

HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus
Editor-in-Chief*

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How Inflammatory Disease Causes Fatigue

<http://www.sciencedaily.com>

ScienceDaily (Feb. 28, 2009) — New animal research in the February 18 issue of *The Journal of Neuroscience* may indicate how certain diseases make people feel so tired and listless. Although the brain is usually isolated from the immune system, the study suggests that certain behavioral changes suffered by those with chronic inflammatory diseases are caused by the infiltration of immune cells into the brain. The findings suggest possible new treatment avenues to improve patients' quality of life.

Chronic inflammatory diseases like rheumatoid arthritis, inflammatory bowel disease, psoriasis, and liver disease cause "sickness behaviors," including fatigue, malaise, and loss of social interest. However, it has been unclear how inflammation in other organs in the body can impact the brain and behavior.

The researchers found that in mice with inflamed livers, white blood cells called monocytes infiltrated the brain. These findings support previous research demonstrating the presence of immune cells in the brain following organ inflammation, challenging the long-held belief that the blood-brain barrier prevents immune cells from accessing the brain.

"Using an experimental model of liver inflammation, our group has demonstrated for the first time the existence of a novel communication pathway between the inflamed liver and the brain," said the study's senior author Mark Swain, MD, Professor of Medicine at the University of Calgary.

Swain and his colleagues found that liver inflammation triggered brain cells called microglia to produce CCL2, a chemical that attracts monocytes. When the researchers blocked CCL2 signaling, monocytes did not enter the brain despite ongoing inflammation in the liver.

Liver inflammation also stimulated cells in the blood to make an immune chemical (TNF α). When the researchers blocked the signaling of this immune chemical, microglia produced less CCL2, and monocytes stayed out of the brain.

In the mice with inflamed livers, preventing the entry of monocytes into the brain reduced sickness behaviors; mice showed more mobility and social interaction. These findings suggest that people with chronic inflammatory diseases may benefit from treatments that limit monocyte access to the brain.

"Sickness behavior significantly impacts quality of life. Our findings further our understanding and may generate potential new avenues for treatment of these often crippling symptoms," said Swain.

"The brain is the master coordinator of many of our bodies' defense responses, so it must be able to sense injury and inflammation in distant body organs. This study starts to explain the peripheral communication signals that activate the brain," said Nancy Rothwell, PhD, DSc, at the University of Manchester, an expert on brain inflammation who is unaffiliated with the study.

The research was supported by the Canadian Institutes of Health Research, the Canadian Liver Foundation, and the Alberta Heritage Foundation for Medical Research.

Adapted from materials provided by Society for Neuroscience, via EurekAlert!, a service of AAAS.

Economic Recovery Payments Coming For People Who Receive Social Security And SSI Benefits

By Elizabeth Wertime
Social Security Public Affairs Specialist in Albany, NY

The American Recovery and Reinvestment Act of 2009, which the President signed into law in February, provides for a one-time payment of \$250 to people receiving Social Security and Supplemental Security Income (SSI) benefits.

The one-time recovery payments will go out in May 2009 and all payments should be received by the end of May. In April, Social Security will send a letter with additional information to each person who is eligible for the one-time payment. The payments will be sent automatically, meaning no action is required on the part of the person receiving benefits. The economic recovery payments will be made separately from a person's regular monthly payments.

All adults who receive Social Security benefits, including disabled adult children (but not minor children) are eligible for \$250 payment. In addition, all persons who receive SSI payments, including minor children, are eligible for the payment. Anyone who receives benefits or who was eligible to receive benefits during any of the three months prior to enactment (November and December of 2008 and January 2009) will receive the one-time payment as long as the address of record is in one of the 50 states, the District of Columbia, Puerto Rico, Guam, U.S. Virgin Islands, American Samoa, or the Northern Mariana Islands.

The payments will be made in the same way that regular monthly payments are made. People with direct deposit will receive their payments electronically. Those who receive paper checks will receive their payments in the mail. People who receive regular payments through the Direct Express debit card will receive their one-time payments through the card.

If someone receives both Social Security and SSI, only one payment of \$250 will be made. The economic recovery legislation also provides for a one-time payment to recipients of Department of Veterans Affairs (VA) and Railroad Retirement Board (RRB) benefits. However, if you receive Social Security or SSI benefits and you also receive VA and/or RRB benefits, you will only receive one \$250 payment. The Social Security Administration will send you this payment.

To assist in processing the payments as efficiently as possible, please do not contact Social Security unless do not receive a payment by June 4, 2009. Information is available at www.socialsecurity.gov and will be updated regularly.

To learn more about the American Recovery and Reinvestment Act of 2009, visit www.recovery.gov.

High hepatitis C viral load increases risk of death in HIV/HCV coinfecting patients

www.aidsmap.com

Liz Highleyman

A high level of hepatitis C virus (HCV) in the blood is associated with an increased risk of death in HIV/HCV coinfecting individuals, according to data presented on February 10th at the Sixteenth Conference on Retroviruses and Opportunistic Infections in Montreal, Canada.

Jürgen Rockstroh from the University of Bonn in Germany presented results from a study evaluating the influence of HCV viral load and genotype on disease progression and response to antiretroviral therapy amongst all HIV/HCV coinfecting participants in EuroSIDA, a prospective observational cohort of more than 16,000 HIV-positive individuals from more than 30 mostly European countries.

Having previously shown that being HCV antibody-positive was not associated with increased mortality amongst people with HIV, the investigators looked at rates of death due to any cause and due to liver-related disease, comparing coinfecting people with high (500,000 IU/ml or more), low (less than 500,000 IU/ml) and undetectable (less than 615 IU/ml) HCV viral load, and those with HCV genotypes 1, 2, 3 and 4.

Out of 1952 identified HIV/HCV coinfecting cohort members, 821 (42%) fell into the high HCV viral load group, 716 (37%) fell into the low HCV group, and 415 (21%) had undetectable HCV. Amongst the 1537 participants with measurable HCV, just over half had hard to treat genotype 1, nearly one-third had genotype 3, about 14% had genotype 4 and only 3% had genotype 2. Very few (about 2%) had taken interferon-based therapy for hepatitis C, though the numbers increased over time.

A total of 78 people in the undetectable HCV viral load group died due to any cause compared with 96 in the low HCV group and 158 in the high HCV group. All-cause mortality rates for the three groups were 3.12, 1.74, and 4.17 per 100 person-years, respectively.

A similar pattern was seen for deaths due to liver disease, though the numbers were smaller: 17 people in the undetectable HCV group died due to liver-related causes compared with 32 in the low HCV group and 49 in the high HCV group, translating to rates of 0.68, 0.58, and 1.29 deaths per 100 person-years, respectively.

After adjusting for potential confounding factors including sex, age, race/ethnicity, HIV transmission risk group, immune status (CD4 cell count and history of AIDS diagnosis), type of antiretroviral therapy, region of Europe, and triple infection with hepatitis B, people with undetectable and low HCV viral load had similar rates of death due to any cause, but the rate was nearly doubled in the high HCV group (adjusted incidence rate ratio of 1.94).

Restricting the adjusted analysis to liver-related deaths, people with undetectable and low HCV viral load again had statistically similar liver-related mortality rates, whilst those in the high HCV group were 77% more likely than to die of such cause than those in the low viral load

group (adjusted incidence rate ratio of 1.77).

After adjustment, people with HCV genotypes 2 and 3 had a lower rate of all-cause death than those with genotype 1, but this was only significant for genotype 3. A similar pattern was seen for liver-related deaths, but differences did not reach statistical significance, possibly due to small numbers. This finding is noteworthy because HCV genotype 3 is associated with liver steatosis (fat accumulation), which might be expected to predict worse outcomes.

