

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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May 17th, 2004

InterMune Reports Positive Data On Combination Therapy

Karen M. Lee
Source: Dow Jones

NEW ORLEANS--InterMune Inc. (ITMN) reported positive data on Infergen-Ribavirin and Infergen-Actimmune combination therapies for Hepatitis C nonresponders.

In a press release Monday, the biopharmaceutical company said in the two investigator-sponsored Infergen-Ribavirin trials, there was a clinically significant end-of-treatment virologic response rate of 43%.

The analyses reviewed 137 patients in combination therapy for 48 weeks who had failed to respond to 12 weeks of pegylated interferon alpha 2 plus ribavirin therapy.

InterMune said therapy was well-tolerated in all patients. Flu-like symptoms and fatigue were reported in most patients, but no patients discontinued therapy. The company also said it would monitor these patients 24 weeks after end-of-treatment to determine the sustained virologic response rate.

In the clinical analysis of Infergen in combination with Actimmune, InterMune said the interim results after 24 weeks of therapy showed that 47% of patients had undetectable levels of Hepatitis C virus RNA in their blood.

In addition, having received 12 weeks of pegylated interferon alpha 2a plus ribavirin therapy, all patients had depressed hemoglobin levels prior to receiving Infergen plus Actimmune therapy.

During the course of therapy, hemoglobin levels returned to normal without the addition of growth factors and no patients discontinued therapy. Eight patients received growth factor therapy for reductions in absolute neutrophil counts, a recognized side effect of alpha interferon therapy.

Shares of InterMune traded recently at \$14.99, up 13 cents, or 0.9%, on Nasdaq volume of 286,891 shares. Average daily volume is 590,391 shares. The company's shares traded up earlier Monday at \$15.15. Its previous 52-week low was set a week earlier at \$14.19, compared with a 52-week high of \$28.44 on June 6.

Company Web site <http://www.intermune.com>

May 18th, 2004

Preliminary Results Presented at American Transplant Congress on Largest Ever Hepatitis C Trial Conducted in Liver Transplant Recipients

Source: PRNewswire

Early Data Shows Steroid-Free Protocol May Be Safe with Low Rejection Rates

BOSTON-- Goran Klintmalm, M.D., Ph.D., chief of Baylor Regional Transplant Institute and principal investigator of a study comparing three immunosuppressant treatment regimens in liver transplant recipients with hepatitis C, presented preliminary data from the trial yesterday in Boston, Mass., at the American Transplant Congress.

Hepatitis C is present in approximately 4 million Americans, and affects 50% of all patients receiving liver transplants. Hepatitis C frequently recurs following liver transplantation, leading to death or retransplantation.

"The data obtained from this study will provide important information to improve the management of hepatitis C patients after liver transplantation," said Dr. Klintmalm.

Corticosteroids have been the cornerstone of immunosuppression in transplantation since the 1960s; however, there is much controversy that corticosteroids may in fact increase recurrence of hepatitis C. In addition, the role and effect of mycophenolate mofetil, an immunosuppressant (non- steroid), in hepatitis C liver transplant patients is unclear.

"The purpose of this study is to determine the effect that the withdrawal of steroids, as an immunosuppressant, has on the recurrence of hepatitis C, as well as whether mycophenolate mofetil can reduce and slow down the development of hepatitis C as it recurs in the transplanted

liver," said Dr. Klintmalm. "While definitive analysis and conclusions will have to await completion of the trial in approximately 2 years, the early results are very encouraging."

A total of 312 patients enrolled in this prospective, multicenter, randomized study at 18 leading U.S. transplant programs. Patients were randomized to one of the three treatment regimens at the time of transplantation and will be maintained on this regimen for two years. Enrollment began in August 2002 and concluded in March 2004.

Treatment regimen 1 includes conventional therapy (tacrolimus) and corticosteroids, but no mycophenolate mofetil; treatment regimen 2 includes tacrolimus, corticosteroids and mycophenolate mofetil; and treatment regimen 3 includes tacrolimus, mycophenolate mofetil and daclizumab (an antibody given to prevent early acute rejection), but no steroids. Liver biopsies will be performed at various times throughout the study to assess treatment failure.

Data presented today by Dr. Klintmalm on 261 patients enrolled through Dec. 31, 2003, focused on day 90 post transplant data. The early data from this trial showed that the steroid-free protocol may be safe with low rejection rates. This preliminary analysis demonstrated that all three regimens had similar excellent early patient survival rates ranging between 95-100%, and graft survival rates ranging between 95-97%. In addition, protocol-defined acute rejection rates and hepatitis C recurrence rates were low in all three regimens. The complete avoidance of corticosteroids in regimen 3 had no negative impact on acute rejection incidence or recurrent hepatitis C. However, there appeared to be a decrease in diabetes and hypertension in this group of patients. Further, the use of mycophenolate mofetil in regimens 2 and 3 did not increase hepatitis C recurrence or severity at 90 days post transplant. Finally, in regimen 3, daclizumab appeared to be safe and did not increase early hepatitis C recurrence or severity.

