

HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus
Editor-in-Chief*

Week Ending: Aug 1, 2009

In This Issue:

- [Case of Hepatitis C Confirmed in Audubon Patient](#)
- [Hepatitis A linked to Milan McDonalds tops 25 and that number may likely grow - over 5,000 people received IG or Hepatitis A vaccines](#)
- [Celebrity chefs are trying to make undercooked pork fashionable. But could it kill you?](#)
- [Hepatitis C co-infection increases risk of many AIDS-defining illnesses](#)
- [Helping those with hepatitis C](#)
- [Fighting Hepatitis E Atom By Atom](#)
- [Doctor at center of hepatitis C outbreak deemed competent for hearing](#)
- [State Trains Inmates In Preventing Hepatitis C](#)
- [Probe position may change results in liver stiffness measurements in transient elastography](#)
- [Celsion and Yakult Honsha Announce Start-up of Japanese Clinical Trial Sites in Celsion's Global Phase III ThermoDox\(R\) Trial for Primary Liver Cancer](#)
- [URI wins \\$13-million federal grant for vaccine research](#)
- [U.S. House panel limits comparative medical studies](#)
- [Unstable housing and hepatitis C incidence among injection drug users in a Canadian setting](#)
- [Authorities raid office of Chinese health activist](#)
- [Studies reveal hepatitis C virus carriers experience substantial increase in mortality](#)
- [Site change aids local hepatitis research](#)
- [Anadys Pharmaceuticals Receives FDA Clearance of Phase II Protocol to Study ANA598 in Combination with Interferon-Alpha and Ribavirin in HCV Patients](#)
- [Advice to patients after hep C scare: Ask questions](#)

- [Pharmasset Reports Positive Preliminary Antiviral Data With PSI-7851 for the Treatment of Hepatitis C](#)
- [Nutritional Supplement, SAME, Effective in Preventing Formation of Primary Liver Cancer in Rats](#)

July 26, 2009

Case of Hepatitis C Confirmed in Audubon Patient

<http://www.krdo.com>

By Stephanie Wurtz

COLORADO SPRINGS - The Colorado Department of Health and Environment reported Friday the first confirmed case of Hepatitis C from the Audubon Surgery Center. Test results continue to come in and that number could go up.

"It was disappointing to see the first case linked to Audubon Surgery Center," says Mark Salley a spokesman for the Department of Health and Environment. Now, the total number of confirmed case linked to surgical tech Kristen Parker is 15. 14 are patients from Rose Medical Center in Denver.

13 of those cases will go on to further genetic testing called sequencing. That gives additional confirmation that the patient's Hepatitis C Virus is the same genotype as Parker's. "According to the CDC, it's 99.4% certain to be linked to the former employee," Salley says.

Audubon says about a 1,000 patients have tested out of the 1,200 patients it notified about testing. Some good news: the negative results at Audubon nearly doubled over the past week.

"They grew from 400-something last Friday to 894 this Friday," Salley says, "and ideally that's the number that continues to grow." But the state says it does expect to see more positive Hepatitis C cases come in.

"There was no knowing if the employee would continue her activity here," Salley says, "but with this case, it appears she may have." The Department of Health and Environment is still moving forward with the testing and investigation, but it won't release any new numbers until next Friday.

The more specific, genetic sequencing results take weeks. Here's a link to the latest numbers and more information.

Hepatitis A linked to Milan McDonalds tops 25 and that number may likely grow - over 5,000 people received IG or Hepatitis A vaccines

<http://www.foodpoisonjournal.com>

Bill Marler

Hepatitis A is a communicable (or contagious) disease. The virus is transmitted by the “fecal – oral route,” (human feces gets into your mouth) generally from person-to-person, or via contaminated food or water.

Outbreaks, like the one at the Milan, Illinois McDonalds, associated with food have been increasingly implicated as a significant source of Hepatitis A infection. Such outbreaks are usually associated with contamination of food during preparation by a Hepatitis A-infected food handler.

Food contaminated with the virus is a common vehicle transmitting hepatitis A. The food preparer or cook is the individual most often contaminating the food. He or she is generally not ill: the peak time of infectivity (i.e., when the most virus is present in the stool of an infectious individual) is during the 2 weeks before illness begins to be noticeable.

The incubation period (time from exposure to onset of symptoms) is 15-50 days, with an average of 30 days. Thus far at least 25 people have contracted Hepatitis A and over 10,000 or more were exposed. 5,000 have received IG or Hepatitis A vaccines to hopefully prevent illness onset. William Marler, food safety attorney from Seattle, has filed suit on behalf of those who received vaccines and one family whose 16 year old contracted Hepatitis A.

As Marler said, "it appears the second Ill McDonald's employee last worked on July 13 or 14. That means that the number of ill may well rise over the next month during the height of the incubation period."

The Rock Island County Health Department will conduct walk-in clinics at its office at 2112 25th Ave., Rock Island, from 8 a.m. to 4:30 p.m. Monday and Tuesday. These additional dates are being made available for those who went to the Milan, Ill., McDonald's on July 13 or 14. If they went there previous to these dates, receiving either of these shots may be beyond the time period to provide protection from potential exposure.

A second dose of hepatitis A vaccine, administered six months after the first one, will provide additional effectiveness against the disease. Second doses will be available at the health department, but they will not be free as the first-dose clinics have been. The cost of the second dose will be \$45 for adults and \$15-\$25 for pediatric patients, depending upon income guidelines.

July 27, 2009

Celebrity chefs are trying to make undercooked pork fashionable. But could it kill you?

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

By George Winter

'New' disease: You can catch hepatitis E by eating undercooked pork

When David Thorne walked into the doctor's surgery to have his eyes examined, the doctor asked if he'd just been on holiday.

‘He thought I looked tanned,’ says David, 74. ‘It seemed quite a bizarre question as it was the middle of February and I hadn’t been anywhere hot.’

Then during his examination, the doctor also noted that David’s eyes had a yellow tinge.

‘My wife Pat and I hadn’t noticed anything, but when he pointed it out we could see it,’ says David.

He was immediately referred to a jaundice clinic near his home in Treliske, Cornwall, where tests confirmed that the problem was hepatitis E.

This is one of a family of viral diseases. Hepatitis B and C are better known and affect many hundreds of thousands of people in Britain. But although few will have heard of it, hepatitis E is on the rise, and experts are concerned that it is often going undiagnosed.

Each type of hepatitis has a different cause, but all attack the liver, causing inflammation. The symptoms vary, but hepatitis E can cause jaundice.

One of the liver’s jobs is to process bilirubin, a waste product formed from old red blood cells.

If the liver isn’t working properly, bilirubin builds up in the blood, leading to the characteristic yellow hue.

The worry is that the disease puts patients at risk of severe liver damage or cirrhosis, where the liver becomes scarred and is unable to function, leading to liver failure, which can be fatal.

Though hepatitis E can be transmitted through blood transfusions and by eating contaminated shellfish, experts say that the main culprit is pigs — around 85 per cent of swine have been infected with the virus.

By coming into contact with pig waste - perhaps through a contaminated water supply - or eating undercooked pork, many people are unknowingly contracting the disease, says Dr Harry Dalton, a consultant gastroenterologist at the Royal Cornwall Hospital Trust, and one of the country’s leading experts on hepatitis E.

‘The source and route of hepatitis E infection are uncertain, but the most convincing evidence suggests that it is an infection derived from pigs,’ he says.