In addition, Dr Rockstroh reported that HCV viral load level was not correlated with differences in response to antiretroviral therapy, either HIV suppression or CD4 cell recovery. However, people with HCV genotypes other than 1 had poorer virological and immunological response to anti-HIV therapy, reaching statistical significance for genotype 4 - a finding he said has not been observed in HIV-negative hepatitis C patients.

These findings prompted some debate, as prior research in HIV-negative people with hepatitis C has not revealed a link between HCV viral load or genotype and liver disease progression.

Dr Rockstroh acknowledged that mortality rates were not adjusted for fibrosis stage in this analysis, as this information was not generally available (it is now being collected). Assessment of alcohol use, he added, is "extremely difficult" in this type of observational study.

In closing, Dr Rockstroh suggested that the effect of HCV viral load on mortality may be more apparent in HIV-positive individuals, who tend to have higher HCV RNA levels and more rapid liver disease progression than HIV-negative hepatitis C patients.

Reference

Rockstroh J et al. High HCV is associated with an increased risk for mortality in HIV/HCV-co-infected individuals. Sixteenth Conference on Retroviruses and Opportunistic Infections, Montreal, abstract 101, 2009.

FTC Clears ZymoGenetics-Bristol-Myers Deal For Hepatitis C Drug Development - Update

<http://www.rttnews.com>

(RTTNews) - Monday, ZymoGenetics Inc. (ZGEN: News) announced that its collaboration with Bristol-Myers Squibb Co. (BMY: News) for hepatitis C compound PEG-Interferon lambda has been cleared by the United States Federal Trade Commission and Department of Justice clearance under provisions of the Hart-Scott-Rodino Antitrust Improvements Act.

PEG-Interferon lambda, (IL-29) is a novel type 3 interferon currently in Phase 1b development for Hepatitis C and is expected to be a more targeted therapy. Now that the collaboration agreement has become effective, following clearance, ZymoGenetics will receive payment of an \$85.0 million licensing fee.

Under the terms of the agreement signed in January, apart from the upfront cash payment of \$85 million, ZymoGenetics will receive an additional license fee of \$20 million this year. In addition, ZymoGenetics could receive payments of up to \$430 million based on pre-defined development

and regulatory milestones for PEG-Interferon lambda in Hepatitis C, up to \$287 million in development and regulatory milestones for other potential indications, and up to \$285 million based on pre-defined sales-based milestones.

ZGEN closed Friday's trade at \$4.15, unchanged from the previous day's close. BMY closed the day's trade at \$18.41.

Study Showing Improved Virologic Response with Nitazoxanide in Chronic Hepatitis C Published in Gastroenterology

<http://news.prnewswire.com>

Editorial Accompanies Manuscript in March Issue

TAMPA, Fla., March 2 /PRNewswire/ -- A study evaluating nitazoxanide in combination with peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C virus (HCV) infection with genotype 4 was published in the March issue of *Gastroenterology*, the official journal of the American Gastroenterological Association Institute (AGA Institute). The study showed that the addition of nitazoxanide to standard-of-care therapy increased the rate of sustained virologic response when compared with patients given peginterferon plus ribavirin alone.(1) An accompanying editorial commenting on the study was also published in the Journal.(2)

"The results published today in *Gastroenterology* represent an important milestone in the development of nitazoxanide, the first thiazolide, for the treatment of chronic hepatitis C," said Jean-Francois Rossignol, MD, PhD, Romark Institute for Medical Research, the inventor of this new class of antiviral drugs and lead author of the study. "Nitazoxanide is currently being evaluated along with the standard-of-care treatment in patients with chronic hepatitis C genotype 1 in clinical trials in the U.S., and we look forward to reporting interim data from those trials in the coming months."

Study Details

The randomized, controlled study published in *Gastroenterology* evaluated the safety and efficacy of nitazoxanide plus peginterferon, with or without ribavirin, in 97 patients with previously untreated genotype 4 chronic hepatitis C at 2 centers in Egypt. Participants were sequentially allocated into 3 treatment arms (one patient immediately dropped from the study):

- Peginterferon alfa-2a 180 mcg/week plus ribavirin 1000-1200 mg/day for 48 weeks (standard of care) (n = 40);
- Nitazoxanide 500 mg twice daily monotherapy for 12 weeks followed by nitazoxanide plus peginterferon for an additional 36 weeks (n = 28);
- Nitazoxanide monotherapy for 12 weeks followed by nitazoxanide plus both peginterferon and ribavirin for 36 weeks (n = 28).

The primary endpoint was sustained virological response (SVR), or serum HCV RNA <12 IU/mL 24 weeks after the end of treatment. Secondary endpoints included HCV RNA <12 IU/mL at week 4 (rapid virological response, or RVR), at week 12 (complete early virological response, cEVR), and at the end-of-treatment (ETR).

Results

The percentages of patients with RVR, defined as undetectable serum HCV RNA at week 4 of combination therapy, and SVR were significantly higher in patients given the triple therapy compared with the standard of care (64% versus 38%, $p=0.048$ and 79% versus 50%, $p=0.023$, respectively). Patients given nitazoxanide plus peginterferon alfa-2a had intermediate rates of RVR (54%) and SVR (61%). Adverse events were similar across treatment groups except for a higher rate of anemia in the groups receiving ribavirin. In the nitazoxanide group, virologic responses were maintained through the end of treatment with no virologic breakthroughs. Of note, the use of nitazoxanide was associated with reduced relapse rates (3/20 patients in the peginterferon plus nitazoxanide arm, and 1/23 patients in the triple arm with peginterferon, ribavirin and nitazoxanide) versus 10/30 patients in the standard-of-care arm.

About Nitazoxanide and Hepatitis C

Nitazoxanide, the first of a new class of broad spectrum antiviral drugs known as the thiazolides, is undergoing worldwide development as a treatment of chronic hepatitis C. Nitazoxanide is a potent inhibitor of hepatitis C virus (HCV) replication in HCV genotype 1-derived replicon cell lines, and in vitro studies have shown that it does not induce mutations in the virus that confer resistance. Phase II clinical trials are ongoing in the United States in patients with chronic hepatitis C and genotype 1 infection.

A recent Phase II study of low and high doses of a controlled-release nitazoxanide tablet showed favorable pharmacokinetics and significant reduction in viral load, with good tolerability and safety.(3) Romark recently entered into an agreement granting Chugai Pharmaceutical Co., Ltd., a member of the Roche Group, an exclusive license to develop and market nitazoxanide for the treatment of chronic hepatitis C in Japan.

About Romark Laboratories

Romark Laboratories (www.romark.com), a privately held biopharmaceutical company, has discovered and developed a new class of small molecule antivirals known as thiazolides. The Company is developing nitazoxanide, the first of the thiazolide class, for the treatment of chronic hepatitis C, and is developing other new thiazolides for treating viral diseases including chronic hepatitis B. Alinia(R) (nitazoxanide) is approved by the U.S. Food and Drug Administration and marketed by Romark for the treatment of infections caused by *Cryptosporidium* or *Giardia*.

(1)"Improved Virologic Response in Chronic Hepatitis C Genotype 4 Patients Given Nitazoxanide, Peginterferon and Ribavirin," J.F. Rossignol, M.D. et. al., *Gastroenterology*, Vol. 136 issue 3, pp 856-862, March 2009

(2)"Nitazoxanide: Beyond Parasites Toward a Novel Agent for Hepatitis C," Jama M. Darling, Michael W. Fried, *Gastroenterology* Vol. 136 issue 3, pp 760-763, March 2009

(3)"Controlled Release Tablet Improves Pharmacokinetics, Viral Kinetics and Tolerability of Nitazoxanide for Treatment of Chronic Hepatitis C," Emmet B. Keeffe, M.D., of the Romark Institute for Medical Research, Tampa, FL. 19th Conference of the Asian Pacific Association for the Study of the Liver (APASL), abstract FP052, February 14, 2009

SOURCE Romark Laboratories

Q&A: could I catch hepatitis C?