Baylor University Medical Center at Dallas initiated this trial and recruited the other 17 participating study sites. CTI, Clinical Trial and Consulting Services, is managing the trial on behalf of Baylor. Other participating members of the study include Emory University School of Medicine, Lahey Clinic, Mayo Clinic Rochester, Mayo Clinic Arizona, Medical University of South Carolina Medical Center, New York Presbyterian Hospital, New York University School of Medicine, Northwestern University Feinberg School of Medicine, Oregon Health and Science University, University of Alabama at Birmingham School of Medicine, University of California - San Francisco Medical Center, University of Chicago Medical Center, University of Cincinnati Medical Center, University of Medicine and Dentistry in New Jersey, University of Southern California Keck School of Medicine, University of Texas, Health Science Center at San Antonio, and University of Virginia Medical Center.

"It was particularly gratifying to work with this group of committed liver transplant programs on this study. Enrollment was completed early and participating investigators have been diligent about obtaining all protocol specified procedures," stated Lynn Fallon, senior vice president, CTI.

For more information about this research, visit <http://www.BaylorHealth.com> .

*Baylor Regional Transplant Institute is the integration of transplant services at Baylor University Medical Center at Dallas and Baylor All Saints Medical Center at Fort Worth.
SOURCE Baylor University Medical Center at Dallas
Web Site: <http://www.BaylorHealth.com>

New Drugs Show Promise In Hepatitis C Fight

Charlene Laino and Charlotte Grayson, MD

Source: WebMD

Mistletoe, Green Tomatoes, Novel Antiviral Drug May Work When Standard Treatments Don't

With current hepatitis C treatments, about half of all patients can now be cured -- that's great if you're in that half. Now, two novel therapies -- one conventional, one unconventional -- show promise for treating those people for whom standard medications fail.

"About one in four patients can't tolerate current hepatitis C drugs because of harsh side effects," says Harald Matthes, MD, medical director and chief of the department of gastroenterology at Havelhohe Hospital for Anthroposophically Extended Medicine in Berlin. "And there are other patients that just don't respond."

In one study, an experimental pill that prevents replication of the hepatitis C virus worked in more than 70% of patients for whom traditional measures failed.

In the other study, a novel agent made from compounds found in mistletoe and green tomatoes cured about half of patients who didn't respond to conventional therapy. Both studies were presented here at Digestive Disease Week.

Most Unaware They Have Hepatitis C

About 4 million Americans are infected with hepatitis C -- most of whom don't know it, according to the National Institutes of Health. That's because hepatitis C often causes few symptoms. The virus can be transmitted from an infected person by sharing needles or from an infected mother to her baby during birth. Alternatively, many have had the virus for years, having contracted it from a blood transfusion or organ transplant before 1992, when supplies began to be screened for the disease.

Despite its silence, hepatitis C can be deadly. According to Eliot W. Godofsky, MD, hepatitis C will be responsible for up to 30,000 deaths a year over the next decade. Godofsky is president and co-founder of Bach and Godofsky, the largest private infectious disease practice specializing in the treatment of viral hepatitis in the U.S., and clinical assistant professor of medicine at the University of Southern Florida in Tampa.

"The good news is that despite popular misconceptions, hepatitis C is curable [for many patients]," he tells WebMD.

Standard treatment with the immune system-boosting drug interferon (known as Intron A, Pegasys, or Peg-Intron) and the antiviral drug ribavirin (known as Copegus and Rebetol; the combination drug is called Rebetron) achieves a "sustained response" in about 50% of people with the most common subtype of hepatitis C, he says. That means that the virus has been eliminated from their blood -- and doesn't return even after treatment is stopped.

Novel Drug Interferes With Viral Life Cycle

Enter the novel therapies. In an early study of 48 patients infected with HCV-1 (the most common form of the virus in the U.S.), virus levels dropped in 70% of those who were given the novel anti-viral drug dubbed NM283. In comparison, none of those given a placebo experienced a dip in the amount of virus present, Godofsky tells WebMD.

"Unlike current therapies, NM283 actually interferes with a specific step in the virus' life cycle, much like the drugs used to treat HIV or hepatitis B," he says. "That's dramatically different from available treatments, which work by boosting the immune system."

Also, there were no major side effects -- just some transient gastrointestinal ailments such as nausea or vomiting that subsided after two days, Godofsky says. In contrast, interferon can cause flu-like symptoms, fatigue, depression, muscle aches, and hair loss.

NM283 is made by Idenix Pharmaceuticals of Cambridge, Mass., which funded the study.

The next step, he says, is to test it in larger numbers of people, and then in combination with interferon. "Lab data shows that NM283 and interferon work better [together] than either by itself," Godofsky explains.

Anna Suk-Fong Lok, MD, professor of internal medicine at the University of Michigan Health Systems in Ann Arbor and a board director for the American Liver Foundation, says the drug looks promising.

Nevertheless, she tells WebMD, "Its true effectiveness can't be gauged until we have longer, larger studies. You have to give the drug for enough time to see if there is a sustained viral response, if the virus comes back, when you stop it."

