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Hepatitis C Combination Therapies in Pill Form Move Nearer

Liz Highleyman,

The latest data on three experimental hepatitis C drug candidates were presented at the American Association for the Study of Liver Diseases meeting, held November 11-15 in San Francisco. Current standard treatment for hepatitis C is based on interferon, an injected cytokine that stimulates immune response. In contrast, several investigational oral agents work by directly targeting the hepatitis C virus, similar to antiretroviral agents used to treat HIV.

Valopicitabine

Christopher O'Brien from the University of Miami presented the first interim data from an American Phase IIb trial of valopicitabine, or NM283, a nucleoside analogue hepatitis C polymerase inhibitor being developed by Idenix Pharmaceuticals.

The study included 190 patients randomly assigned to receive 800mg valopicitabine monotherapy, one of three doses (400mg, ramped dosing from 400 to 800mg, or 800mg once daily) of valopicitabine plus pegylated interferon alpha-2a (Pegasys) 180mg/week, or pegylated interferon plus ribavirin 1000-1200mg daily; 152 participants completed 12 weeks of treatment. Baseline characteristics were similar in the five arms, with a mean age

of about 50 years. By ethnicity, 51-76% were Caucasian, 10-23% were East Asian, 10-23% were Middle Eastern or Indian, and fewer than 2% were African-American.

All were previous non-responders who did not clear hepatitis C with twelve weeks or more of pegylated interferon plus ribavirin, the standard treatment for HCV infection; relapsers were excluded. All had genotype 1 hepatitis C, baseline hepatitis C RNA of at least 100,000 copies/ml, and compensated liver disease.

After twelve weeks, patients in the two higher-dose valopicitabine combination arms achieved significantly greater suppression of hepatitis C RNA compared with the pegylated interferon/ribavirin arm. Hepatitis C viral load declined by 0.78 log₁₀ copies/ml in the valopicitabine monotherapy arm, 1.92 log₁₀ copies/ml in the pegylated interferon/ribavirin arm, 2.22 log₁₀ copies/ml in the 400 mg valopicitabine combination arm, 2.51 log₁₀ copies/ml in the in 400-800 mg valopicitabine combination arm, and 2.77 log₁₀ copies/ml in the 800mg valopicitabine combination arm (p=0.001 for the latter two arms compared with pegylated interferon/ribavirin).

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Standard of Care

Note to the Readers: The following opinion article is from a "Longtime" member of the Hemophilia Association of the capital area.

Definition of 'Standard of Care': 'A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness, or clinical circumstance....' (MedicineNet.com) The standard of care reflects the combined wisdom and experience of healthcare providers; but it isn't always right! In fact, I can remember four occasions in which the standard of care for hemophilia was substantially incorrect.

Certainly the most inspiring example was the one set by Dr. Michael Kuhn of New Jersey, who passed away far too early in a tragic accident. This story dates back to the late 60's when cryoprecipitate (cryo), the first truly effective hemophilia A drug, had become available. But cryo required deep freezing, careful thawing, plus monitoring during administration for allergic reaction. So, hemophiliacs were still tethered to the hospital visit for therapy. This was miserable for many reasons: wasted time traveling to hospitals and waiting in emergency rooms (often in the middle of the night), prolonged unnecessary bleeding, unavailability of therapy anyplace far from a major city, etc. etc. Dr. Kuhn took on a mission to allow all hemophiliacs in New Jersey to maintain and administer cryo in their own homes. This was a direct challenge to the standard of care. And it opened him up to serious medical and legal challenge. But he did it; and he was right; and people's joints were saved because of his heroism. There are saints in this world.

And then, of course, there was the standard of care in the early 80's as the AIDS epidemic began: "continue to infuse" with product. I'm a little less sure about this one; this whole period remains a bitter memory to me. But I understand that one hemophilia treatment center in Ohio, and one in the Pacific NW, moved their patients over to cryo as soon as they began to suspect that something horrible was in the commercial product. As I understand it, those centers saved most of their patients from HIV.

But I also remember some considerably less inspiring

situations.

There was the period in the late 50's when a decision was made that the standard of care for active joint bleeds should include maintaining the joint outstretched. This was supposed to prevent 'contractures' (deformation and loss of joint mobility). It was a painful and nonsensical standard.

There was also a period in the late 50's the standard of care pain medication for hemophilic bleeds was Darvon with aspirin. How I remember those pink pills as I lay in the hospital. They didn't work. It was a drug firm fraud. Darvon is a synthetic opiate with a low maximum ceiling of effectiveness. It works to a point, but increased doses don't relieve the pain at all. But other opiate effects, like suppression of respiration, those were still there. So, people died from overdoses of Darvon because they were trying to obtain pain relief. Many many people just suffered. And the pain of a severe joint bleed...it was very very very very hard.

Two footnotes here.

1. The standard Darvon preparation in those days included aspirin. So the drug was not only ineffective for severed pain. It was also toxic to hemophiliacs.
2. Public Citizen's Health Research Group has recently petitioned FDA to 'phase out' Darvon because hundreds of people die each year from overdose.

The message I'm trying to leave is that standard of care isn't gospel. And I guess that I'd also like to indicate my own suspicion that the next situation where I expect to see dramatic changes in standard of care is in Hepatitis C therapy, particularly for long established cases. I'm educated in this suspicion from two facts: first, the treatment for long-established cases is not only difficult, but also often ineffective; and two, we are beginning to see reports of experimental medicines that attack the virus metabolism directly. Just a suspicion folk, and at that, just from an educated layman.