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

How easy is it to catch hepatitis C from a partner who is carrying the virus? I have just heard that an ex of mine has it

Dr Mark Porter

How easy is it to catch hepatitis C from a partner who is carrying the virus? I have just heard that a past boyfriend of mine is awaiting a liver transplant because of the infection, which he probably picked up when he dabbled with drugs at university. That was more than 15 years ago, but I am now worried that he may have had the virus when we were together and passed it on to me.

Hepatitis C is an infection that was first identified in 1989. Some people will eliminate the virus without any trouble, but most develop a slow-burning, chronic infection that, in as many as one in five people, can lead to serious liver disease some 20 years later.

Hep C is blood borne and the most common route of transmission in the UK is sharing dirty needles and syringes. There is also a risk to anyone who received a blood transfusion before routine screening was introduced in 1991, or blood products (as used to treat people with haemophilia) before 1986.

In theory the virus can be spread during any activity where blood may come into contact with cuts or a nick in the skin but sexual transmission is quite uncommon. Studies suggest that fewer than one in twenty regular sexual partners of people with Hep C become infected themselves: good odds for you.

Screening involves a simple blood test and if you turn out to have the virus, there are treatments that can clear the infection in around half of cases, but the earlier this is done the better. Visit www.nhs.uk/hepc for more details.

March 3, 2009

Vertex Pharmaceuticals Strengthens HCV Drug Development Portfolio, Adds Novel Polymerase Inhibitors to Shape New Combinations with Telaprevir

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

- Vertex to acquire privately-held ViroChem Pharma in cash and stock transaction -- Two HCV polymerase inhibitors, VCH-222 and VCH-759, have demonstrated significant antiviral activity in early clinical trials -- First STAT-C combination trial with telaprevir planned for 2H 2009 start -

CAMBRIDGE, Mass. & LAVAL, Quebec, Mar 03, 2009 (BUSINESS WIRE) -- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX), which is developing the hepatitis C virus (HCV) protease inhibitor telaprevir, will add two polymerase inhibitors to its HCV drug development portfolio through a definitive agreement to acquire privately-held ViroChem Pharma Inc. in a

stock and cash transaction. With the addition of these compounds, Vertex will advance its strategy to pursue novel combinations of Specifically Targeted Antiviral Therapies for hepatitis C (STAT-Cs) for the treatment of HCV infection. Following completion of the transaction, Vertex will own worldwide rights to ViroChem's HCV drug development portfolio, including VCH-222 and VCH-759, which have demonstrated substantial reductions in plasma HCV RNA when dosed as single agents and have been well-tolerated in clinical studies to date. In particular, VCH-222 dosed as 750 mg twice daily resulted in a median 3.7 log₁₀ decrease in HCV RNA at the end of dosing in a three-day viral kinetic study, representing the most substantial reduction in viral load reported to date with an investigational HCV polymerase inhibitor dosed as a single agent. Vertex expects to begin clinical evaluation of novel combination regimens of its HCV protease inhibitor telaprevir, currently in Phase 3 clinical development, in the second half of 2009. The transaction is subject to customary pre-closing conditions.

"This acquisition significantly strengthens our pipeline in hepatitis C by bringing together Vertex's telaprevir, our HCV protease inhibitor in registration studies, with the HCV non-nucleoside polymerase inhibitors being developed by ViroChem," said Joshua Boger, Ph.D., Chief Executive Officer of Vertex. "Through this acquisition, we're well positioned as a leader in the development of HCV therapies. Our goal is to further advance HCV care for patients through the creation of novel and highly potent STAT-C combination regimens."

"This move expands Vertex's global presence in HCV and has the potential to enhance the profile and lifecycle of our telaprevir-based combination regimens. We believe it strengthens our ability to compete and stay at the forefront in developing novel STAT-C combination regimens," added Kurt C. Graves, Executive Vice President, Chief Commercial Officer and Head, Strategic Development at Vertex. "We selected ViroChem's compounds following careful evaluation of the STAT-C landscape for more than a year. Key data has emerged that suggest that these compounds could uniquely complement telaprevir and provide a foundation for shaping a potentially new treatment paradigm."

ViroChem HCV Drug Development Portfolio

Two ViroChem HCV polymerase inhibitors, VCH-222 and VCH-759, are currently in clinical development. ViroChem also has a preclinical program directed at the discovery of novel HCV NS5a inhibitors. The status and profile of each clinical compound is detailed below.

VCH-222: VCH-222 is an oral non-nucleoside inhibitor of the HCV NS5B polymerase that recently completed a viral kinetic study in HCV patients. In this study involving five treatment-naive genotype 1a and 1b HCV infected patients, VCH-222 dosed as 750 mg twice daily resulted in a median 3.7 log₁₀ decrease in HCV RNA - equivalent to a 5,000-fold reduction in virus in the blood - at the end of three days of dosing. The results were consistent from patient to patient, and across HCV genotype 1 subtypes, and represent the most substantial reduction in viral load reported to date with an investigational HCV polymerase inhibitor dosed as a single agent. In clinical evaluations to date, VCH-222 has been well-tolerated, with no serious adverse events observed. VCH-222 has completed 28-day non-clinical toxicology studies in two species.

VCH-759: VCH-759 is an oral non-nucleoside inhibitor of the HCV NS5B polymerase that has completed Phase 1b clinical development. In a Phase 1b trial reported at a medical conference in 2007, VCH-759 dosed as 800 mg three times daily showed a mean maximal 2.5 log₁₀ reduction in HCV RNA and a median 1.7 log₁₀ reduction in HCV RNA at the end of 10 days. VCH-759

was also well-tolerated with no serious adverse events observed in clinical studies to date. VCH-759 has completed 28-day non-clinical toxicology studies.

Future clinical plans: Vertex plans to conduct additional dose-ranging studies of VCH-222 as a single agent and in combination with pegylated interferon and ribavirin. Vertex plans to initiate a first clinical study combining telaprevir with a ViroChem HCV polymerase inhibitor in the second half of 2009. Data from in vitro HCV replicon studies suggest that VCH-222 and VCH-759 may provide synergistic or additive antiviral activity to the HCV protease inhibitor telaprevir, thus creating the potential for a non-cross resistant, complementary profile in exploratory clinical studies.

Terms of the Transaction

Under the terms of the agreement, which have been approved by the Boards of Directors of both companies, ViroChem shareholders will receive \$100 million in cash and 9.9 million shares of Vertex common stock. The stock portion of the consideration is subject to a collar, and the actual number of shares of Vertex stock to be issued will be based on an average Vertex share price prior to the acquisition closing, but per the agreement will not exceed 11.0 million shares. Vertex expects the shares issued in this transaction will be immediately tradeable under a resale registration statement which Vertex plans to file at the time of closing. Goldman, Sachs & Co. is acting as exclusive financial advisor to Vertex.

Vertex HCV Portfolio

Vertex is developing telaprevir, one of the most advanced investigational agents in development that specifically targets HCV. Telaprevir is being evaluated in a broad Phase 3 registration program, which has enrolled more than 2,200 genotype 1 HCV patients, including patients who have both failed prior treatment with pegylated interferon and ribavirin, as well as patients who are naive to treatment. Vertex plans to file an NDA for telaprevir in the second half of 2010 assuming successful completion of its ongoing Phase 3 program. In addition, Vertex is developing two other novel HCV protease inhibitors, VX-813 and VX-985, currently in Phase 1 and preclinical development respectively.