Mistletoe-Green Tomato Combo Wipes Out Virus

In the other study, "unconventional therapy" with an extract of mistletoe and green tomatoes wiped out the virus in nearly half of patients for whom standard interferon therapy had failed, Matthes tells WebMD.

"We used a whole extract of mistletoe, which stimulates the immune system" to fight off the virus, he says. "And green tomatoes contain a key enzyme called caspase-8 that stimulates cell suicide."

In the study, 85 patients were given the new treatment. At one year, 18% were cured; by two years, the cure rate had reached 44%, Matthes reports.

"It's not quite as high a response rate as you see with interferon and ribavirin," he says. "But for the patients who can't tolerate that treatment and who currently have no alternative, we now have an option."

Godofsky says he sees a day when hepatitis C patients will be treated with a combination of therapies, much like people with HIV/AIDS. "We need combinations of different drugs that target different aspects of the disease. But drug development is a timely process."

Valeant Pharmaceuticals Presents Details of Viramidine 24-Week Data From Phase 2 Trials

Source: PRNewswire

COSTA MESA, Calif.,-- Valeant Pharmaceuticals (NYSE: VRX) today presented detailed 24-week data from Phase 2 clinical trials of Viramidine, a nucleoside (guanosine) analog Valeant is developing in oral form for the treatment of chronic hepatitis C (HCV) in conjunction with a pegylated interferon. Valeant presented its data at the Digestive Disease Week (DDW) Conference in New Orleans. This presentation complements data presented at the European Association for the Study of the Liver (EASL) in April 2004.

The Viramidine Phase 2 study consists of 180 treatment-naive subjects with chronic HCV. The on-going study was an open-label, randomized, active control trial, being conducted at multiple centers in the United States and with patients stratified by genotype. The study consists of four demographically comparable treatment groups: Viramidine 400 mg BID, Viramidine 600 mg BID, Viramidine 800 mg BID and ribavirin 1000/1200 mg daily all in combination with peginterferon alfa-2a. Treatment duration was based on genotype, with genotypes two and three receiving 24 weeks of treatment and genotype one receiving 48 weeks of treatment, each with a post-treatment follow-up period of 24 weeks.

The data demonstrate that a smaller portion of patients who received Viramidine 800-1200 mg/day had hemoglobin levels 10 g/dL or greater than or equal to 2.5 g/dL drop from baseline during the 24-week treatment period when compared to patients who had received ribavirin (48 percent versus 82 percent, respectively).

Among patients who received Viramidine 800-1200 mg/day, there were no instances of hemoglobin 10g/dL in either male or female patients. In the ribavirin group, 19 percent of male patients and 38 percent of female patients experienced hemoglobin levels 10g/dL. Differences between genders were not observed in the occurrence of a greater than or equal to 2.5 g/dL decrease in hemoglobin.

Data addressing effects on hemoglobin levels were also presented at DDW. After 12 weeks of treatment, the mean RBC ribavirin C(min) was 159 (mu)g/mL in patients who received Viramidine 1200 mg/day compared to 235 (mu)g/mL in ribavirin-treated patients. Thirteen percent of ribavirin-treated patients experienced declines in hemoglobin, requiring dose reduction or discontinuation, versus zero percent for the Viramidine group. These differences were reflected in the clinical outcomes at week 24, where a smaller proportion of patients who received Viramidine 800-1200 mg/day had hemoglobin 10 g/dL (zero percent versus 24 percent) or greater than or equal to 2.5 g/dL decrease from baseline (48 percent versus 82 percent) when compared with ribavirin-treated patients.

Data were presented by Robert Gish, M.D., the lead investigator on the Viramidine Phase 2 study and Medical Director of the Liver Transplant Program at California Pacific Medical Center in San Francisco and Sanjeev Arora, M.D., Professor of Gastroenterology and Internal Medicine Vice Chairman of Clinical Affairs for the Department of Medicine at the University of New Mexico.

A Phase 3 clinical trial, called VISER1, comparing Virmidine to ribavirin in combination with Peg-Intron was initiated in the fourth quarter of 2003 and is ongoing.

The Phase 3 trial compares the 600 mg BID dose of Virmidine to ribavirin, each in conjunction with pegylated interferon alpha 2b.

Data presented at EASL earlier this year demonstrate a sustained reduction in HCV RNA of approximately two-and-a-half log(10) for all three doses of Virmidine, comparable to the ribavirin group in the same study. The proportion of patients with greater than or equal to 2 log(10) reduction or non-detectable HCV RNA was 83 percent for both Virmidine (800-1600 mg/day) and ribavirin at 24 weeks. The results also show the percent of patients with non-detectable HCV RNA at 12 weeks and 24 weeks were similar between all treatment groups.

There were also fewer patients in the Virmidine groups with anemia (defined as hemoglobin 10g/dL) when compared with the ribavirin arm (2 percent versus 24 percent; p 0.001). In the Virmidine 400 mg BID and 600 mg BID dosage groups, defined anemia (hemoglobin 10g/dL) did not occur, while there were only two occurrences of anemia in the 800 mg BID group. Other adverse events were similar among treatment groups.

