

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Week Ending: November 15, 2008

In This Issue:

- [Lamivudine-Resistant Mutation Among Treatment-Naïve Hepatitis B Patients May Be Associated With Treatment Failure: Presented at AASLD](#)
- [I caught hepatitis C at birth - but now I'm cured](#)
- [Roche, InterMune And Pharmasset Announce Initiation Of INFORM-1, The First Dual-Combination Clinical Trial With Oral Antivirals In Hepatitis C](#)
- [Profectus BioSciences Executes an Assignment and License Agreement with Wyeth for Vaccines against HIV, HCV, HPV and HSV](#)
- [Triglycerides may be blood fat to watch: studies](#)
- [Going to the doctor? Go prepared, expert advises](#)
- [Spike in Hepatitis C cases reported; health officials attribute increase to change in reporting method](#)
- [Does HBV infection induce acute cellular DNA damage?](#)
- [AASLD 2008: Biomarkers May Guide Sorafenib Treatment for Liver Cancer](#)
- [AASLD 2008: Mortality Lower for Early Liver Transplant in Healthier Patients](#)
- [Rifaximin Plus Lactulose Reduces Severity of Hepatic Encephalopathy](#)
- [Healthcare reform gets backing in Congress](#)
- [HIV treatment safe and effective in South African patients with hepatitis B co-infection, but co-infection frequent](#)
- [Human Genome Sciences Awaiting Crucial Albuferon Data](#)
- [Migrants, drinking push up liver cancer rates](#)
- [Biotech Mailbag: Vertex Has Verve](#)

Lamivudine-Resistant Mutation Among Treatment-Naïve Hepatitis B Patients May Be Associated With Treatment Failure: Presented at AASLD

<http://www.docguide.com>

By Arushi Sinha

SAN FRANCISCO -- November 7, 2008 -- Patients with hepatitis B virus (HBV) appear to have a high prevalence of lamivudine resistance genetic mutations that result in treatment failure, researchers reported here at the Liver Meeting 2008, the 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD).

In these patients, treatment with adefovir or tenofovir proved more effective than treatment with lamivudine, said investigator Scott Fung, MD, Department of Medicine, University of Toronto, Toronto, Ontario.

The aim of this study was to examine the role of a patient's genetic profile in influencing the efficacy of treatment for HBV, he said in a presentation on November 2.

The goal was to document the incidence of antiviral resistance (AVR) mutations among a population of patients diagnosed with chronic HBV who had not received prior treatment. The researchers hypothesised that AVR mutations in a patient may prevent effective treatment with lamivudine and thus reduce clinical outcomes.

"We thought that there might be a low level of natural resistance," explained Dr. Fung.

The study enrolled 209 treatment-naïve patients aged a mean of 38 years with a mean HBV DNA of 5.7 +- 2.3 log₁₀ IU/mL (male, 69%). Incidence of cirrhosis in the cohort was 15%.

The range of HBV genotypes was type A (8%), type B (32%), type C (47%), and type D (10%). Patients' AVR mutations were the following: rtL180M 10%; rtM204V/I, 12%; rtL80V/I, 9%; rtV173L, 3%; rtA181V/T, 0%; rtN236T, 0%.

Of these patients, 6 patients with genetic AVR mutations were treated with nucleoside therapy; 3 patients received lamivudine 100 mg daily for an average of 11 months, while 3 patients were treated with adefovir 10 mg daily or tenofovir 300 mg daily for an average of 7 months.

One of the patients treated with lamivudine exhibited a primary nonresponse, and 2 exhibited breakthrough infection. By contrast, all 3 patients treated with either adefovir or tenofovir demonstrated undetectable HBV DNA levels.

It was also found that those patients who were both male and exhibited a high viral load were at greater risk of having AVR mutations.

Results showed that 21 patients (10%) had lamivudine resistance at baseline.

Mutations resulting in a resistance pathway were fairly common, occurring in about 10% of patients. For those patients who did have the resistant mutation, treatments other than lamivudine, such as adefovir or tenofovir, proved more effective.

Overall, the findings suggested that creating a genetic profile for antiviral resistance is important and can influence therapeutic regimens.

"In this study, we probed over 200 treatment-naïve patients, and to our surprise we found that there is resistance to a commonly-used agent for the treatment of chronic hepatitis B," said Dr. Fung. "We should therefore be using agents that have no known resistance at baseline."

[Presentation title: Lamivudine-Resistant Mutation Among Treatment-Naïve Hepatitis B Patients Is Common and May Be Associated With Treatment Failure. Abstract 888]

Nov 9, 2008

I caught hepatitis C at birth - but now I'm cured

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

By Hilary Freeman

Six years ago, doctors told Louise Davage she might be dead before the age of 50.

Like the majority of the estimated 500,000 affected in the UK, the 24-year-old from Bedfordshire was unaware she had hepatitis C.

Louise had contracted the virus - which can survive in blood outside the human body for up to three months - from her mother who had herself been infected by a blood transfusion while giving birth.

'Mum was diagnosed in 2000 after reading a magazine article that advised those who'd had a blood transfusion before routine screening began in 1991 to get tested,' says Louise.

'We were all tested but while my brother and sister got the all-clear, I was positive. It was a terrible shock.'

There is no vaccine and it was, until recently, incurable. There are five major hepatitis viruses, A to E, all of which are distinct and transmitted in different ways, but all of which cause similar problems in the body.

Although hepatitis C is often symptomless, some people suffer fatigue, aches, anxiety and loss of appetite. Long-term infection causes liver damage and can lead to liver failure and liver cancer. Left untreated it can dramatically shorten life expectancy.

Thanks to advancements in medical treatment, Louise is now free of the virus - and the stigma it brought with it.

'Some people didn't understand it wasn't because of anything I'd done,' says Louise. 'One girl at college assumed I was a drug addict and would not use the same toilet in case she caught it. I was devastated.'

Today, Louise is proud that her portrait is in a photography exhibition called FaCe It, the Department of Health's hepatitis C public awareness campaign, touring the UK for the past three years. She agreed to take part to help dispel the misconceptions surrounding the disease.

The hepatitis C virus is spread through contact with the blood of an infected person. It cannot be caught through everyday contact, although it is possible but rare to pass on during unprotected sex.

Famous sufferers include Pamela Anderson and the late Body Shop founder, Anita Roddick.

Methods of transmission include injecting or snorting (inhaling) drugs, which can also cause bleeding; having a tattoo or piercing with unsterilised equipment; receiving a blood transfusion before 1991 or a blood product before 1986 (pre-screening); or having medical or dental treatment abroad.