Vertex retains commercial rights to telaprevir in North America. Vertex and Tibotec are collaborating to develop and commercialize telaprevir in Europe, South America, Australia, the Middle East, and other countries. Vertex is collaborating with Mitsubishi Tanabe Pharma Corporation to develop and commercialize telaprevir in Japan and certain Far East countries. Vertex retains worldwide rights to VX-813 and VX-985.

HCV Protease and Polymerase as Targets for New Drug Development

Since the identification and sequencing of the hepatitis C virus in 1989, efforts to discover new drugs for HCV infection have focused on specific antiviral targets, including the HCV NS3 protease and the HCV NS5B polymerase. Several specifically targeted antiviral therapies for HCV (known as STAT-Cs) have demonstrated promising clinical results, with the potential for a significant advancement in HCV treatment and disease outcomes when dosed in combination with the currently available treatment of pegylated interferon and ribavirin. As investigational compounds targeting HCV protease and polymerase have advanced in development, clinicians have expressed interest in combining these investigational approaches, with the goal of further optimizing HCV treatment regimens, including treatment of certain hard to treat populations, by potentially increasing SVR rates, decreasing the duration of HCV therapy and increasing the

tolerability of HCV treatment regimens.

About Vertex

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical companies. Vertex's product pipeline is focused on viral diseases, cystic fibrosis, inflammation, autoimmune diseases, cancer, and pain. Vertex co-discovered the HIV protease inhibitor, Lexiva, with GlaxoSmithKline.

Lexiva is a registered trademark of the GlaxoSmithKline group of companies.

Vertex's press releases are available at www.vrtx.com.

Conference Call

Vertex Pharmaceuticals will host a conference call and webcast on Tuesday, March 3, 2009 at 5:15 p.m. EST to review recent developments. This call and webcast will be broadcast via the Internet at www.vrtx.com. It is suggested that webcast participants go to the web site at least 10 minutes in advance of the call to ensure that they can access the slides. The link to the webcast is available on the Events and Presentations button on the home page.

To listen to the call on the telephone, dial (800) 374-0296 (U.S. and Canada) or (702) 696-4937 (International) and the conference ID number is 88366180. Vertex is also providing a podcast MP3 file available for download on the Vertex website at www.vrtx.com.

The call will be available for replay via telephone commencing March 3, 2009 at 8:00 p.m. EST running through 5:00 p.m. EST on March 9, 2009. The replay phone number for the U.S. and Canada is (800) 642-1687. The international replay number is (706) 645-9291 and the conference ID number is 88366180. Following the live webcast, an archived version will be available on Vertex's website until 5:00 p.m. EST on March 16, 2009.

Vertex Pharmaceuticals Incorporated Investors Michael Partridge, 617-444-6108 or Lora Pike, 617-444-6755 or Media Jane Kramer, 617-444-6924 or Zachry Barber, 617-444-6470

SOURCE: Vertex Pharmaceuticals Incorporated

Combination therapy eases fibromyalgia symptoms

www.reuters.com

NEW YORK (Reuters Health) - A review of previous clinical trial results shows that a multifaceted approach can be effective for treating fibromyalgia, German researchers report.

Fibromyalgia is characterized by pain, fatigue and difficulty sleeping. It's a somewhat mysterious condition with no clear-cut cause.

Dr. Winfried Haeuser told Reuters Health that German guidelines recommend "multicomponent treatment" of fibromyalgia -- "at least two components: patient education or psychological

therapy and exercise as second-line therapy for patients whose symptoms and restrictions in daily life are not sufficiently reduced by a single therapy, such as medication."

To investigate how well this strategy works, Haeuser, of Klinikum Saarbruecken, and her colleagues examined pooled evidence from nine clinical trials of multicomponent therapy involving more than 1100 patients. The researchers report the results in the medical journal *Arthritis and Rheumatism*.

The findings, Haeuser explained, "demonstrated that multicomponent treatment was superior to monocomponent treatment in relieving pain, depressed mood and fatigue and improving physical fitness."

However, she and her colleagues found, "There is strong evidence that the positive effects of multicomponent therapy on the key symptoms of fibromyalgia syndrome decline with time."

The longest follow-up was for 15 months. The researchers conclude, "Strategies to maintain the benefits of multicomponent treatment in the long term need to be developed."

SOURCE: Arthritis and Rheumatism, February 15, 2009.

Hep C highest on North Coast

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

Luke Keioskie

THE NORTH Coast has the highest rate of infection for hepatitis C in the State, despite the fact that up to 80 per cent of sufferers can be cured.

The Hepatitis C Council of NSW has found that our State houses 100,000 people infected with the disease, with the North Coast area showing the highest rates of infection at 97.4/100,000 population.

Hepatitis C is an infectious disease spread by blood-to-blood contact that can cause inflammation of the liver and lead to liver failure and cancer.

Hepatitis C Council executive officer Stuart Loveday said the need to increase treatment rates is critical.

"More than 200,000 ordinary Australians have hepatitis C, but less than two per cent of them receive treatment," he said. "This year 10,000 more people will get hepatitis C, and most of these will be young people."

Mr Loveday said awareness of the fact that the infection can cure 50 to 80 per cent of people undergoing treatment is low among both the community and health professionals.

"Some people are put off by treatment side effects, which can be severe for some people," he said.

“But liver damage often occurs slowly and silently, making it very important for people to understand their options and not wait too long to consider treatment.”

The Hepatitis C Council has launched a \$20,000 grants program to assist community health organisations and health workers to raise awareness about the risk, prevention and treatment of the disease.

For information, go to website www.hepatitisc.org.au .

Call for EU action on hepatitis death toll

<http://www.theparliament.com>

Slovenian MEP Alojz Peterle has thrown his weight behind calls for early diagnosis for those at risk from hepatitis.

Speaking in parliament, the centre-right deputy accused member states of "inertia" in their efforts to tackle the condition.

He said, "Hepatitis represents one of the major challenges for public health in Europe.

"If policy makers want to lower tomorrow's mortality and morbidity rates, they have to act today," added Peterle, who has survived a cancer scare.

His comments came at the presentation of the findings of a survey to gauge the political commitment to combat hepatitis in Europe.

The study, by the European liver patients association (ELPA), reveals that hepatitis awareness amongst national policymakers and the general public is very low.

In view of this "ignorance and neglect of a major disease" ELPA has called on the EU to promote targeted screening strategies to ensure early diagnosis for those at risk.

The event in parliament on Monday was told that current estimates indicate that in the EU 14 million people have chronic hepatitis B, while approximately nine million are infected with the hepatitis C virus.

Up to 90 per cent of hepatitis patients are unaware of their infections.

The study also found that in Austria, only nine per cent of newly diagnosed hepatitis C patients were aware of the disease and only three per cent realised that they were at risk once they had been diagnosed.

It says that only France, Spain and the UK have conducted hepatitis awareness campaigns and that France, the Netherlands, the UK and Sweden are the only countries to have developed a comprehensive national plan to fight hepatitis.

ELPA president Nadine Piorkowsky said, "If member states don't act, the EU has to guide them

in the development of targeted screening campaigns for hepatitis risk groups.

"Countries like France have proven that investment in the fight against hepatitis pays off. There is no reason why this should not be replicated by other member states."

She said the consequences of inaction will be "terrible," adding, "People infected with the virus and treated too late frequently experience severe liver damage such as liver scarring, liver cancer, or liver failure."

She said that since the vast majority of those who carry the hepatitis virus are unaware of their infection, the number of patients with such follow-on diseases will rise "dramatically".

Heiner Wedemeyer, deputy secretary of the European association for the study of the liver, said, "Liver cancer is almost always fatal and incidence has already doubled in the past 20 years.

"Since there is a strong relationship between hepatitis and liver cancer, concrete efforts have to be made to find those hepatitis carriers, so they can become patients and receive treatment before cancer can set in."