There are reports of vets and other pig industry workers with a high prevalence of hepatitis E antibodies, indicating they’ve come into contact with the virus.’

Last year, Dr Dalton’s team highlighted the case of a 59-year- old Cornwall resident who died of liver failure after contracting hepatitis E.

His job involved hosing down equipment using pond water filled by a stream from an adjacent pig farm.

Another possible method of transmission is through eating undercooked pork.

‘Pork should be cooked thoroughly and stored, handled and prepared properly, as recommended by the Food Standards Agency,’ says Dr Dalton.

‘What certainly doesn’t help is the trend of some celebrity chefs, who suggest that pork tastes better when it’s undercooked and still pink in the middle. This is potentially hazardous to human health.’

For instance, Gary Rhodes’ pork tenderloin with cabbage recipe suggests the pork be cooked until it is ‘still pink and moist in the middle’.

Indeed, many chefs agree that ‘overcooking’ pork (that is, cooking it through) makes the fibres too tough.

So how common is this ‘new’ disease? Scientists have discovered that 16 per cent of blood donors in South-West England have antibodies to the virus, meaning they have come into contact with it at some point.

The disease is rife in the developing world, but it is increasingly common in Britain. As many as 800,000 people in England alone have the infection, according to the Health Protection Agency, with the vast majority unaware of it. ‘The problem is that hepatitis E in developed areas such as Britain is often misdiagnosed,’ says Dr Dalton.

‘A side-effect of many drugs is damage to the liver, and this is what might be blamed for the patient’s condition, rather than hepatitis E.’

Misdiagnosis is ‘particularly common in elderly people who are most likely to be taking a lot of medication’.

While the causes of hepatitis E virus infection are to be investigated in a new study funded by the Prince of Wales’s Duchy Health Charity, David Thorne has little doubt about how he caught the disease - eating his favourite meal of underdone pig’s liver.

‘Pat and I probably eat pig’s liver every three weeks and I have to admit that we do like it slightly undercooked because it tastes so much nicer,’ he says.

Fortunately, because David is in good health, he was told his prognosis is good.

‘Dr Dalton told me go home, rest and drink plenty of water — there was no other treatment. Within a few weeks, the jaundiced look began to disappear and I was given the all-clear.

‘We’ve decided to stop eating pork liver. But if you can’t eat it the way you like it there isn’t much point anyway.

‘Fortunately, the local rare breed pork is very tasty, so that’s some consolation.’

For more on HEV, see this month’s issue of the [HCV Advocate](#).

Hepatitis C co-infection increases risk of many AIDS-defining illnesses

www.aidsmap.com

Michael Carter

HIV-positive patients who are co-infected with hepatitis C virus are twice as likely to develop an AIDS-defining illness than individuals who are only infected with HIV, Italian investigators report in the August 15th edition of *Clinical Infectious Diseases*. Moreover, co-infected patients with cirrhosis had an even more marked increase in their risk of developing an AIDS-defining condition.

The author of an accompanying editorial described the research findings as “important”, adding that they “may affect the clinical management of hepatitis C virus-HIV coinfection.”

Liver disease, often due to hepatitis C, is now an important cause of illness and death in people with HIV. Hepatitis C infection has been independently associated with an increased risk of non-Hodgkin’s lymphoma, which is an AIDS-defining illness. However, the association between the infection and the development of other AIDS-defining illnesses in co-infected patients has not been established.

Therefore Italian investigators from the ICONA Foundation Study Group designed a study involving 5397 HIV-positive patients, approximately half of whom were co-infected with hepatitis C. They compared the risk of developing AIDS-defining illnesses between these two groups. These illnesses were divided into broad categories: non-Hodgkin’s lymphoma; viral (such as Kaposi’s sarcoma); bacterial infections; HIV-related illnesses (for example, wasting); protozoal infections (like toxoplasmosis); and fungal infections (including pneumocystis).

A total of 25,000 person-years of follow-up were available for analysis. The co-infected patients took hepatitis C treatment for 1% of the follow-up period.

AIDS-defining rates were rare, with only 496 observed. Bacterial infections were the most common (five events per 1000 person years).

However, co-infected individuals had a significantly increased risk of developing an AIDS-defining condition compared to those only infected with HIV (adjusted relative rate [ARR] = 2.61; 95% CI, 1.88-3.61, $p < 0.001$).

Furthermore, co-infection was associated with a three- to five-fold increased risk in the development of bacterial, fungal, and protozoal infections. The investigators emphasise, however, that no significant relationship was found between co-infection and an increased risk of non-Hodgkin’s lymphoma.

For all patients, a CD4 cell count below 200 cells/mm³ significantly increased the risk of all AIDS-defining conditions with the exception of non-Hodgkin’s lymphoma and toxoplasmosis ($p < 0.01$). Each one log₁₀ increase in current viral load was associated with an approximately 50% increase in the risk of non-Hodgkin’s lymphoma ($p = 0.03$).

The investigators also found that each 1 log₁₀ increase in current viral load increased the risk of developing a viral AIDS-defining condition ($p < 0.001$). Older age was associated with an increased risk of fungal infections such as pneumocystis ($p = 0.05$).

Next the investigators analysed the effect of antiretroviral treatment on the risk of the development of AIDS.

They found that patients only infected with HIV and who were taking antiretroviral therapy, were significantly less likely to develop a fungal-related AIDS-defining illness than were co-infected patients taking HIV treatment ($p = 0.008$). By contrast, there was a greater risk of HIV-related diseases such as wasting for co-infected patients taking anti-HIV drugs, than co-infected patients who were naive to antiretrovirals (ARR = 10.26; 95% CI, 3.63-28.96).

Finally the investigators looked at the relationship between cirrhosis and the risk of AIDS-defining illnesses. This showed that co-infected patients who had progressed to this condition were significantly more likely to develop fungal diseases ($p = 0.003$), bacterial infections ($p = 0.009$), toxoplasmosis ($p = 0.01$), and HIV-related conditions ($p = 0.01$) than either co-infected patients who did not have this degree of liver damage or patients only infected with HIV.

“To our knowledge, this is the first study to investigate whether the risk associated with hepatitis C virus infection may be different according to specific AIDS-defining events and whether it is exacerbated in patients with liver cirrhosis”, write the investigators. They add, “our results have important implications because hepatitis C coinfection is frequent among HIV-infected individuals.”

The investigators suggest that the findings of their study should be taken into account by doctors treating co-infected patients, “in particular when deciding when to start antiretroviral therapy”.

This recommendation is endorsed by the editor of the accompanying editorial, who suggests the study “highlights and strengthens the need for careful follow-up of hepatitis C-HIV-coinfected patients, including preventative methods (screening, prophylaxis, and vaccination of preventable diseases), effective management of co-morbidities...and early and effective therapies against HIV and hepatitis C virus.”

Reference

Monteforte A d'A et al. Risk of developing specific AIDS-defining illnesses in patients coinfecting with HIV and hepatitis C virus with and without liver cirrhosis. Clin Infect Dis 49: 612-622, 2009.

Piroth L et al. Coinfection with hepatitis C virus and HIV: more than double trouble. Clin Infect Dis 49: 623-625, 2009.

Helping those with hepatitis C

<http://www.denverpost.com>

By Nancy Steinfurth

There have been many people who have said that the potential and actual transmission of

hepatitis C at Rose Medical Center and Audubon Surgery Center are teachable moments for the organization I run, Hep C Connection.

