

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Editor-in-Chief*

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Desai, ex-patient settle but other defendants remain in lawsuit

<http://www.lasvegassun.com>

By Jeff German

Amount to be paid man who says he contracted hepatitis C in endoscopy clinic not disclosed

Dr. Dipak Desai has settled with the first of thousands of former patients suing over last year's hepatitis outbreak springing from his clinics.

Lawyers for Desai filed court papers this week disclosing they have reached a deal with Michael Washington, who alleges he was infected with the potentially deadly hepatitis C virus during a colonoscopy at Desai's Endoscopy Center of Southern Nevada in 2007.

Washington's suit, the first to go before a jury, is to be tried before District Judge David Wall on Oct. 19. But Washington will square off with one less defendant — Desai — if Wall, at a hearing Thursday, finds that both sides reached the settlement in good faith.

Several defendants would remain in Washington's suit, including the nurses involved in his colonoscopy, the Endoscopy Center, and the pharmaceutical companies that manufactured and distributed Propofol, the anesthetic used in the procedure. Washington, a 69-year-old retired Air Force veteran, contends that sloppy handling of vials and syringes containing Propofol led to his infection.

In their court papers, Desai's lawyers did not reveal the amount of the settlement, saying both sides agreed it would be confidential and disclosed only to the judge.

But there is some idea of the amount because there is a cap of \$350,000 under state law on what Washington could receive for noneconomic damages. Washington's wife, Josephine, is also a plaintiff in the suit, and the settlement likely included some noneconomic damages to her, as well.

Nevada Mutual Insurance, the company that provided Desai with malpractice insurance, is expected to pay the settlement.

Brett Schoel, one of the Sacramento lawyers who filed the court papers on Desai's behalf, declined to comment Friday. So did Washington's attorney, Ed Bernstein, who also would not allow Washington to be interviewed.

But in their court papers, Desai's lawyers said the agreement, the result of extensive "arms-length" negotiations, "represents a fair compromise of the risks of both sides of proceeding to trial in this case."

Desai's risks were considerable because the Southern Nevada Health District was able to determine through genetic testing that Washington was infected with the hepatitis C virus during his procedure at the Endoscopy Center on July 25, 2007.

And records show that Desai is the one who performed the colonoscopy on Washington. As the owner of the center, Desai is also a defendant in cases where he didn't perform the procedures and may face a lesser liability.

Professor Robert Correales, a torts expert at UNLV's Boyd Law School, said Desai's agreement in the Washington case is significant because it could prompt other settlements.

"I think it demonstrates that there may be a willingness to settle other cases with similar facts," he said.

The key to striking deals in those cases will be the ability of the plaintiffs to establish the cause of their infections at the center, Correales said.

Aside from Washington, the Health District has linked only a small number of hepatitis C infections to Desai's clinic through genetic testing. The district determined that a half-dozen patients contracted the disease on Sept. 21, 2007. Plaintiffs' lawyers this week, however, revealed in court documents that they have discovered independent of the Health District a new cluster of infections at the center on March 15, 2007, and they're working to uncover more clusters.

In all, about 300 former patients are alleging in lawsuits that they were infected. More than 4,000 noninfected former patients are suing over the stress of having to get tested for hepatitis C and other viruses.

Will Kemp, a lead plaintiffs' lawyer in the endoscopy litigation, said he also thinks the Desai agreement will lead to other settlements.

But he added he doesn't expect to see a rush to reach agreements until a jury holds one of the wealthy pharmaceutical companies liable for the infections. The damage caps in Nevada apply only to the health care providers, not the pharmaceutical manufacturers.

In their court papers, Desai's lawyers contended that the evidence uncovered by the plaintiffs is stronger against the center's employees than against Desai.

But the lawyers also said Desai risked a "sympathy verdict" in taking the case to trial and that there was a possibility that a jury would find him liable for what happened to Washington because of "the publicity of the case rather than its merits."

Jeff German is the Sun's senior investigative reporter.

September 28, 2009

How Should I Manage the Pregnant HBeAg-Positive Woman?

www.medscape.com

William F. Balistreri, MD

How should the pregnant HBeAg-positive woman and newborn be managed before, during, and after delivery?

Response from William F. Balistreri, MD,
Dorothy M. Kersten Professor of Pediatrics, University of Cincinnati College of Medicine,
Cincinnati, Ohio; Medical Director, Liver Transplantation Program, Cincinnati Children's
Hospital Medical Center, Cincinnati, Ohio

The hepatitis B virus (HBV) can be transmitted from an infected mother to her infant. In fact, the risk of developing chronic HBV infection after acute exposure ranges from 90% in newborns of hepatitis B e antigen (HBeAg)-positive mothers to approximately 25% in infants and children under 5 years of age, to less than 5% in adults.[1-4] According to the recently revised guidelines approved by the American Association for the Study of Liver Diseases and endorsed by the Infectious Diseases Society of America,[5] screening is recommended for all pregnant women. Newborns of HBV-infected mothers should receive both hepatitis B immune globulin (HBIG) and the HBV vaccine at the time of delivery and should complete the recommended vaccination series. The guidelines further state that hepatitis B surface antigen (HBsAg)-positive women who are pregnant should be counseled to make sure that they inform their providers of their hepatitis B status so that HBIG and the HBV vaccine can be administered to their newborns immediately after delivery.[5,6] This has become an established and highly effective practice. Concurrent administration of HBIG and the HBV vaccine to the newborn is 95% effective in the prevention of perinatal transmission of HBV. However, efficacy is lower for maternal carriers with very high serum HBV DNA levels ($> 8 \log_{10}$ IU/mL).[6-8] Because infants of HBsAg-positive mothers remain at risk for HBV infection, they should be tested for response to vaccination. Postvaccination testing should be performed at 9-15 months of age in infants of carrier mothers.

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Achillion Completes Phase 1a Trial of ACH-1625; Begins Dosing in Phase 1b Segment with HCV-Infected Patients

<http://www.globenewswire.com>

ACH-1625 Safe and Well-Tolerated in Single Ascending and Multiple Ascending Dose Trial Segments

NEW HAVEN, Conn., Sept. 28, 2009 (GLOBE NEWSWIRE) -- Achillion Pharmaceuticals, Inc. (Nasdaq:ACHN), a leader in the discovery and development of small molecule drugs to combat the most challenging infectious diseases, today announced that the Company has completed Phase 1a of its ongoing clinical trial of ACH-1625, a protease inhibitor for the treatment of hepatitis C virus (HCV) infection, and has begun dosing HCV-infected patients in the Phase 1b segment of the trial.

ACH-1625 is a potent small molecule inhibitor of HCV protease, an enzyme necessary for viral replication. The drug candidate was discovered and is being advanced by Achillion, with the objective of developing a best-in-class protease inhibitor for treatment of HCV infection featuring potency, safety, tolerability and convenient once-daily dosing.

"We are pleased that the outstanding safety profile established in preclinical testing continues to be seen in this human clinical trial. ACH-1625 was safe and well-tolerated in both the single and the multiple ascending dose segments," stated Elizabeth A. Olek, D.O., Vice President and Chief Medical Officer of Achillion. "Clinical data gathered thus far support our belief that ACH-1625 has the potential to offer convenient once-daily dosing and an improved safety and tolerability profile compared with other protease inhibitors being studied for the treatment of hepatitis C."

"This first clinical trial of ACH-1625 has proceeded exactly as planned and we are quite pleased and encouraged with the results to date. The HCV-infected cohort of the trial has begun, and we expect it should conclude within the next few months. We are eager to demonstrate ACH-1625's efficacy and anticipate being able to announce those data early next year," added Michael Kishbauch, Achillion's President and Chief Executive Officer.

