

VISER2: Viramidine Trial Results Released



Alan Franciscus, Editor-in-Chief

On September 12, 2006 Valeant Pharmaceuticals reported the results from a phase III study called VISER2 (Viramidine's Safety and Efficacy vs. Ribavirin). The study compared Viramidine (600 mg BID (twice a day dose) to ribavirin (weight-based 1000/1200 mg BID dose) in combination with pegylated interferon alfa 2a (Pegasys)). The two co-primary endpoints of the study were safety and efficacy (sustained viral response or SVR).

A total of 962 HCV positive patients (treatment naïve) were enrolled in the United States, Canada, Europe, Israel, Argentina and Australia. Treatment duration was 24 weeks for genotype 2, 3 and 48 weeks for non-genotype 2, 3 patients. The post treatment

follow-up period was 24 weeks. The study was also stratified for genotype, weight and viral load although this information has not yet been released.

Viramidine (taribavirin) is a prodrug of ribavirin. A prodrug is a drug that is concentrated in a certain organ such as the liver rather than distributed throughout the entire blood system. The safety endpoint of the study was to find out if treatment with Viramidine resulted in lower rates of anemia (Hgb < 10g/dL) when compared to ribavirin. This was an intent-to-treat basis (all patient results counted).

The study confirmed that treatment with Viramidine resulted in lower anemia than in the patients

IN THIS ISSUE



Hep C Aware – Internet Telethon.....2

Healthwise:

Not Trivial Liver Trivia.....3

Extrahepatic Manifestations:

Cryoglobulinemia.....4

Tuberculosis in People with Hepatitis C.....5

treated in the ribavirin group (6% compared to 22%; $p < 0.001$).

The other study endpoint was the effectiveness of Viramidine compared to ribavirin (in combination with pegylated interferon alfa 2a). Overall SVR rates were 40% for the Viramidine arm compared to 55% for the ribavirin arm. The SVR rate of Viramidine did not meet the non-inferiority efficacy

continued on page 2

Table 1

VISER 1 and VISER 2: Safety and Efficacy (Intent-to-Treat Analysis)

Study	Anemia (Hgb < 10g/dL)		Sustained Virologic Response*	
	Viramidine	Ribavirin	Viramidine	Ribavirin
VISER 1 (N = 970)	5%	24%	38%	52%
VISER 2 (N = 962)	6%	22%	40%	55%

*Percent of Patients with Undetectable HCV RNA; NGI SuperQuant Assay, sensitivity to 39 IU/mL (100 copies/mL)

Source: Company press release

VISER2

continued from page 1

goal. A non-inferiority efficacy trial examines whether the new drug (Viramidine) is at least as effective as the drug it is being compared to (ribavirin).

The data from this study is consistent with the VISER1 study results that were released earlier this year. VISER1 results showed similar lower anemia rates and lower treatment response rates (SVR) in the Viramidine group compared to the pegylated interferon alfa 2b (Peg-Intron) plus ribavirin group (see table 1).

A retrospective analysis of the drug exposure in both the VISER1 and VISER2 found that the higher exposure of Viramidine in the blood resulted in a higher SVR, but without the corresponding higher rates of anemia. The information on the blood exposure of ribavirin was not available.

Based on the higher exposure rate of Viramidine found in the analysis, Valeant announced that it is starting a new phase 2b study to evaluate the effectiveness and safety of higher doses of Viramidine (20 mg/kg, 25 mg/kg, and 30 mg/kg per day) in combination with Peg-Intron. There will also be a control group that will receive pegylated interferon and ribavirin. A total of 240 genotype 1 treatment naïve patients will be enrolled. Based on the interim 12 week data from the new study, Valeant may decide to go forward with a new phase III study of higher doses of Viramidine in combination with pegylated interferon.

**Hep C Aware – The Internet Telethon 2006****Saturday October 21st – 3rd Annual Event!**<http://www.hepcaware.org>

Hep C Aware - The Internet Telethon is the signature event of Hep C Aware, a non-profit foundation that is dedicated to raising awareness of Hepatitis C.