Indeed, the State of Colorado, and now two other states, have developed awareness about the virus, have learned that it is transmitted by blood, that re-using a needle or syringe that was used by someone who is HCV positive is the most common route of transmission these days, and that people with the virus who are employed are protected by the Americans with Disabilities Act.

While these are all relevant and important topics, we're missing the teachable moment with one big group - the people who have tested positive for the hepatitis C virus and the thousands still waiting to be tested or waiting for results.

What's missing in the coverage are strategies to cope with the emotions they're feeling as they wait, or the anger they have at the surgery technician who may have made them ill.

There are many reasons why this unique group of people should seek emotional support for the short and long-term journey they may be facing.

Seeking counseling in any form, whether through a therapist, member of the clergy, support group, or other means, will give you an opportunity to discuss your feelings with someone who will empathetically listen to your comments, provide feedback without judgment, and outline constructive ways of dealing with the variety of emotions. You may think you don't need to seek professional help, but this may be too great of a burden for a family member or friend to truly provide the assistance you need. A support group can be a great way to seek counseling.

Doctors don't necessarily explain information about hepatitis C in a way that everyone understands. Hepatitis C is a complicated disease, much of which is still being studied.

If someone chooses to go through treatment (and there are valid reasons not to undergo treatment), there are a battery of tests that happen throughout the treatment phase and it's important to understand what the results are telling you and to discuss the side effects that you may be feeling.

Meeting with a support group facilitator who is trained about hepatitis C can provide a layman's perspective on test results while explaining what may happen as next steps. Support groups provide information as well as emotional support. Use it as your information clearinghouse.

Compliance with treatment is easier if you are in a hepatitis C support group. Treatment for genotype 1b can involve taking two medications for 48 weeks. This is a long time in anyone's book and following the dosing schedule, while important for success, can get difficult over time. Support group members have been there - they can talk about side effects and ways of reducing them that were effective for them, and they can be your cheerleaders when you're feeling tired and want to stop.

The stigma of hepatitis C can be overwhelming and people in the same circumstance can provide effective tools for how to deal with it in the future. Do you tell an employer? What about friends? In what situations does it make sense not to disclose?

Hep C Connection has organized a special one-time support group for anyone affected by the exposure to hepatitis C at Rose Medical Center or Audubon Surgical Center. It will be held on Wednesday, July 29 from 6:30 P.M. to 8:30 P.M. To ensure privacy for anyone who attends, we request that you call 720-917-3960 to RSVP and receive the location. Patient confidentiality is our utmost concern. The group will be led by a long-time Hep C Connection support group leader who has personal experience with the disease.

Whether you choose to attend a support group or not, we encourage you to reach out to a mental health professional to discuss what you are feeling. Don't ignore your mental health while focusing on your physical health. There are ways to cope with what you are going through.

Nancy Steinfurth is executive director for the Hep C Connection.

Fighting Hepatitis E Atom By Atom

<http://www.sciencedaily.com>

ScienceDaily (July 27, 2009) — Researchers at Rice University and their international colleagues have for the first time described the atomic structure of the protein shell that carries the genetic code of hepatitis E (HEV). Their finding could mean that new ways to stop the virus may come in the not-too-distant future.

Rice graduate student Tom Guu was part of the research team led by Yizhi Jane Tao, an assistant professor of biochemistry and cell biology. Guu said researchers have had a difficult time analyzing HEV, a particularly nasty form of viral hepatitis that flourishes in the developing world, where poor sanitation is common.

"About 10 years ago, researchers began to describe what the virus looks like," said Guu. "They found protrusions and indentations on its surface. While it looked a bit like a buckyball, or a geodesic dome, researchers were still stuck."

Without a more detailed description of the virus, it has been hard to design drugs to stop it. To do that, you have to look at it very closely, as the Rice team has done.

Tao's lab specializes in X-ray crystallography, a powerful technique that can pinpoint the exact location of every atom in a biomacromolecule or a large biomacromolecular assembly. In this case, the assembly was the viral capsid shell, made from a network of individual capsid proteins from a strain of HEV that had been made in insect cells, then purified and crystallized.

After two years of intense study, Guu calculated the position of each of the approximately 500,000 atoms that make up the capsid, an icosahedron-shaped particle that roughly resembles a buckyball. The resulting 3-D computer model gives researchers the ability to identify the particle's host-cell binding sites, through which HEV spreads.

"Dr. Tao has already identified potential sites on the new model," said Guu. "If we can prove these sites to be correct, labs around the world can start to design drugs, called competitive inhibitors, to interrupt the binding process and prevent the virus from attaching to cell receptors in the first place."

Guu compared the virus's capsid protein to a hollowed-out watermelon. "You have the outer shell of the virus, but you take out its insides," he said. "It retains its outside properties." The empty capsid may still bind to a cell, but it contains no genetic material to transfer, rendering it noninfectious and therefore an excellent candidate for a vaccine.

"In fact, other researchers have used the empty viral shell to vaccinate monkeys, and even humans. Later on, when the researchers challenged them with the real virus, they discovered that prior exposure to this virus-like particle conferred some sort of protection," Guu said.

"This virus has been less studied than others in the pathogenic human virus domain," Tao said. "It has been rather difficult to generate a culture in the lab to study how the virus invades the cell. The only way to work with it is to overexpress the protein on its own."

It took nearly six months for Rice researcher Qiaozhen Ye to identify the right construct, isolate the protein and form the first crystals, after the project was initiated through an international collaboration with Jingqiang Zhang at Sun Yat-sen University in early 2006. Former Rice undergraduate student Douglas Mata then successfully reproduced one of these crystallization conditions. They were surprised to discover that, in the crystallization process, HEV capsid proteins extracted from the cultured cells self-assembled into virus-like particles. This in turn may lead to another strategy: "If you can prevent the protein from assembling, you can stop the virus," Ye said.

Tao sees great potential for their discovery. "There are so many things you can do with the structure that I think it will be useful for many years to come."

The research was supported by the National Institutes of Health, the National Natural Scientific Foundation of China, the Welch Foundation, the Hamill Foundation and the Kresge Science Initiative Endowment Fund at Rice University.

Tao, Guu, Ye, Mata and Zhang co-authored the paper with Zheng Liu and Changcheng Yin of Peking University in China and Kunpeng Li of Sun Yat-sen University in Guangzhou, China.

Journal reference:

Tom S. Y. Guu et al. Structure of the hepatitis E virus-like particle suggests mechanisms for virus assembly and receptor binding. PNAS, DOI: 10.1073/pnas.0904848106

Adapted from materials provided by Rice University.

For more on HEV, see this month's issue of the [HCV Advocate](#).

July 29, 2009

Doctor at center of hepatitis C outbreak deemed competent for hearing

<http://www.lvrj.com>

Adrienne Packer

Las Vegas Review-Journal

The central figure of an investigation into the hepatitis C outbreak might have been impaired by

a stroke a year ago, but he is competent enough to face medical malpractice charges, according to the state Board of Medical Examiners.

Based on results from an examination performed by Dr. Thomas Kinsora, a clinical neuropsychologist, Dr. Dipak Desai is “borderline” regarding his ability to assist defense attorneys in his medical board licensing hearing.

But, according to Kinsora’s findings, Desai “is clearly aware of the charges against him, has a good knowledge of the facts of the case and understanding the role of all the key players in the judicial system.”