Mark Antell

March 1, 2006

Longtime member of HACA with a bleeding disorder.

HCV/HIV Today is published bi-monthly by the Hemophilia Association of the Capital Area. Comments and questions from our readers are strongly encouraged. Please address all correspondence to Editor: HACA, 3251 Old Lee Highway, Suite 3, Fairfax, VA 22030-1504 or call (703) 352-7641. Any information contained in this newsletter related to the diagnosis or treatment of either hemophilia, HIV or HCV is intended for educational purposes only; HACA does not recommend or discourage any specific medical services or treatments. All questions regarding medical care should be decided by patients in consultation with their physicians or medical providers. Any reader wishing to learn more about any topic contained in this newsletter can contact HACA, and will be directed to the appropriate source.

HCV News Reports from the 2006 Retrovirus Conference

Liz Highleyman

Although this year's Conference on Retroviruses and Opportunistic Infections, held February 6-9 in Denver, did not feature any groundbreaking news on hepatitis or coinfection, some 70 presentations dealt with various aspects of this topic. For conference abstracts and webcasts of oral presentations, visit the website at www.retroconference.org/2006.

Kicking off the conference, Takaji Wakita from Japan (abstract 15) reviewed a new method of cultivating HCV in the laboratory. This method offers "a powerful tool with which to study the viral life cycle," he concluded, compared with existing replicon models that produce non-infectious virus-like particles. At a Wednesday symposium, T. Jake Liang of the National Institutes of Health (abstract 170) presented an overview of HCV, its impact on the liver, and the body's immune response. Stuart Ray of Johns Hopkins (abstract 171) looked at current challenges in the management of HIV/HCV coinfection. Also, Ann Kwong from Vertex Pharmaceuticals (abstract 172) reviewed the development of novel therapies targeting HCV, including the protease inhibitors VX-950 and SCH 5030304, while Daria Hazuda from Merck (abstract 173) followed with a discussion of HCV polymerase inhibitors.

HCV Treatment

Manel Crespo and colleagues from Barcelona (abstract 81) reported on treatment of genotype 2/3 HCV in HIV positive patients. In this retrospective review, they looked at data from 42 subjects (41 with genotype 3; 1 with genotype 2) treated with either conventional or pegylated interferon (Peg-Intron) plus ribavirin for 24 weeks. Sustained virological response (SVR) rates were 43% using conventional interferon and 71% using Peg-Intron. End-of-treatment (EOT) and SVR rates were higher among patients who achieved undetectable HCV viral load by four weeks, and relapse rates were lower (46% vs 5%). These results suggest that 24 weeks of pegylated interferon/ribavirin is sufficient for a majority of HIV positive people with genotype 2 or 3 HCV, and that rapid virological response (RVR) at week 4 could be used to predict the eventual outcome. This contradicts some previous research and recent guidelines suggesting coinfecting patients may benefit from longer treatment.

Based on data from the APRICOT study, Douglas Dieterich and colleagues (abstract 856) reported that rapid virological response at four weeks also predicted SVR in coinfecting patients with genotype 1. Among 176 genotype 1 patients treated with pegylated interferon

(Pegasys) plus ribavirin, 75-83% of those with RVR went on to achieve SVR, regardless of whether they started with high or low HCV viral load. Previous research has shown that lack of early virological response (EVR) at 12 weeks could be used as a cut-off for stopping therapy; these two studies suggest this cut-off may be pushed back even earlier, sparing patients the side effects and cost of additional therapy that is unlikely to produce a sustained response.

In a study by Alison Uriel and colleagues (abstract 854), again, prolonged therapy was not associated with a higher SVR rate. In this multicenter trial, 177 coinfecting participants (80% genotype 1) initially received Peg-Intron/ribavirin for 24 weeks. The 61 patients with undetectable HCV RNA at week 24 were then randomly assigned to receive treatment for 24 (standard course) or 48 (prolonged course) additional weeks; SVR rates were 50% and 54%, respectively. However, more than half of the 61 patients did not complete treatment due to side effects or refusal to consent to further therapy after 24 weeks, leading the researchers to conclude that "longer...therapy may not be feasible for many HIV-infected patients."

Higher-dose therapy has also been suggested for coinfecting patients. However, T. Ruys and colleagues (abstract 852) reported that high-dose induction therapy with Peg-Intron (3 mcg/kg/week for four weeks, 2 mcg/kg/week for four weeks, then 1.5 mcg/kg/week for 40 weeks) plus ribavirin did not appear more effective than standard-dose Peg-Intron (1.5 mcg/kg/week for 48 weeks) plus ribavirin. In this pilot study of 23 coinfecting participants (10 genotype 1; 10 genotype 3; 3 genotype 4), 38% of patients in the induction arm achieved SVR, compared with 35% in the standard-dose arm. Nearly one-third of subjects in the high-dose induction arm required dose reduction or treatment discontinuation due to neuropsychiatric side effects, versus none in the standard-dose arm.

The reason for poorer response to interferon in HIV/HCV coinfecting compared with HCV mono-infected individuals remains unclear. Some researchers have hypothesized that the difference is related to immune status. However, in a study by Susan Hopkins and colleagues (abstract 860), nadir (lowest ever) CD4 count did not predict response to pegylated interferon plus ribavirin. This retrospective analysis included 124 coinfecting patients (about half with genotype 1) in London and Dublin. Median baseline and median nadir CD4 counts were 440 and 208 cells, respectively; about

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HCV News Reports from the 2006 Retrovirus Conference (continued)

60% were on HAART. SVR was achieved by 25% of genotype 1 and 75% of genotype non-1 patients. In a multivariate analysis, genotype was the only statistically significant predictor of sustained response – nadir CD4 count had no significant effect.