This year's event, scheduled for October 21st, will be live on the internet for eight hours, and for 2 of those hours the telethon will run live on TV in Southern California!

Featuring musical performances by over 20 bands, comedians and medical experts as well as special guests, music videos and featured spots about Hepatitis C throughout the entire event.

The 2006 HepCAware Telethon will run from 12pm PST to 8pm PST. The televised portion is from 6-8pm PST.

- Broadcast live all over the world!
- Music & Comedy
- Special Guests and sponsors
- Live on KVMD in Los Angeles and Surrounding Areas
- Hep C Education from medical host
- Special tributes

Artists Performing at the 2006 Telethon*(confirmed as of 8/10/06)*

<http://www.keatonsimons.com/>
<http://www.paperbackhero.com/>
<http://www.muscletonerecords/>
<http://www.edenautomatic.com/>
<http://www.kanary.com/>
<http://www.bigdume.com/>
<http://www.debpasternak.com/>
<http://www.courtneycronin.com/>
<http://www.meleamusic.com/>
<http://www.hardluckstory.com/>
<http://www.peach.us/>
<http://www.laurenadams.com/>
<http://www.digjelly.com/>
<http://www.analoginmusic.com/>
<http://www.detweilermusic.com/>
<http://www.kellyslot.com/>
<http://www.myspace.com/hepctelethon>

HealthWise:

Not Trivial Liver Trivia



Lucinda K. Porter, RN

October is liver awareness month. The liver deserves this attention, especially since most people seem barely aware of their livers. This may be because the liver is a *non-complaining organ*. Three quarters of the liver can be damaged and you might not notice any signs of it. Nobel Laureate Pablo Neruda underscores this in his eloquent poem *Ode to the Liver*. Neruda describes the liver as “modest, together friend, profound worker” and an “invisible machine.”¹

The liver is praised in poetry, art and myth. Prometheus had his liver destroyed daily by an eagle. At night, his liver would mend, only to be pecked at again the next day. Although this exaggerates the capability of the liver, it illustrates that the Greeks recognized the awesome ability of the liver to recover.

Some ancient cultures believed that the liver was the most important organ, more so than the heart. The Greeks believed that the soul resided in the liver. It was the source of love and passion. Journalist Mary Roach noted that if the liver maintained this prestige, we would be seeing bumper stickers declaring “I (liver symbol) New York” rather than “I ♥ New York.”

There are literary connections to the liver. In Shakespeare’s *Macbeth*, a coward is called *lily-livered*. The liver is normally a dark reddish-brown or maroon color. A bloodless liver, white as a lily, refers to a lack of courage. Portraying the mighty liver, Neruda writes: “Seafaring anger soul whose innards measure blood, you live hands on oars and eyes ahead navigating the hidden mysteries, the alchemist’s chamber of life’s microscopic, echoic, inner oceans.”²

In keeping with liver awareness month, here is some liver trivia. These facts may not win you a Jeopardy championship, but you may win at Hepardy.

- The word *liver* traces its origins to a number of languages, Old English and German being two of them. It may mean to “fatten up.” This seems particularly apt, given the rise of fatty liver disease in the United States.
- The liver is the *largest internal organ*. Roughly, the size of a football, a man’s liver typically weighs around three pounds.
- Everything passes through your liver. This includes everything you eat, breathe, and apply to your skin.
- The liver is made up of specialized cells called *hepatocytes*. *Hepatic* comes from the Greek word for liver, *hepar*. *Hepatitis* means inflammation of the liver. A *hepatologist* is a liver disease specialist.
- The liver can re-grow damaged cells. This is known as *regeneration*. The liver can regenerate an entire liver from only one-fourth of a functioning liver.
- A veritable highway system of arteries, veins and capillaries run through the liver. A quart and a half of blood flows through the liver every minute.
- The liver produces bile, which is necessary for the digestion of fats. Bile passes through a duct system that rivals the Alaskan pipeline. Most of the bile pours into the small intestine, where it breaks down fat. Some bile is stored in the gall bladder.
- You can live without your gall bladder. You cannot live without your liver.
- A double-layered membrane encases the liver. This protects the liver against friction from nearby organs.
- Liver cells do not have nerves. This means that technically a liver biopsy would not hurt if doctors could perform a liver biopsy without puncturing the skin, membrane and surrounding tissue. However, the majority of liver biopsy procedures are *percutaneous*, meaning a needle needs to pass through the skin and surrounding tissue in order to get to the liver. This is why a local anesthetic is used to numb the area.
- The liver has over 500 functions. The human body relies on the liver for regulation of energy,