March 4, 2009

RF Ablation Linked to Improved Liver Cancer Survival

www.medscape.com

By David Douglas

NEW YORK (Reuters Health) Feb 24 - Pooled data from a review of randomized trials of percutaneous ablation therapies in hepatocellular carcinoma indicates that a radiofrequency (RF) approach offers a survival advantage, Korean researchers report in the February issue of *Hepatology*.

Lead investigator Dr. Yun Ku Cho told Reuters Health, "Recent studies comparing RF ablation and percutaneous ethanol injection revealed no consistent survival benefit of RF ablation over percutaneous ethanol injection for patients with hepatocellular carcinoma."

However, he explained, "By performing a systematic review and meta-analysis of randomized trials, we demonstrated that RF ablation showed an improved 3-year overall survival status for patients with small hepatocellular carcinomas, compared to percutaneous ethanol injection."

Dr. Cho of Seoul Veterans Hospital and colleagues analyzed data from 4 trials involving 652 patients. The pooled results showed that RF ablation was in fact significantly superior to the ethanol technique, which was associated with an odds ratio for 3-year survival of 0.477.

Nevertheless, the researchers point out that in these studies the number of patients involved was insufficient to determine initial tumor response, and there was "no real consensus regarding the definition of major adverse events. Therefore, quantitative analysis could not be performed for the local tumor progression or adverse events."

Hepatology 2009;49:453-459.

Rates of Liver Cancer are Rising, but Survival is Increasing

www.medscape.com

Roxanne Nelson

March 4, 2009 — The incidence of hepatocellular carcinoma (HCC) in the United States tripled between 1975 and 2005, with much of the increase between 2000 and 2005 occurring among men 50 to 59 years. But even though incidence and mortality have increased substantially, HCC survival rates are improving, according to a report published online February 17 in the *Journal of Clinical Oncology*.

Researchers found that the 1-year survival rate nearly doubled between 1992 and 2005, increasing from 25% to 47%. Improvement in survival rates coincided with increasing numbers of patients being diagnosed with localized stage HCC (28% in 1992 to 1993 and 44% in 2003 to 2004).

"Early screening for patients with hepatitis C, a leading risk factor for liver cancer, has directly contributed to increasing survival rates for patients living with liver cancer," said Jennifer Obel, MD, an official of the American Society of Clinical Oncology and an attending physician at NorthShore University HealthSystem, in Illinois. Dr. Obel was not involved in the study.

"When detected early, there are significantly more treatment options for liver cancer — in most cases, the earlier it is caught, the better the prognosis," she said in a statement. "This study points to the need to identify even more at-risk individuals through early-screening programs to improve prognosis with potentially curative therapy."

Infection with chronic hepatitis C virus (HCV) or hepatitis B virus (HBV) is associated with the development of HCC. More than 3 million people are chronically infected with HCV in the United States, but chronic infection with HBV, a major global risk factor for HCC, is less common. However, among certain ethnic groups residing in the United States, the researchers note, HBV is a more common risk factor than HCV.

Etiology Complex, More Data Needed

The etiology of HCC is complex, and most likely involves interactions between multiple risk factors. In this study, Sean F. Altekruze, DVM, MPH, PhD, from the National Cancer Institute (NCI), in Bethesda, Maryland, and colleagues examined data on incidence trends, mortality rates, and survival rates from NCI's Surveillance Epidemiology and End Results (SEER) cancer registries. Their goals were to monitor changes in the burden of HCC and to define the populations most at risk, in an effort to help control the disease.

"SEER registries don't tell us the etiology, so we can only speculate on what may be driving the rates," Dr. Altekruze said in an interview. "Liver cancer typically begins with a hepatic insult, such as chronic inflammation, and then may progress to cirrhosis, and ultimately HCC."

Cancer occurs at a very late stage in the process, and Dr. Altekruze emphasized that not all patients infected with hepatitis will go through these stages, although infection with HBV and/or HCV is associated with an increased risk. "It is believed that there was an epidemic of hepatitis C that began in the 1960s and extended into the 1970s," he said. "It was projected that we would be seeing an increase in rates of HCC because of that."

But hepatitis infection is not the only risk factor. "We do need studies to better understand the proportion of HCC that is attributable to hepatitis, and we need to better understand the etiology of hepatitis C," Dr. Altekruse told Medscape Oncology. "We also need to study other possible contributing factors, such as alcohol consumption, obesity, diabetes mellitus, and iron-storage diseases."

Incidence Rising Among All Ethnic/Racial Groups

Their results showed that between 1975 and 2005 the rate of HCC tripled, from 1.6 cases to 4.9 cases per 100,000 people, and incidence was also approximately 3 times higher among men than among women during this time. Between 1992 and 2005, overall incidence rates of HCC increased, with an annual change of 4.3%.

The incidence of HCC increased among all ethnic/racial groups, with the greatest annual percentage change (APC) increase seen in the American Indian/Alaska native group (5.0%). This was followed increases in black (APC, 4.9%), white (APC, 4.6%), and Hispanic (APC, 4.0%) groups. Even though the Asian/Pacific Islander group had the highest incidence of HCC, it experienced a smaller APC (1%) than other groups. During the 5-year period from 2000 to 2005, the researchers observed marked increases in incidence rates among Hispanic, black, and white middle-aged men.

During the 1992 to 2005 time period, patterns of HCC mortality were similar to those of incidence. The overall age-adjusted mortality rates rose, with an APC of 1.6%, and mortality was highest among the Asian/Pacific Islander group, followed by Hispanic, black, American Indian/Alaska native, and white groups. Although the APC significantly increased among the Hispanic (1.7%), white (1.7%), and black (1.3%) groups, it declined for the Asian/Pacific Islander group (-0.9%). Mortality rates remained stable among the American Indian/Alaska native group.

Survival Improving in Patients With Localized Disease

An additional finding was that overall survival rates increased, and 2- to 4-year cause-specific survival rates doubled. The 1-year survival rates jumped from 65% in 1992 to 1993 to 83% in 2003 to 2004 among patients with localized HCC who reported undergoing treatment. Increases in survival were also observed among patients with localized HCC who underwent surgery, from 81% in 1992 to 1993 to 91% in 2003 to 2004.

"The most dramatic improvement in survival has been among people with localized disease," said Dr. Altekruse. "If screening can detect patients with early-stage HCC, it can truly have an important impact on the burden of liver cancer, which is projected to increase over the next 20 years."

The study was supported by the Division of Cancer Control and Population Sciences, Surveillance Research Program, National Cancer Institute, National Institutes of Health. The researchers have disclosed no relevant financial relationships.

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Continuous antiretroviral therapy improves survival in HIV/hepatitis C co-infected patients with liver cirrhosis

www.aidsmap.com

Liz Highleyman & Michael Carter

Antiretroviral therapy - but not treatment for chronic hepatitis C virus (HCV) infection - was associated with significantly improved survival in HIV/HCV co-infected individuals with liver cirrhosis, researchers reported on February 10th at the Sixteenth Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal, Canada.

Maria Luisa Montes from Hospital Universitario La Paz in Madrid, Spain, presented findings from a prospective multicentre study looking at the effect of hepatitis C treatment in HIV/HCV co-infected patients with compensated cirrhosis or advanced fibrosis.

Compensated cirrhosis means that even though the liver has been heavily scarred, it is still able to perform most of its normal functions. Chronic hepatitis C is responsible for more than 90% of cirrhosis cases in HIV-positive people, the researchers noted.

A total of 248 co-infected participants were assessed to determine factors associated with survival and time to a first episode of liver decompensation, and in particular whether hepatitis C treatment improved the prognosis of patients with compensated cirrhosis.

The investigators used an expanded definition of survival that included development of liver cancer and liver transplantation in addition to death.