Progression and Fibrosis

Offering some promising news, Pablo Barreiro and colleagues from Madrid (abstract 859) reported that successful hepatitis C treatment can reverse liver damage in HIV/HCV coinfecting individuals. In this study of 112 patients (70% genotype 1; 44 with SVR; 68 nonresponders or relapsers), moderate to severe fibrosis (stage F3-F4) was less common in sustained responders. Further, fibrosis scores decreased as elapsed time since completion of hepatitis C treatment increased. Several past studies have shown that patients with HCV mono-infection who achieve SVR experience regression of liver fibrosis, and it is reassuring to learn that this can also occur in coinfecting individuals – although the researchers noted that “long periods of time seem to be required to show this benefit.”

Barreiro's study offered evidence that the noninvasive FibroScan elastometry test is useful for coinfecting individuals as well as those with HCV alone. Mark Sulkowski and colleagues (abstract 867) also reported on a noninvasive metric – the Johns Hopkins Fibrosis Index – comprised of laboratory measures (albumin, AST, and platelet count) and history of alcohol use that accurately predicted fibrosis in coinfecting patients. In addition, Huda Al-Morhi and colleagues from Montreal (abstract 869) used the noninvasive APRI index to assess fibrosis in 162 coinfecting patients. In a multivariate analysis, any amount of past alcohol use was linked to more severe fibrosis, but not history of injection drug use or tobacco or marijuana smoking. Higher CD4 cell count was associated with less severe fibrosis, but current HAART use had no significant effect.

HIV Treatment

Research continues to provide conflicting data on treatment of HIV in coinfecting individuals. Renato Maserati and colleagues (abstract 846) analyzed 201 coinfecting and 684 HIV mono-infecting subjects in the Italian MASTER Cohort who were on HAART with undetectable HIV viral load for at least 12 months. In contrast to some past studies, the researchers found that having HCV did not appear to reduce CD4 cell recovery. However, presence of genotype 2 or 3 HCV was signifi-

cantly associated to worse CD4 recovery compared with genotypes 1 or 4. Marina Nuñez and colleagues from Madrid (abstract 847) presented data showing that HIV/HCV coinfection is associated with increased T-cell apoptosis (programmed cell death), which may help explain impaired CD4 cell recovery following HAART initiation.

Certain antiretroviral medications used to treat HIV, in particular protease inhibitors, have been linked to increased blood cholesterol and triglyceride levels. Jack Stapleton and colleagues (abstract 878) analyzed 1440 HIV positive participants (161, or 11% with HCV) starting HAART for the first time in the ACTG 5001 (ALLRT) study. Blood fat levels rose over time in both HIV mono-infecting and HIV/HCV coinfecting subjects. In contrast to some past studies, fasting cholesterol levels were similar in the two groups after 48 weeks. However, more HIV mono-infecting than coinfecting subjects required lipid-lowering medications (4% vs none). In a study of 415 HIV mono-infecting and 307 HIV/HCV coinfecting subjects (13% with genotype 3), G. Lapadula and colleagues (abstract 877) found that coinfecting patients were less likely to develop high cholesterol and triglyceride levels while on HAART, but that this effect was driven by those with HCV genotype 3.

One of the major stories at this year's conference was a report by Kenneth Lichtenstein and colleagues suggesting that earlier initiation of HAART in HIV mono-infecting individuals is associated with better outcomes and fewer adverse side effects. Laure Valerio and colleagues (abstract 891) presented evidence that starting HAART earlier benefits coinfecting patients as well. Using a mathematical model, Valerio's team estimated that a cohort of coinfecting individuals with a mean age of 37 starting HAART for the first time with a CD4 cell count of 200-350 had a projected life expectancy of 13.21 years (assuming that antiretroviral therapy would remain effective for 10 years). However, life expectancy increased to 14.48 years when HAART was initiated with 350-500 CD4 cells, leading the researchers to conclude that, “Earlier ART initiation is likely to increase life expectancy of HIV/HCV-co-infected patients by at least 1.27 years.”

HCV Advocate March 2006

HealthWise: Stigma: Living with the Labels of Others

Lucinda K. Porter, RN, CCRC

In the latest issue *Hepatitis* magazine, the staff conducted an informal web poll about stigma and viral hepatitis. (Jan. 2006, Vol. 8, No. 1, p. 53) The article reported both good and bad news. First the good news: 42% of the participants felt they had not faced any stigma due to living with hepatitis B (HBV) or hepatitis C (HCV). Now the bad news: 20% felt they had experienced job discrimination due to HBV or HCV; 13% reported hepatitis-related social stigma; 13% had been alienated from family and friends because of viral hepatitis. The most remarkable report was that 8% of those in this informal survey felt that medical professionals had denied service to them because of HBV or HCV.

According to the Oxford Dictionary, the definition of stigma is, "a mark of disgrace associated with a particular circumstance, quality or person." The Greek and Latin roots of stigma mean "to mark, brand or tattoo." The dictionary Encarta defines stigma as "a sign of social unacceptability: the shame or disgrace attached to something regarded as socially unacceptable." Merriam-Webster's descriptions of stigma include "a mark of shame or discredit; an identifying mark or characteristic; a specific diagnostic sign of a disease."