continued on page 7

Extrahepatic Manifestations: *Cryoglobulinemia*

■■■
Alan Franciscus, Editor-in-Chief

A large study by the MULTIVIRC group reported that 74% of patients with hepatitis C had at least one extrahepatic (outside the liver) manifestation. The most common conditions included essential mixed cryoglobulinemia (40%), arthralgia or joint pain (23%), paresthesia (17%), myalgia (15%), pruritus (15%), and sicca syndrome (11%). This article will discuss one of the most common conditions associated with hepatitis C called essential mixed cryoglobulinemia (EMC).

Cryoglobulinemia is a blood disorder that is caused by abnormal proteins in the blood called cryoglobulins that precipitate or clump together when blood is chilled and then dissolve when rewarmed. These proteins can be deposited in small and medium-sized blood vessels which can lead to restricted blood flow to joints, muscles, and organs.

The cause of cryoglobulinemia is not completely understood, but it is thought to be an autoimmune disorder (caused by the body's immune system producing antibodies that attack healthy cells). The term frequently used is essential mixed cryoglobulinemia because the exact cause is unknown. There are three types of cryoglobulinemia—type I, type II and type III. Type I does not have rheumatoid factor activity whereas type II and III have rheumatoid factor activity. Rheumatoid factor is an antibody found in the blood of people afflicted with

rheumatoid arthritis (a chronic autoimmune disease characterized by inflammation of the joints).

HCV AND CRYOGLOBULINEMIA

The direct relationship between HCV and cryoglobulinemia has not been established but it is believed that the hepatitis C virus attaches itself to B lymphocyte cells, which causes the immune system to produce autoantibodies.

The high prevalence of HCV in people with cryoglobulinemia leads us to believe that there is a direct link between HCV and cryoglobulinemia. In fact, one study found that 95% of patients with cryoglobulinemia had evidence of the hepatitis C virus or HCV antibodies. Cryoglobulinemia is also associated with hepatitis B infection and other liver disorders, but to a much lesser extent. Longer duration of HCV infection, female gender and the presence of cirrhosis are factors that are strongly correlated with cryoglobulinemia.

In people with hepatitis C only about 10% of people with cryoglobulinemia show signs or symptoms of this condition. The other 90% of people with HCV and cryoglobulinemia have no symptoms or any of the blood or organ disorders associated with the condition.

SYMPTOMS

The people with symptomatic hepatitis C-related cryoglobulinemia can have ongoing problems

Arthralgia: joint pain

Paresthesia: burning, prickling, itching or tingling

Myalgia: muscle pain and tenderness

Pruritus: severe itching

Sicca syndrome: an autoimmune disorder that can damage the glands that produce tears and saliva

that can cause many symptoms and disorders. The most common symptoms and disorders associated with the condition include:

- **Vasculitis:** inflammation of the small blood vessels of the skin, kidneys, gastrointestinal tract and other organs of the body. It can also cause red or purple blotching skin (especially on the lower extremities of the body), rashes, sores, and ulcers

- **Renal (kidney) disease:** caused by the deposition of proteins in the kidney. Symptoms include blood and proteins in the urine

- **Arthralgias and arthritis:** pain and/or inflammation in the joints

- **Itching:** mild to severe

continued on page 7

Tuberculosis in People with Hepatitis C



Liz Highleyman

Tuberculosis (TB) is one of the leading causes of disease-related mortality. It is estimated that approximately 2 billion people worldwide are infected with *Mycobacterium tuberculosis*, the bacterium that causes TB, with about 8 million new cases and 2 million deaths per year. TB is most common in the developing world, especially in Africa and Asia, but remains a concern in the United States.