It can also be passed on by sharing a razor or toothbrush with an infected person and it may be passed by an infected mother to her baby before or during the birth.

According to Ray Poll, nurse consultant for viral hepatitis at the Royal Hallamshire Hospital, 80 per cent of those infected develop the chronic form of the disease.

'Once infected, the virus travels to the liver where it replicates,' says Poll. 'The immune system fights it, causing inflammation and, over time, this leads to scarring within the liver, causing it to lose function.'

There are seven different strains of hepatitis C, labelled with numbers. It is possible to be infected with one or more strain.

Hepatitis C used to be treated with standard Interferon, a drug that stimulates the immune system to attack the virus, but it often proved ineffective.

However, since January 2004, the National Institute for Health and Clinical Excellence (NICE) has recommended a combination of a drug called Pegylated Interferon Alpha, which is administered by weekly injections, and Ribavirin, taken as daily tablets.

Treatment lasts up to 12 months, after which time up to 80 per cent of patients are completely cured.

Louise began six months of treatment in July 2007 and by November last year she was clear of the virus.

'I cannot describe my relief. Now I'm a young woman with a future.'

'Although my liver won't ever repair itself fully, it won't deteriorate any more and I should live a normal, healthy life.

'I would urge anyone who thinks they're at risk to get a blood test done. That simple test saved my life.'

www.nhs.uk/hepc .

Nov 10, 2008

Roche, InterMune And Pharmasset Announce Initiation Of INFORM-1, The First Dual-Combination Clinical Trial With Oral Antivirals In Hepatitis C

<http://www.medicalnewstoday.com>

Roche (SWX:ROG), InterMune, Inc. (Nasdaq: ITMN) and Pharmasset (Nasdaq: VRUS) today announced that the first patients have been dosed in an innovative clinical trial in patients chronically infected with the hepatitis C virus (HCV). The trial (run in centers in Australia and New Zealand) is the first to investigate the combination of two oral antiviral molecules in the absence of interferon.

The initial study will evaluate the safety and combined antiviral activity of R7227 (ITMN-191), a protease inhibitor, and R7128, a polymerase inhibitor, in 14 days of combination therapy in treatment-naïve patients infected with HCV genotype 1.

This direct antiviral combination study represents an important first step in evaluating the therapeutic potential of an all-oral, interferon-free combination treatment for HCV. Roche is uniquely positioned to develop all-oral combination studies in HCV through its collaborations with InterMune and Pharmasset, which provide access to both protease and polymerase inhibitors, respectively.

With InterMune, Roche is developing R7227, an HCV protease inhibitor compound to be used in combination with PEGASYS® (peginterferon alfa-2a) and COPEGUS® (ribavirin), the current standard of care (SOC). Concurrently with Pharmasset, Roche is developing R7128, an HCV RNA polymerase inhibitor, also for therapy in combination with PEGASYS® and COPEGUS®. Both of these molecules have successfully completed Phase 1 monotherapy studies, have been dosed in combination with PEGASYS® and COPEGUS® and both have individually demonstrated their efficacy against HCV.

Current standard of care for HCV comprises pegylated interferon plus ribavirin, for a duration that is dependent upon factors such as genotype of the virus. For the most difficult to treat genotype 1 virus, a 48-week treatment course generally results in sustained viral response in about 50% of patients. PEGASYS® and COPEGUS® are the current foundation of HCV treatment and the preferred pegylated interferon therapy of choice for most HCV antiviral agents in development.

Nick Cammack, Leader of the Virology Disease Biology Leadership Team at Roche stated: "It is exciting to be at the forefront of designing innovative clinical approaches in fighting this chronic disease together with our partners, InterMune and Pharmasset. Our approach demonstrates our strong interest in combining molecules in development and investigating all possibilities that may enable us to deliver a new standard of care for patients with HCV."

Dan Welch, Chairman, Chief Executive Officer and President of InterMune, said, "The goal is to develop a treatment regimen that is better tolerated, shorter in duration and delivers higher sustained viral response rates. We are pleased to participate in the first clinical exploration of an all-oral, direct antiviral regimen towards that goal."

"The combination of oral antiviral therapies for HCV represents an exciting step in the evolution of HCV treatment" stated Patrick Higgins, Executive Vice President of Marketing and Sales at Pharmasset. "We believe the development of an all oral treatment regimen may help attract many more patients into therapy that are currently not on treatment."

About R7227 (ITMN-191)

R7227 is an inhibitor of HCV NS3/4A protease activity, and has produced multi-log₁₀ reductions in circulating HCV RNA in chronic HCV patients when administered for 14 days as monotherapy. In support of clinical studies that will combine R7227 with R7128, including the INFORM-1 study, InterMune, Roche and Pharmasset have investigated in vitro the combined antiviral effect of these compounds.

About InterMune

InterMune is a biotechnology company focused on the research, development and commercialization of innovative therapies in pulmonology and hepatology. InterMune has a pipeline portfolio addressing idiopathic pulmonary fibrosis (IPF) and hepatitis C virus (HCV) infections. The pulmonology portfolio includes the Phase 3 program, CAPACITY, which is evaluating pirfenidone as a possible therapeutic candidate for the treatment of patients with IPF and a research program focused on small molecules for pulmonary disease. The hepatology portfolio includes HCV protease inhibitor ITMN-191 (R7227) in Phase 1b, a second-generation HCV protease inhibitor research program, and a research program evaluating a new target in hepatology. For additional information about InterMune and its R&D pipeline, please visit <http://www.intermune.com>.

About R7128

R7128, being developed for the treatment of chronic HCV infection, is a pro-drug of PSI-6130, a cytidine nucleoside analog inhibitor of HCV RNA polymerase. A pro-drug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. R7128 has shown in vitro activity against all of the most common HCV genotypes (1, 2, 3 and 4).

About Pharmasset

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

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America and Europe. Clevudine is already approved for HBV in South Korea and marketed by Bukwang Pharmaceuticals in South Korea under the brand name Levovir. R7128, an oral treatment for chronic HCV infection, is in a 4-week Phase 1 clinical trial in combination with Pegasys(R) plus Copegus(R). Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.
<http://www.pharmasset.com>.

Source: Roche

Profectus BioSciences Executes an Assignment and License Agreement with Wyeth for Vaccines against HIV, HCV, HPV and HSV
<http://www.centredaily.com>

Leading R&D Company Will Continue Research for Both Therapeutic and Preventative Vaccines of Chronic Viral Diseases

Profectus BioSciences, Inc. (Profectus) announced today that it has executed an Assignment and License Agreement with Wyeth Pharmaceuticals that provides Profectus therapeutic/prophylactic vaccine programs for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Human Papilloma Virus (HPV) and Herpes Simplex Virus (HSV). These programs combine the Wyeth proprietary technologies in the fields of DNA and vectored vaccines used alone and in a prime-boost strategy to prevent and treat infections.