Sadly, hepatitis C does carry a stigma. I believe this is for three reasons. First, HCV is potentially infectious. Although not easily transmitted, people are nevertheless fearful and shun those who have the disease. My neighbor would not let her teenager visit my family after she learned I had HCV. Fear and ignorance have cost patients their jobs, friendships and marriages. Hugs and kisses cease. Sexual relationships stop or are never initiated. In the extreme, even marriages have been challenged.

Another stigma associated with HCV is connected in a more general way. Some people do not like to be around people who are "sick." The disease itself does not seem to matter. It does not have to be an infectious disease, nor one with obvious symptoms. I speculate that this is a fear-based response. Some people are afraid of illness and death and they shun others who have a disease or illness. They may also be afraid that someone they care for will die, so they reject that person rather than risk the loss.

A third stigma connected to hepatitis C is from its association with injection drug use. Misinformed people sometimes assume that all hepatitis C patients have a history of injection drug use in spite of the many ways hepatitis C can be acquired. Our society lacks compassion and understanding about injection drug use. Those

who never used injection drugs do not want to carry that label. Former injection drug users feel haunted by their past. Active injection drug users carry the burden of having two stigmatized diseases – addiction and hepatitis C¹.

It is tragic to witness this unnecessary and avoidable ostracism. Those struggling to live with a chronic disease need more support, not less. To some, the isolation is worse than the virus. It is heartbreaking to witness, especially when patients are newly diagnosed and need the most support.

On TV, commercials freely discuss erectile dysfunction, but hepatitis C remains in the closet. This despite an HCV mortality rate that is projected to triple in the next 10 years. It is a sad commentary about our priorities.

My feelings are this: how those acquired HCV is nobody's business; that they acquired HCV is everybody's business. HCV is a community problem that needs a community response. It is time to look at solutions rather than problems. Dropping the stigma is a good place to start.

What can we do about this? First, start with yourself. Do you label yourself? Do you expect to be shunned? Do you fear that others will reject you in some way? Do you have your own fears about having HCV? If so, talk about this. The best place to discuss these feelings is at an HCV support group. Learn how others live with HCV.

Do you feel like you deserve HCV as a consequence for current or past behavior? If so, there is something you need to know – no one deserves HCV. It does not matter how you acquired HCV. This virus is not a punishment or natural consequence – it is an unfortunate but unintended outcome. Guilt and remorse will not improve your health and may have a negative effect. If you struggle with negative emotions, talk to your medical provider. You may need some counseling. Important **Note: If you have thoughts of suicide or hurting yourself or others, seek immediate professional help.**

One final thought to reflect on – there is another definition of stigma. In botany, the stigma is the part of a plant where bees deposit pollen. The stigma bears the fragrant sweet solution that attracts bees. It is a place of fertilization. For those with HCV, it may be the place where shame blossoms into hope. It is time to bring hepatitis C out of the closet and into the sunshine.

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HCV/HIV Bytes

Extrahepatic Manifestations: Non-Hodgkin's Lymphoma (NHL)

Alan Franciscus, Editor-in-Chief

First of all, NHL in people with hepatitis C is uncommon. In addition, most studies show that the incidence of NHL in people with hepatitis C usually occurs after many years of infection with hepatitis C.

The designation "Non-Hodgkin's Lymphoma" encompasses a variety of cancers of white blood cells that affect lymphoid tissues. The exact cause of these cancers is not fully understood but it is believed to be caused by an altered or depressed immune system. Other conditions and medications that have been linked to NHL include HIV infection, immunosuppressive medications, rheumatic diseases and hepatitis C.

The lymphatic system is a circulatory system that collects white blood cells which are taken from veins, circulated throughout the body, and returned to the bloodstream. Once the lymphatic fluid is returned to the blood supply, the kidneys are responsible for removing the waste products. Lymphatic organs include the spleen, tonsils, appendix, and thymus. Moreover lymphatic glands are also found in patches located in the intestines. The lymphatic system carries white blood cells that help fight infection.

Typically, lymphoma occurs when white blood cells divide continuously without pause, which prevents them from maturing. This process can cause an overproduction of the immature cells which can crowd out the mature white blood cells, platelets and red blood cells.

It is not fully understood how HCV causes NHL. There are theories that the virus might be the causative agent, or that the constant immune system stimulation from hepatitis C causes NHL. However, we do know that the incidence of NHL in people with hepatitis C is higher than in the general population.

One very large study from Sweden of 27,150 HCV infected persons found that the incidence of NHL was nearly double in persons with hepatitis C who had been infected with hepatitis C for longer than 15 years. Other studies have found a similar or even a higher risk for HCV-infected patients developing NHL. Smoking cigarettes also has been found to increase the risk of NHL even without hepatitis C. In 2005 a study from Italy linked smoking to the development of NHL. The same study found that people with hepatitis

C who are heavy smokers have about a 4-fold increased risk for developing NHL.

In the general population the treatment of NHL consists of chemotherapy. But, as with many HCV-related extrahepatic manifestations treatment also consists of treating the underlying disease – hepatitis C. In fact, some studies have found that interferon with or without ribavirin leads to a remission of NHL especially in people who achieve an SVR. But remission with treatment of interferon only occurred in the hepatitis C group. This further supports the association between HCV and NHL.

HCV Advocate March 2006

Factors Influencing Adherence

Non-adherence of antiretroviral therapy can lead to higher viral loads and viral resistance, while proper adherence is linked with viral suppression. Data show that adherence of over 95 percent is needed for effective viral suppression. Adherence to anti-HIV medications is critical because of the increased chance of developing drug resistance and, according to the U.S. Department of Health and Human Services (DHHS) HIV/AIDS Bureau, "a treatment's success can begin to diminish when patients are less than 95 percent compliant."