About the Phase 1 Program

The Phase 1a/1b clinical trial is a randomized, double-blind, placebo-controlled trial to investigate the safety, tolerability, pharmacokinetic profile and antiviral activity of ACH-1625 after single and multiple ascending oral doses in healthy volunteers, and oral repeat doses for 5-days in subjects with hepatitis C infection. The trial is taking place in Europe and is designed to enroll at least 54 subjects, including both healthy volunteers and HCV-infected patients. The trial is anticipated to be completed in the first quarter of 2010.

Subjects in the phase 1a single ascending dose (SAD) segment of the study received single doses of ACH-1625 ranging from 50 mg to 2000 mg. Subjects in the phase 1a multiple ascending dose (MAD) segment of the study received 5 days of ACH-1625 up to a maximal dose of 2000 mg per day.

Preliminary data from the SAD and MAD trial segments demonstrate:

- No serious adverse events
- No clinically significant changes in vital signs, ECGs, or laboratory evaluations
- Adverse events were mild and transient

About ACH-1625

ACH-1625 is an HCV protease inhibitor designed and synthesized based on crystal structures of enzyme/inhibitor complex. ACH-1625 is an open chain, non-covalent, reversible inhibitor of NS3 protease. In preclinical studies, ACH-1625 demonstrated high potency, unique pharmacokinetic properties and an excellent safety profile at high drug exposures. With its rapid and extensive partitioning to the liver, as well as high liver/plasma ratios demonstrated in preclinical studies, Achillion believes that ACH-1625 has the potential for once daily dosing. ACH-1625 has shown low single-digit nanomolar potency that is specific to HCV. It is equipotent against HCV genotypes 1a and 1b at IC₅₀~1nM.

About Achillion

Achillion is an innovative pharmaceutical company dedicated to bringing important new treatments to patients with infectious disease. Achillion's proven discovery and development teams have advanced multiple product candidates with novel mechanisms of action. Achillion is focused on solutions for the most challenging problems in infectious disease -- hepatitis C, resistant bacterial infections and HIV. For more information on Achillion Pharmaceuticals, please visit www.achillion.com or call 1-203-624-7000.

Can Vitamin B-12 Help Hepatitis-Related Fatigue?

<http://www.hepatitis-central.com>

by Nicole Cutler, L.Ac.

To ease the exhaustion typical of hepatitis, people are constantly looking for an energy booster. Find out if vitamin B-12 could help power you through your fatigue.

Anyone living with chronic hepatitis knows that fatigue is one of this illness's biggest challenges. Thus, rumors of vitamin B-12 shots or supplements miraculously restoring energy levels have generated a lot of interest in the hepatitis community. Before beginning a campaign to find and receive this shot, pill or tablet, learn about the situations that actually warrant taking vitamin B-12.

Essential for many of the body's functions, vitamin B-12 is known as the "energy vitamin." While vitamin B-12 deficiency was previously regarded as rare, recent studies from the U.S. Framingham trial show that one in four adults in the U.S. don't have enough of this vitally important nutrient.

About Vitamin B-12

Present only in animal food sources, vitamin B-12 is an essential water-soluble vitamin that is found in fish, shellfish, meat and dairy products. Also known as cobalamin, this nutrient plays many roles including helping to:

- Maintain healthy nerve cells
- Create red blood cells
- Produce DNA, the genetic material in all cells

Bound to the protein in food, hydrochloric acid in the stomach releases vitamin B-12 from protein during digestion. Once released, B-12 combines with intrinsic factor so that it can be absorbed into the bloodstream.

Vitamin B-12 Deficiency

There are two primary ways to become deficient in vitamin B-12: not getting enough in your food and losing the ability to absorb it.

- Diet - While most Americans get plenty of cobalamin from their diet, those who are strict vegetarians or vegans have trouble getting enough B-12 from their food.
- Age - With advanced age, the likelihood of a vitamin B-12 deficiency rises. This is because the stomach's lining gradually loses its ability to produce hydrochloric acid.
- Drugs - The use of antacids or anti-ulcer drugs will lower stomach acid secretion, thus decreasing the ability to absorb vitamin B-12.
- Pathogen - Infection with *Helicobacter pylori*, a common contributor to stomach ulcers, can also result in vitamin B-12 deficiency.
- Cobalamin malabsorption syndrome - This newly coined term is when the stomach lining loses the ability to produce intrinsic factor (which enables vitamin B-12 absorption). The suggested reasons for this syndrome span atrophic gastritis, *Helicobacter pylori* infection and long-term ingestion of antacids and biguanides.

Fatigue

Because it is involved with red blood cell production, cobalamin is crucial for bringing oxygen throughout the body to provide energy. This is why many people with anemia (insufficient red blood cells) are energized after taking a vitamin B-12 supplement or receiving a shot. However, those with hepatitis can have many causes for their fatigue.

Before someone with hepatitis assumes that cobalamin is the answer to his/her prayers, a physician must first look carefully at what factors could be responsible for the person's fatigue. For more information about why someone with Hepatitis C might be tired, read *Fatigue and Hepatitis C*. While most people with hepatitis have fatigue for reasons unrelated to vitamin B-12, there are some exceptions:

- Alcohol - Those with alcoholic hepatitis who obtain the bulk of their nutrients from alcohol are likely to develop a vitamin B-12 deficiency. In addition, alcohol can interfere with the absorption of vitamin B-12. Thus, a cobalamin deficiency may develop if a person consumes alcohol even if a well-balanced diet is maintained.
- Encephalopathy - Those with hepatitis who have progressed to chronic encephalopathy are instructed to avoid eating red meat. Because they may be vegetarians, a vitamin B-12 deficiency can occur in individuals with chronic encephalopathy.
- Diminished absorbability - Due to advanced age (over 60 years old) or a history of medications that block stomach acid, those with diminished ability to absorb vitamin B-12 could be tired due to cobalamin deficiency.

B-12 and Hepatitis C

Although there are only a few reasons that someone with hepatitis could benefit from vitamin B-12 for an energy boost, there is some interesting evidence tying this nutrient to Hepatitis C suppression.

- As published in the April 2001 Proceedings of the National Academy of Science of the

United States of America, Australian researchers found that in those with Hepatitis C, high concentrations of cobalamin inhibited Hepatitis C viral replication. While these results have not been implemented into a treatment strategy, they do demonstrate a favorable relationship between vitamin B-12 and Hepatitis C suppression.

- According to a study by researchers from the Karolinska Institute in Stockholm presented at the 2009 Digestive Disease Week meeting in Chicago, Hepatitis C combination therapy was more effective in recipients who had high serum levels of vitamin B-12. While this provides more recent evidence that cobalamin could restrict Hepatitis C from replicating, there is not yet enough data to make this conclusion.

Hepatitis-induced fatigue can be severe. Understandably, those affected often try a wide range of products in search of a safe and effective energy boost. Whether administered by a syringe-yielding physician or purchased in a grocery store, vitamin B-12 could be a step in the right direction. Especially if you have reason to believe that you are not getting cobalamin from your diet or are not properly absorbing it, involve your doctor in your consideration of vitamin B-12 deficiency.

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Bluesman Kenny Neal battles tragedy, illness and comes out on top

<http://www.tahoe.com>

By Tim Parsons

Tommy Castro may have said it best: Kenny Neal is the real deal.

Neal's latest record epitomizes the essence of blues music. There was death all around him, and he too appeared to be on his death bed when he optimistically wrote about life.

“Let Life Flow” won every award imaginable, and Neal drove hepatitis C out of his veins.

A native of Baton Rouge, La., who now is based in Palo Alto, Calif., Neal will bring his guitar, lap steel guitar and harmonica to Saturday, Oct. 3's Legendary Rhythm & Blues Revue at Harrah's Lake Tahoe with the Tommy Castro Band, Janiva Magness and John Nemeth.

Neal's father, sister, brother and one of his best friends died in an 11-month period, at the end of which Neal was diagnosed with hepatitis C and stage 4 liver disease. Stage 5 is death.

"I was knocking at the door, man," Neal, 51, said.