The Agreement also provides Profectus with access to an extensive portfolio of intellectual property, research reagents, equipment, governmental funding and clinical trial products.

"Bringing the Wyeth portfolio into Profectus boosts our ability to develop innovative ways to treat patients inflicted with some of the most destructive viral diseases of our day," said Profectus President & CEO Shawn O'Brien. "The breadth and strength of the Wyeth portfolio, coupled with our expertise, will enable us to deliver a new class of vaccines into infected individuals with the first human trials projected to begin in 2009 for HIV followed closely by HCV. We are proud and honored to be the recipient of this portfolio and look forward to advancing this exciting class of vaccines to reduce morbidity and mortality."

The newly formed world-class team has over 150 years of combined experience in developing and delivering vaccines. One notable addition is John Eldridge, Ph.D., former VP of Wyeth Vaccines who joined Profectus as CSO, Vaccines.

About Profectus BioSciences Inc.

Profectus Biosciences is an R&D company dedicated to harnessing the immune system to prevent and treat chronic viral diseases and cancers through the delivery of proprietary prime/boost vaccines and small molecules. Profectus BioSciences Inc. commenced operations in early 2005. For more information please visit: www.profectusbiosciences.com.

Nov 11, 2008

Triglycerides may be blood fat to watch: studies

www.reuters.com

By Julie Steenhuysen

CHICAGO (Reuters) - For people keeping track of their blood fats, triglycerides may be the new lipid to watch, researchers said on Tuesday.

A study earlier this week found that the percentage of U.S. adults with high triglycerides had doubled over the past three decades, likely driven by climbing obesity rates.

In another study, the largest yet, Danish researchers reported on Tuesday that a blood test that does not require fasting showed a strong link between high triglyceride levels and the risk of stroke caused by a blood clot.

Taken together, the studies suggest the need for better management of triglycerides, a blood fat that typically has played second fiddle to low-density lipoprotein or LDL, known as the "bad" cholesterol because of its role in causing heart attacks and strokes.

Cholesterol-lowering drugs known as statins help reduce LDL, but they often do not address high triglycerides, a blood fat derived from the fats people eat and fats in the body. Triglycerides are an independent risk factor for heart disease, the leading cause of death in the United States.

Triglycerides and other lipids are typically measured after an eight- to 12-hour fast.

In the Danish study, published in the Journal of the American Medical Association, Borge Nordestgaard of Copenhagen University Hospital studied levels of nonfasting triglycerides to see how well they could predict stroke risk.

The study followed nearly 14,000 people in Copenhagen for 31 years and found a clear correlation between higher levels of triglycerides and stroke.

For example, a man 55 or older with the highest triglyceride levels -- above 443 milligrams per deciliter -- has a 17 percent risk of a stroke in 10 years.

That compared with about a 3 percent risk for men in the lowest triglyceride group -- 89 milligrams per deciliter.

"Nonfasting triglycerides may be even better than fasting at predicting risk," Nordestgaard said in a telephone interview.

He said the nonfasting tests were far more convenient for patients, a factor that may lead more people to get tested.

Triglyceride Levels Double

A U.S. study presented earlier this week at a meeting of the American Heart Association in New Orleans found triglyceride levels were on the rise.

The 30-year study of a large government health survey found that while LDL levels had fallen, the percentage of adults with high triglyceride levels had doubled.

"As the LDL story gets solved by the use of statins, triglycerides are emerging as the new important lipid risk factor," Dr. Jerome Cohen of St. Louis University School of Medicine in Missouri, who worked on the study, said in a telephone interview.

He said the study suggested the dramatic increase in the number of obese Americans may help explain the spike.

Dr. Irene Katzan of the Cleveland Clinic in Ohio, who was not involved in either study, said the studies and others like them reflected a growing focus on controlling triglycerides, which have been "one of these poor sisters of the lipid world."

"It's finally going to get its due attention," she said.

(Editing by Maggie Fox and Peter Cooney)

Going to the doctor? Go prepared, expert advises

www.reuters.com

By Megan Rauscher

NEW YORK (Reuters Health) - To make the most of your next visit to the doctor -- be prepared, proactive and "pleasantly assertive," Dr. Michael Pignone, chief of general internal medicine at University of North Carolina at Chapel Hill advises.

"Have an agenda. Write down the problems that need to be addressed. It helps the doctor a whole lot if you can give him a quick synopsis of your agenda for the visit. The more you can have a plan going in the better," Pignone noted in a telephone interview with Reuters Health.

It's also important to know your medical history and medications. "Doctors need to know what tests you've had - and when - as well as what medications you're taking," Pignone said. "Without that information, they might mistakenly re-order tests or prescribe medication that has a bad interaction with something you're already taking."

It's also important to tell your doctors about your values and lifestyle. It's not something patients think about, Pignone said, but "it doesn't make sense to agree to a treatment plan you know you won't follow."

Research has shown that patients who prepare for a doctor's appointment are likely to get better care and come away more satisfied than those who do not.

If you don't go in prepared, odds are you'll forget something, Pignone noted, and in the current "fee-for-service" health care model, "you can't just pick up the phone and ask the doctor."

"The current system is antiquated and rewards face-to-face visits and especially rewards procedures over the cognitive work, when it turns out that most of the care that needs to happen, especially in the care of older adults, is that cognitive work," he said.

In the era of chronic disease, Pignone said, only a minority of patients have conditions that require a face-to-face office visit. "Especially if the patient has been appropriately trained in some of the self-monitoring -- like checking their blood sugar or blood pressure or assessing their shortness of breath if they have lung disease -- then much of it can be done over the phone, with various adjustments to medication dose."

Pignone predicts that 5 years from now, the future doctor's office might look very different. One health care reform proposal called the "medical home" model would grant reimbursement to doctors for time spent caring for patients by phone or email.

"If I could get paid at the same rate for my time by doing email or talking on the phone as I can for doing exactly the same work in the office, it would allow me to structure my day better and it certainly would be better for patients," Pignone said.

Spike in Hepatitis C cases reported; health officials attribute increase to change in reporting method

<http://www.sanluisobispo.com>

Bob Cuddy

The number of chronic Hepatitis C cases has more than doubled San Luis Obispo county this year, but the spike is due to a change in the way cases are reported, rather than more people having the disease, health officials said.