Recently Richard Day Research conducted a study underwritten by Bristol-Myers Squibb of 403 HIV-infected persons taking antiretroviral therapy on average for eight years and who had switched regimens four times. A number of important findings are identified below.

As this survey defined adherence in terms of doses missed or taken late, the results showed only 48 percent were considered adherent. Breaking medication habits down further, based solely on the number of doses missed during the past seven days, 69 percent were considered adherent (defined as taking 95 percent or more of all required doses), while 31 percent were not. Sixty-six percent said they were fully adherent in that they had not missed a single dose in the past week, while 17 percent reported missing a single dose and another 17 percent reported missing two or more doses within the past seven days.

According to survey participants, the primary reason for becoming less adherent (cited by 29 percent in open-ended format) is due to being busy with work or

life demands. More than one-third (38 percent) reported that although they “strongly” or “somewhat agree” that they want to take their medications, they sometimes forget or fall asleep. Twenty-two percent said forgetting to carry their medications with them when they were away from home was a problem. Psychological and personal control issues are important barriers for some patients, who do not yet feel they are fighting HIV on their own terms; these individuals continue to be challenged by side effects and by disruptions to their daily routines and eating habits. Consistently, one-quarter to one-third of respondents felt they are not yet controlling how HIV affects their lives: thirty-three percent reported they have had to tailor their life to their HIV treatment regimen, 24 percent agreed that “HIV is controlling me, instead of me controlling it” and 37 percent said having to take HIV medications means having less freedom. Twenty-seven percent felt having to take HIV medications was embarrassing.

While 87 percent felt a strong commitment to taking their antiretrovirals as prescribed, side effects (47 percent), feeling ill (21 percent), or being depressed (23 percent) were the most frequently cited reasons offered for why adherence can be difficult. They reported that the following side effects had the greatest influence on adherence: fatigue (42 percent), diarrhea (40 percent), nausea (29 percent), problems with sleep (28 percent), depression (26 percent), and body shape changes (26 percent). In addition, 34 percent cited concerns about the long-term effects of HIV medications as a reason taking HIV medications can sometimes be difficult. Although cited less often than side effects, other barriers to adherence included too many pills to take at one time (23 percent), difficulty coordinating medications with daily schedule, changing schedule, or with their job (19 percent). However, it is noteworthy that the frequency of dosing was cited as a major barrier by only 11 percent. In open-ended format, “being too busy” and “forgetting” was the top reason cited by 46 percent of those providing open end answers as the reason for missed or late doses within the past seven days.

Sixty-two percent have been able to tailor an antiretroviral regimen that suits their lifestyle. Patients said taking personal responsibility for their won success was essential, and recommended strategies to keep dosing easy and pills accessible. Ninety-three percent declared they themselves had the strongest influence on their success with adherence; 22 percent cited the influence of their health care providers, and 20 percent relied on immediate family members and partners. The most effective adherence strategies were ranked and the ones most frequently cited were using a pill container (48 percent), keeping pills in an obvious place (42 percent), switching to simpler regimens with lower pill burdens (40 percent), linking dosing to specific aspects of their daily routines (37 percent), working with

their provider to tailor a regimen that suits their daily schedule and lifestyle (20 percent) and switching to a regimen with more tolerable side effects (30 percent).

There are a number of benefits to complete adherence, such as better HIV suppression and limiting the emergence of resistance. This survey showed that other important benefits are the improved sense of control over patients’ lives reported by 62 percent, worrying less about having HIV (44 percent), feeling healthier (43 percent) and possessing a sense of well-being (41 percent).

However, nearly one quarter (22 percent) did not believe their healthcare providers really understood how hard it is for them to take their antiretrovirals. Twenty-six percent said they had not been given a choice of treatment regimens that suits their lives best. According to the DHHS Guidelines, healthcare providers can and should adjust regimens to suit a patient’s lifestyle and address other issues such as side effects. When this is done, the chance of adherence success has been found to increase.

This survey was designed by Richard Day Research of Evanston, IL and edited by Dr. Judith Feinberg, professor of medicine at the University of Cincinnati College of Medicine and principle investigator at the University of Cincinnati AIDS Clinical Trials Unit. It was conducted online in June, 2005 by Richard Day Research. This educational initiative is underwritten by Bristol-Myers Squibb.

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Patient Assistance Programs

Alan Franciscus, Editor-in-Chief

Many Americans do not have insurance for health-care services and/or prescription coverage. In order to provide free or low cost medicines to those who qualify, patient assistance programs were created by the pharmaceutical industry. In addition to these services some pharmaceutical companies will work with patients to see if the prescription for their drug is covered by the patient’s insurance company or other drug plans.

Partnership for Prescription Assistance was launched in 2005 as a centralized site for help with patient assistance prescription coverage. Pharmaceutical, and local and national organizations participate to bring more than 475 public and private patient assistance programs together in one place.

The *Partnership for Prescription Assistance* was

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formed because many Americans do not know that they may qualify for free or low cost medication. A centralized location will make it easier for patients to locate assistance programs. The goal or mission of the *Partnership for Prescription Assistance* is to bring about more awareness of the patient assistance programs and to help put people in touch with these programs.

To find out if you qualify for an assistance program go to the *Partnership for Prescription Assistance* Web Site <https://www.pparx.org> or call 1-888-477-2669 (toll free) for more information.