About Valeant Valeant Pharmaceuticals International (NYSE: VRX) is a global, publicly traded, research-based specialty pharmaceutical company that discovers, develops, manufactures and markets a broad range of pharmaceutical products. More information about Valeant can be found at www.valeant.com.

FORWARD-LOOKING STATEMENTS This press release contains forward-looking statements within the meaning of the federal securities laws relating to expectations, plans or prospects for Valeant Pharmaceuticals, including funding and conducting clinical trials and expected research and development expenses. These statements are based upon the current expectations and beliefs of Valeant Pharmaceuticals' management and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include market conditions and other factors beyond Valeant Pharmaceuticals' control, the company's success in identifying and enrolling patients in the clinical trials program, the absence of adverse events that would require the clinical trials to be prematurely terminated, clinical results that indicate continuing clinical and commercial pursuit of Virmidine is advisable, and the risk factors and other cautionary statements discussed in Valeant Pharmaceuticals' filings with the U.S. Securities and Exchange Commission.

Idenix Pharmaceuticals, Inc. Announces First Human Clinical Trial Data For NM283 for the Treatment of Hepatitis C

Source: PRNewsire

Phase I/II clinical trial data presented at Digestive Disease Week (DDW)

NEW ORLEANS,-- Idenix Pharmaceuticals, Inc. announced today the results of the first human clinical trial of NM283, a novel once-daily oral treatment for hepatitis C. In a Phase I/II dose escalation clinical trial, NM283, Idenix's first candidate for the treatment of hepatitis C, demonstrated consistent, dose-related antiviral effects in adult patients with chronic hepatitis C.

The patient cohort that received the highest overall dose exposure of NM283 achieved a mean viral load reduction of 92 percent ($1.1 \log^{10}$) within 15 days of treatment. All patients were infected with HCV genotype 1, a difficult to treat strain, which is the predominant strain in the U.S., Western Europe and Japan. Among the NM283-treated patients in the clinical trial to date, 87 percent had previously failed interferon-based therapies. The overall safety profile for NM283 in the Phase I/II trial was satisfactory, with no dose-limiting toxicities. These data were presented by Dr. Eliot Godofsky, the lead investigator in the study, at the Digestive Disease Week conference in New Orleans.

Study description: The double blind, randomized Phase I/II dose escalation clinical trial was designed to evaluate the safety, pharmacokinetics and antiviral activity of NM283 during 15 days of treatment with a two-week follow up period. All patients were chronically infected with the genotype 1 strain of HCV and were either previously untreated or had failed interferon-based therapy. Entry criteria for patients included serum HCV RNA levels greater than $5 \log_{10}$ (100,000 international units (IU) per mL), ALT (a measure of liver disease) levels less than five times the upper limit of the normal range, and compensated liver disease without cirrhosis.

The design of the Phase I/II clinical trial included five once-daily dosing cohorts: 50, 100, 200, 400 and 800 mg and one twice-daily dosing cohort of 200 mg. Two further cohorts explored methods for optimizing tolerance of higher daily doses: one cohort initially received NM283 at 100 mg/day, advancing progressively to 800 mg/day for the second week of the clinical trial; the second cohort initially received NM283 at 400 mg/day, advancing progressively to 800 mg/day for the second week of the clinical trial, with anti-emetic treatment given together with NM283 for the first two days and for one day in conjunction with each of the two dose escalations. Each cohort included 12 patients, randomized so that 10 patients received NM283 and two received placebo. The once-daily 800 mg cohort is currently ongoing.

To date, a total of 82 patients comprising seven dose groups have completed treatment including 68 patients receiving assigned doses of NM283 and 14 receiving placebo. Patients enrolled in this clinical trial had a high baseline serum viral load (HCV RNA) with an average of $6.7 \log_{10}$ IU/mL and the average serum ALT level at baseline was moderately elevated at 64 IU/L, reflecting underlying liver inflammation typical of hepatitis patients. The average age of the enrolled patients was 50 years (age range: 39 to 65 years).

Six clinical centers in the United States participated in the trial, including three university-based trial centers and three community-based trial centers. The trial was conducted under a U.S. FDA Investigational New Drug (IND) Application.

Study results: Consistent, dose-related reductions in serum HCV RNA were observed in patients receiving NM283. The greatest antiviral effect, with a mean HCV RNA reduction of $1.1 \log^{10}$ IU/mL (92 percent), was experienced by patients who received the highest cumulative dose of NM283 over the 15-day treatment period. In this dosing group, 10 out of 10 patients demonstrated a significant reduction in HCV RNA ranging from 0.7 to $1.9 \log^{10}$ IU/mL, corresponding to 79 to 99 percent viral load reductions. In this group, nine of the 10 patients had previously failed to respond to interferon-based therapies. For the three highest-dose groups in the clinical trial, antiviral responses over the 15-day treatment period exceeded the average serum viral level reduction of $0.3 \log_{10}$ IU/mL per week observed in hepatitis C patients who respond to treatment with the current standard of therapy, ribavirin in combination with pegylated interferon.