According to the Health Department's report on communicable diseases, there were 835 cases of the disease reported through September. That is up from 366 for all of last year. But the numbers should not be taken as alarming, said Penny Borenstein, health agency director. "It doesn't mean the person is ill," Borenstein said. "It means that at some point the person has been exposed." A vagueness in the way cases are reported has been clarified, she said, and it has caused the numbers to jump. It's "an artifact of increased reporting."

Hepatitis C is most commonly transmitted through intravenous drug use. The numbers of reported cases of Chlamydia, Valley Fever, and gonorrhea are all down from last year, according to the chart, published in the county's public health bulletin.

Does HBV infection induce acute cellular DNA damage?

<http://www.eurekalert.org>

Eukaryotic cells employ multiple strategies of checkpoint signaling and DNA repair mechanisms to monitor and repair damaged DNA. There are two branches of the checkpoint response pathway, ataxia telangiectasia-mutated (ATM) pathway and ATM-Rad3-related (ATR) pathway. Virus replication presents the host cells with large amounts of exogenous genetic material, including DNA ends and unusual structures. Therefore, infected cells recognize viral replication as a DNA damage stress and elicit DNA damage signal transduction, which ultimately induces apoptosis as part of host immune surveillance. There was no evidence so far that the ATM/ATR kinases or their downstream pathways are triggered by HBV infection.

A research article to be published on October 28, 2008 in the *World Journal of Gastroenterology* addresses this question. This research group was led by Dr Hui Zhong from Beijing Institute of Biotechnology, China.

Using HL7702 hepatocytes with HBV-positive serum as material, they evaluate protein expression levels in HBV infected cells or in non-infected cells; immunofluorescence to show ATR foci and Chk1 phosphorylation foci formation; flow cytometry to analyze the cell cycle and apoptosis; ultraviolet radiation (UV) and ionizing radiation (IR) treated cells to mimic DNA damage; Trypan blue staining to count the viable cells.

They found that HBV infection induced increased steady state of ATR protein and increased phosphorylation of multiple downstream targets including Chk1, p53 and H2AX. In contrast to ATR and its target, the phosphorylated form of ATM at Ser-1981 and its downstream substrate Chk2 phosphorylation at Thr-68 did not visibly increase upon infection. However, the level of Mre11 and p21 were reduced beginning at 0.5 h after HBV-positive serum addition. Also, HBV infection led to transient cell cycle arrest in the S and the G2 phases without accompanying increased apoptosis. Research on analyzing cell survival change upon radiation followed HBV infection showed that survival of UV treated host cells was greatly increased by HBV infection, owing to the reduced apoptosis. Meanwhile, survival of IR treated host cells was reduced by HBV infection.

Their result indicated that HBV induces cellular DNA damage response dependent on ATR but escapes the consequences of activation of the DNA damage checkpoint by degradation of checkpoint proteins on different levels. The implication of this is that with time, persistent HBV infection may lead to the accumulation of a variety of mutations which would ultimately give rise to HCC.

Reference:

Zhao F, Hou NB, Yang XL, He X, Liu Y, Zhang YH, Wei CW, Song T, Li L, Ma QJ, Zhong H. Ataxia telangiectasia-mutated-Rad3-related DNA damage checkpoint signaling pathway triggered by hepatitis B virus infection. *World J Gastroenterol* 2008; 14(40): 6163-6170
<http://www.wjgnet.com/1007-9327/14/6163.asp>

Nov 12, 2008

AASLD 2008: Biomarkers May Guide Sorafenib Treatment for Liver Cancer

Laurie Bouck
www.medscape.com

November 5, 2008 (San Francisco, California) — Certain tumor and plasma biomarkers can indicate whether **sorafenib (Nexavar, Bayer HealthCare Pharmaceuticals in collaboration with Onyx Pharmaceuticals)** will extend the time to progression of hepatocellular carcinoma (HCC), according to new research.

In an analysis of data from 602 advanced HCC patients from the phase 3 Study of Heart and Renal Protection (SHARP), researcher Joseph Llovet, MD, from the Barcelona Clinic Liver Cancer Group, Hospital Clinic Barcelona, in Spain, and the Division of Liver Diseases Recanati/Miller Transplantation Institute, Mount Sinai School of Medicine, in New York City, and colleagues looked at 7 biomarkers to see how sorafenib affected disease progression and survival. Dr. Llovet presented his findings here at The Liver Meeting 2008, the 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD).

Sorafenib is an approved renal cancer treatment, from Bayer HealthCare, now being tested as a promising liver cancer treatment. It is also being investigated as an adjuvant therapy for breast cancer, melanoma, and non-small-cell lung cancer.

In Dr. Llovet's study, patients were randomized to receive either oral sorafenib 400 mg twice a day or placebo. Researchers used tumor biopsies to analyze the biomarker pERK, and analyzed 6 plasma biomarkers (BEGF, soluble (s) vascular endothelial growth-factor receptor [VEGFR]-2, s VEGFR-3, s-c-Kit, hepatocyte growth factor [HGF], and Ras p21) at baseline and 12 weeks. About half the patients were available at 12 weeks for plasma analysis.

Independently, VEGF and c-Kit were associated with survival. At 12 weeks, patients in the sorafenib cohort had decreased levels of most of the plasma biomarkers, including c-Kit (–33.9%; $P < .0001$), but increased VEGF levels (+195.7%; $P = .010$).

"VEGF plasma levels were independently associated with survival in HCC patients," Dr. Llovet and colleagues write in the study abstract, although "low HGF levels and high c-Kit levels were associated with longer survival in patients treated with sorafenib."

Fewer data were available for the tumor biomarker ($n = 107$), but patients with high pERK (based on area percent staining positive) had a longer time to progression than those with low pERK. Combined with lowered HGF levels, positive pERK increased time to progression in the sorafenib cohort.

Session moderator and AASLD president Arthur J. McCullough, MD, found the data "very impressive." He told Medscape Gastroenterology that "it's very early, but it's a concept more important than the individual data, that you will be able now to predict early on in treatment who will respond to therapy." Although it is too early to apply the data to clinical practice, he said, sorafenib combined with other treatments could add an unknown amount of time to a patient's life.

In other sessions on sorafenib, audience members questioned whether the price of sorafenib, which runs more than \$5000 per month, is worth the 2 or 3 months of extended life for patients with terminal liver cancer.

Dr. Llovet has received research support from Bayer. Four of Dr. Llovet's coauthors are employed at Bayer; the fifth consults for Bayer. Dr. McCullough has received research support from Takeda.

The Liver Meeting 2008: 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD): Abstract 149. Presented November 3, 2008.