To speed up the process, have the following information available:

1. Age
2. State of residence and zip code
3. Estimated gross annual household income
4. Number of people living in the household
5. Brand name of the prescription medicines that you are currently taking or have been prescribed (Pegasys/Copegus – Roche; PegIntron/Rebetol – Schering)
6. Type of health insurance and/or prescription coverage (if any)
7. Name and contact information of physician who prescribed or will prescribe the medication.

The people who assist you are specially trained to be courteous and sensitive to the special issues of information related to money and issues surrounding illness. All of the information is strictly confidential.

If it is determined that you may be eligible for a particular program you will be asked to fill out an application. For most people this process is stressful for a variety of reasons so it is highly recommended that you involve a caregiver, social worker, benefits counselor, healthcare professional, or friend to help with the initial process and fill out the application. After you fill out the patient information, the application will have to be sent to your medical provider to complete.

The pharmaceutical companies that provide patient assistance programs can also be contacted directly:

- Roche – Pegasys plus Copegus (ribavirin): Pegassist Patient Assistance Foundation – 1-877-734-2797
- Schering – PegIntron plus Rebetol (ribavirin): Commitment to Care – 1-800-521-7157

HCV Advocate March 2006

Three Rivers Pharmaceuticals Announce FDA Final Approval of Ribasphere® (ribavirin, USP) Tablets 600mg, 400mg and 200mg for the Treatment of Chronic HCV

CRANBERRY TOWNSHIP, PA., Dec. 5/ PRNewswire/--Three Rivers Pharmaceuticals, LLC today announced that the U.S. Food and Drug Administration (FDA) has granted final approval for its Ribasphere® (ribavirin, USP) Tablets 600 mg, 400 mg, and 200 mg in combination with interferon alfa-2a for the treatment of Hepatitis C ("HCV"). Three Rivers Pharmaceuticals and PAR Pharmaceuticals will be shipping product immediately.

"Ribasphere® Tablets 600 mg, 400 mg, and 200 mg provide the patient and physician an opportunity to significantly reduce the number of tablets a patient has to take each day. "Three Rivers believes that this has the potential to lead to better patient compliance and improved patient outcomes," said Three Rivers President and CEO Donald J. Kerrish, R.Ph. These new dosage strengths represent the first significant advance in the treatment of HCV since the launch of Pegasys®.

Ribavirin is a synthetic nucleoside analogue with antiviral activity currently marketed by Roche Pharmaceuticals under the brand name Copegus®. Annual U.S. sales of the product are approximately \$200 million. The products will be co-marketed by Three Rivers and its marketing partner PAR Pharmaceuticals (NYSE:PRX) of Spring Valley, New York.

Three Rivers Pharmaceuticals is a closely held, privately owned company. Three Rivers Pharmaceuticals' mission is to develop and market brand and **generic** prescription drugs through product acquisition and in house development.

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SOURCE Three Rivers Pharmaceuticals, LLC

URL: <http://www.prnewswire.com>

PR Newswire US
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HealthWise: Living with the Label of HCV

Lucinda K. Porter, RN, CCRC

We live in a label-conscious society. Clothes, sports apparel, handbags, even our eyewear sports some sort of label. But what happens if you wear a label? What would you say if you were asked, "Who are you?" Take a moment and answer that question. Make a list of everything you are. You might answer, "I am a mother or a father; a son or a daughter; a sister or brother; a spouse, a partner, or a friend; a Buddhist, a Hindu, a Methodist, a Jew; a computer programmer; a carpenter; a dentist; a hepatitis C patient. If you labeled yourself as a hepatitis C patient, this article was written for you.

Labels define us. They tell others who we are. They tell us about our values and beliefs. Some labels describe our relationships and identify the people in our lives. Some labels describe what we do, such as an occupation or hobby. Declaring our religious preferences gives insight into our spiritual beliefs. However, being a hepatitis C patient is quite different from being a parent or a nurse. Saying, "I am a hepatitis C patient" defines us. It says, "I am sick." It ties us to a state of disease rather than to a state of health.

It is easy to identify with an illness. Hepatitis C (HCV) can be all encompassing at times. Sometimes it is in the foreground; other times in the background. Nevertheless, it is always there. However, living with HCV is not the same as being an HCV patient.

To some of you, this may seem like hair splitting; but before you dismiss this idea, try an experiment. If you imagine or describe yourself as an HCV patient, try substituting words and images that are more powerful. Imagine yourself as strong and calm. Say to yourself, "I am living with hepatitis C, but I am much more than this." How does this feel as compared to "I am a hepatitis C patient."

There is a healthy side of identifying with an illness. We can't let go of something without first accepting it. An important part of moving through HCV is to acknowledge it, assess it and recognize the meaning of it. In *Man's Search for Meaning*, Viktor Frankl notes, "seriously ill people are often not given the opportunity to suffer bravely, and thereby retain some dignity." He goes on to say that when we tell people to cheer up and be optimistic, the ill are made to feel ashamed of their pain and unhappiness.

Frankl is imminently qualified to speak about the human search for meaning. His contributions to modern psychotherapy were forged by his experiences as a Holocaust survivor. Frankl spent three years in Nazi death camps, including Auschwitz. The Nazis slaughtered his family.

Frankl endured more than most of us. He did not let pain, torture, or grief interfere with living a life filled with compassion and integrity.