The overall clinical safety profile seen in this trial has been good with no serious or treatment-limiting side effects. All 82 compliant patients completed treatment and follow-up; one patient was discontinued from the study for non-compliance. At the higher doses, some patients had mild-moderate gastrointestinal side effects that most often appeared in the first two days of treatment and typically resolved quickly. No patients changed or discontinued treatment due to any side effects.

Pharmacokinetics data revealed that NM283 was well absorbed by patients on treatment. There was no significant drug accumulation as Day 15 drug levels were comparable to Day 1 levels. Observed drug levels were proportional to the dose.

About NM283: NM283 is a novel antiviral drug that, after absorption, is metabolized to a form that inhibits the HCV RNA polymerase. NM283 has been shown to have synergistic antiviral effects with interferon-alpha in vitro. NM283 also inhibited HCV genotype 1 replication in chronically infected chimpanzees.

The next clinical trial will evaluate the combination of NM283 and pegylated interferon over a four-week treatment period. Longer-term trials of NM283 will follow in the second half of 2004.

About hepatitis C: There are approximately 170 million people worldwide with chronic hepatitis C virus (HCV) infection, of which approximately 2.7 million are in the United States. Chronic HCV infection accounts for 40 percent of end-stage cirrhosis, 60 percent of liver cancer and 30 percent of liver transplants in the United States and other industrialized countries. Available treatment options have tolerance issues and are often limited in their effectiveness; particularly in patients infected with HCV genotype 1, a specific strain of HCV that is the most treatment-resistant HCV genotype and that causes more than 70 percent of the reported cases of hepatitis C in the U.S., Western Europe and Japan.

About Idenix: Idenix Pharmaceuticals, Inc. is a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral and other infectious diseases. Idenix's current focus is on the treatment of infections caused by hepatitis B virus, hepatitis C virus and human immunodeficiency virus (HIV). Idenix headquarters are located in Cambridge, Mass. and has drug discovery operations in Montpellier, France and Cagliari, Italy.

About DDW: Digestive Disease Week (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW takes place May 15-20, 2004 in New Orleans, Louisiana. The meeting showcases approximately 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology.

Contact:

Idenix Pharmaceuticals, Inc.	Ruder Finn, Inc.
Teri Babine	Catherine London
(617) 995-9905	(212) 593-6309
Idenix Public Relations	Media Relations

SOURCE Idenix Pharmaceuticals, Inc.

Large-Scale Nationwide Study of Hepatitis C Treatment Patterns

Source: Business Wire

Finds Nearly 30% of Treatment Candidates Not Receiving Therapy

Study finds significant variations in treatment patterns and reported outcomes

BOSTON-The Bruckner Group (BGI), a strategy and research firm for the pharmaceutical and biotechnology industries, today announced the results of a large-scale nationwide study on hepatitis C treatment patterns conducted with Brooke Army Medical Center. Select findings are being presented today at the Digestive Disease Week conference in New Orleans.

This nationwide study, developed and performed by The Bruckner Group through its non-profit Academic Collaboration Program, was undertaken to understand the diagnostic and clinical practice patterns of gastroenterologists and hepatologists treating hepatitis C patients. 1,002 clinicians from private practices, hospitals, academic research centers, and government hospitals participated in the study, representing a 20% response rate.

Some key findings include:

1. While 71% of all hepatitis C-infected patients are considered by clinicians to be treatment candidates, only 52% of all hepatitis C-infected patients actually initiate therapy.
2. 78% of clinicians offer re-treatment to patients who relapse after initial therapy, and 64% provide re-treatment to previous non-responders.
3. 75% of clinicians discontinue combination therapy at 12 weeks if the early virologic response data indicates failure to achieve a 2 log or greater reduction in viral load. Combination therapy consists of pegylated interferon and ribavirin: Peg-Intron + Rebetol from Schering-Plough, or Pegasys + Copegus from Roche.
4. Patients treated in private practices are more likely to be considered candidates for treatment, and to actually commence therapy.

“This is the first large-scale study—with over 1,000 participating clinicians—of hepatitis C treatment patterns,” Major Sean Hurley, staff gastroenterologist said. “The majority of gastroenterologists follow an acceptable approach to the management of patients with hepatitis C, but we have learned that substantial practice variations do exist. We also see linkages between practice variations and physician-reported patient outcomes.”

“This large study establishes a baseline of practice patterns from which future trials can be developed to enhance side effect management,” said senior author and staff gastroenterologist Dr. (Maj.) Eric Lawitz.

An abstract from the study, “Assessment of Patients Infected with Hepatitis C Among Gastroenterologists in the United States: A National Survey” is being presented today by Dr. Sean Hurley. In the poster session, a second abstract from this study, “Hepatitis C Therapeutic Management Patterns Among Gastroenterologists in the United States: A National Survey,” is also being presented today with co-authors Dr. Eric Lawitz; Michael Russo, Bruckner Group Partner and Managing Director of BGI’s Academic collaboration Program; Dr. Matthew Hepburn, and Dr. Hurley.