AASLD 2008: Mortality Lower for Early Liver Transplant in Healthier Patients

www.medscape.com

November 3, 2008 (San Francisco, California) — Patients with low to mid Model for End-Stage Liver Disease (MELD) scores benefit more from early liver transplantation than sicker patients, said Michael Goldstein, MD, from Columbia University, in New York City, here at The Liver Meeting 2008, the 59th Annual Meeting of the American Association for the Study of Liver Diseases.

Dr. Goldstein and his colleagues looked at the 5-year survival rate from the time patients were put on the waitlist, analyzing United Network for Organ Sharing (UNOS) data from a 2002 to 2006 study of 22,863 liver-only adult transplant recipients and 43,497 liver transplant waitlist patients. They looked at both waitlist and posttransplant mortality. The organ transplants studied included both living-donor organs and deceased donor high-donor-risk index organs (DRI >2.0) and low-donor-risk index organs (DRI <1.5). Study methods included a Cox proportional hazards regression and a Kaplan–Meier analysis.

Early timing of liver transplants was key to the analysis. Dr. Goldstein calculated a "break even" 5-year mortality rate for high- and low-risk organs to find the best timing for high DRI organ transplantation. For example, for patients with a MELD score of 11 to 14, survival improved with transplantation at 15 months instead of a projected 21 months, he stated in his presentation.

He also said during his presentation that living-donor allografts worked well for patients with MELD scores lower than 15. Dr. Goldstein said that "living donor allografts actually outperformed all deceased-donor allografts," in the UNOS data.

In his presentation, Dr. Goldstein said that the 5-year mortality rate for those on the transplant waitlist is probably higher than it appears. "No one knows really how to predict 5-year mortality [from] MELD," he said, and a lack of follow-up on transplant patients probably skews the data as well.

In the 4 MELD-score cohorts (<10, 11–18, 19–24, and >25), those with the lowest and highest MELD scores who received an early living-donor transplant had 5-year mortality rates higher than the national average: those with a MELD score lower than 10 had a 3.5% increased mortality rate, and those with a MELD score higher than 25 had a 7.6% increased mortality rate. However, 5-year mortality decreased for early living-donor transplants given to patients with MELD scores of 11 to 18 (a 13.4% decrease) and of 19 to 24 (a 14.8% decrease).

Patients who received a high DRI organ followed a similar pattern. Those with a MELD score higher than 25 had a slight improvement in 5-year mortality rates, but those with MELD scores in the middle 2 cohorts (11 to 18 and 19 to 24) benefited most.

"The small differences in posttransplant mortality by donor type are offset by the greater benefit in early access to transplantation, regardless of donor type," Dr. Goldstein stated in his abstract. "Living-donor and high DRI allografts are best utilized in mid-MELD recipients and offer the most benefit when utilized early to balance waitlist mortality."

Clinicians who want to apply these data need to look at the average wait time for their patients and the number of patients who would benefit from early transplantation, Dr. Goldstein told Medscape Gastroenterology.

Dr. Goldstein admitted that his conclusions are "somewhat contradictory to the general MELD principles" of treating the sickest patients first, since the patients he recommends for early transplant are "exactly those patients who no one transplants early," he told Medscape Gastroenterology. However, he said that patients with lower MELD scores "have the most to gain" because they have a better quality of life before and after transplantation and live longer posttransplant than the sicker patients. When making transplantation decisions with limited organs, "we should look at the total benefit for society as a whole," he said.

Session moderator Sandy Feng, MD, PhD, from the Department of Surgery, University of California, San Francisco, who was not involved with the study, told Medscape Gastroenterology that each patient must be viewed as an individual. "I think it's always dangerous to make individual decisions based on modeling data," she said. "I think the weakest argument is really in the low-MELD group.... We don't really know that people with MELD scores of 11 to 14 have that waitlist mortality curve all the way out to 20 months," she said. "So I still am nervous in particular about his conclusions regarding the very low MELD-score patients and that they should proceed to living-donor transplantation."

Dr. Feng added that transplant outcomes vary by transplant center. "I don't think you should undergo those transplants at low MELD scores unless you're at a very, very experienced center with the best outcomes," she said.

Dr. Goldstein received no commercial support for his analysis. Neither Dr. Goldstein nor Dr. Feng have disclosed any relevant financial relationships.

The Liver Meeting 2008: 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD): Abstract 22. Presented November 2, 2008.

Rifaximin Plus Lactulose Reduces Severity of Hepatic Encephalopathy

www.medscape.com

By Martha Kerr

SAN FRANCISCO (Reuters Health) Nov 04 - The non-absorbed antibiotic rifaximin (Xifaxan, Salix Pharmaceuticals) added to standard treatment of hepatic encephalopathy with lactulose

significantly reduces the number of hospitalizations for hepatic encephalopathy and shortens the length of hospital stay.

Those findings were presented here at The Liver Meeting 2008, the annual meeting of the American Association for the Study of Liver Diseases (AASLD) by Dr. Parvez S. Mantry of The Liver Institute at Methodist Dallas Medical Center, Texas.

Dr. Mantry described a retrospective review of medical records of 123 patients with end-stage liver disease seen on the liver transplantation unit at his institution. Fifty-eight of the patients received lactulose monotherapy for a mean duration of 24 months, while 65 patients received adjunctive rifaximin, 400-1200 mg/day, for a mean duration of 14 months after lactulose monotherapy.

"The risk of hospitalization for hepatic encephalopathy during adjunctive rifaximin treatment was 87% lower than during the preceding period with lactulose monotherapy," Dr. Mantry told meeting attendees.

Mean hospitalizations per patient were 0.26 with rifaximin plus lactulose and 0.95 with lactulose alone, for an odds ratio (OR) of 0.13.

The mean duration of hospitalizations for hepatic encephalopathy was shorter during adjunctive rifaximin (1.1 days) compared with lactulose monotherapy (2.4 days).

Treatment, age, and MELD score were independent predictors of hospitalization for hepatic encephalopathy.

"By reducing hospitalizations, rifaximin may reduce morbidity associated with hospitalization and overall costs associated with hepatic encephalopathy," Dr. Mantry concluded, adding, "Prospective studies to further investigate the potential therapeutic and pharmaco-economic benefits of rifaximin for hepatic encephalopathy are ongoing."

Healthcare reform gets backing in Congress

www.reuters.com

By Maggie Fox, Health and Science Editor

WASHINGTON (Reuters) - Efforts to reform the U.S. healthcare system got a big boost on Wednesday as a powerful Democratic senator unveiled a plan similar to President-elect Barack Obama's and an analysis said the financial crisis could accelerate any efforts, not hinder them.

Max Baucus, a Montana Democrat who heads the U.S. Senate Finance Committee, proposed creating a national insurance exchange, similar to Obama's idea, through which millions of uninsured Americans and businesses could get health coverage.