Liver decompensation included bleeding in the oesophagus or stomach, abdominal fluid accumulation (ascites), brain damage (encephalopathy), spontaneous bacterial infection of the abdominal lining (peritonitis) and kidney failure (hepatorenal syndrome).

The factors the investigators included in their analysis were current and nadir (lowest-ever) CD4 cell count, HIV viral load, type of antiretroviral therapy, HCV genotype, whether patients had received hepatitis C treatment and whether they achieved sustained virological response (continued undetectable HCV viral load 24 weeks after completing treatment), concurrent chronic hepatitis B, and Child-Pugh score (a measure of liver disease prognosis).

More than three-quarters (78%) of the study participants were men and the median age was 42 years. Most had a history of injecting drug use. Overall, they had well-controlled HIV disease, with 88% taking combination antiretroviral therapy at baseline, 60% receiving continuous antiretroviral treatment without interruptions for the duration of the study, and 60% with undetectable HIV viral load; the median CD4 cell count was 437 cells/mm³.

With regard to liver disease, participants had been infected with HCV for 23 years on average and had cirrhosis or advanced bridging fibrosis, diagnosed for one year on average. About three-quarters had the harder to treat HCV genotypes 1 and 4. In addition, 27% were heavy alcohol drinkers and 4% also had chronic hepatitis B.

About three-quarters were currently taking or had received treatment for hepatitis C - mostly using the standard of care regimen of pegylated interferon plus ribavirin - and the sustained

virological response rate was 24%, leaving 74% as relapsers or non-responders (1% were still undergoing treatment).

During a median 34 months of follow-up, a total of 30 endpoints were recorded: 25 deaths, 2 cases of liver cancer and 5 liver transplants. In addition, 28 patients experienced a first episode of liver decompensation, most often ascites.

The overall survival rate for co-infected patients with compensated cirrhosis was 85% at three years. In a univariate analysis, participants treated for hepatitis C were significantly more likely than untreated patients to survive during the follow-up period (91% vs 71% at three years), but the difference between sustained responders and non-responders was not significant (95% vs 90% at three years).

Hepatitis C treatment did not increase the time to a first episode of decompensation, nor did sustained response compared with non-response.

In a multivariate analysis controlling for potential confounding factors, only a baseline Child-Pugh score of 'B' or 'C' (indicating 81% and 45% probability of one-year survival, respectively) and non-continuous use of antiretroviral therapy were significantly associated with first liver decompensation and decreased survival, whilst decompensation during follow-up also predicted death, liver cancer or transplantation.

Although treatment of chronic hepatitis C was significantly associated with increased survival over three years in the univariate analysis, the investigators noted, this association disappeared after controlling for other factors.

“Continuous antiretroviral therapy and Child-Pugh scores are more important prognostic factors than anti-hepatitis C treatment”, they concluded.

They added the caveat that this study does not rule out a possible survival benefit of sustained response to hepatitis C treatment due to the low number of participants, and said longer follow-up might be needed to see an effect.

Because the success rate of hepatitis C treatment in co-infected individuals with liver cirrhosis is low, the researchers recommended that "every effort should be made to avoid progression to cirrhosis" in HIV/HCV co-infected patients - an argument for timely HCV screening, regular monitoring of liver health and prompt treatment when indicated.

Reference

Montes ML et al. Survival of HIV/HCV-co-infected patients with compensated liver cirrhosis: effect of HCV therapy. Sixteenth Conference on Retroviruses and Opportunistic Infections, Montreal, abstract 106, 2009.

Proteomics Prove Accurate In Identifying Liver Cancer

<http://www.thebostonchannel.com>

By Bonnie Prescott

Beth Israel Deaconess Medical Center staff

As the incidence of liver cancer continues to grow-- fueled in large part, by rising rates of hepatitis C infections – so too does the need for tests to help diagnose the disease at an earlier stage.

A study appearing in the January 15, 2008, issue of *Clinical Cancer Research* demonstrates that a novel mass-spectrometry based form of proteomic profiling is more accurate than traditional biomarkers in distinguishing liver cancer patients from patients with hepatitis C liver cirrhosis, particularly with regard to identifying patients with small, curable tumors. Led by researchers at Beth Israel Deaconess Medical Center (BIDMC), the study could help lead to earlier diagnostic methods – and subsequent treatments -- for liver cancer.

“Proteomics represents a potentially powerful tool for the serologic recognition of protein profiles associated with cancer,” explains co-senior author Towia Libermann, PhD, Director of the Genomics Center at BIDMC and Associate Professor of Medicine at Harvard Medical School. “Although this particular proteomics technology, SELDI-TOF MS [surface enhanced laser desorption/ionization time of flight mass spectrometry] had already proven capable of identifying liver cancer in some limited studies, this was the first time that the technology was compared side-by-side with the clinical standard biomarker in a cohort of patients at risk for developing the disease,” adds Liebermann, who is also Director of the Dana-Farber/Harvard Cancer Center Proteomics Core in the Division of Interdisciplinary Medicine and Biotechnology at BIDMC.

Over a single decade, the incidence of liver cancer (hepatocellular carcinoma) increased from 1.8 to 2.5 per 100,000 patients, in large part due to a rise in the spread of hepatitis C virus.

“Hepatitis C has become a tremendous public health problem,” explains co-senior author Nezam Afdhal, MD, Director of the Liver Center at BIDMC and Associate Professor of Medicine at Harvard Medical School. “And a significant number of hepatitis C-infected patients will go on to develop liver cirrhosis.”

Cirrhosis results when healthy tissue is replaced by scar tissue, preventing the liver from properly functioning. Cirrhosis itself is responsible for more than 25,000 deaths each year. But, adds Afdhal, secondarily, cirrhosis greatly increases a person’s chances of developing liver cancer.

“Each year, cirrhosis patients have a two to five percent chance that their condition will escalate to cancer,” he explains. “And the problem is that, right now, there is no reliable means of detecting liver cancer at an early stage, when surgical treatment is an option. Typically by the time the disease is discovered, the cancer has advanced and treatment options become much more limited.”

The best hope for early detection is cancer biomarkers, serum proteins found in altered amounts in blood or other body fluids. The current biomarker for liver cancer in clinical use is alpha fetoprotein (AFP). In many cases, patients with hepatitis C undergo routine monitoring for AFP levels as an indicator of whether tumors may have developed in their livers.

But, as Libermann explains, the AFP biomarker has a number of shortcomings, including false positives and false negatives. “AFP not only fails to detect many early tumors, but it also lacks

specificity. Consequently, elevated AFP levels could be indicators of not only cancer, but also of other liver diseases or even benign conditions, while on the other hand, many patients with small tumors will test negative for AFP.”

The authors, therefore, decided to evaluate the sensitivity and specificity of SELDI-TOF MS for the detection of liver cancer and to compare its effectiveness with AFP.

Examining serum samples of 92 patients – including 51 patients with liver cirrhosis and 41 patients with liver cancer, and among the cancer patients, individuals with both large and small (less than 2 cm) tumors -- by SELDI-TOF mass spectrometry, the investigators were able to identify an 11-protein signature that accurately discriminated between the cirrhosis and cancer patients, first in a training set (made up of 26 cirrhosis and 20 liver cancer patients), and then again in an independent validation set (consisting of 25 cirrhosis and 19 liver cancer patients). The resulting diagnostic value – 74 percent sensitivity and 88 percent specificity – compared favorably with the diagnostic accuracy of AFP (73 percent sensitivity and 71 percent specificity) as well as with two other biomarkers currently in clinical development for liver cancer, AFP-L3 and PIVKA-IL.

“Most strikingly,” notes Libermann, “in patients with small tumors (less than 2 cm), where AFP identified only three, and AFP-L3 and PIVKA-II only one each, the 11-protein signature correctly identified seven of eight patients at this early stage of disease.