Health officials have linked two of Desai’s now-shuttered endoscopy clinics to nine contracted cases of hepatitis C. An additional 105 cases have been characterized as possibly related to the clinics.

Examinations conducted by Kinsora earlier this year indicated that the residual effects of Desai’s stroke would make it difficult for him to assist his defense team with the case. But after further tests, Kinsora reported that Desai might be impaired but not to the point of being “unable to assist counsel.”

His findings were detailed in an order Tuesday by hearing officer Patrick Dolan.

Dolan’s ruling means hearings regarding disciplinary action by the board can move forward. Louis Ling, the board’s executive director, said Tuesday a hearing will not be scheduled until fall and likely would take place early next year.

Desai also faces a civil lawsuit filed by patients infected with hepatitis C.

The medical board’s ruling should have no effect on those proceedings because Desai was expected to invoke his Fifth Amendment rights all along in the civil proceedings, said attorney Will Kemp, who represents Desai’s former patients. “He would have taken his Fifth Amendment rights or, if he was unable to, his attorney would have to come in and pled the Fifth for him,” Kemp said.

Desai’s attorney, Richard Wright, declined to comment.

Desai also could face criminal charges related to the outbreak, which health officials say resulted when reused syringes contaminated medical vials used to treat patients.

In early 2008, about 50,000 patients of the clinics received notices saying they could have been exposed to hepatitis, HIV or other blood-borne diseases.

The clinics filed for Chapter 7 bankruptcy last week, raising further questions about whether the civil litigation would proceed. Bankruptcies automatically postpone any lawsuits involving the clinics until a bankruptcy judge lifts the postponement. A bankruptcy hearing is scheduled for Aug. 19.

Desai suffered the stroke in July 2008.

Dolan's order said that, according to Kinsora, current treatment of Desai "may improve his ability to assist legal counsel, but will in all likelihood not significantly improve over time."

Although a "sound argument can be made either way," Kinsora's findings state, Desai is "likely acceptably competent, but certainly not optimally competent."

Though Kinsora in April opined that Desai would have difficulty assisting in his defense, he noted that he would like to have access to additional medical records, including current imaging of Desai's brain and radiological tests. Kinsora had also recommended that Desai be referred to a clinical psychologist and a speech and language pathologist for evaluation.

"The question at issue was whether Dr. Desai's medical conditions were debilitating," Ling said. "We needed to know that before we tried the case."

"The process worked. We are glad we will now be able to proceed with the hearing against Dr. Desai," he said.

State Trains Inmates In Preventing Hepatitis C

<http://www.kfoxtv.com>

SANTA FE, N.M. -- Health officials and the New Mexico Corrections Department are teaching state inmates how to educate other inmates about the Hepatitis C virus.

Hepatitis C is a liver disease caused by the Hepatitis C virus. The Centers for Disease Control says it can lead to cirrhosis of the liver and liver cancer.

About 38 percent of New Mexico Corrections Department inmates are living with the virus. As of June, there were more than 2,400 confirmed cases in state prisons.

The virus is often transmitted by inmates sharing needles.

This week, ten male inmates will be receiving 32 hours of training in Hepatitis C and other infectious diseases.

Probe position may change results in liver stiffness measurements in transient elastography

<http://www.eurekalert.org>

A major clinical challenge is to find the best method to evaluate and to manage the increasing numbers of patients with chronic liver disease. Liver biopsy, due to its risks and limitations, is no longer considered mandatory as the first-line indicator of liver injury, and several markers have been developed as non-invasive alternatives.

The assessment of liver fibrosis by non-invasive techniques, such as biomarkers FibroTest® (FT) and liver stiffness measurement (LSM) by Fibroscan®, is now widely performed in

countries where these techniques are available and approved. It is therefore essential to identify factors associated with a variability of the results of the techniques to reduce the risk of false positives or false negatives. There are no published procedures for the most accurate position of the probe in LSM.

A research article recently published on July 21, 2009 in the *World Journal of Gastroenterology* addresses this issue. The research team led by Professor Thierry Poynard from the Hepatology Department of the Pitié-Salpêtrière Hospital in Paris, France, found that the applicability of Fibroscan examinations may increase when the probe is placed in a more anterior position. So far, recommendations for Fibroscan examinations derive from a spot vaguely defined as the "liver biopsy zone" which is in the axillary line in the 8th to 10th intercostal space. The article further investigates possible changes in fibrosis grades due to the different probe positions. The mean LSM was significantly lower (0.5 kPa) at the anterior position versus the reference position. This difference was also clinically significant. When using the anterior position instead of the reference position, 7% of patients changed status from advanced fibrosis to non-advanced fibrosis when a cutoff of 7.1 kPa was chosen. The difference of 0.5 kPa is particularly clinically relevant in the zone of 7 kPa to 9 kPa for the risk of a false negative/positive diagnosis of advanced fibrosis; it is less relevant for the diagnosis of cirrhosis as LSM cutoffs are usually recommended at a 12.5 kPa or 14 kPa cutoff with a range to 75 kPa.

Interestingly, the estimated fibrosis scores were compared with FibroTest® and not with liver biopsy in this study. The diagnostic value of LSM and FT has been validated in the most common chronic liver diseases and FT has shown as having at least a similar prognostic value to liver biopsy (which is also an imperfect gold-standard) in patients with chronic hepatitis C and B.

Non-invasive techniques will increasingly replace liver biopsy in chronic liver disease because they are easy-to-do and well accepted by patients. This study helps to improve the understanding of possible limitations of transient elastography. Further research will be needed to define advantages and pitfalls of this technique.

Reference:

Ingiliz P, Chhay KP, Munteanu M, Lebray P, Ngo Y, Roulot D, Benhamou Y, Thabut D, Ratziu V, Poynard T. Applicability and variability of liver stiffness measurements according to probe position. *World J Gastroenterol* 2009; 15(27): 3398-3404

Celsion and Yakult Honsha Announce Start-up of Japanese Clinical Trial Sites in Celsion's Global Phase III ThermoDox(R) Trial for Primary Liver Cancer

<http://www.medicalnewstoday.com>

Celsion Corporation (NASDAQ: CLSN) and Yakult Honsha Co., Ltd. (Tokyo: 2267) announced that Celsion's global Phase III ThermoDox trial for the treatment of primary liver cancer will be extended to Japan by Yakult's expertise. This is an important step towards a potential application to market the drug in Japan. Yakult Honsha is the exclusive licensor of Celsion's ThermoDox in Japan.

"We are proud to announce that Yakult will initiate trial sites and begin patient enrollment in Japan for our Phase III liver cancer trial, and we look forward to working with Yakult," stated Michael H. Tardugno, President and Chief Executive Officer. "The extension of our PIII study to Japan will enable us to accelerate patient enrollment in the trial and has the potential to decrease the time to market in Japan."

"Japan has the highest rate of liver cancer in industrialized countries," said Dr. Kiyoshi Terada, Head, Pharmaceutical Division/Senior Managing Director, Member of the Board of Yakult Honsha. "Given there are limited effective treatment options for these patients, we are pleased to have the opportunity to provide ThermoDox to them in the clinical trial setting,"

Under the license agreement between Celsion and Yakult, Yakult is financially responsible for the patients enrolled in clinical trials in the Japanese sites and all the data generated in Japan will be jointly owned by Celsion and Yakult and can be used by Celsion to support regulatory filings in territories outside of Japan. Additional information on Celsion's Phase III ThermoDox trial for primary liver cancer can be found at <http://www.clinicaltrials.gov/>

About ThermoDox

ThermoDox in combination with hyperthermia has the potential to provide local tumor control and improve quality of life. ThermoDox is a proprietary heat-activated liposomal encapsulation of doxorubicin, an approved and frequently used oncology drug for the treatment of a wide range of cancers including breast cancer. Localized mild hyperthermia (40-42 degrees Celsius) releases the entrapped doxorubicin from the liposome. This delivery technology enables high concentrations of doxorubicin to be deposited preferentially in a targeted tumor.