But Baucus would eventually require everyone to have health insurance while Obama proposes making health coverage more affordable but not mandatory. But both plans would be expensive and come amid financial turmoil.

Both major parties, Congress, consumer groups and employers agree the U.S. healthcare system is in shambles and needs reworking. Obama will have to work with Congress to make any significant changes.

Nearly 46 million Americans have no health insurance and while Americans pay more per capita for healthcare than citizens of any other industrialized country, many studies show they have poorer health, suffer more medical mistakes and are in general unhappier with what they do get.

Consultants PriceWaterhouseCoopers released a report on Wednesday that said the Obama plan would cost the federal government \$75 billion the first year but would provide health insurance for 95 percent of Americans.

This would grow to \$130 billion a year by 2018.

Dr. David Levy, health industry specialist at the consulting firm, said the financial crisis could make waste unacceptable and speed healthcare reform. "Maybe this crisis has helped unleash more market forces to drive this system toward more value for patients," Levy told a telephone briefing.

"The financial crisis and culminating market forces could accelerate health reform, not be a roadblock," the report reads.

The effects could be enormous for the \$2.3 trillion healthcare industry, which accounts for about 16 percent of the U.S. economy.

Quick Backing

Congress has been waiting for years to enact healthcare reform, and a quick and enthusiastic response to Baucus's plan suggests considerable backing.

"He has rightly sounded the urgent plea to get comprehensive reform done early in the next Congress and recognizes that the failure to act has dire and unacceptable consequences for working families, businesses and our national economy," AFL-CIO President John Sweeney said in a statement.

"There has never been a more auspicious opportunity to secure meaningful health care reform: The President-Elect has made it a top priority; key congressional committee chairs have made it their top priority; and the large and diverse health care interest groups are working cooperatively to find common ground," Ron Pollack of Families USA, a liberal-leaning health reform advocacy group, said in a statement.

Massachusetts Sen. Edward Kennedy, a senior Democrat and a life-long supporter of expanded healthcare access, has said he wants lawmakers united behind one bill.

Baucus, who as head of the tax-writing Finance Committee will play a major role, said he plans to work closely with Obama, who takes office on January 20, Kennedy and other lawmakers.

But Iowa Republican Sen. Chuck Grassley, ranking member of the Committee on Finance, said any reform would be hampered by the budget deficit.

"Right now, we already have a deficit of at least \$400 billion before the \$700 billion bailout and the economic downturn being factored in," Grassley said in a statement.

"We're heading toward a deficit that's 10 percent of the economy. So, paying for health care reform needs to be done in an intellectually honest way for the fiscal health of our country, and the broader the support for any health policy changes, the more durable and effective they will be."

(Editing by Eric Beech)

Nov 13, 2008

HIV treatment safe and effective in South African patients with hepatitis B co-infection, but co-infection frequent

www.aidsmap.com

Michael Carter

South African patients who are co-infected with HIV and hepatitis B virus have a comparable response to HIV treatment to patients who only have HIV, according to a South African study published in the December 1st edition of *Clinical Infectious Diseases*. For most of the HIV/hepatitis B co-infected patients, antiretroviral therapy did not cause liver toxicity, and there was no difference in the risk of death for patients with or without hepatitis B co-infection. However the study found a high frequency of hepatitis B/HIV coinfection in an urban cohort - almost one in five were co-infected.

Most of the world's HIV infections are located in Africa, a region which also has a high prevalence of hepatitis B infection. Antiretroviral therapy is becoming increasingly available in Africa, but there is currently uncertainty about the impact of hepatitis B co-infection on responses to HIV treatment.

Investigators in South Africa therefore designed a study involving 537 HIV-positive individuals receiving antiretroviral therapy through work-place treatment programmes. A fifth of these individuals (106) had evidence of chronic hepatitis B infection (hepatitis B surface antigen-positive, [HBsAg-positive]). A high hepatitis B DNA viral load is considered to be 10,000 copies/ml or above and the investigators tests indicated that 46 patients were in this category and that a further 60 patients had hepatitis B DNA loads below 10,000 copies/ml.

All the patients in the study started antiretroviral treatment between 2001 and early 2006. They were followed until the end of November 2006 or for a maximum of 72 weeks.

The investigators divided the patients into three exclusive groups according to their hepatitis B infection status: those who were HBsAg-negative; patients who were HBsAg-positive with a low hepatitis B DNA load; and individuals who were HBsAg-positive with a high hepatitis B DNA load.

All the patients were antiretroviral-naïve at the start of the study and commenced HIV treatment with a combination that included efavirenz, 3TC (a drug with activity against both HIV and hepatitis B) and AZT.

Four outcomes were monitored by the investigators:

- The achievement and maintenance of a HIV viral load below 400 copies/ml.
- Increases in CD4 cell count.
- Liver toxicity indicated by increases in ALT/AST levels of five times or more the upper limit of normal.
- Death.

Viral load was measured during the study at weeks six, 24, 48 and 72 and at all these points all three groups of patients were equally likely to achieve and maintain a viral load below 400 copies/ml. For example, at week 48, 84% of patients who only had HIV had a viral load below 400 copies/ml, as did 85% of the hepatitis B co-infected patients with low hepatitis B DNA-levels and 86% of the co-infected patients with high DNA levels.

Next the investigators looked at changes in CD4 cell count amongst the three groups of patients. During the first six weeks of antiretroviral treatment, the average weekly increase in CD4 cell count was 16 cells/mm³ each week and once again this did not differ between the three patient groups. The only factors that predicted CD4 cell count increase during early antiretroviral therapy were baseline CD4 cell count ($p = 0.02$), baseline haemoglobin ($p = 0.05$) and baseline HIV viral load ($p < 0.01$), and these values were all comparable between the three categories of patients at baseline.

In the longer-term, CD4 cell count increased by an average of 1 cell/mm³ per week with no difference between the three groups of patients.

At baseline, patients with hepatitis B coinfection and a high hepatitis B DNA viral load had significantly higher liver-enzyme levels than the other groups of patients (median 56 iu/dl vs. 38 iu/dl for patients who only had HIV and 40 iu/dl for coinfecting patients and a low hepatitis B DNA viral load, difference with this two patient groups, $p = 0.004$).

Although liver enzyme levels decreased in this group of patients after starting HIV therapy, at week 48 it was still significantly higher (median, 46 iu/dl) than in patients with a low hepatitis B DNA load at baseline (29 iu/dl) and HIV-negative patients (33 iu/dl, $p = 0.004$).