The problem occurs when a line is crossed between finding the meaning in the illness versus letting the illness define you. What does having HCV mean to you? Does it mean a lifetime of fatigue? Loss of opportunity? Perhaps HCV is a wake-up call, motivating you to make lifestyle choices that bring renewed vigor. Maybe you appreciate life more because of HCV. A Buddhist principle is that our energy follows our attention. If we focus on illness, that is where our energy will go. Illness can takeover, robbing meaning and joy from our lives. The entire self becomes defined by illness.

If any of this rings true for you, consider an attitude adjustment. Try to live in the positive rather than the negative side of life. Optimism is not wishful thinking. If an earthquake is rocking the world around, it is foolhardy to act as if you are on steady ground. The wise thing is to protect yourself and others, and to try to minimize the damage. Once the shaking stops, assess the damage and make a plan for recovering. The optimist looks at what is left and plans around this. The pessimist looks at what is gone and in doing so, lives in the loss and pain.

Here are some tips on how to cultivate a healthy attitude:

- ☞ Be honest and realistic. Do not build your attitude on thinking things are worse than they are or better than they are.
- ☞ Make sure you know the truth. Get accurate information about HCV. Some people think that HCV is an automatic death sentence. This is not true. The majority will die with HCV, not of HCV.
- ☞ Stay in the present. Don't make things worse by imagining a future with pain, disability or loss.
- ☞ Accept your situation, but don't overly identify with it. HCV may be a part of your life, but that doesn't mean it should control your life.
- ☞ Maintain your perspective. Focus your attention on something that brings peace, joy, laughter and meaning.
- ☞ Watch your words. If you hear yourself talking negatively, substitute positive phrases. Say, "I will find a way to live with HCV" rather than "HCV is ruining my life."
- ☞ Try to relax. Tell yourself that difficult moments will pass.

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It's Not Only About the Pills

By Gary R. McClain

"It looks like I'm going to be starting a new drug regimen."

As a counselor, I often find myself sitting across from a client who begins the conversation with these words. Each has his or her own reasons for changing regimens, including efficacy, side effects and compliance issues.

If you are facing a change in your regimen, or have been presented with this possibility by your physician and are talking about the next steps, chances are you are experiencing your own thoughts and emotions. What I have learned from my clients is that a new drug regimen presents both challenges and opportunities. And like other life changes, the best way to tackle them is through acknowledging our emotions, harnessing the power of your rational mind, and taking action.

Are you ready to get started?

Remember that you are not at square one. In the immortal words of Joan Crawford in the film *Mommie Dearest*: "This ain't my first time at the rodeo."

As you approach your regimen change, don't forget that you have been down this path before. Whether this is the first time, or if you have changed too many times to count, or feel that way, you are not a stranger to facing the uncertainties of putting new medications into your body. You've been through whatever period of time it takes your body to adjust, the temporary and potentially long term side effects, and the frequent monitoring.

So you've got an edge here. I have clients who, because of past experiences, approach their regimen with bravado—a "dare you to defeat me" attitude and a lot of chest pounding. This attitude may result from having worked closely with their physicians to evaluate potential regimens and to determine when to begin the new therapy, with confidence that they have chosen the optimal route. Enthusiasm may also be related to an intense sense of relief due to the end of regimen that has been difficult to maintain, or has resulted in intolerable side effects or has become less effective. But is there another side to the bravado?

Some clients use their bravado as a way of avoiding some of the less acceptable, uncomfortable feelings that a new regimen may provoke—anger, fear, frustration—while others don't even attempt to hold back on the dark side but instead go there and stay. They recall past experiences with new regimens that caused intestinal distress, or nightmares, or fatigue. If they had to face it in

the past, how could this one be any better? They can't help but wonder: what next?

Are your coping skills rusty?

Let me tell you about a client who I will call Doug, who has been HIV positive for 15 years. As a veteran of AZT, he is no stranger to changes in his medication. He has gone through a few of them over the years. He has been on his current regimen for more than two years but has gradually become resistant to it, so he finally agreed with this physician that it was time to change. But that doesn't mean Doug was looking forward to this change.

I had my treatment down to a routine. I was calling my meds my vitamins. Now, that's a joke. I mean I wasn't even thinking about them any more and was barely aware that I was popping them at the same times every day. It's like they were just pills that had nothing to do with HIV.

Doug was overwhelmed by the idea of having to make changes in his routine to accommodate the new regimen, along with the adjustment that his body would have to go through. But more important, he didn't want to face the feelings that went along with this change. With a comfortable medication routine, HIV stayed in the background. With a regimen change, he was going to need to be conscious of how he was feeling physically and emotionally from the perspective of his HIV. He was going to have to adjust his schedule to accommodate his regimen. Basically, the prospect of paying more attention to his medications made Doug feel like a patient and disempowered. He thought he had long ago left the patient label behind and wondered how much old territory he was going to have to cover again.

You may want to ask yourself the question I asked Doug: ***What worked and didn't work the last time you went through this?***

Take a moment and think about past experiences with regimen changes, or even back to when you first began taking HIV meds. What helped you to handle the emotions you were experiencing around this new chapter in your life? Did you get informed? Connect with supportive people? Make lifestyle changes? Get in touch with your spiritual side? In other words, how did you get to the other side of what may have seemed like a very deep valley? Just as important, what did you do that didn't help at all? What bumps in the road could have been avoided?

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Treatment Success

Alan Franciscus, Editor-in-Chief

In this article, I will briefly describe my treatment experiences and my general feelings about what it means (to me) to be hepatitis C virus free. First of all, I am not recommending treatment for anyone. Not everyone should be treated and treatment is not for everyone. Treatment decisions should be made after gathering as much information as possible and weighing the pros and cons as they apply to each person. No one should rush into it because I or someone else you know has had a successful treatment outcome. The ultimate decision is between you and your medical provider. Below are my thoughts, experiences and feelings, but as the saying goes "It don't make it so."