Neal's Stanford doctor told him he needed to stop playing music for a year or two. He objected.

"She said, 'If you want to live you have to follow my orders,'" Neal said. "I said, 'You've got my attention.'"

Neal was too ill to get out of bed when he penned "Let Life Flow."

*"Life is so unpredictable; that's the way it is.
Gets a little hard to bear sometimes; things out of nowhere blow your mind.
One thing I know for sure; You got to let life flow."*

"I was seven months into my treatment," he said. "That's when your body really breaks down because they had to kill off 80 percent of my white cells for the medicine to work. ... A lot of people can't take it. A lot of people's bodies reject it and a lot get so sick they just can't take it. I got real bad there, but I didn't let it get me down. But a lot of people just can't take that bad feeling. That nausea. It's just crazy."

During his 58 weeks of treatment, Neal, who more than a decade earlier was a lead actor on Broadway, started an entertainment talk show on a public access station. During an interview with E.C. Scott, Neal mentioned he had put together material for an album but hadn't yet looked for a label.

San Francisco's Blind Pig Records President Edward Chmielewski saw the program, and made an offer to Neal. It was a fortuitous development for everybody.

"We put that record out and it took off like wildflower," Neal said.

The 2009 Blues Music Awards named "Let Life Flow" song of the year. The album was voted the year's best by Blueswax, Blues Critics Awards and the West Coast Blues Hall of Fame. Neal also won the Monterey Bay Blues Artist of the Year Award. In addition, Neal was nominated for a Grammy Award in four categories.

All 10 of the Neal brothers and sisters are professional musicians.

"I don't even remember learning the stuff," Neal said. "I got it from my dad. I remember crawling up his legs and grabbing the harmonica from his hands or pick from his guitar. ... When we got older, the other kids started joining football and baseball teams, but we started putting bands together and making music on weekends with our dad."

Castro, who also lives in the Bay Area, recruited Neal to join the Legendary Rhythm & Blues Revue, which has annual week-long Caribbean and Mexican cruises.

"Kenny's amazing because he is so much the real deal for a guy his age," Castro said. "He's as close as you're going to get to another generation of blues guys. He grew up around this music."

“We're all just learning this stuff. We learn it from listening to records and pop culture — somehow we find out about this stuff. But guys like Kenny, he just grew up in that type of music. That's cool because he can give us a little bit of schooling.”

Neal's father, Raful, was the bandleader of a Baton Rouge group which included Buddy and Phillip Guy, who both moved to Chicago to start their own bands.

“Buddy and my dad were very close and Buddy told him he needed a bass player,” Neal said.

So at the age of 19, Neal joined Guy's band in 1976 for a gig at Antone's in Austin, Texas. Neal decided to move to Chicago where he played with Guy for a few years.

“I went to Chicago and it did change me in having a look at different artists who were playing guitar and singing, and all of them had their contracts in their back pockets telling me, ‘Hey I'm going to Europe next week,’” Neal said. “I'm going, ‘Damn, these guys are not that good and they're taking off to Europe with their own band. I think I need to get me a band.’ That opened my eyes up to a much broader music business. We were just playing weekends in the South at the regular local scene. So when I went to Chicago, I just saw everything just open up for me. Yeah man, I can make a living at this and travel all over the world.”

Now a bandleader and lead guitarist, Neal landed a deal with Chicago's Alligator Records.

Neal's first hit song with Alligator, “Outside Looking In,” was released in 1988, around the time he met Albert Collins.

“He was always my idol, so when I made my first record, I was nervous about going up and introducing myself to him,” Neal said. “He was on his bus. I knocked on the bus door and walked in and he goes, ‘Wow man, you're that little dude from Baton Rouge.’ He said, ‘Check this out,’ and he turned the volume up. He was listening to “Outside Looking In.”

Shortly after releasing his third record on Alligator, Neal received a singular offer.

The 1930 play, “Mule Bone,” written by the African-American poet Langston Hughes and folklorist Zora Neale Hurston, was being put together for Broadway. Taj Mahal wrote the music, and a 27-member cast was assembled. But producers struggled finding a lead actor to play the role of a young bluesman. None of the actors who auditioned were authentic enough to land the part. So instead, a real bluesman was taught to become an actor. Neal received intensive training.

“They just drilled me, man,” Neal said. “Broadway don't believe in mistakes and they don't believe in being slouchy about anything. You need to be on the button, on time and you can't ad lib. They really drill you in rehearsal and that made me much more disciplined when I came back to the blues stage.”

“Mule Bone” played for more than a year and won a Theater World Award for “The Most Outstanding New Talent On and Off Broadway.”

Although he said he may someday return to acting, Neal is content playing the blues and letting life flow. He recently had his third six-month test for hepatitis C. He came up clean.

“Prayers work,” he said. “I’m one of the lucky ones. I beat this hepatitis. Your time up ain’t till it’s ready.”

If you go

The Legendary Rhythm & Blues Revue

Who: the Tommy Castro Band, Kenny Neal, Janiva Magness and John Németh

When: 7:30 p.m. Saturday, Oct. 3

Where: Harrah's Lake Tahoe South Shore Room

Tickets: \$25 plus fees

Purchase: Visit www.harrahslaketahoe.com or call (800) 786-8208

September 29, 2009

InterMune Announces Initiation of Ritonavir-Boosted ITMN-191/RG7227 Study in HCV Patients

<http://in.sys-con.com>

PR Newswire

BRISBANE, Calif., Sept. 29 /PRNewswire-FirstCall/ -- InterMune, Inc. (Nasdaq: ITMN) today announced that its partner Roche has begun dosing in a Phase 1b multiple ascending dose (MAD) study of **ITMN-191 (RG7227) boosted by low-dose ritonavir** in patients chronically infected with hepatitis C virus (HCV) genotype-1.

Ritonavir boosting is an option to enhance and improve pharmacokinetic profiles of protease inhibitors. It is well established in the treatment of HIV where it leads to more convenient dosing, reduced resistance development and high efficacy. Not all HCV protease inhibitors are suitable for ritonavir boosting. However, as InterMune announced on August 6, 2009, ITMN-191 showed high promise in a Phase 1 single ascending dose (SAD) study in healthy volunteers. Important PK parameters showed marked improvement and significant increases in AUC and drug concentrations were observed. There were no remarkable safety findings.

"We and our partner Roche are very pleased by the performance of ITMN-191 in twice-daily regimens when un-boosted with ritonavir," said Dan Welch, Chairman, Chief Executive Officer and President of InterMune. "However, if results of ritonavir boosting of ITMN-191 in human volunteers are replicated in this study of HCV patients, the approach could lead to achieving more sustained exposures with lower twice-daily doses of ITMN-191 or perhaps allow once-daily administration. Either of these two possibilities could provide patients a regimen with more convenient administration and with the clinical advantages associated with sustained drug exposure."

The objective of the MAD study is to determine the pharmacokinetic (PK), viral kinetic and safety profiles of ascending doses of once-daily and twice-daily ITMN-191 co-administered with low doses of ritonavir and standard dose Pegasys® (peginterferon alfa-2a) and Copegus® (ribavirin) in HCV-infected patients and for 14 days. On August 6, the company announced results of a Phase 1 study of ITMN-191 co-administered with low dose ritonavir in healthy volunteers.

About ITMN-191/RG7227

ITMN-191/RG7227 is a potent, macrocyclic inhibitor of HCV NS3/4A protease activity currently in Phase 2b development. The compound is being developed in collaboration with Roche. ITMN-191 has produced multi-log₁₀ reductions in HCV levels in chronic HCV patients, when administered for 14 days as monotherapy. When ITMN-191 was combined with Pegasys and Copegus, or the NS5B polymerase in Phase 1b studies, it reduced HCV viral loads below the limit of quantification in the majority of study-treated patients. The safety and antiviral activity of ITMN-191 is also under clinical investigation in combination with the NS5B nucleoside inhibitor RG7128 in the INFORM clinical development program. To date, ITMN-191 has been safe and well tolerated in these studies.