ThermoDox has also demonstrated evidence of efficacy in a Phase I study for primary liver cancer. Celsion has been granted FDA Orphan Drug designation for ThermoDox and is conducting a pivotal global Phase III study in primary liver cancer under a FDA Special Protocol Assessment.

ThermoDox® is a registered trademark of Celsion Corporation

URI wins \$13-million federal grant for vaccine research

<http://www.projo.com>

C. Eugene Emery Jr.
Journal Staff Writer

PROVIDENCE — Dr. Annie De Groot and her colleagues think they have a better way of speeding the development of vaccines against Lyme disease, hepatitis and stomach cancer.

The federal government apparently believes their ideas are worth a \$13-million investment.

The University of Rhode Island, where De Groot works, announced Tuesday it will receive a five-year grant from the National Institutes of Health to throw new resources at De Groot's vision of using computer software to design lean, mean, more potent vaccines, and then use a faster process for testing their effectiveness in humans.

“The objective, actually, is to get some of this basic research into the clinic, to go from 20 years for making a vaccine to, perhaps, 5. And that’s why I love it,” she said. “The whole idea is to get people out of the laboratories and, instead of focusing on their models in mice, actually getting vaccines into people.”

The grant will also pay for training researchers in the novel techniques to encourage the development of vaccines against tropical diseases in developing countries.

She called the NIH award “a dream come true” because it will provide “a team of researchers — based right here in Rhode Island — with the exciting opportunity to collaborate across disciplines and to teach the next generation of scientists to use tools that are accelerating the development of vaccines” and drugs.

At least 10 people will be hired to help do the work.

The funds will go to De Groot and several other researchers at URI and Lifespan, which owns Rhode Island Hospital.

At URI’s main campus in South Kingstown, Thomas Mather will be trying to fine-tune a vaccine that will protect people against Lyme disease and other tick-transmitted illnesses, not by directly vaccinating them against those diseases but by sensitizing the immune system to attack tick saliva.

The hope is that if the body can be sensitized to tick saliva, it will block the nasty bugs that come with it.

That’s one reason why guinea pigs don’t get Lyme disease, De Groot said.

In Providence, researchers Lenny Moise of URI and Steve Moss of Lifespan will be developing a vaccine against *Helicobacter pylori*, a bacterium responsible for most ulcers. It also increases the risk of stomach cancer.

Steve Gregory of Lifespan will use the money to continue working on a vaccine against the potentially deadly liver disease hepatitis C.

De Groot herself will be developing a multi-purpose vaccine against a group of microorganisms you’ve probably never heard of and definitely wouldn’t want to meet — some “really nasty pathogens that could be used as bio-warfare agents.”

“Soldiers need this because you never know what concoction someone will come up with,” she said.

Their new method of developing vaccines relies heavily on a computer analysis of the DNA that bacteria and virus use to build the proteins that allow them to function.

“The way they used to make vaccines was shake and bake,” the researcher said. “They would take the bacteria, they would grow it up, they would bake it [to kill it], then they would give you the shot. Everything goes in. That’s not necessary.”

Instead, their “vaccine design toolkit” uses a computer program to predict which proteins in the genetic code will most easily trigger the body’s immune system. The toolkit has been in development for a decade.

“The small pieces can then be tested with human cells [to see if] it would be good for a vaccine,” she said.

The next step is testing in mice that have been genetically engineered to have a human, not rodent, immune system.

If human immune cells attack the virus or bacteria after inoculation, the vaccine can go on to human testing.

This is the second major NIH grant URI has received in recent months. In May, it was awarded an \$18-million five-year grant for research into cell biology, molecular toxicology and behavioral science.

July 30, 2009

U.S. House panel limits comparative medical studies

www.reuters.com

By Kim Dixon

WASHINGTON (Reuters) - A panel of U.S. lawmakers voted on Thursday to prohibit the federal government from "denying or rationing" medical care based on studies comparing medical drugs and devices.

The U.S. House of Representatives Energy and Commerce Committee passed the Republican-sponsored amendment, despite objections from Democrats. It is a potential win for drug and medical device makers, which argue that such comparison studies could favor cheaper treatments.

The panel is debating its version of legislation winding its way through Congress to overhaul the \$2.5 trillion healthcare system, aimed at expanding coverage and cutting costs.

The current House bill sets up a federal center for comparative effectiveness research.

"Alarmingly the bill has no restrictions on how the federal government can use this research," said Republican Michael Rogers of Michigan, the amendment's sponsor.

"Comparative effectiveness research is about general average assumptions," not about individuals seeking unique treatment, he said.

House Energy and Commerce Committee Chairman Henry Waxman and several other Democrats objected to the amendment, but then let the amendment pass on a voice vote without taking roll-call. Democrats hold a majority on the panel.

Backers of comparative effectiveness, which include insurers and large employers, say the

government-funded research is crucial for learning which treatments work best because manufacturers have little incentive to compare their products with those of competitors.

Currently, drugmakers must only test their new products against a sugar-pill placebo to win U.S. approval. Drug companies, devicemakers and others also do not have to compare their treatments with other options, such as surgery.

The medical product industry contends that comparative effectiveness research will favor older, cheaper therapies and that the results could be used to deny insurance coverage for newer, more expensive treatments.

The Senate is expected to include comparative effectiveness language in its healthcare reform bill. One key senator, Finance Committee Chairman Max Baucus, backs establishment of a nonprofit corporation for the research, but it would be barred from issuing medical practice guidelines or coverage recommendations for insurers.

Later today, the House panel will consider a highly watched amendment that would give biotech drugmakers 12 years of marketing exclusivity, free of generic competition.

(Additional reporting by Lisa Richwine and Susan Heavey; Editing by Steve Orlofsky)

Unstable housing and hepatitis C incidence among injection drug users in a Canadian setting

<http://7thspace.com>

There has emerged growing recognition of the link between housing and health. Since Vancouver, Canada has had increasing concerns with homelessness brought about by urban renewal in the lead-up to the 2010 Winter Olympic Games, we evaluated hepatitis C virus (HCV) incidence among injection drug users (IDU) with and without stable housing.

Data were derived from a collaboration between two prospective cohort studies of IDU in Vancouver, Canada.

Using Cox Proportional Hazards regression, we compared HCV incidence among participants with and without stable housing, and determined independent predictors of HCV incidence.

Overall, 3074 individuals were recruited between May 1996 and July 2007, among whom 2541 (82.7%) were baseline HCV-infected. Among the 533 (17.3%) individuals who were not HCV-infected at baseline, 147 tested HCV antibody-positive during follow-up, for an incidence density of 16.89 (95% confidence interval: 14.76 - 19.32) per 100 person-years.

In a multivariate Cox regression model, unstable housing remained independently associated with HCV infection (relative hazard = 1.47 (1.02 - 2.13)).