TRANSMISSION AND RISK FACTORS

TB is spread through sputum droplets that spread when infected people cough, sneeze, or spit. In the United States, the disease occurs most often among individuals in communal residential settings such as homeless shelters, prisons, and long-term care facilities. Healthcare providers exposed to infected patients are also at risk. The risk of transmission can be reduced by using disposable face masks and HEPA air filters.

People with compromised immunity are more susceptible to TB. This includes young children, the elderly, malnourished individuals, people taking immune-suppressing drugs, and people with HIV. It is estimated that people with HIV are about ten times more likely to develop active TB compared with HIV negative persons. Injection drug users also have higher TB rates than the general population.

People at risk for TB, including HIV positive individuals and

healthcare providers, should be screened regularly. This is done using a test in which a small amount of tuberculin protein (PPD) is injected under the skin. The site is checked after 2-3 days to see if a hypersensitivity reaction (a hard swelling) develops. People exposed to TB may test positive even if they do not have active disease; other tests, including lung fluid examination (sputum smear) and chest X-rays, are performed to confirm active disease.

SYMPTOMS AND DISEASE PROGRESSION

Not everyone infected with TB bacteria develops active disease. Most people (about 90%) with healthy immune systems control the infection without treatment. People with latent (inactive) TB have no symptoms and do not spread the disease to others. TB may remain inactive for life, or may become active if a person's immunity later becomes compromised.

TB usually attacks the lungs, settling in the alveoli (air sacs). The immune system mounts a response and builds structures called tubercles to wall off the bacteria; these may burst, leaving cavities and scars. If the immune response is inadequate, the bacteria may enter the bloodstream and migrate to other parts of the body, including the brain, bones, kidneys, and liver (known as extrapulmonary TB). People with active TB typically

have symptoms including:

- Persistent productive cough (longer than 2-3 weeks)
- Coughing up blood
- Chest pain
- Fever (possibly night sweats)
- Persistent fatigue
- Loss of appetite
- Weight loss (possibly severe wasting)

TREATMENT

There are two types of TB treatment: prophylaxis to prevent latent TB from developing into active disease, and treatment for active disease. Prophylaxis typically consists of either isoniazid (INH) for 6-9 months or a 2-month course of rifampin (also known as rifampicin) plus pyrazinamide.

Treatment of active TB requires combination therapy, which typically consists of INH, rifampin or rifapentine (Priftin), and pyrazinamide, plus either ethambutol (Myambutol) or streptomycin. The standard course of treatment is 6 months; if resistance testing shows that an individual's bacteria are susceptible to isoniazid and rifampin, ethambutol or streptomycin can be discontinued. Combination pills containing INH plus rifampin (Rifamate) and INH, rifampin, and pyrazinamide (Rifater) are available.

People with active TB should be isolated to prevent transmission. Once a person starts treatment, they typically are no longer infectious after 2-3 weeks. Although patients usually start to feel better within a few weeks, it is important to complete the full course of therapy. Because TB is a serious public health concern, directly-observed therapy is often employed.

continued on page 6

TUBERCULOSIS

continued from page 5

DRUG-RESISTANT TB

TB can mutate to develop resistance to drugs, especially if an agent is used as monotherapy, if adherence is poor, or if treatment is not completed. Strains of TB resistant to the major first-line drugs – known as multidrug-resistant TB or MDR-TB – are increasingly common. Treatment of MDR-TB requires intensive therapy with more drugs for a longer period of time (up to 2 years). Some of the additional drugs used to treat MDR-TB include aminoglycosides, fluoroquinolones, cycloserine, and ethionamide.