SOURCE: The Bruckner Group Inc.

HIV and Hepatitis C Coinfection Within The CAESAR Study

Source: www.gastrohep.com

People with HIV and a history of intravenous drug use or elevated liver function tests should be targeted for hepatitis C testing, find investigators in the May issue of *HIV Medicine*.

There is a declining incidence of AIDS-related opportunistic diseases in people with HIV infection. This has shifted the focus of clinical management toward prevention and treatment of comorbidities.

The increased risk of hepatitis C virus (HCV)-related advanced liver disease in people with HIV infection makes early HCV diagnosis a priority.

In this study, investigators from Australia and England assessed HCV prevalence and predictors of HIV/HCV coinfection.

The team conducted a retrospective analysis of people enrolled in the CAESAR (Canada, Australia, Europe, South Africa) study. This is a multinational randomized placebo-controlled study of the addition of lamivudine to background antiretroviral therapy.

In addition, the team evaluated the impact of HCV on HIV disease progression.

HIV/HCV coinfection was low in homosexual men.

The investigators determined that study participants had an HIV/HCV coinfection prevalence of 16%. This varied from 2% in South Africa to 49% in Italy.

The team found that the strongest predictor of HIV/HCV coinfection was HIV exposure category: injecting drug use (IDU), transfusion or blood products, or both homosexuality and IDU.

They established that HIV/HCV coinfection was low (4%) in homosexual men without reported IDU.

Other predictors of coinfection were alanine aminotransferase (ALT), country of residence, ethnicity, and stage of HIV disease.

The team found that HIV disease progression was similar in HIV monoinfected and HIV/HCV coinfecting patients.

Dr Amin's team concluded, "People with HIV and a history of IDU or elevated liver function tests should be targeted for HCV testing".

"The low prevalence of HIV/HCV coinfection among homosexual men without a history of IDU suggests low efficiency of sexual HCV transmission."

HIV Medicine 2004; 5(3): 174-9

Playing Field For Liver Transplants Is Not Level, Studies Find

By Robert Davis, USA TODAY

BOSTON — A process meant to equitably allocate human livers for transplant is flawed, medical experts say, costing lives among those most in need and putting relatively healthy patients at risk.

Studies presented this week at the American Transplant Congress reveal that U.S. surgeons are transplanting livers into their own patients first, even when those patients are not as sick as others.

Officials say the federal regulation governing transplant eligibility should be changed so that organs go to the sickest patients first. That is not always the case, even though the rule, imposed in February 2002, ranks patients based on the severity of their disease.

The rule came about because of widespread allegations that doctors were bending the rules in favor of their own patients, including putting them in hospital intensive care units and on transplant waiting lists long before they needed the surgery.

Studies presented at the international scientific meeting indicate that the rules are still being bent.

Today, when a liver suitable for transplant is identified, local Status One patients are considered first. Status One patients are those who are near death.

About liver transplants

The good news and bad news: Fewer people are awaiting liver transplants because of rule changes that rank patients by severity of illness. The number of transplants has increased. But fewer people have opted to be living donors because of the elevated risk of complications.

	2001	2002	Change
People waiting for organs			
Total	77,334	79,387	+2.7%
Livers	18,047	16,974	-5.9%
Number of transplants			
Total	23,902	24,544	+2.7%
Livers	4,986	5,060	+1.5%
Deceased donor	4,468	4,701	+5.2%
Living donor	518	359	-30.7%

Source: Scientific Registry of Transplant Recipients

If no Status One patients are in the local area or if the organ is not a biological match, the search for a recipient then expands to the organ transplant region, which can include several states.

If no Status One patient in the region is a match, the transplant surgeons in the city where the liver was recovered can give the organ to the patient ranked highest by the disease severity score, known as the Model for End-stage Liver Disease.

The problem, researchers say, is that even by following these steps, surgeons are still allowed to send too many livers to patients who rank the lowest.

Ironically, the practice puts patients who are relatively healthy at a higher risk of death, the researchers say. Surgeons have developed an expanded criteria to accept livers for the sickest patients, believing that a marginal liver is better than no liver.

But transplanting a liver considered medically marginal into a person who is not critically ill puts that patient in greater danger of death from complications, infections or organ rejection, the researchers say. They say nearly 30% of the patients ranked with the least severe disease are receiving marginal livers.

At the same time, sicker patients are dying. "Our focus has to be on what's best for the patient," says Robert Merion, professor of surgery at the University of Michigan. "There may be somebody right across the river who doesn't have access to that organ." Merion is clinical transplant director for the Scientific Registry of Transplant Recipients, a federally funded database of transplant outcomes.

Officials are considering changes in the transplant system regulated by the United Network for Organ Sharing that would ensure that organs go only to patients who rank high on the disease severity scale.

"We need to ensure that people who need the livers the most are getting them," says Clive Callender, who heads the transplant program at Howard University in Washington, D.C. "As we get more information, we change our policies. When you shine a light on things, people change their behavior."