Our conclusions are that HCV prevalence and incidence are high in this setting and were predicted by unstable housing. Efforts to protect existing low-income housing and improve access to housing may help to reduce HCV incidence.

Authors:

Christina Kim Thomas Kerr Kathy Li Ruth Zhang Mark Tyndall Julio Montaner Evan Wood

Credits/Source: BMC Public Health 2009, 9:270

Authorities raid office of Chinese health activist

<http://www.google.com>

By Alexa Olesen (AP)

BEIJING — Chinese authorities seized dozens of newsletters from a nonprofit group that fights discrimination against people with hepatitis B, a campaigner said Thursday, calling the move retribution for the group's advocacy work.

Two officials from the Beijing Cultural Law Enforcement Agency, in charge of campaigns against printed and DVD pornography and piracy, on Wednesday confiscated about 90 copies of a legal guide to fighting discrimination for people with hepatitis B.

A spokeswoman for the agency, Li Fei, confirmed the group was being investigated for publishing material without a required license. She would not comment further.

The 40-page guides, published by the Beijing non-governmental organization Yirenping, include information about Chinese law, a practical guide to reporting violations and filing lawsuits, as well as details about successful anti-discrimination cases, said Lu Jun, the group's founder. He denied doing anything illegal.

"It's part of our job to put out material like this, to educate people," he said, adding that many other Chinese NGO's have similar types of publications.

The raid appeared aimed at reining in the group's legal advocacy and comes fast on the heels of a clampdown on activist lawyers in the capital.

Earlier this month, a legal research center in Beijing was shut and the licenses of more than 50 lawyers — many known for their politically sensitive human rights work — were revoked. China is also preparing for the communist state's 60th anniversary on Oct. 1, a particularly sensitive period when dissent is not tolerated.

The New York-based rights group, Human Rights in China, said in a statement Thursday that the raid of Yirenping showed the "increasingly restrictive legal environment under which China's civil society organizations must operate."

Lu and his organization campaign for awareness about the hepatitis B, which infects the liver and is endemic in China, with an estimated 120 million sufferers. They often face discrimination and are sometimes denied jobs, even though the disease cannot be transmitted by casual contact.

Yirenping has assisted individuals in filing over 40 lawsuits, mostly discrimination claims, since it was founded in 2006, according to background posted on its Web site. Lu said he thought the seizure of the newsletters was punishment for such legal activism, which has pitted the group

against some large companies and government organizations.

"I think we offended some people and they wanted to get back at us," he said.

Studies reveal hepatitis C virus carriers experience substantial increase in mortality

<http://www.scienceblog.com>

Hepatitis C virus (HCV) is a blood-borne disease that causes inflammation of the liver and to which there is currently no vaccine available. The World Health Organization (WHO) estimates that 3% of the world's population, approximately 170 million people, are infected with HCV and it is a leading cause of liver cirrhosis, end stage liver disease, hepatocellular carcinoma (HCC) and liver transplantation.

Researchers at Kagoshima University Graduate School of Medical and Dental Sciences concluded a 10-year study in Japan (where there is a greater incidence of HCV) and found the overall mortality rate was higher in HCV carriers. A second study, led by Dr. Adeel Butt from the University of Pittsburgh School of Medicine, looked at the effect of HCV on survival rate and also confirmed individuals infected with HCV had much higher death rates. Both findings appear in the August issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases.

The Kagoshima research team, led by Hirofumi Uto, studied 1,125 individuals with the HCV antibody from 1995 through the end of 2005 or to their earlier death. Of the total, 758 (67.4%) had detectable HCV core antigen (HCVcAg) or HCV Ribonucleic Acid (HCV RNA) and were classified as carriers meaning the patients were viremic. The 367 (32.6%) individuals who had a prior HCV infection, but tested negative for both HCVcAg and HCV RNA were considered non-carriers or non-viremic.

According to the study, a total of 231 deaths occurred in the subjects over an average of 8.2 years of follow-up with 176 deaths in the HCV carrier group and 55 of the non-carriers. Using death certificates, researchers classified the deaths into 7 categories: hepatocellular carcinoma, liver disease (excluding HCC), neoplasms (excluding HCC), stroke, heart disease, pulmonary disease (excluding lung cancer) and unknown/other causes.

"Adjusting for age and gender," researchers concluded, "the elevated mortality rate among the subjects with HCV viremia was due to a much higher occurrence of liver-related deaths, but was not significantly associated with death from other malignancies such as stroke, heart disease, or pulmonary disease." The study notes that the higher overall mortality rate is explained by the higher rate of liver-related deaths from HCC and non-HCC with a cumulative risk of death of 28.0% for carriers, compared to 17.8% for non-carriers (based on Kaplan-Meier estimates).

Additionally, researchers observed that high HCVcAg levels were predictive of liver-related deaths, including HCC, in the HCV carriers. "Monitoring HCV load and ALT level in HCV carriers may be important for identifying those individuals at increased risk for HCC or other liver disease, particularly among older carriers who are less likely to respond to HCV treatment," said the authors.

Dr. Butt's team studied a national sample of 34,480 HCV infected subjects versus a non-infected control of the same number from the Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES) and found that those infected were more likely to have a shortened survival rate. "HCV increased the risk of death by about 37% after adjusting for demographic characteristics and common comorbidities." Treatment for HCV was associated with a significant decrease in mortality. Individuals who received at least 48 weeks of treatment had the lowest mortality, while those who received less than 48 weeks of treatment had intermediate mortality compared with untreated individuals. "Strategies to identify appropriate candidates for treatment, and to ensure completion of treatment may substantially reduce mortality in HCV infected persons," concluded the authors.

Site change aids local hepatitis research

<http://www.dailyiowan.com>

by Tyler Lyon

Researchers for Vertex Pharmaceuticals of Cambridge, Mass., are developing a medication that could cut treatment time for hepatitis C in half. But until Wednesday, they were almost crawling over each other to do it.

The company officially opened a new research facility at the UI BioVentures Center on the Oakdale Campus on Wednesday afternoon, moving across the street from its old, less-adequate facility.

Now, the seven members of the Iowa team have space tailored to their needs, said the associate director and site head for the Vertex Iowa team, Ute Müh.

Müh said one of the biggest advantages of the move is gaining four labs and four offices, including a dedicated conference room.

"We are no longer crowding into my office, all seven of us practically sitting on my desk so we can video conference with Cambridge," she said.

The researchers also now have space for their robots, a new isotope room, and wet labs, which are used for chemical research, Müh said. All of which will help the company complete research on its new treatment for hepatitis C.

The drug is called Telaprevir; Ann Kwong, the Vertex head of infectious diseases, said it could cut the usual recovery time in half.

It usually takes 48 weeks to complete treatment using current medication, she said, and 24 more weeks to guarantee the treatment is successful. However, she said, the current treatment has a fail rate of about 60 percent as well as another downside.

"It also makes you feel terrible," Kwong said. "These people feel like they have the flu for a year."

The reason for the lower recovery time is because the drug Telaprevir — when taken with the

other drugs — prevents the virus from replicating, and patients experience an improvement in recovery by more than 20 percent.

The drug is in its third stage of development — determining the ideal dose — which is the last stage needed to submit the drug for approval in the United States and Europe, Kwong said.

“For the clinical trials, we have to monitor whether the patients who don’t get [sustained virological response] if they become resistant to the drug,” she said.