About InterMune

InterMune is a biotechnology company focused on the research, development and commercialization of innovative therapies in pulmonology and hepatology. InterMune has an R&D portfolio addressing idiopathic pulmonary fibrosis (IPF) and hepatitis C virus (HCV) infections. The pulmonology portfolio includes pirfenidone for which a Phase 3 program in patients with IPF (CAPACITY) has been completed and the compound is currently in the pre-registration stage. The company also has a research program focused on a pirfenidone analog named ITMN-520. The hepatology portfolio includes the HCV protease inhibitor compound ITMN-191 (referred to as RG7227 at Roche) that entered Phase 2b in August of 2009 and a second-generation HCV protease inhibitor research program. For additional information about InterMune and its R&D pipeline, please visit www.intermune.com.

Bone Problems among Women, but Not Men, with HIV and Hepatitis

<http://www.aidsmeds.com>

HIV-positive women who are also infected with hepatitis B virus (HBV) or hepatitis C virus (HCV) have lower bone density than positive women not infected with HBV or HCV, according to a study published online September 23 in *AIDS*. Among men in the study, however, no connection between HIV, viral hepatitis and bone mineral loss was documented.

As increasing numbers of people with HIV are now living well into their 50s and 60s, diseases typically associated with aging have become a greater concern. Low bone mineral density can increase the risk of serious fractures, which in turn increase the risk of further illness and death.

Previous research has documented that HIV-positive men appear to lose bone mineral at a more rapid rate, at a younger age, compared with HIV-negative men. No studies, however, have looked specifically at this condition in people coinfecting with HIV and HCV or HBV—two additional viral infections that, for unknown reasons, have been linked to bone mineral depletion.

To determine the potential influence of coinfection on bone mineral density, Vincent Lo Re, MD, MSCE, from the University of Pennsylvania School of Medicine in Philadelphia, and his colleagues conducted bone scans in 1,237 people with HIV in Italy. Among this group, 624 were also infected with viral hepatitis—92 percent with HCV, 14 percent with HBV and 5 percent with both HCV and HBV. The average age overall was 43.

Lo Re's team found that coinfecting women were more likely to have more pronounced bone mineral loss in their spines than women infected only with HIV. Among men, however, no

differences between HIV-monoinfected and HIV/viral hepatitis-coinfected patients was found.

When the team looked at bone density in the upper thighbone, coinfecting women once again had weaker bones than women with just HIV. This difference, however, was not statistically significant, meaning that it could have occurred by chance.

When looking at low bone mineral density in both the spine and thighbone, coinfecting women were more likely to have low bone density, and this time the result was statistically significant.

Other factors that likely contributed to reduced bone mineral density in this study included being older, being underweight, smoking and engaging in less physical activity.

The authors concede that because the study participants are all from the same country, Italy, the results may not be true for people in other countries. They are calling for future studies to examine the reasons why HIV and hepatitis coinfection might increase bone mineral loss and to determine whether this actually translates into higher fracture rates.

Marcial: Pharma Firms May Vie for Vertex

<http://www.businessweek.com>

By Gene Marcial

Telaprevir is a potential blockbuster drug for treating hepatitis C, with a multibillion-dollar market. Vertex could get FDA approval for it next year

Expect merger-and-acquisition activity to heat up in the biotechnology sector. That's the prognostication of many analysts who have become more upbeat about the industry, with share prices now outpacing most other small-to-mid-cap stock groups.

The Nasdaq biotech stock index gained 3.15% in the week of Sept. 14, vs. the broader Nasdaq composite index's 2.50%, notes Simos Simeonides, senior biotech analyst at investment firm Rodman & Renshaw (RODM), who believes the biotech rally will likely persist this year. Both the profitable biotech companies as well as those that are still trying to develop and produce drugs for approval by the Food & Drug Administration have been gaining ground, he adds.

Analysts note that the young biotechs that have yet to earn a penny are again attracting accelerated interest from large pharmaceutical companies. Health-care analysts at Credit Suisse (CS) believe there is a higher likelihood of large drugmakers pursuing smaller biotech outfits to augment their drug pipelines. They believe there will be less likelihood of megamerger deals occurring among the major drugmakers.

One of the biotechs the Credit Suisse analysts believe will be a target of major drug firms: Vertex Pharmaceuticals (VRTX), which focuses on the discovery and development of small-molecule drugs to treat viral infections, inflammation, and cancer. Its chief product is telaprevir for the treatment of hepatitis C (HCV).

Expiring Patent Pressure

Vertex's name emerges whenever the subject of merger deals in the biotech sector pops up, says

Steven Silver, biotech analyst at Standard & Poor's. (S&P, like BusinessWeek, is a unit of The McGraw-Hill Companies (MHP).) He notes that a number of the major pharmaceuticals, particularly those likely to lose huge revenues because of drugs facing patent expiration, are eager to buy biotechs with drugs that could replace those medicines.

Vertex's attraction: Telaprevir is a potential blockbuster drug with a multibillion-dollar market that could get approval next year, notes Silver. The product, he says, is "likely to emerge as a leader in treating hepatitis C (HCV), which afflicts more than three million people in the U.S."

He rates Vertex a buy with a 12-month target of 43. However, "My price objective of 43 doesn't include a takeover premium," he adds.

Vertex spokesman Cach Barber declined comment, saying the company doesn't respond to market speculation.

Analyst Rachel McMinn of Bank of America Merrill Lynch (BAC), who rates Vertex a buy, projects a higher price target of 48, mainly based on her "high expectations" for telaprevir. Vertex is "well positioned," she says, to be the first to bring to market a "novel, highly potent oral medicine to treat a broad range of patients with HCV." She forecasts telaprevir sales of \$3.6 billion in 2013, which she says would make it "one of the highest-profile biotech product launches in the next 18 months." (Bank of America Merrill Lynch has done business with Vertex.)

Embraced by J&J

Who could be the potential suitors? Credit Suisse believes Vertex could well be a takeover target of Johnson & Johnson (JNJ), Bristol-Myers Squibb (BMY), or Gilead (GILD).

Other biotechs the Credit Suisse analysts believe could also be targets of big drugmakers: Alexion (ALXN), Amylin (AMNL), Biomarin (BMRN), Rigel (RIGL), and Salix (SLXP).

But some analysts believe Vertex may be the more attractive target as it is already in a close embrace with Johnson & Johnson. Vertex partnered with J&J in 2006 to develop and commercialize telaprevir in Europe and several other regions. Vertex received an upfront payment of \$165 million from J&J and could potentially "receive a total of \$545 million in license and milestone payments," says S&P's Silver.

Shares of Vertex have been on a roll, hitting a 52-week high of 38.50 a share on Sept. 21 from a 52-week low of 18.43 on Oct. 28, 2008. The stock's advance is in part ascribed to the takeover speculation. It climbed as high as 45 in 2006 when the deal with Johnson & Johnson was announced. The stock closed on Sept. 25 at 36.39.

Analyst Maged Shenouda of investment bank UBS (UBS), who met with senior executives of Vertex on Sept. 21 for an update on telaprevir, says that while numerous compounds to treat hepatitis C are in development, telaprevir "possesses the most competitive efficacy, safety, and treatment duration profile."

"Superior Efficacy," Shorter Treatment

Rating Vertex a buy, Shenouda says the drug is a "major advance in the treatment of HCV." The

company, he adds, is studying more competitive dosing regimens for telaprevir. It has completed three phase III clinical studies on dosing. Vertex on Sept. 24 disclosed that it will announce data results on the twice-daily dosing of telaprevir at the 60th annual meeting of the American Association for the Study of Liver Diseases in Boston on Oct. 30 through Nov. 3, 2009. Drugs in existence have a three-dose regimen,

"We believe the drug has shown superior efficacy to rivals," says S&P's Silver, and notes that telaprevir's treatment duration of 24 weeks vs. the 48 weeks in current standard-of-care drugs would be a big advantage.