More recently, extensively drug-resistant strains of TB (XDR-TB) have emerged, which are resistant to all first-line and most second-line drugs. The Centers for Disease Control and Prevention has documented more than 350 cases of XDR TB worldwide. At the International AIDS Conference in Toronto in August, researchers reported an outbreak of more than 50 cases of XDR-TB among HIV positive people in the KwaZulu-Natal province in South Africa; since then, XDR-TB strains have been detected at 28 hospitals. This type of TB is extremely aggressive, with 98% of patients dying during follow-up, after an average of just 16 days.

HEPATOTOXICITY OF TB TREATMENT

Like most drugs, agents used to treat TB drugs can cause side effects and drug interactions. INH, rifampin or rifapentine, and pyrazinamide can all cause liver toxicity, which may be indicated by elevated liver enzymes (ALT and AST), fatigue, loss of appetite, abdominal pain, and jaundice (yel-

lowing of the skin and eyes). Use of these drugs in combination further increases the risk.

INH appears to cause liver damage due to the production of a toxic metabolite as the drug is broken down. While about 10%-20% of patients taking INH develop mild, transient liver enzyme elevations, usually within the first few months after starting the drug, in rare cases (about 1%-2%) it can lead to life-threatening liver failure. Severe INH-related hepatotoxicity is more common in women and the risk also increases dramatically with age. It is thought that some people are genetically predisposed to INH liver toxicity, but specific genes have not been identified.

Several studies suggest that people with pre-existing liver disease, including chronic hepatitis C, are more susceptible to liver toxicity while taking anti-TB drugs. In one study, for example, patients with HCV were five times more likely to develop liver toxicity related to INH, while HIV/HCV coinfecting patients had a 14-fold higher risk. Other studies, however, indicate that only patients with elevated liver enzymes or fibrosis before starting INH are at increased risk. People with hepatitis C should avoid alcohol in any case, but this is especially important during TB treatment.

Because most first-line anti-TB agents carry a risk for liver toxicity, there are limited options for hepatitis C patients who require TB therapy (for example, not using INH in combination with pyrazinamide). Such individuals should be treated by physicians who have experience with both diseases. In most cases, HCV positive individuals can be successfully treated for active TB with careful monitoring (one group of experts recommends twice weekly during the first 2

weeks, once weekly through the remainder of the first 2 months, then once monthly). Some experts do not recommend prophylaxis for patients with latent TB who are at elevated risk for liver toxicity – believing the likelihood of liver failure may be greater than the risk of active TB – but this approach is controversial.

TB drugs can interact with other medications, which may require dose adjustment, selection of alternative agents, or delayed treatment for another condition while TB therapy is completed. Rifampin and rifapentine, in particular, may interact with antiretroviral drugs used to treat HIV, especially protease inhibitors. There is little research concerning interactions between TB drugs and interferon or ribavirin. There have, however, been case reports of latent TB becoming active during treatment with interferon, which can impair immune function.

CONCLUSION

In contrast with HIV, there has not been much research on coinfection with hepatitis C and TB. More studies in this area are needed, as well as the development of anti-TB drugs that carry less risk for liver toxicity.

References:

American Thoracic Society, CDC, and Infectious Diseases Society of America. Treatment of Tuberculosis. *Morbidity and Mortality Weekly Report* 52(RR11). June 20, 2003. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm>.

Weisiger, R. Isoniazid Hepatotoxicity. WebMD E-Medicine. August 2, 2005. <http://www.emedicine.com/med/topic1193.htm>.



LIVER

continued from page 3

hormonal balance and clotting. It also filters nutrients, poisons and bacteria.

- The immune system depends on the liver. The liver produces approximately one quart of lymphatic fluid daily.
- Drugs and alcohol are metabolized by the liver.
- The liver is an important player in the metabolism of carbohydrates, protein, and fats.

The liver is always doing something such as storing, converting, producing, maintaining, breaking down, processing, filtering, regulating, or removing something. Neruda's ode puts it like this: "you suck and score, you distinguish and divide, you increase and lubricate, you give home to life's enzymes and grams of experience."