May 20th, 2004

Thimerosal-Related Changes in Hepatitis B Vaccine Recommendations

Source: www.Gastrohep.com

Reductions in hepatitis B vaccine birth-dose coverage persisted after recommendations were made to resume previous newborn vaccination practices, find physicians in this week's issue of the Journal of the American Medical Association.

In July 1999, the hepatitis B vaccination of all US infants at birth was temporarily suspended due to concerns about the vaccine preservative thimerosal.

This suspension was lifted in September 1999 when preservative-free hepatitis B vaccine became available.

In this study, physicians evaluated the effects of these changes on vaccination coverage.

The team performed a cohort analysis of the vaccination status of 41,589 children born before, during, and after the recommendation to suspend the birth dose. Coverage with other recommended vaccinations did not decline. *Journal of the American Medical Association*

They assessed the association between birth cohort and age at receipt of hepatitis B vaccine dose 1, as well as receipt by 19 months of age of all recommended vaccines.

The physicians determined that 47% of infants born before the suspension received dose 1 at birth, compared to 11% of infants born during the suspension.

They also found that birth-dose coverage remained significantly lower in the year after the suspension was lifted.

In addition, the team found that children who received 3 doses of hepatitis B vaccine by 19 months of age declined from 88% before the suspension to 81% in those born during the suspension. The rate increased to 85% in children born in the 6 months after the suspension, and then returned to baseline levels.

The team calculated that the reductions represent 750,000 fewer newborns vaccinated during 2000 compared with 1998. An additional 182,000 children were undervaccinated for hepatitis B at 19 months of age compared with 1998 coverage levels.

Dr Elizabeth Luman's team concluded, "Reductions in hepatitis B vaccine birth-dose coverage persisted after recommendations were made to resume previous newborn vaccination practices".

"Although the recommendation to complete the series by 19 months of age was never changed, infants born between July and December 1999 were less likely to have completed the series by 19 months, compared with infants born during the previous year".

"The lack of impact on other vaccinations suggests that public confidence in immunization remained strong."

JAMA 2004; 291: 2351-8

PR Newswire

SciClone Achieves Enrollment Milestone For U.S. Phase 3 Hepatitis C Trials; Earns \$1,000,000 Milestone Payment

Source: Business Wire

SAN MATEO, Calif.---SciClone Pharmaceuticals, Inc. (Nasdaq:SCLN) today announced that a total of 1,000 patients have been enrolled in its two U.S. phase 3 hepatitis C (HCV) clinical trials evaluating its lead product ZADAXIN(R). SciClone has earned a \$1,000,000 milestone payment from Sigma-Tau for successfully meeting the enrollment objective. SciClone expects all patients to have completed therapy and the observation period by the end of 2005. Data from both trials are expected to be available in early 2006.

Dr. Eduardo Martins, Vice President of Medical Affairs of SciClone, commented, "We are pleased to reach this milestone in our efforts to develop the combination of ZADAXIN and pegylated interferon alpha to treat hepatitis C patients who fail to respond to current HCV

therapy." The first trial includes 534 HCV non-responder patients with no cirrhosis of the liver and was fully enrolled in September 2003. The second clinical trial of HCV non-responders with cirrhosis currently has enrolled 467 patients, which surpasses the number of patients required to satisfy the protocol's statistical design. Qualified patients who are currently undergoing screening procedures will be allowed to enroll in the second clinical trial.

Approximately half of all HCV patients fail to respond to current therapy of pegylated interferon alpha with or without ribavirin. SciClone's objective is for ZADAXIN in combination with pegylated interferon alpha to be the first FDA approved therapy for the treatment of HCV non-responder patients. If this combination is approved by the FDA, SciClone believes that ZADAXIN also could be beneficial in a triple combination with pegylated interferon alpha and ribavirin for all HCV patients.

SciClone's two U.S. phase 3 clinical trials are multi-center, randomized and double-blinded studies. Patients are assigned to a 12-month course of treatment of either ZADAXIN and pegylated interferon alpha or placebo and pegylated interferon alpha. After completing treatment, the patients will be closely followed for a six-month observation period. Primary endpoints are the absence of HCV RNA and an improvement in the liver histological activity index measured at the end of the six-month observation period.

About SciClone

SciClone Pharmaceuticals is a biopharmaceutical company engaged in the development of therapeutics to treat life-threatening diseases. SciClone is currently evaluating its lead product ZADAXIN in several clinical trials, including two phase 3 hepatitis C clinical trials in the U.S., a completed phase 3 hepatitis B clinical trial in Japan, a phase 2 malignant melanoma clinical trial in Europe, two phase 2 liver cancer pilot studies in the U.S., a hepatitis C triple therapy open-label clinical trial in Mexico, and a hepatitis B combination therapy trial in Taiwan. The Company's other principal drug development candidate is SCV-07, a potentially orally available therapeutic to treat viral and infectious diseases. For more information about SciClone, visit www.sciclone.com.

This press release includes forward looking statements regarding our expectations for timing of events related to our clinical trials. Actual timing and results could differ based on a number of factors, including delays in the trials due to unexpected events.