A total of 23 episodes of grade 3 or 4 liver toxicity were observed in 23 patients during the course of the study. The rate of these events was highest in patients with a high hepatitis B DNA load (17 per 100 person) years compared to a rate of 1.7 per 100 patient years in co-infected patients with a low hepatitis B DNA load and 3.8 per 100 person years in patients who only had HIV.

Most of these events occurred during the first six months of antiretroviral therapy, and the investigators believe that immune reconstitution inflammatory syndrome is the most likely explanation in the hepatitis B-infected patients. However, three events occurred after six months of HIV treatment, all involving patients with co-infection and the investigators suggest that the emergence of 3TC-resistant hepatitis B and the subsequent loss of viral control is the most likely cause.

There were a total of 24 deaths, 17 of which were non-traumatic. There was no difference in the risk of death between the three groups of patients.

“Hepatitis B co-infection did not affect early mortality or response to highly active antiretroviral therapy that included agents active against hepatitis B virus” write the investigators, adding, “even the group of patients with the highest pre-[antiretroviral] hepatitis B virus DNA levels achieved increases in their CD4 cell count and HIV [viral load] suppression at rates similar to those among patients who were HBsAg-negative. Furthermore, we demonstrated that the risk of [antiretroviral]-related hepatotoxicity can be stratified by hepatitis B DNA level”.

The investigators conclude, “chronic hepatitis B infection does not alter response to [antiretroviral therapy] or increase mortality during the first 18 months of therapy and, thus, should not deter clinicians from initiating [antiretroviral therapy].”

An accompanying editorial says there are five important messages from this study:

- There is a high prevalence of hepatitis B in South Africa and it is therefore essential to test HIV-positive patients for hepatitis B and vaccinate patients who are negative.
- Viral load and CD4 cell count responses to antiretroviral therapy was not affected by hepatitis B co-infection. They note that treatment guidelines, which are largely based on poorer outcomes of antiretroviral therapy in patients co-infected with hepatitis C, recommend the early initiation of HIV therapy in patients with hepatitis co-infection.
- There was a low rate of liver toxicity.
- High hepatitis B DNA levels were associated with an increased risk of liver toxicity suggesting that regular monitoring of hepatitis B viral load would be of value.
- 3TC resistant-hepatitis B may be contributing to liver toxicity.

Research presented earlier this year at the HIV Implementers' Meeting in Kampala, also conducted in South Africa, among 502 patients about to start therapy in the Themba Lethu clinic cohort at Helen Joseph Hospital in Johannesburg, found that 5.6% were hepatitis B SAg-positive, but 10.6% had antibody to hepatitis B core, accompanied by detectable HBV DNA in liver or serum in 91% of cases, indicating that they had an "occult" or silent infection. In one case a patient who was hepatitis B surface antigen-negative had an HBV DNA viral load of 1 million copies/ml. No correlation between occult infection and CD4 count, gender or any other variable could be detected.

The study also found that of those patients who were hepatitis B surface antigen-positive, 57% had grade 1 elevated liver enzyme levels. Yet a chart audit in the clinic found that none of 22 HIV-positive patients with grade 1/2 elevated liver enzymes was referred for hepatitis serology testing, despite the fact that raised liver enzymes should be a cause for suspicion of hepatitis.

Cynthia Firnhaber of WITS Consortium at the University of Witwatersrand, who carried out the research, said that the prevalence of occult hepatitis B infection in the South Africa context was cause for concern because patients may receive inappropriate first-line therapy. In particular she highlighted the risk of giving what amounts to long-term hepatitis B monotherapy with 3TC if that drug is the only anti-HBV drug in an antiretroviral combination. The [South African HIV Clinicians Society](#) recommends that people with HIV and hepatitis B coinfection should receive tenofovir in addition to 3TC in first-line treatment, or tenofovir and FTC (a similar drug to 3TC), since both drugs suppress hepatitis B replication.

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Nov 14, 2008

Human Genome Sciences Awaiting Crucial Albuferon Data

<http://seekingalpha.com>

Recent headlines that Susquehanna analysts have downgraded their rating on Human Genome Sciences (HGSI) from “positive” to “neutral”, whilst negative for sentiment, may have initially appeared relatively innocuous given the tough financial climate.

However, this “neutral” rating masked some pretty damning opinions from the analysts, including: “our enthusiasm for HGSI’s products and our confidence in management’s ability to execute has waned”. With HGSI’s shares losing 81% of their value this year and now trading at record lows of \$1.95, shareholders will be desperate that the company’s first ever set of phase III results, due in December for hepatitis C drug Albuferon, prove doubters such as Susquehanna wrong and stimulates the return of some of the enthusiasm and confidence that clearly used to exist when the stock traded at \$100 during the biotech-boom in 2000.

Albuferon needs to achieve its targets

Albuferon, developed using HGSI’s albumin-fusion technology, is a longer-acting form of Roche’s recombinant interferon alpha, Pegasys, which is already approved to treat hepatitis C and B and achieved sales of \$1.37bn last year.

With Albuferon required to demonstrate non-inferiority to Pegasys as a bare minimum, HGSI is pinning its hopes for regulatory and commercial success on the fact Albuferon requires half as many injections as Pegasys and may offer the potential for improved quality of life and fewer lost days of work whilst on treatment.

Two phase III trials are ongoing for Albuferon: Achieve 1 in 933 treatment-naïve patients with genotype 1 chronic hepatitis C and Achieve 2/3 in 1,331 treatment-naïve patients with genotype 2 or 3 chronic hepatitis C. It is the top-line results from Achieve 1 next month that investors will be hoping provides a much-needed boost to HGSI’s ailing share price.

Commercial potential

Having struck a global development and commercialisation deal over Albuferon with Novartis in 2006, which included a \$45m upfront fee, a further \$508m in milestones and allows HGSI to co-promote and book US sales, the commercial infrastructure is already in place; the issue remains the delivery of positive clinical trial results and regulatory approval.

With a potential NDA filing in late 2009, consensus forecasts of \$70m in 2010 are then set to rise to \$726m by 2014. On a risk-adjusted basis, HGSI’s US sales could reach \$376m by 2014

and coupled with rest-of-world royalties from Novartis, Albuferon is worth \$1.33bn to the company, according to EvaluatePharma's NPV Analyzer.

Compared to a market capitalisation of \$264m, or an enterprise value of \$690m, the potential for positive Albuferon data to dramatically improve HGSI's market value is clear.

Safety concerns

Whilst the valuations for Albuferon may look compelling, a major setback to the drug's chances of clinical success occurred in January when the highest dose of 1200-mcg had to be withdrawn from both trials due to a greater incidence of serious adverse pulmonary events in patients treated with the high dose.