In short, the liver is more of a factory than a house for the soul. However, what a grand factory it is! Neruda dubs it a *visceral warehouse*. So as you eat, drink, breathe, work, and play, remember to care for your liver. Be aware, not just in October but all year. "Do not betray me! Work on! Do not arrest my song."³

¹ Neruda, Pablo, "Oda al Hgado", translated by Morales, H. and Hochman, W.

² *ibid.*

³ Neruda, Pablo, "Oda al Hgado", translated by Kalant, O.

**CRYO**

continued from page 4

- *Fatigue*: mild to severe
- *Pain*: mild to severe
- *Lymph node enlargement*: swollen gland-like tissue in the lymphatic vessels containing cells that become lymphocytes (white blood cells)
- *Peripheral neuropathy*: numbness and tingling in the hands, legs and feet that is due to decreased blood and/or inflammation of the peripheral nerves.
- *Stomach pain*
- *Bleeding disorders*: internal bleeding and abnormal blood clot formations

Other conditions associated with cryoglobulinemia include non-Hodgkin's lymphoma (cancers of the lymphoid system), Raynaud's syndrome (a disorder that causes the blood vessels in the fingers, toes, ears, and nose to constrict or narrow), and multiple myeloma (cancer of the bone marrow). The more serious consequences of cryoglobulinemia are usually only seen after many years or decades of infection with HCV.

DIAGNOSIS

Cryoglobulinemia is usually noticed in patients because of the blotchy skin rash seen on the lower extremities. A simple blood test is performed to diagnose cryoglobulinemia, but the blood sample has to be handled very carefully – drawing the blood sample at room temperature then cooling it to see if the blood precipitates or clumps together.



**HEPATITIS C
SUPPORT PROJECT**

**Executive Director
Editor-in-Chief,
HCSP Publications**

Alan Franciscus
alanfranciscus@hcvadvocate.org

Managing Editor, Webmaster

C.D. Mazoff, PhD
cdmazoff@hcvadvocate.org

Contributing Authors

Liz Highleyman
Lucinda K. Porter, RN

Design

Paula Fener
Blue Kangaroo Design
blueroodesign@aol.com

Contact information:

Hepatitis C Support Project
PO Box 427037
San Francisco, CA 94142-7037

The HCV Advocate offers information about various forms of intervention in order to serve our community. By providing information about any form of medication, treatment, therapy or diet we are neither promoting nor recommending use, but simply offering information in the belief that the best decision is an educated one.

Reprint permission is granted and encouraged with credit to the Hepatitis C Support Project.

© 2006

Hepatitis C Support Project

continued on page 9

SOUTH CAROLINA ORGAN DONOR REGISTRY

Just like their northern neighbor, the state of South Carolina does not maintain its own organ donor registry. South Carolina residents may signify their wishes on their driver's license or state identification. South Carolina residents, who wish to carry a record of their wishes, may download a universal organ donor card at:

www.shareyourlife.org/become_donor_card.pdf

South Carolinians are encouraged to convey their preferences to their loved ones. A family notification form can be downloaded at:

www.shareyourlife.org/become_notifi_form.pdf

October is liver awareness month. Perhaps this is a good time to promote liver donation. Talk to family, friends, co-workers, classmates and others about this. For more information about organ donation, check out: *www.carolinadonorservices.org*

Help Us Reach More People with Hepatitis C!
SUPPORT US THROUGH EITHER A PAID SUBSCRIPTION OR DONATION

YES! I'd like to subscribe

\$20 one year—12 issues

\$10 one year—12 issues
 (for those with fixed incomes)

Renewal

NAME _____

ADDRESS _____

CITY _____

STATE _____ ZIP _____

**YES! I'd like to make
 a tax deductible donation**

\$10 \$25
 \$100 other

Please make checks payable to: HCSP/The Tides Center

Please mail form to:

HCV ADVOCATE
 P.O. Box 427037
 San Francisco, CA 94142-7037



The Hepatitis C Support Project does not share its mailing list with any individual or organization. All subscribers' names and addresses are strictly confidential

CRYO

continued from page 7

TREATMENT

The approach to treating HCV related cryoglobulinemia is to treat the underlying cause, hepatitis C. Prior to pegylated interferon and ribavirin therapy, interferon monotherapy was used with very little effectiveness. However, studies have found that the use of pegylated interferon plus ribavirin has produced better results especially in patients who achieve a sustained virological response. Cryoglobulin disappearance, improvement in kidney response and complete or partial cryoglobulinemia syndrome response has been found in some people successfully treated with pegylated interferon therapy. It should be noted that interferon may exacerbate some autoimmune disorders so monitoring for these potential problems during interferon/ribavirin treatment is needed.

Other treatment strategies include medication to reduce the inflammation and suppress the immune system with a combination of nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen, corticosteroids) to reduce the inflammatory response, plasmapheresis (removing the plasma from the body, returning the blood cells to the body, and replacing the plasma with a saline solution to remove the cryoglobulins) and hypo-antigenic-content diet (LAC diet). Immunosuppressive therapy is not recommended for HCV-related cryoglobulinemia since immunosuppressant drugs can lead to increased hepatitis C viral replication.

Rituximab is a drug currently used to treat non-Hodgkin's lymphoma and rheumatoid arthritis, and it is being studied to treat cryoglobulinemia. In the studies to date, rituximab has been found to

be effective in most patients with cryoglobulinemia, but, since the drug can increase HCV viral replication, more studies are needed to further understand the implications of increased viral replication.

In conclusion, HCV-related cryoglobulinemia is one of the most common extrahepatic manifestations of HCV. Approximately 40% of people with hepatitis C have blood markers for this condition. However, only a small fraction (10%) of the people with hepatitis C who have these markers are symptomatic. In addition, severe consequences of hepatitis C-related cryoglobulinemia usually require a long period of infection with hepatitis C virus before the severe damage occurs. Treatment of symptomatic HCV-related cryoglobulinemia usually consists of treating the underlying cause—HCV. Talk to your medical provider or a specialist in cryoglobulinemia if you have any of the signs or symptoms of cryoglobulinemia.

Be sure to checkout these other publications on Extrahepatic Manifestations of HCV. They can be found on the Fact Sheet page of our website:

- Extrahepatic Manifestations (overview)
- Lichen Planus
- Non-Hodgkin's Lymphoma (NHL)
- Porphyria Cutanea Tarda (PCT)
- Pruritus (Itching)
- Sjögren's (Show grins) Syndrome

H CSP CUSTOMIZABLE GUIDES

The Hepatitis C Support Project is pleased to announce a new service: *Downloadable Customizable Guides*.

Just go to <http://www.hcvadvocate.org/Customize/Guides.html> and follow the instructions. Simply enter in the name and address of your support group or your medical practice, and then select the Guide you wish to customize with your information.

Below are just a few of the Guides that you can customize:

- *A Guide to Understanding Clinical Trials and Medical Research in Hepatitis C*
- *A Guide to Understanding Hepatitis C*
- *A Guide to Understanding Hepatitis C Basics*
- *Aging and Hepatitis C: An HCSP Guide*
- *Coping with Depression and Hepatitis C*
- *Easy C - A Guide to HIV and Hep C Coinfection*
- *Easy C - A Guide to Understanding Hepatitis*
- *First Steps with HCV for the Newly Diagnosed*
- *HCV Treatment: A Guide to Help You Stay on Treatment*
- *Hepatitis C Support Group Manual*
- *Management of Hepatitis C by the Primary Care Provider: Monitoring Guidelines*
- *Next Steps: When HCV Treatment Isn't Working*
- *Stigma and Hepatitis C*
- *Women and Hepatitis C: An HCSP Guide*



For Living Positively. Being Well.



www.hcvadvocate.org

HCSP

P.O. Box 427037
San Francisco, CA
94142-7037