Vertex is expected to file a new-drug application for telaprevir in the second half of next year, and could launch the product in 2011 if it's approved.

Besides telaprevir, Vertex has also begun clinical studies on next-generation hepatitis C protease inhibitors. It also is studying novel small molecules for the treatment of cystic fibrosis in partnership with the Cystic Fibrosis Foundation.

On Wall Street, Vertex has been attracting significant support, with 16 of 24 analysts who follow it recommending a buy for its stock, with 8 others rating it a hold. Big shareholders include Fidelity Management, which holds an 11.7% stake, Capital World Investors with 5.3%, and Barclays Global Investors with 4.9%.

Those institutions—and lots of smaller shareholders—should not be too surprised if a takeover bid emerges as drug companies discover the virtues of Vertex.

Unless otherwise noted, neither the sources cited in Gene Marcial's Stock Picks nor their firms hold positions in the stocks under discussion. Similarly, they have no investment banking or other financial relationships with them.

Marcial writes the Inside Wall Street column for BusinessWeek. In 2008, FT Press published the book Gene Marcial's 7 Commandments of Stock Investing.

Dynavax starts new hepatitis test

<http://sanfrancisco.bizjournals.com>

Steven E.F. Brown

San Francisco Business Times

Dynavax Technologies Corp. has started a Phase III clinical trial of its hepatitis B vaccine in people with chronic kidney disease.

This trial will enroll 600 people and will test the vaccine against a currently available vaccine.

According to the company, the phase III registration trial, which has been initiated, is enrolling approximately 600 patients with chronic kidney disease. The patients will be randomized to receive either 3 doses of Hcpisav (at 0, 1, and 6 months) or 8 doses of the current licensed vaccine Engerix-B (2 doses at 0, 1, 2, and 6 months). The primary endpoint is seroprotection rate at month 7.

A second phase III registration trial -- a lot-to-lot consistency trial, is expected to begin in early 2010. The company expects to complete the two registration trials within the next 24 months.

The Dynavax treatment, Heplisav, is designed to provide protection in fewer doses than vaccines now in use. Dynavax data say two doses of Heplisav provide a higher rate of protection than three doses of current vaccine.

People with chronic kidney disease don't always respond to traditional vaccination, or require more doses.

The Food and Drug Administration lifted a clinical hold on the vaccine early in September.

Should Those with Hepatitis C Get a Swine Flu Shot?

<http://www.hepatitis-central.com>

by Nicole Cutler, L.Ac.

Just in time for flu season, swine flu vaccines will be distributed and administered. If you think having Hepatitis C is cause for receiving this vaccination, become familiar with who is at highest risk from swine flu complications - and why you may want to think twice about this injection.

Officially known as H1N1, just about everyone is aware of swine flu since its first outbreak in March of 2009. In response to the worldwide panic that H1N1 could evolve into a deadly plague, pharmaceutical companies have been racing to develop a vaccination before flu season is in full swing. As of September 2009, the U.S. Food and Drug Administration approved four vaccines against H1N1. While vaccine distribution is expected to begin by mid-October, many (including those with Hepatitis C) are unsure if they should sign up to get vaccinated.

As an influenza virus, the H1N1 strain appears to cause a comparatively mild illness. Despite having a relatively mild course, H1N1 has claimed a moderate number of lives. While the elderly are typically at a higher risk from the typical seasonal flu, swine flu has caused more flu-related complications and deaths in young people than expected.

The likelihood of there being enough vaccine doses available for everyone who desires it is slim. The Centers for Disease Control has urged hospitals and other H1N1 vaccine providers to prioritize who gets the vaccine. At Texas Health Harris Methodist Hospital Fort Worth, providers are preparing a protocol to decide who is approved for H1N1 vaccination:

- At the top of the list are those who have daily contact with patients: doctors, nurses and other healthcare workers.
- Next are people considered high risk. According to Jacie Russell, infection preventionist at the hospital, "That includes patients who have cancer or people with chronic organ disease, such as liver disease or heart disease, or people who take care of children."
- Pregnant women complete the hospital's priority list.

According to this Texas hospital, those with chronic Hepatitis C certainly qualify for receiving a potentially limited swine flu vaccine. The question then becomes, is getting this vaccine in

someone with Hepatitis C's best interest?

Advantage

Obviously, the one advantage of getting vaccinated against swine flu is that your chance of getting sick with this disease is reduced. With the swine flu vaccination under your belt, you can safely go in public without worrying about whether the sneezing person next to you is infected.

Disadvantage

One of the reasons many are less than enthused about the H1N1 inoculation is that its fast-tracked status could lead to reduced effectiveness or side effects. Considering how quickly drug developers had to scramble to devise these vaccines, this is a valid concern. If clinical studies were rushed, there is a chance that the vaccine will have side effects. Such a problem arose from a vaccine developed to counter a supposed swine flu outbreak at Fort Dix, New Jersey in 1976, where four people got sick and one person died. This caused millions of people in the United States to take the swine flu vaccine available then. Unfortunately, many who received this vaccination became ill with Guillain-Barre syndrome, an autoimmune disease where parts of the nervous system are attacked.

Thus, a fast-tracked vaccine with unknown side effects is feasible. However, all flu vaccinations are typically created quickly as infectious disease specialists attempt to isolate what they presume will be the most prevalent and destructive flu virus that next season. According to Jesse Goodman, M.D., the FDA's acting chief scientist, "The H1N1 vaccines approved today (September 15, 2009) undergo the same rigorous FDA manufacturing oversight, product quality testing and lot release procedures that apply to seasonal influenza vaccines."

According to a global survey published in the August 20, 2009 issue of *Eurosurveillance*, at least half of the fatal swine flu cases involved underlying disease. A majority of fatalities involved people in the 20 - 49 year-old age group. In addition, the conditions most often linked to flu deaths were obesity and diabetes. Hepatitis C in and of itself was not recognized as a risk factor for swine flu complications. However, a number of fatal cases did involve people with immune suppression due to other causes, including cancer, organ transplants and autoimmune diseases.

Hepatitis C and H1N1 Vaccine

As we move into the flu season, those with chronic Hepatitis C must decide if the H1N1 vaccine is for them. While some institutions are advising those with chronic liver disease to get vaccinated, this decision is not one-dimensional. Just like with any medication, there are benefits and risks associated with a flu vaccine.

In and of itself, Hepatitis C does not imply a mandatory H1N1 vaccination. Some of the indicators of a high swine flu complication risk are age, chronic disease, diabetes, immune system strength and being overweight. There are some with Hepatitis C who are strong, have no detectable liver damage and are able to fight off pathogens. These individuals may opt to focus on lifestyle practices to stay healthy instead of receiving a shot.

Due to multiple health problems, having a more advanced stage of liver disease or demonstrating other swine flu complication risk factors, there are others with Hepatitis C who are more susceptible to ill health. In these circumstances, discussing swine flu concerns with a physician can help with the decision of whether or not to receive an H1N1 vaccination this fall.

The latest flu information and public health recommendations from the CDC are available at <http://www.cdc.gov/h1n1flu>.

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Massie '78 finds new liver with alums' help

<http://www.dailyprincetonian.com>

By Erica Che
Staff Writer

Many alumni would probably say that Princeton became a part of them in one way or another. In the case of Bob Massie '78, who received a new liver in July with the help of a few classmates, this metaphor could be interpreted a bit more literally.

A hemophiliac, Massie has received many blood transfusions, one of which carried hepatitis C and caused advanced cirrhosis of his liver. Despite his disease, Massie became an Episcopal priest, political candidate — he ran for the post of lieutenant governor of Massachusetts in 1994 — and director of Ceres, a nonprofit network that addresses sustainability concerns. The development of hepatitis C-related cirrhosis, however, took a heavy toll on Massie's health and involvement in many activities.