HGSI's shares plummeted 44% on the day this event was announced and failed to recover, before sliding a further 69% in just the past six weeks, albeit it in a very weak and depressed overall market.

With the withdrawal of the highest dose, hopes that Albuferon may prove to be superior to Pegasys have been dashed, leaving a more limited claim of non-inferiority as the basis for a regulatory filing. Therefore, with a major safety scare now associated with the drug and the FDA taking an increasingly hard line against 'me-too', and even 'me-better' drugs with delivery or dosing advantages, major question marks over Albuferon will remain unless both Achieve trials produce dramatically positive data.

Highly geared

With \$280m in convertible debt due in 2011 and a further \$230m in 2012, HGSI clearly needs to start generating some decent revenues over the next few years. As such, news that \$120m in revenues for supplying anthrax antibody ABthrax to the US government would not be coming in this year overshadowed the fact that third-quarter losses were narrower than expected.

Although HGSI still believes it will receive \$150m related to ABthrax in 2009, the vagaries of government contracts mean some commentators see this as an increasingly risky assumption.

As such, HGSI needs Albuferon data to be very positive next month, otherwise the recent trend for ailing biotech companies having to restructure their operations could become necessary.

Migrants, drinking push up liver cancer rates

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

Kate Benson, Medical Reporter

An influx of migrants from developing countries where hepatitis is rife and a boom in binge drinking have caused liver cancer rates to skyrocket in the past 10 years, the latest statistics from the NSW Cancer Institute reveal.

Rates have increased by 70 per cent in men and 134 per cent in women, pushing up death rates and putting a huge strain on liver transplant waiting lists.

Chronic hepatitis B and C is the biggest risk factor in liver cancer and is endemic throughout Asia and the Middle East. In some Asian countries, up to 20 per cent of the population is infected with hepatitis B and 18 per cent have hepatitis C.

Dramatic increases in thyroid and lung cancer rates for women, with both surging by 84 and 22 per cent respectively in the past decade, have also alarmed doctors.

Thyroid cancer, caused by a lack of dietary iodine, was most prominent in cities where shoppers had greater access to table salts that did not contain iodine, such as rock and sea salt, the NSW chief cancer officer, Jim Bishop, said on Wednesday.

"We've been urging people to buy salt with iodine for some time, and pushing for manufacturers to include it in breads, because we have long seen this as a problem."

But Professor Bishop said the increase in lung cancer rates for women was more alarming because it had one of the lowest survival rates of all cancers, with only about 14 per cent of people diagnosed still alive after five years.

"We've seen a decline of about 16 per cent in the number of men contracting lung cancer, which is promising, but most women took up smoking later and are now suffering a lag in regard to the effects of that so while we think the anti-smoking message has had an impact, it will be some time before we see that reflected in the statistics for women."

Melanoma, which is increasing in men and women, was four times more prevalent in NSW than in the United States and an increase in the number of overweight and obese women in the past 10 years had contributed to an increase in cancers of the uterus, breast and colon, Professor Bishop said.

The report, *Cancer In NSW: Incidence And Mortality 2006*, showed that more than 35,000 new cases of cancer were detected in 2006, 590 more than in 2005. Prostate cancer was still the most common with 6158 cases (18 per cent), followed by bowel cancer with 4710 (13 per cent), breast cancer on 4173 (12 per cent) and 3559 cases of melanoma (10 per cent).

"Cancer rates have increased by about 10 per cent for men and 7 per cent for women in the past decade mainly due to an ageing population and an increase in screening programs, but the positive aspect is that the mortality rate has declined by about 14 per cent of men and 8 per cent for women so we are heading in the right direction," Professor Bishop said.

Biotech Mailbag: Vertex Has Verve

www.thestreet.com

Adam Feuerstein

Wes P. writes, "Adam, did I miss your final verdict on Vertex Pharmaceuticals (VRTX Quote - Cramer on VRTX - Stock Picks) after the hepatitis C meeting last week? The stock has held up well since that meeting ended."

I wrote some about Vertex's showing at the American Association for the Study of Liver Disease (AASLD) annual meeting, but Wes is right about me not getting around to summarizing after the confab of hepatitis C researchers ended Nov. 4.

Vertex's stock price, at around \$27, tells the tale. It has held up well, in large part because Vertex emerged from AASLD as a winner. The company's experimental hepatitis C drug telaprevir took some shots from competitors but no one landed a knockout punch.

What a difference one year makes. At the November 2007 gathering of the American Association for the Study of Liver Disease (AASLD), Vertex shares took a beating because many investors believed that competing drugs from the likes of Boehringer Ingelheim, Merck(MRK Quote - Cramer on MRK - Stock Picks), the Tibotec division of Johnson & Johnson (JNJ Quote - Cramer on JNJ - Stock Picks) and InterMune(ITMN Quote - Cramer on ITMN - Stock Picks) were going to be superior to telaprevir in one way or another.

Never mind that there weren't any data on this crop of alleged telaprevir killers; their mere existence was enough to ratchet up the Vertex worry factor to near panic mode.

At this year's AASLD meeting, we had the first opportunity to dig into early but meaningful data from a lot of these competitor drugs. The results were good, but not unexpectedly good. And none of the data pointed to serious trouble for Vertex.

Boehringer's drug, BI201, for instance, reported a maximum median viral load reduction of 4.2 log at 14 days when used as a monotherapy dosed once daily. This compares to a 4-log reduction in viral load with Vertex's telaprevir monotherapy in a previous 14-day study. And telaprevir, recall, is dosed three times daily while Boehringer is dosed BI201 once daily.

But there were also a lot of patients in the BI201 study reporting significant viral rebound by the time the monotherapy portion of the study ended at Day 14. This means that while BI201 was able to suppress the hepatitis C virus, the effect was somewhat short-lived. This raises the risk that BI201 might not be as effective in some hepatitis C patients, particularly those who have not responded well to previous treatment.

By comparison, Vertex's telaprevir caused far less viral rebound in its 14-day monotherapy study, and so far, Vertex appears to be very potent in treatment-resistant patients.

"Investors have been paranoid about telaprevir competition, but at this year's meeting, I think we saw that there doesn't appear to be anything more potent than telaprevir, and we still need to see a lot more data on safety," Cowen & Co. biotech analyst Rachel McMinn told me in a phone conversation after AASLD. She has an outperform rating on Vertex.

As a reminder, Vertex's phase III studies of telaprevir in both treatment-naïve and treatment-experienced hepatitis C patients are expected to report results in the first half 2010.

Before those data are released, competitors will continue to have their say. The European liver disease meeting is scheduled for April 22-26, 2009, while the next U.S. meeting will be held in November 2009.