*CONTACT: SciClone Pharmaceuticals
Richard A. Waldron, 650-358-3437*

FDA Finalizes New Rule on Donor Eligibility for Human Tissues and Cells

Source: www.pharmalive.com

ROCKVILLE, Md.,-- FDA today published a final rule establishing donor eligibility criteria for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps) to help prevent the transmission of communicable disease when these products are transplanted. This new rule is the second of three proposed rules that have been finalized as part of the Agency's plan to regulate tissues and related products with a comprehensive, risk-based approach. The requirements are comprehensive, yet adequately flexible, and they provide needed protections for patients without imposing unnecessary regulation.

Along with the potential for great benefit, products derived from the human body such as HCT/Ps may pose risks of transmitting communicable diseases especially if donors are not

properly screened and tested. For this reason, this final rule requires that, before the use of most HCT/Ps, the cell or tissue donor must be found eligible, based on the results of screening for risk factors and testing for relevant communicable diseases. In most cases, a donor who tests positive for a particular disease or who possesses clinical signs or risk factors for such a disease would be considered ineligible, and cells and tissues from that donor would not ordinarily be used.

"Transplanted human tissues and cells have the potential to treat or cure a wide range of health conditions including skin replacement after severe burns and corneas to restore eyesight," said Acting FDA Commissioner Dr. Lester M. Crawford. "We now have new tissue technologies that hold the potential to provide treatments for diseases such as cancer, Parkinson's Disease, hemophilia and many other serious conditions. Our comprehensive approach helps make these novel products as safe as possible while still encouraging innovation. We have achieved this by tailoring our regulations to the degree of risk posed by each product."

The new rule on donor eligibility pertains to donors of traditional tissues such as musculoskeletal, skin and eye tissues that have been required to be screened and tested for HIV, Hepatitis B virus (HBV) and Hepatitis C virus (HCV) since 1993. Under this new rule, reproductive tissue (semen, ova, and embryos), hematopoietic stem cells derived from cord blood and peripheral blood sources (circulating blood sources as opposed to bone marrow), cellular therapies and other innovative products are also regulated.

"This new rule was developed with input from many concerned consumers, associations and tissue establishments. In all cases, we carefully considered the comments we received in the proposed rule and made changes in the final rule when the science supported the change," Dr. Crawford said.

In addition to including a broader range of tissues and cells, the new rule extends the scope of protection against additional communicable diseases that can be transmitted through transplanted tissues and cells. The new regulation adds requirements to screen for human transmissible spongiform encephalopathies, including Creutzfeldt-Jakob disease (CJD), and to screen and test for syphilis. Screening and testing for still other relevant communicable disease agents (human T-lymphotropic virus (HTLV) would be required for viable cells and tissue rich in leukocytes such as semen and hematopoietic stem cells. For reproductive tissues, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* also pose potential risks and are included.

The new rule also provides a framework for identifying emerging diseases that may pose risks to recipients of transplanted HCT/Ps and for which appropriate screening measures or testing are available. Thus, this new regulation gives FDA the flexibility to rapidly address new disease threats as they appear, providing substantial new protections for patients receiving tissue transplants. Examples of such diseases include West Nile virus, Severe Acute Respiratory Syndrome (SARS) and sepsis.

The behavioral risk factors that are used to screen donors are consistent with 1994 Centers for Disease Control and Prevention (CDC) guidelines for preventing transmission of HIV through organ and tissue transplantation and with the scientific literature as reviewed by CDC in 2000. Professional groups, such as the American Association of Tissue Banks, have adopted the recommendations contained in the CDC guidelines.

The rule also contains requirements related to record-keeping, quarantine, storage and labeling of the HCT/Ps, all important to the prevention of disease transmission.

Certain exceptions from the requirements for donor eligibility testing and screening exist. These tissues and cells include:

- autologous HCT/Ps (Cells or tissue removed from and transplanted back into the same person) and reproductive cells or tissues from a sexually intimate partner.
- Other cells and tissues are subject to donor testing and screening, but may be used with appropriate communication, labeling and documentation of the relevant results even if the donor is determined to be ineligible. These are:
 - reproductive cells or tissues from a directed donor, those for use in first or second-degree blood relatives, and those that meet a documented urgent medical need.

The new framework does not include whole organs or minimally-manipulated bone marrow, which are regulated by HRSA, another agency of the Department of Health and Human Services. It also does not cover blood products for transfusion or products derived from animals, which FDA regulates under the biologics license requirements and other applicable regulations.

The final rule becomes effective on May 25, 2005. It is accompanied by draft guidance that provides recommendations for complying with the requirements in the donor eligibility rule. Comments on the draft guidance should be received by August 23, 2004 (90 days from the publication date) to assure consideration in the final guidance. The rule is available on FDA's website at www.fda.gov/OHRMS/DOCKETS/98fr/97N-484S-nfr0001.pdf and the guidance is available at www.fda.gov/cber/gdlns/tissdonor.pdf.

Media Inquiries: 301-827-6242

Consumer Inquiries: 888-INFO-FDA

Questions and Answers for Roll-Out of Donor Eligibility Final Rule and Draft Guidance