Earlier this year, Class of 1978 president Gwen Feder e-mailed her classmates on Massie's behalf, asking them to consider "a potentially life-changing act of generosity on behalf of one of our classmates," a living-donor liver transplant, the Princeton Alumni Weekly said.

"Bob Massie was a much beloved classmate for those of us in the Class of 1978. Because his hemophilia limited his mobility, Bob had a little motorcart, painted orange and black, that he drove around campus," said Dave Douglas '78, a friend and classmate of Massie's at both Princeton and Yale Divinity School. "We all thought it quite appropriate that the cover of our yearbook, published during our senior year, had a photograph of Bob's motorcart parked next to Nassau Hall."

When Douglas received the e-mail from Feder, he forwarded it to a roommate from Princeton, Stuart Knechtle '78.

“Stuart had recently moved from the University of Wisconsin to Emory to take the position as director of Emory’s liver transplantation program,” Douglas explained. “As a result of his move, I thought that he might not be on the Princeton Class of 1978 e-mail list and hence would not have received Gwen’s e-mail.”

Knechtle offered to review Massie’s case and found that Massie was a blood-type match for Jean Handler, a woman who suffered from Maple Syrup Urine disease and also needed a liver transplant, though her liver could be transplanted without carrying her disease to the recipient.

Handler, who was assigned high priority for a transplant, agreed to be Massie’s donor. After around six years of waiting on Massie’s part, on July 10, both patients received new livers in a successful domino transplant at Emory.

“He waited a long time because his [Model for End-Stage Liver Disease] (MELD) score, used to prioritize allocation of donor livers in the U.S., was low despite him having significant symptoms of his illness.” Knechtle explained in an e-mail. “He was chosen because he was the same blood type as the donor and because we felt that his medical needs were not well reflected by his MELD score.”

Coincidentally, both patients have ties to Princeton: Handler is the daughter of Princeton alumnus Henry Handler '75.

“The main message to take away from this particular transplant was that the generosity of one deceased donor family and one living donor ... allowed two patients to be cured of metabolic diseases ... and also hepatitis C-related cirrhosis for Massie,” Knechtle said. “Both patients ... have courageously confronted their illness and come through well.”

A mother’s crusade

<http://www.boston.com>

By Adrian Walker

Globe Columnist

Laura Linehan’s death was the end of a life, but the start of a quiet crusade.

Since the young Melrose woman died, far too early, from liver disease, her family and friends have waged a low-key but effective campaign to get Massachusetts to care about organ donation and transplantation.

They will be in a hearing room at the State House tomorrow, urging lawmakers to support a bill making it easier for people to donate, and receive, organs.

Ann Linehan, Laura’s mother, has seen both the urgency of the cause and the resistance it sometimes encounters.

“People come up to me and say they don’t want to donate their organs or a loved one’s,” she said, weariness and frustration evident in her voice. “They think it will never happen to them.”

Laura Linehan received her first liver transplant at the age of 2. By her teens, hepatitis C, contracted through a blood transfusion, had ravaged her second liver, requiring another transplant. The Linehans quickly discovered that the waiting list in Massachusetts might be longer than her life expectancy.

So Laura and her mother moved to Florida, where the waiting list was shorter. Laura became a patient at the Mayo Clinic in Jacksonville. After an emergency last-minute plea, a donor surfaced. But it was too late. By the time the transplant surgery began, Laura was too weak. She died shortly after surgery on April 4, 2008. She was 20.

A variety of efforts sprung up in her memory. Friends ran the Boston Marathon in her honor. The Registry of Motor Vehicles moved to make organ donation easier by allowing people to register as donors on its website. The Department of Revenue did the same.

The bill now being debated would revive a long-dormant committee in the Department of Public Health and put it to work educating people about organ donation and transplants. It would also establish a fund to support the cause.

Its major sponsor is Representative Katherine Clark of Melrose, a family friend of the Linehans.

“She was just a wonderful, wonderful spirit,” Clark said yesterday. “We were so hopeful when they moved to Florida that this would be a new beginning. We thought all our prayers had been answered, and to hear later that day that she has passed away was just devastating.”

Linehan believes that making organ donation as easy as possible is one of the keys to creating a larger supply.

The idea of approaching the Registry about getting involved came to her when she was doing her late daughter’s taxes: There was a box asking people to contribute to an organ donation fund, and she thought filers should be asked whether they wanted to donate organs as well as money.

Her crusade is rooted in the heartbreaking idea that her daughter didn’t have to die.

“I remember her looking at me in the ICU and saying, ‘Mom, please don’t let me die.’ And there was nothing I could do,” she said.

Finding an outlet for grief does little to lessen it.

“There’s a giant hole in our family,” Linehan said yesterday. “I miss her more every day. Working on this bill does not make me miss her any less. I feel that I’m doing something to honor her, but the bottom line is that no parent should have to watch their child die because there’s something that could save them, but you can’t put your hands on it.”

Since Laura died, Linehan has experienced an outpouring of sympathy and support. But she has also witnessed the wariness that comes with asking people to think about a subject that inevitably

involves their death.

She gives speeches in schools and public places - she will talk to anyone who will talk to her - and finds that people connect to her family's struggle.

"If you walked in my shoes," she said, "you would do anything to get someone to be an organ donor."

Adrian Walker is a Globe columnist. He can be reached at walker@globe.com.

September 30, 2009

Metabolic Syndrome Linked to Liver Disease in Obese Teenaged Boys

www.medicalnewstoday.com

Researchers studying a large sample of adolescent American boys have found an association between metabolic syndrome, which is a complication of obesity, and elevated liver enzymes that mark potentially serious liver disease.

The link between metabolic syndrome and the suspected liver disease did not appear in adolescent girls, said study leader Rose C. Graham, M.D., a pediatric gastroenterologist at The Children's Hospital of Philadelphia. There were ethnic differences among the boys as well, she added, between Hispanic and non-Hispanic males.

The study appears in the October 2009 print edition of the *Journal of Pediatric Gastroenterology and Nutrition*.

Metabolic syndrome is of concern as a risk factor for cardiovascular disease and type 2 diabetes, and is estimated to occur in 22 percent of U.S. adults and 4 percent of U.S. adolescents. It is defined by insulin resistance, increased waist circumference, high blood pressure, and abnormal measures of high density lipoprotein ("good cholesterol") and triglycerides in the blood. The criteria are similar for pediatric metabolic syndrome, although there is some dispute over details of the definition.

In adults, researchers have shown an association between metabolic syndrome and a group of diseases called nonalcoholic fatty liver disease (NAFLD), which at its most severe, may progress to irreversible liver damage. The purpose of the current study was to investigate to what extent metabolic syndrome in adolescents was associated with elevated levels of the liver enzyme alanine aminotransferase (ALT), a marker of NAFLD.

Graham and colleagues analyzed a nationally representative sample of 1,323 U.S. adolescents, aged 12 to 19, from the National Health and Nutrition Examination Survey. They found a strong association between metabolic syndrome and elevated ALT levels in adolescent males, but not in adolescent females.

While looking more carefully at this association in boys, they found that among Hispanic males, this association largely coincided with being obese, as measured by body mass index. The researchers expected to find this correlation, because for all ethnicities, obesity was already

known to be a risk factor for both metabolic syndrome and NAFLD. However, they also found that among non-Hispanic adolescent boys, metabolic syndrome and high ALT levels were associated with each other, independent of obesity. "Something else seems to be going on, in addition to the effects of obesity," said Graham. "Some unknown factors may be at work here."

The finding may have implications for treatment, she added. Currently, the only known treatment for NAFLD is weight loss. "If some adolescents with metabolic syndrome may be susceptible to this liver disease regardless of whether or not they are obese, there may be other treatments yet to be discovered."

