up, the state kept people from getting treatment at the best time."