The data gathered in this stage of research will go toward a new drug application, she said. Diane Gallagher, the UI interim director of the Research Park & BioVentures Center, said the success of the drug could have a positive effect for the university.

“Anything that Vertex does bodes well for the university, because it is a spin-out from technology here at the university,” she said. “And the fact that Vertex Pharmaceuticals — which is in Cambridge, Mass. — decided to keep this unit here, I think really says something about the University of Iowa.”

July 31, 2009

Anadys Pharmaceuticals Receives FDA Clearance of Phase II Protocol to Study ANA598 in Combination with Interferon-Alpha and Ribavirin in HCV Patients

<http://www.medicalnewstoday.com>

Anadys Pharmaceuticals, Inc. (Nasdaq: ANDS) announced finalization of the protocol for the Company's Phase II trial of ANA598 in combination with pegylated interferon-alpha and ribavirin in hepatitis C patients. Allowance of the protocol has been received from the United States Food and Drug Administration (FDA), and patient dosing is expected to commence within the next several weeks.

In the Phase II study, naive genotype 1 patients will receive ANA598 or placebo in combination with Pegasys(R) (peginterferon alfa-2a) and Copegus(R) (ribavirin, USP) (a current standard of care, or SOC) for 12 weeks at dose levels of 200 mg or 400 mg twice daily (bid), each with a loading dose of 800 mg bid on day one. After week 12, patients will continue to receive SOC. Patients who achieve undetectable levels of virus at weeks 4 and 12 will be randomized to stop all treatment at week 24 or 48. The primary endpoint of the study is the proportion of patients with undetectable virus at week 12 (defined as complete Early Virological Response, or cEVR). Additional endpoints include safety and tolerability as well as the proportion of patients with undetectable virus at week 4 (defined as Rapid Virological Response, or RVR), weeks 24 and 48, and 24 weeks after stopping all treatment (defined as Sustained Virological Response, or SVR).

Ninety patients are planned to be enrolled in this study - thirty patients receiving ANA598 and fifteen receiving placebo at each dose level. The study will be conducted at a number of clinical sites in the United States. Anadys expects to receive 28-day safety and response (RVR) data from the 200 mg dose level by year-end and additional on-treatment safety and response data from both cohorts during the first two quarters of 2010.

"ANA598 has demonstrated potent antiviral activity and good tolerability as a single agent in Phase I, as well as preclinical properties indicative of likely synergy when used clinically in combination regimens," said Steve Worland, Ph.D., President and CEO of Anadys. "We are now in a position to demonstrate the value of ANA598 when used in combination in a Phase II trial to treat hepatitis C patients. This trial incorporates several attractive features designed to further enhance the competitive position of ANA598, including twelve weeks of triple combination treatment and a randomized exploration of shortening the overall duration of HCV therapy in conjunction with ANA598 treatment."

About ANA598

ANA598 is a non-nucleoside inhibitor of the HCV RNA polymerase. Anadys has completed three Phase I clinical studies of ANA598 that have demonstrated potent antiviral activity and good tolerability. In a monotherapy study in naive genotype 1 patients, treatment with ANA598 for three days led to median declines in viral load ranging from 2.4 to 2.9 log₁₀ in three separate dose groups. No patient at any dose level showed evidence of viral rebound while on ANA598, and there were no serious adverse events.

Anadys has completed dosing in two long-term chronic toxicology studies of ANA598 (26 weeks duration in rats and 39 weeks duration in monkeys). At the 13-week interim, the toxicology profile of ANA598 in both species was very favorable. A preliminary assessment of the results from the 26-week study in rats indicates a similar profile to that seen in rats at 13 weeks, in which the only adverse finding was a marginal decrease in the rate of weight gain in females at 1000 mg/kg, the highest dose tested. Complete results from both studies, including 39-week data from the monkey study, are expected at the end of the third quarter 2009.

Anadys has presented in vitro data supporting the use of ANA598 in combination with interferon-alpha as well as with direct antivirals currently in development. In particular, data has shown that ANA598 is synergistic in vitro with interferon-alpha as well as representative HCV protease and polymerase inhibitors. Furthermore, ANA598 retains full activity in vitro against mutations conferring resistance to protease inhibitors, nucleoside polymerase inhibitors and non-nucleoside polymerase inhibitors that act at binding sites distinct from that of ANA598, and protease and nucleoside polymerase inhibitors retain full activity against mutations conferring resistance to ANA598.

ANA598 has received Fast Track Status from the FDA for the treatment of chronic hepatitis C.

Advice to patients after hep C scare: Ask questions

<http://www.rockymountainindependent.com>

by Tillie Fong

Don't be afraid to ask questions, and lots of them.

In the wake of a hepatitis outbreak that may be tied to a hospital surgical technician, that's the advice advocates are giving to patients who worry the same thing could happen to them.

"There is no way to know about (the background) of every employee at every hospital. You need to learn to ask questions and get as much information as you can." said Patty Skolnik, founder

and director of Colorado Citizens for Accountability.

Surgical technician Kristen Diane Parker is suspected of exposing hundreds of patients at Denver's Rose Medical Center and Colorado Springs' Audubon Surgical Center to hepatitis C, a liver disease. She is accused of stealing a powerful painkiller, Fentanyl, from surgical carts, injecting it into herself and refilling the syringes with saline. The same syringes were later used on patients.

As a result, 5,800 people are being tested for hepatitis C. At least 19 patients at Rose and one patient at Audubon have tested positive, although the investigation is ongoing. Last week, a federal grand jury indicted Parker on 42 counts — 21 each of product tampering and obtaining a controlled substance by deceit.

In the Rose case, Skolnik said she believes that there was a system breakdown.

“We need to look at systems — it's a lot more than looking at a person,” she said. “You need to ask, ‘What didn't we do to allow that to happen?’ You learn from your mistakes, so let's do something about it, so that this doesn't happen again.”

The Colorado Hospital Association is planning a meeting next month to do exactly that, according to Donna Kasuda, director of the newly formed Rocky Mountain Patient Safety Organization, which was spun off from the hospital association.

“We want to get all the hospitals together and see who really has the best practices in keeping medication secure,” she said. “Maybe we can standardize things in some way and learn from each other.”

But what can a patient do?

“If I was going into surgery, I would ask, ‘Let me see which leg you marked for surgery. Are you sure you have systems in place so that I will get Fentanyl and not get a contaminated needle when I get put to sleep?’ ” Skolnik said. “Make everyone aware that the patient is aware of what's going on.”

Skolnik has first-hand experience with the issue. Her son Michael died in 2004 from multiple organ failure, but she said she believes that his death was caused in 2001 by unnecessary brain surgery that left him in a vegetative state.

She later learned that, despite the surgeon's assertions that he had performed the procedure numerous times, her son was only his second operation. She also learned the doctor had a malpractice suit in another state.

Skolnik pushed hard for a Colorado law that would allow consumers to check on doctors' backgrounds. In 2007, the Michael Skolnik Medical Transparency Act was signed into law.

“It's like CarFax but for doctors — DocFax,” she quipped.

Kasuda said that most doctors, nurses and hospital staff are willing to answer patients' questions.

“All hospitals have a Patients’ Bill of Rights,” she said. “You have a right to be involved in your care, and asking questions is part of that.”

All hospitals are required to have measures in place to keep medications secure, but the particular methods may vary from hospital to hospital, so patients will have to ask to find out.

“If they are concerned about it — they should ask: ‘How do you keep medications secure? How do you lock it up?’ ” Kasuda said. “Most hospital staff would explain that to anybody.”