NAFLD is increasingly being recognized among overweight teenagers. "Our findings suggest that NAFLD in adolescents merits closer attention, and its treatment may require more than just weight loss," said Graham.

The National Institutes of Health provided grant support for Graham and another investigator of this study. Graham's co-authors were Nicolas Stettler, M.D., of The Children's Hospital of Philadelphia; and Ann Burke, of the University of Pennsylvania Medical Center.

About The Children's Hospital of Philadelphia: The Children's Hospital of Philadelphia was founded in 1855 as the nation's first pediatric hospital. Through its long-standing commitment to providing exceptional patient care, training new generations of pediatric healthcare professionals and pioneering major research initiatives, Children's Hospital has fostered many discoveries that have benefited children worldwide. Its pediatric research program is among the largest in the country, ranking second in National Institutes of Health funding. In addition, its unique family-centered care and public service programs have brought the 430-bed hospital recognition as a leading advocate for children and adolescents.

Source: Children's Hospital of Philadelphia

Viral Load Criteria Help Distinguish Acute from Chronic HCV

www.medscape.com

By David Douglas

NEW YORK (Reuters Health) Sep 29 - Viral load features can help to distinguish acute hepatitis C virus (HCV) infection from chronic infection, researchers report in the October 1st issue of *Clinical Infectious Diseases*.

"The diagnosis of acute hepatitis C infection is problematic," lead investigator Dr. Barbara H. McGovern told Reuters Health, "because HCV antibody does not distinguish between acute and chronic infection and seroconversion is often not documented, particularly in injection drug users."

"Use of virologic parameters that are uncommon in chronic infection," she added, "namely fluctuating viremia... and low level viremia... can help identify those who may have acute infection."

In an earlier prison-based pilot study, Dr. McGovern of Lemuel Shattuck Hospital in Jamaica

Plain, Massachusetts and her colleagues found that serial monitoring of HCV RNA levels over 10 weeks could differentiate seroconverters who developed persistent viremia from those who attained spontaneous resolution.

In their pilot study, 81% of subjects with acute HCV infection had low-level viremia and 86% had viral load fluctuations. In contrast, only 13% of patients with chronic HCV had low-level viremia.

To validate these earlier findings, the researchers went on to prospectively study 35 high-risk injection drug users who were entering prison with suspected acute HCV infection. Patients with HCV RNA fluctuations >1 log were classified as being at "high probability" of acute HCV infection, as were patients with any single HCV RNA measurement above 100,000 IU/mL. Patients with fluctuations <1 log were "moderate probably" or "low probability" depending on their peak alanine aminotransferase level. Patients with spontaneous clearance were classified as "definite" acute infection.

Using standard diagnostic criteria, all received a diagnosis of acute HCV infection.

Using the novel criteria, however, "we were able to reclassify the (patients)...as having 'definite' (n=8), 'high probability' (n=20), 'moderate probability' (n=5), and 'low probability' (n=2) acute HCV infection," the investigators said.

Dr. McGovern commented to Reuters Health that "early treatment interventions can lead to sustained viral eradication," and indeed, her team writes, "the veracity" of the novel criteria "is reflected by...high sustained virologic response rates...in those who accepted therapy."

"The diagnosis of acute infection in HCV-seropositive patients is strengthened by the use of virologic parameters that are uncommon in chronic disease," the investigators conclude.

Clin Infect Dis 2009;49:1051-1060.

October 1, 2009

Hypertension and Diabetes Are Concern in Long-Term Care of Liver Transplant Patients

www.medicalnewstoday.com

A recent study by researchers from the University of Colorado looked at post-transplant care to determine whether primary care physicians (PCPs) or hepatologists are better suited to manage the overall health care of patients who received a liver transplant (LT). Researchers learned that hepatologists believe metabolic complications to be common in LT patients, but not well controlled. The hepatologists surveyed also felt that PCPs should be responsible for managing these conditions, but that this group was not taking an active role. Full details of this study appear in the October issue of *Liver Transplantation*, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases.

In the U.S. approximately 6,000 liver transplants are performed annually. Since liver transplantation began in 1963, survival rates have increased dramatically with overall 1-year and

5-year patient survival rates at 86.9% and 73.6%, respectively. As long-term survival rates increase, metabolic complications such as cardiovascular diseases, diabetes, chronic renal insufficiency and bone disease become a concern to the welfare of LT patients.

Lisa Forman, M.D. and colleagues surveyed 280 hepatologists in programs that transplanted at least 8 adult livers during the 2004 study year. Of the 191 respondents, 86% were male with a mean age of 50 years and had been in practice for an average of 13 years. Close to half of the hepatologists who replied noted that they cared for 21-50 liver transplant patients each month, while only 2.1% stated that a PCP was a working member of the practice group's post-transplant team.

Researchers found that more than 70% of hepatologists surveyed noted hypertension, chronic renal insufficiency, diabetes, and osteoporosis were present in at least 25% of patients 1 year post-transplant. The majority of respondents felt that these metabolic complications significantly contributed to morbidity and mortality 10 years after liver transplantation. Based on survey responses, the most commonly cited barriers to control post-transplant complications were dietary non-adherence, adverse effects of immunosuppressive agents, and inadequate primary care.

Approximately 75% of respondents felt that metabolic complications should be managed by PCPs, but believe that PCPs are adequately managing these health issues in only 38%-51% of LT recipients. "While there are many factors which influence the management of metabolic health concerns, the transplant community needs to be aggressive in influencing aspects that are modifiable such as PCP involvement," stated Dr. Forman. "If PCPs are reluctant to treat LT patients, and hepatologists assume their overall care, perhaps transplant hepatology fellowships should include rotations in cardiology, endocrinology, rheumatology and nephrology to give fellows more exposure to the management of metabolic complications," she suggested.

"Despite the fact that this study was based on perception rather than hard data, it does serve as a basis for future studies," stated Bashar Aqel, M.D., from the Mayo Clinic in his editorial also published in the October issue of Liver Transplantation. The authors acknowledged this study was based on the perception of hepatologists without hard data collected on the prevalence of metabolic complications and noted that PCPs were not surveyed likely leading to a bias toward the hepatologist. "More research is needed to address the real prevalence of metabolic complications, adequacy of treatment and to identify the barriers to care in the treatment of metabolic complications after liver transplantation," added Dr. Aqel.

Citations:

Article:

"Long-term management after liver transplantation: Primary care physician versus hepatologist," J. Christie Heller, Allan V. Prochazka, and Lisa M. Forman. Liver Transplantation; Published Online: September 29, 2009 (DOI: 10.1002/lt.21786); Print Issue Date: October 2009.

Editorial:

"Should or could transplant hepatologist become primary care physicians?" Bashar A. Aqel. Liver Transplantation; Published Online: September 29, 2009 (DOI 10.1002/lt.21837); Print Issue Date: October 2009

Source: University of Colorado

A Chinese Hepatitis B Health-Related Quality of Life Questionnaire

www.medicalnewstoday.com

Health-related quality of life (HRQoL) assessment is an important aspect of the overall management of hepatitis B virus (HBV) infection. However, a major challenge is to find a valid and reliable disease-specific HRQoL instrument designed for hepatitis B patients. This is particularly important among Chinese-speaking individuals, as a substantial portion of the 400 million hepatitis B sufferers worldwide is ethnic Chinese.

A recent study, "Reliability and Validity of A Chinese Version's Health-related Quality of Life Questionnaire for Hepatitis B Patients," published in *Value in Health*, reports the study findings of the Chinese Hepatitis B Health-Related Quality of Life Questionnaire being tested for its reliability and validity. The study was performed in Singapore, a multiracial country with a sizable ethnic Chinese population (75%), where the availability of a validating Chinese questionnaire would contribute to the management and monitoring of hepatitis B disease progression among Chinese patients. The study was co-authored by Dr Siew Chin Ong, Professors Seng Gee Lim and Shu Chuen Li of National University of Singapore and University of Newcastle, Australia.