“Biomarkers play a major role in all aspects of personalized medicine, not only in early disease detection, but also in outcome prediction and evaluation of therapeutic responses,” he adds. “This study provides strong evidence that serum contains early detection biomarkers and supports the notion that a combination of multiple biomarkers may prove more effective than individual biomarkers for diagnosis of liver cancer, as well as other cancers.”

This study was funded by grants from the National Institutes of Health.

March 5, 2009

Sick, seeking answers

<http://news.therecord.com>

Greg Mercer
Record Staff

After living with hepatitis C for more than 20 years, Troy Anderson knows the end is near. But he says it didn't have to be this way.

Kitchener – Troy Anderson was already carrying the virus that was silently attacking his liver when he walked into a navy recruiting office on Duke Street in 1986.

Twenty-three years later, he has only to look a few blocks from his Queen Street apartment to be reminded of his eagerness and ignorance that day.

But Anderson, now 43, doesn't have to look nearly as far for a reminder of the virus that was with him then and is with him now. With his hepatitis C in its advanced stages, he lives with

wild swings in his weight, fatigue, near-constant pain and an expert opinion that he only has a few years left to live.

For 15 years, Anderson was sick with the disease without knowing it. Eight of those years were spent in the navy, where he received regular blood tests -- but he alleges incompetence or irresponsibility kept military doctors from diagnosing his illness.

It wasn't until 2000 that his hepatitis C was diagnosed by a civilian doctor. The physician suggested he had 10 years left to live.

"When I heard that, I lost it," said Anderson, who lives alone in his 10th-floor apartment with a grey cat, Rocky.

"I know I'm not going to live past 45."

That diagnosis launched the former sailor on a long struggle with his former employer -- a string of letters, appeals and dead-ends.

Anderson's fight with the Canadian military isn't just about money, though he is asking for financial things -- including increased long-term disability pension and coverage of his funeral costs.

He wants the navy to admit its doctors made mistakes.

"This is not about revenge," he said. "What's happened to me is unacceptable."

In January 1991, when he was still a fit and trim young sailor, he became suddenly ill in Puerto Rico. There on military exercises, he visited a U.S. army hospital because he was having intense stomach pain and vomiting bright red blood.

The staff diagnosed him with alcoholic hepatitis, or inflammation of the liver, caused by excessive drinking. A U.S. doctor recommended he return to Halifax for further testing, which Anderson declined, saying he didn't understand the severity of his illness.

The doctor also asked his Canadian counterparts to follow up with the sick sailor. Anderson said the base surgeon in Halifax never contacted him.

Blood tests done at the time of his discharge in 1994 showed his liver enzymes were 20 times above normal, a sign that could suggest hepatitis C.

But no one told him, he said. No more testing was ordered.

Unknown to Anderson at the time of his release, earlier blood tests conducted by military doctors had already suggested his liver was showing signs of disease.

A civilian doctor who examined his medical records after he left the military concluded those tests were red flags that could have led to an earlier diagnosis of hep C.

"The pattern of liver-test abnormalities was not consistent with alcohol-induced liver injury and was more indicative of a viral disease," Dr. Mark Levstik, a liver specialist at the University of Western Ontario, wrote in a letter to Veterans Affairs Canada after Anderson left the military.

The Canadian Forces declined to speak about Anderson's case for this story, citing privacy rules.

Instead, an official offered this: "The (Canadian Forces) considers the health needs of military members a priority. If the medical personnel become aware of any medical condition they would be obligated to inform a CF patient," Major André Berdais, a spokesperson for Canadian Forces' health services, said in an email.

He also said a test for hep C was not discovered until 1990, four years before Anderson left the navy.

Berdais added that outgoing members of the military are only given their medical records upon request. Anderson obtained his through an access-to-information request.

There's no way of telling how many people Anderson may have unknowingly infected. From Canadian Blood Services, though, he knows of at least one -- the recipient of a blood donation he gave in 1987 while stationed at CFB Esquimalt in B.C. Unfortunately, the agency said it can't find the person. Anderson suspects the recipient was a military colleague.

"I want to find this person and I want to apologize to their family," Anderson said. "Because I know no one else will."

The Canadian Blood Services agency traced his infection back to an operation he had in an Owen Sound hospital in 1985 to fix a bleeding ulcer. He received tainted blood in that operation, and last November the agency give him a compensation package.

It's enough to allow him to "live comfortably" for his remaining years, which he says aren't many. He used part of the money to buy a big-screen TV and a leather recliner for his living room.

He also receives a \$1,900-a-month veterans' disability pension for post-traumatic stress disorder and for an injury to his arm while working in a navy shop in Halifax.

He appealed a decision by Veterans Affairs to deny him a disability pension for his Hep C. The department's review board upheld the decision, ruling there was "no medical evidence that his delayed diagnosis caused irreversible harm."

His physician, Dr. Ketan Patel, strongly disagrees. So, too, does much of the civilian medical community, which believes early detection of hepatitis C can slow or stop the disease's progression.

"I feel my life was absolutely worth nothing to them," said the Pakistan-born Anderson.

He doesn't regret his career in Canada's navy, though. It gave him a chance to travel the world as a hull technician, a sort of jack-of-all-trades called upon when things break on ships.

But Anderson wonders how his life might have been extended had he had known earlier about his hep C. He suspects his indulgence in the navy's heavy-drinking culture -- endorsed by bar prices like 25-cent shots and 50-cent bottles of beer -- worsened the damage to his liver.

He admits he's an alcoholic. When he was posted in Bosnia, a position he volunteered for six months before he left the military, he was drinking at least a dozen beers every night.

Since his diagnosis, he says, he's reduced his consumption to the occasional glass of red wine.

He says he tried to recruit a lawyer three times but was invariably told his case would be too costly, too time-consuming and had little guarantee of success.

Former Kitchener Centre MP Karen Redman also backed his bid for a resolution, writing letters of support to the ministers of Veterans Affairs and National Defence. Nothing changed.

Anderson asked the military's ombud to investigate but was told the office's mandate only stretches back to the date of its creation in June 1998.

That's not to say the ombud's office didn't review his files. It did, and found he had been handled fairly.

"My conclusion is that your concerns were treated seriously," wrote Aviva Farbstein, an ombud lawyer who asked Anderson to stop contacting her office.

Farbstein also wrote that further investigation into Anderson's complaint "would not be in the public interest."

Anderson, meanwhile, has grown weary of his fight with the military. This is no way to treat a dying sailor who served his country, he said.

He's tired of being sick, tired of being alone, tired of being tired all the time. He just wants to find a way to enjoy his remaining years.

"I don't want to fight this anymore," Anderson said. "But this . . . it's always lingering over my head."

NYC dialysis center tied to 9 hepatitis C cases

<http://www.mercurynews.com>

By KAREN MATTHEWS Associated Press Writer

NEW YORK—A New York City kidney dialysis center remains closed after state health inspectors found that nine patients contracted hepatitis C there over a seven-year period, according to a report released Thursday.

The Life Care Dialysis Center in Manhattan shut its doors in September after the inspectors found unsanitary conditions including blood on chairs and machines, the federal Centers for Disease Control and Prevention said in its summary of the investigation results.

Hepatitis C is a liver disease caused by a virus and spread by contact with the blood of an infected person.

According to the report in the CDC's *Morbidity and Mortality Weekly Report*, Life Care Dialysis Center staff members failed to change gloves between patients or to clean and disinfect equipment properly.

Once the patients tested positive for hepatitis C, the clinic failed to inform the patients or to notify the city Health Department, the CDC said.

After the first case was discovered, letters went out to more than 600 patients who had received dialysis there urging them to get tested.

The for-profit dialysis center was operated by DaVita Inc., an El Segundo, Calif.-based company that runs more than 1,400 outpatient dialysis centers. A message left at the company Thursday was not immediately returned.