She also said that with some medications, a nurse can unwrap the packaging right before administering it to the patient at bedside. “You can ask to see the packaging,” Kasuda said.

She also said that patients should definitely ask about the medication that they’re getting, especially if they are unfamiliar with it or have never taken it before.

“They should ask: what is it, how does it work, why am I getting it, are there any side effects,” said Kasuda, adding that patients should also ask about the dosage.

Kasuda said that many patients are reluctant to voice their concerns.

“If you think someone hasn’t washed their hands, you can ask about it,” she said. “People may not feel comfortable doing that, but it’s good if they do — for their own sake.”

Also, most hospitals have advocates whose job is to help patients get the care that they need.

“Just ask questions — it’s like getting your car fixed, except this is much more serious,” Kasuda said.

Pharmasset Reports Positive Preliminary Antiviral Data With PSI-7851 for the Treatment of Hepatitis C

<http://news.prnewswire.com>

- PSI-7851 achieves a 1 log(10) reduction in HCV RNA after 3 days of monotherapy

- No discontinuations or serious adverse events reported

- Conference call at 8:00 AM ET today

PRINCETON, N.J., July 31 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS) reported today positive preliminary results from its phase I clinical trial of PSI-7851 for the treatment of hepatitis C (HCV). PSI-7851 is a second generation nucleotide polymerase inhibitor of HCV.

PSI-7851 Phase 1 Multiple Ascending Dose Study Overview

In June 2009, Pharmasset initiated a phase 1 multiple ascending dose study with PSI-7851. The trial was conducted at two US centers, as a blinded, randomized, and placebo-controlled study, in 30 patients chronically infected with HCV genotype 1. The primary objective was to assess the



safety, tolerability, and pharmacokinetics of PSI-7851 after once-daily (QD) dosing for 3 days. The secondary objective was to assess antiviral activity by measuring the change in HCV RNA. Patients were randomized to receive either PSI-7851 (8 patients per cohort) or placebo (2 patients per cohort). Three dose cohorts of PSI-7851 (50mg QD, 100mg QD, 200mg QD) were evaluated.

PSI-7851 Antiviral Activity Summary

Preliminary Antiviral Response Observed Following PSI-7851 Administered as Monotherapy for 3 Days

Dose	N	Mean Change in HCV RNA at Day 3 (Log(10))
50mg QD	8	-0.49
100mg QD	8	-0.61
200mg QD	8	-1.01
Placebo	6	-0.03

PSI-7851 demonstrated potent antiviral activity with a mean HCV RNA decrease of -0.49 log(10) IU/mL, -0.61 log(10) IU/mL and -1.01 log(10) IU/mL in patients receiving 50mg QD, 100mg QD, and 200mg QD, respectively.

PSI-7851 Pharmacokinetic and Safety Summary

Pharmacokinetics were similar between healthy subjects in the single ascending dose study and HCV infected patients in the multiple ascending dose study. PSI-7851 was generally safe and well tolerated across all cohorts with no discontinuations. There were no serious adverse events and no dose-related trends in adverse events or laboratory abnormalities.

"We are very encouraged by the preliminary efficacy and safety data with PSI-7851, our second generation nucleotide analog," said Michelle Berrey, MD, MPH, Pharmasset's Chief Medical Officer. "The data from these first three cohorts demonstrate that we have achieved our goal of identifying a nucleotide analog with good efficacy that can be administered once daily at a low milligram dose. Given these characteristics and the potential benefits of nucleotide analogs over other classes of HCV direct acting antivirals, we continue to believe that PSI-7851 could become a key component of any future combination treatment regimen for HCV."

Conference Call and Webcast

Members of Pharmasset's management team will host a conference call today, Friday, July 31, 2009, at 8:00 a.m. ET to discuss the preliminary results of the multiple ascending dose trial with PSI-7851. Investors may listen to the webcast of the conference call live on the "Events & Presentations" section of Pharmasset's website, www.pharmasset.com. Alternatively, investors may listen to the call by dialing (888) 806-6208 from locations in the U.S. and (913) 312-0640 from outside the U.S. The webcast replay will be available for at least 72 hours following the call.

About PSI-7851

PSI-7851 is a uridine nucleotide analog currently in development for the treatment of chronic HCV infection. PSI-7851 has demonstrated potent in vitro anti-HCV activity with EC(90) values

of 31 +/- 12 nM, which is approximately 15-fold more potent than Pharmasset's first generation nucleoside polymerase inhibitor, RG7128 (formerly known as R7128). In vitro studies of PSI-7851 have not shown evidence of any mitochondrial or other cellular toxicities that may be associated with some nucleoside analogs. Like RG7128, PSI-7851 has demonstrated pan genotype activity in vitro.

Nutritional Supplement, SAME, Effective in Preventing Formation of Primary Liver Cancer in Rats

<http://www.sciencedaily.com>

ScienceDaily (July 30, 2009) — A new study investigated the effectiveness of S-adenosylmethionine (SAME) in the prevention and treatment of hepatocellular carcinoma (HCC) or primary liver cancer. SAME, a widely available nutritional supplement, with little known side effects, was found to be effective in preventing the formation of HCC in rats. However, high enough levels of SAME were not attainable to successfully treat established HCC.

The findings are available in the August issue of *Hepatology*.

HCC is the fifth most common cancer and the third most frequent cause of cancer death worldwide. Risk factors for HCC include chronic infection with hepatitis B virus, hepatitis C virus (HCV), dietary aflatoxin, excessive alcohol use, cigarette smoking, diabetes and obesity. The overall 5-year survival for HCC patients is less than 10% and the disease rate is expected to rise due to the high prevalence of HCV in many areas of the world.

Shelly Lu, M.D., of the Keck School of Medicine at the University of Southern California, and colleagues studied the effects of SAME on chemoprevention and treatment of HCC. In the U.S. the incidence of HCC doubled from 1979 to 1995 and the number of HCC cases for the following 20 to 30 years is projected to increase. "Given these projections, there is a tremendous interest in developing effective chemoprevention strategies," said Dr. Lu. "And an important property of SAME that makes it an attractive agent for chemoprevention and treatment of HCC is its ability to selectively kill liver cancer cells," she added.

During the study researchers injected H4IIE cells into rats and found a 1cm tumor developed in the liver two weeks after injection. A regimen of IV SAME was started one day after injecting the cells and continued for ten days. The researchers monitored the animals using MRI, ultrasound, and visual inspection to assess the liver tumors. "Treatment with IV SAME by continuous infusion significantly reduced the tumor size and significantly prevented tumor development after 11 days," researchers discovered.

Researchers found that if SAME infusion was started after sizable tumors had already formed it failed to reduce the rate of tumor growth after 24 days of treatment. This is because of a compensatory response of the liver to metabolize SAME and prevent its accumulation. "The observation that SAME failed to exert any therapeutic effect in already established HCC is disappointing," said Dr. Lu. "But whether SAME can be effective in treating HCC in man remains unclear because this compensatory mechanism may not work properly in human HCC. Nevertheless, effectiveness of SAME in chemoprevention of human HCC deserves study now."

Journal reference:

Lu et al. S-adenosylmethionine in the chemoprevention and treatment of hepatocellular carcinoma in a rat model. *Hepatology*, 2009; 50 (2): 462 DOI: 10.1002/hep.22990
Adapted from materials provided by Wiley-Blackwell.