Says Dr Ong, "Our results showed that this version of the culturally adapted questionnaire has good validity and reliability, making it a potentially useful outcome measure in the evaluation of HBV patients in Singapore, and possibly among Chinese patients worldwide".

The study is discussed in *Value in Health*, the official journal of the International Society for Pharmacoeconomics and Outcomes Research.

Value in Health (ISSN 1098-3015) publishes papers, concepts, and ideas that advance the field of pharmacoeconomics and outcomes research and help health care leaders make decisions that are solidly evidence-based. The journal is published bi-monthly and has a regular readership of over 4,000 clinicians, decision-makers, and researchers worldwide.

ISPOR is a nonprofit, international organization that strives to translate pharmacoeconomics and outcomes research into practice to ensure that society allocates scarce health care resources wisely, fairly, and efficiently.

Source: ISPOR

New Data on Four Bristol-Myers Squibb Compounds to Be Presented at AASLD 2009

<http://www.businesswire.com>

PRINCETON, N.J.--(BUSINESS WIRE)--New data on four Bristol-Myers Squibb Company



(NYSE:BMJ) compounds will be presented at the 60th annual meeting of the American Association for the Study of Liver Diseases (AASLD) in Boston from October 30 to November 3.

Data will be presented on **BARACLUDGE®** (entecavir) in patients with chronic hepatitis B, and on two compounds in early clinical development for the treatment of hepatitis C -- **BMS-650032**, an NS3 inhibitor, and **PEG-Interferon lambda**, a novel type 3 interferon. The presentation of data on BMS-650032 will mark the first public disclosure of information about this investigational compound. Data will also be presented on the investigational compound **brivanib**, the first selective dual inhibitor of fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) signaling, which is in Phase 3 development for the treatment of hepatocellular carcinoma.

“The data on Bristol-Myers Squibb compounds that will be presented at AASLD demonstrate the breadth of our research and development portfolio and support the company’s goal of developing innovative medicines for patients with various diseases of the liver,” said Elliott Sigal, M.D., Ph.D., executive vice president, chief scientific officer and president, Research and Development, Bristol-Myers Squibb. “Our established expertise in viral hepatitis and oncology uniquely position Bristol-Myers Squibb to be at the forefront of delivering innovation in the treatment of multiple types and stages of liver disease. We are proud to be releasing new data on our significant portfolio of assets.”

BARACLUDGE, BMS-650032 and brivanib were discovered by Bristol-Myers Squibb Research and Development. BMS-650032 is Bristol-Myers Squibb’s second small molecule under development for the treatment of hepatitis C, joining BMS-790052, a first-in-class investigational NS5A inhibitor of the hepatitis C virus.

PEG-Interferon lambda was discovered by ZymoGenetics, Inc. Bristol-Myers Squibb and ZymoGenetics announced a global collaboration for PEG-Interferon lambda and its related development program earlier this year.

The times, titles and lead authors of the data presentations are as follows:

Date/Time	Presentation Title	Lead Author
Hepatitis B		
October 31, 2:00 – 8:00 p.m. EDT	Efficacy and Safety of Entecavir versus Adefovir in Chronic Hepatitis B Patients with Evidence of Hepatic Decompensation (Abstract #422)	Y. Liaw Chang Gung Memorial Hospital, Chang Gung University College of Medicine Taipei, Taiwan
Hepatitis C		
November 3, 12:00 – 12:15 p.m. EST	Safety, Tolerability, Pharmacokinetics and Antiviral Activity following Single- and Multiple-Dose Administration of BMS-650032, a Novel HCV NS3 Inhibitor, in Subjects with Chronic Genotype 1 HCV Infection (Abstract #225)	C. Pasquinelli Bristol-Myers Squibb
November 3, 8:00 a.m. – 1:00 p.m. EST	Genotypic and Phenotypic Analysis of Samples from HCV-Infected Subjects Treated with BMS-650032 in a Single Ascending Dose Study (Abstract #1607)	F. McPhee Bristol-Myers Squibb
November 3, 8:00 a.m. – 1:00 p.m. EST	A Phase 1b Dose-Ranging Study of 4 Weeks of PEG-Interferon (IFN) Lambda (PEG-rIL-29) in Combination with Ribavirin (RBV) in Patients with Chronic	A.J. Muir Duke University School of Medicine Durham, North

	Genotype 1 Hepatitis C Virus (HCV) Infection (Abstract #1591)	Carolina
Hepatocellular Carcinoma		
November 3, 8:00 a.m. – 1:00 p.m. EST	Time-to-Progression Analysis of Second-line Treatment with Brivanib in Patients with Unresectable, Locally Advanced, or Metastatic Hepatocellular Carcinoma (Abstract #1683)	R. Finn UCLA Los Angeles, CA
November 3, 8:00 a.m. – 1:00 p.m. EST	Cell-dependent Response of BMS-582664 (Brivanib) in Hepatocellular Carcinoma Cells: Gene Expression Profiling Study (Abstract #1668)	J. Park National Cancer Center Goyang, South Korea

Keeping hepatitis C virus at bay after a liver transplant

<http://www.eurekalert.org>

One of the most common reasons for needing a liver transplant is liver failure or liver cancer caused by liver cell infection with hepatitis C virus (HCV). However, in nearly all patients the new liver becomes infected with HCV almost immediately. But now, Hideki Ohdan, Kazuaki Chayama, and colleagues, at Hiroshima University, Japan, have developed an approach that transiently keeps HCV levels down in most treated HCV-infected patients receiving a new liver.

Specifically, the team took immune cells known as lymphocytes from the donor livers before they were transplanted into the HCV-infected patients, activated them in vitro, and then injected them into the patients three days after they had received their liver transplants. Importantly, these infused cells were able to keep the HCV at bay even though the patients were taking immunosuppressive drugs to prevent their immune systems from rejecting the new livers. Despite showing clear clinical effects, the authors are planning further studies in which they will modify the protocol in an attempt to find a way to keep HCV levels down for longer and in all patients.

TITLE: Adoptive immunotherapy with liver allograft–derived lymphocytes induces anti-HCV activity after liver transplantation in humans and humanized mice. *Journal of Clinical Investigation*.

HCV Infection May Be Associated with Risk for Coronary Disease

<http://www.cardiologytoday.com>

Patients with hepatitis C virus may be at a higher risk for coronary artery disease, according to a new study conducted by researchers from the Department of Veterans Affairs.

The increased risk for CAD among patients with hepatitis C was seen even among those who were younger and had lower lipid levels and better BP levels.

Researchers collected data from all Veterans Affairs facilities in the United States and the Electronically Retrieved Cohort of HCV Infected Veterans. They identified 82,083 people with HCV and 89,582 people who were not infected with HCV. Data were collected from 2001 to 2006.

According to the results, patients with HCV were less likely to have hypertension, hyperlipidemia and diabetes, but more likely to experience renal failure, anemia and to have a history of alcohol and drug abuse.

The average total plasma cholesterol was 175 ± 40.8 mg/dL in patients with HCV compared with 198 ± 41.0 mg/dL in those who were not infected ($P < .001$). Patients with HCV also had LDL (102 ± 36.8 mg/dL vs. 119 ± 38.2 mg/dL) and triglyceride levels (144 ± 119 mg/dL vs. 179 ± 151 mg/dL) than those who did not have HCV ($P < .001$ for both comparisons).

Multivariate analysis demonstrated that the hazard ratio for CAD among patients with HCV was 1.25 (95% CI, 1.20-1.30).

Age, hypertension, chronic obstructive pulmonary disease, diabetes and hyperlipidemia were risk factors for CAD among both HCV-infected and HCV-uninfected populations. A lower risk for CAD was observed among ethnic minorities and women.

Butt A et al. Clin Infect Dis. 2009;49:225-232.