March 6, 2009

Results may determine fate of Human Genome Sciences

<http://washington.bizjournals.com>

Vandana Sinha Staff Reporter

Washington Business Journal

Fruition or failure: The test results on a hepatitis drug could be the fruition of years of hard work or lead to the demise of Tom Watkins' company.

Sometime this month, Rockville's Human Genome Sciences Inc. will receive conclusive results from arguably its most crucial clinical trials of a hepatitis C drug, what analysts consider the 16-year-old company's best shot at breaking into the commercial market.

Positive data would boost HGSI's plan to apply by fall for federal approval to begin selling the drug, its first ever for pharmacy shelves.

But market insiders agree that a clinical trial failure would be disastrous for the 880-person company, which has piled up a \$2 billion debt over its lifetime and, more dauntingly, has more than \$400 million in debt coming due by 2012.

"Our view is that the trial should meet its primary endpoint," said Edward Tenthoff, managing director of Piper Jaffray and Co., a research organization. But if the trial fails, which is a "long shot," Tenthoff said, "the company would be in very serious trouble. The stock would be under severe pressure. At this point, the debt level is higher than the cash. We would see the stock basically fold."

This is a test of nerves for HGSI at a time when, ironically, the company is basking in its biggest success so far. HGSI shipped its first product last month, an anthrax treatment called ABThrax to the Department of Health and Human Services, and is expecting \$150 million in its first sales revenue from the contract this year.

“This is likely to be the year a lot of the painstaking work over many, many years comes to positive fruition for our company and our shareholders,” said HGSI’s chief executive officer, Tom Watkins, in a recent interview. “You know that the people around you are doing things right. While everything may not work out, you know you’re doing everything you can. And this company is doing everything it can to serve patients and get these opportunities out. Are we anxious? Sure. But we’re more excited.”

In this final stage of studies, HGSI need only prove that its hepatitis C drug, Albuferon, which is given every two weeks, works as effectively as its competitors’ drugs, which are all weekly doses.

While analysts see room for HGSI in an estimated \$2.4 billion hepatitis C market, the field is still dominated by Roche and Schering-Plough Corp., pharmaceutical heavyweights that make HGSI look skeletal in comparison. HGSI also will have to study Albuferon’s compatibility with emerging antibiotics expected to revolutionize the hepatitis C drug market.

For now, the company argues it is halfway there, having reached its goal of showing Albuferon’s overall effectiveness in similar clinical trials late last year on two different, albeit easier-to-treat, strains of the debilitating disease.

However, HGSI has not escaped skepticism. After receiving reports last year of pulmonary problems with Albuferon, the company had to significantly lower the doses for clinical-trial patients in a high-profile setback that, in one day, chopped its stock price nearly in half. HGSI has been unable to return to its \$10 levels since.

While some observers worried a lower dose would make Albuferon a weaker challenger to its rival drugs, others say they are closely watching the potential for harmful side effects in the upcoming trial data.

Despite HGSI’s enthusiastic lineup of existing late-stage products, most analysts still see Albuferon as the headliner. ABThrax is geared primarily to the government, and two drugs are licensed to other pharmaceutical companies, which are developing them.

HGSI’s other key drug candidate, a lupus treatment called LymphoStat-B, is undergoing advanced clinical trials whose results are due in July and November. But it does not inspire much confidence on Wall Street.

“Most people do not expect the lupus drug to work,” said Liisa Bayko, director and senior analyst with JMP Securities LLC, who believes Albuferon will get a passing grade but describes lupus as an inordinately difficult disease to treat.

“It’s a very high-risk program, frankly,” she said.

That only ups the ante for the Albuferon trials in a recession-weary investor community that dragged HGSI’s stock down below \$2 by the first week of March.

“If this doesn’t work, you’ve got a company with two failed Phase 3 programs, and they’ve dumped a lot of money in it,” Bayko said. “It becomes a solvency issue.”

Electrochemical solution to virus detection

<http://www.rsc.org>

Paul Cooper

A user-friendly approach for detecting the hepatitis C virus has been developed by scientists in China.

Hepatitis C is a blood-borne disease that affects the liver and accounts for almost half of the 4000 liver transplantations done each year. Monitoring the hepatitis C virus (HCV) in the body can be used to diagnose and confirm active infections and can also be used to assess a patient's response to therapy. Now, Hui Zhang, Chenxin Cai and co-workers at Nanjing Normal University have developed an electrochemical way to detect and quantify HCV.

The approach uses a gold electrode coated with a DNA probe labelled with the dye thionine. Samples containing virus are pre-treated with a transcriptase enzyme to produce complementary DNA (cDNA), a synthetic oligonucleotide related to the HCV. When the electrode is placed in the sample, the DNA probe binds to the cDNA to form a DNA double helix. If this is then treated with an endonuclease enzyme, the helix is cleaved, removing the thionine label. The detection works by monitoring the loss of thionine's voltammetric signal after the enzyme treatment: the smaller the signal, the more cDNA in the tested sample. Using this technique, Cai's team was able to detect HCV in real patient samples.

Cai explains that there are other methods for detecting HCV but these are considered to be 'time-consuming and laborious, and require sophisticated and expensive instruments. This electrochemical approach not only allows for ease of performance and good specificity but can also be used as a general method of DNA detection,' he says.

Bernie Kraatz, an expert in biosensors and detection at the University of Western Ontario, London, Canada, says that 'the system appears surprisingly robust to potential contaminants such as proteins that tend to pollute gold surfaces and is able to work under real-to-life conditions. This alone is noteworthy and interesting and demonstrates the potential usefulness of this approach.'

The researchers say that they hope their technique can be further developed and be used for clinical diagnosis.

HBV Polymerase Resistance Mutations May Be Antagonistic

www.medscape.com

By Will Boggs, MD

NEW YORK (Reuters Health) Mar 04 - Susceptibility of hepatitis B virus (HBV) previously resistant to lamivudine may be restored as resistance to adefovir develops, according to a report in the March *Journal of Medical Virology*.

"Most bacterial- and HIV-resistance is cumulative; newly acquired resistance comes on top of existing resistance," Dr. Hans L. Zaaijer from Academic Medical Center, University of Amsterdam, told Reuters Health. "Fortunately, it seems that HBV sometimes is forced to choose

between resistance mechanisms."

Dr. Zaaijer and colleagues described the effect of lamivudine and adefovir combination in two patients who were resistant not only to lamivudine, but also to adefovir. They underwent serial monotherapy with lamivudine and then adefovir.

Complete virological breakthrough occurred in both patients during lamivudine monotherapy and then again during adefovir monotherapy, the authors report.

After lamivudine was ultimately added to adefovir, the adefovir resistance mutation persisted in both patients in all clones, but the lamivudine-related mutations did not return.

During combination therapy, the HBV-DNA level decreased 1000-fold despite the earlier virological breakthrough during lamivudine monotherapy, the researchers note.

"Apparently," the investigators say, "HBV resistance to different HBV polymerase inhibitors may be antagonistic; resistance to one drug may restore the susceptibility to another drug."

"Antagonistic HBV resistance mechanisms deserve further attention," the authors conclude. "If chronic hepatitis B is to be treated with a combination of drugs, a combination of drugs with antagonistic patterns of resistance seems superior to other combinations of HBV inhibitors."

"Prescribing lamivudine plus adefovir for patients who failed on serial monotherapy with these drugs is not advisable," Dr. Zaaijer explained. "Nowadays new potent HBV inhibitors, rarely inducing resistance, are available."

He added, "Regarding long-time suppression of HBV in naive patients, monotherapy with tenofovir or entecavir seems the way to go. Nevertheless, in the long-run it may become necessary again to know which antiviral combinations display antagonistic resistance."

J Med Virol 2009;81:413-416.