In 1994 I was feeling the symptoms of hepatitis C – moderate to severe fatigue and other mild flu-like symptoms, but I didn't know the cause. I went through many tests over a two-year period and no one could medically explain my fatigue or the other symptoms. That was really frustrating because I thought I had this bizarre disease that no one knew about. I'll never forget the day that I had a doctor's appointment with my new primary care physician. After I explained my symptoms, he ordered blood work, including a hepatitis C antibody test. I had never heard of hepatitis C, but luckily, he had. A week or so later I received my test results – I had hepatitis C. Of course, I was devastated by the news, but in some ways, it was a relief to finally find out what was causing the severe fatigue.

About 3 months after I was diagnosed I decided to try treatment with non-pegylated interferon monotherapy (3 injections a week). I was on treatment for a year, but I did not achieve an SVR. In fact, during treatment my viral load never reached a point where it was undetectable. I also had many side effects. The first evening I had severe chills and a fever. After a while, the physical side effects such as the flu-like symptoms seemed to diminish somewhat – at least to the point where I could handle them. However, the psychological side effects (anger and depression) slowly became worse. After about three months, it was decided that I should start on anti-depressant therapy. I also started to meditate regularly and between the meditation and the antidepressants, I felt better and was able to finish treatment.

Looking back, I wished that I had been more educated about the chances for a successful treatment with monotherapy because I am not sure I would have tried it. The data about the treatment at that time showed that I only had a 9% chance of achieving an SVR. However, even though it didn't eradicate the virus, treatment did help with the fatigue, for a while at least.

But eventually the fatigue returned so in 1999 I decided to try high daily dosing of non-pegylated interferon monotherapy. At first, there was a dramatic reduction in HCV RNA (viral load) levels, but after 10 months, the virus came back so I stopped therapy. Again, my energy level dramatically improved, but over the next couple of years the extreme fatigue as well as some of the other symptoms like brain fog, lack of concentration, difficulty with mental retention and other annoying symptoms came back. Surprisingly, the side effects of high daily dosing didn't seem that much worse than when I took interferon three times a week. I think this might be because of what I learned the first time about managing side effects. I also started on anti-depressants a couple of months before I started therapy.

In 2002, I decided that I wanted to try pegylated interferon plus ribavirin therapy. I began towards the end of 2002 and my viral load began to drop, but not as quickly as I had hoped. After about 3 months, I had a 2-log drop in HCV RNA, so I was well on my way. At about the 9-month mark, I began to do some research on treatment duration for people who had characteristics similar to me – older, genotype 1, high viral load, had HCV for a long period of time. Most data suggested that I should be treated for a longer period of time. After consulting with my doctor, it was decided to extend the treatment from 48 weeks to 72 weeks.

The side effects of pegylated interferon plus ribavirin were much less than the side effects I experienced while on the first two courses of therapy. In fact the morning after the first shot I felt so good that I wondered if I really did take the drug at all! That slowly changed and by the third month, the side effects became worse, but I was able to manage them fairly effectively. My blood chemistries looked pretty good throughout therapy, except that eventually I developed anemia. I am VERY fortunate to have insurance to cover all of my medications including erythropoietin (EPO). Epo worked wonders for the anemia and the related fatigue, allowing me to finish treatment.

One of the strategies I put into place was to have a good support system well before I started therapy. I relied a lot on my friends and family for support. The side effects were managed aggressively with early intervention to prevent them from becoming worse. I am very fortunate that I love the work that I do for the Hepatitis C Support Project. This really helped to distract me from the side effects. Don't get me wrong – it wasn't a walk in the park, especially since I was trying to run a

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Treatment Success (continued)

non-profit agency. I traveled extensively during this period and logged about 100,000 air miles. However, I made it through, and it was well worth it.

It has been well over a year since I finished treatment, and I am still negative for the hepatitis C virus. This was not totally unexpected, but, as most people who are treated know, it wasn't totally expected either. Ever since the news, I have been thinking about what successful treatment and getting rid of the virus means for me.

First, it was fantastic news that the virus was out of my body. I only wish that everyone with hepatitis C could experience the feeling of beating HCV. It took awhile but the side effects gradually went away and I began to feel better. The hepatitis C symptoms that I had been experiencing for so long also started to get better. Slowly, my energy returned. In fact, my energy level is better than it has been in 10 years, and most of those hepatitis C flu-like symptoms have gone away. Best of all I now feel clear-headed and I feel a general calmness that I haven't experienced in years. This is a big difference from the way I felt before treatment.

Many issues come up after successful treatment. One of the most frequent questions people ask is if they can drink alcohol again. For me, this was a no brainer. I'm in recovery so drinking again is not an option. Unfortunately, there is no data on whether someone who achieves an SVR can drink alcohol. Until there is significant data on this issue, the general recommendation is to abstain from alcohol.

Another big issue is blood. Should I cover my wounds or take precautions if blood is present? Definitely. Always be cautious where there is any blood present whether it's yours or someone else's.

Feeling infectious is probably one of the strongest emotions that almost everyone with hepatitis C feels especially after being newly diagnosed. I used to be so concerned when my blood was present that I would needlessly become almost hysterical about it. I still believe and practice safety precautions in the presence of blood. But there is a big difference between common safety precautions as opposed to knowing that you have infected blood that could potentially infect another person.

Do I feel like I will live longer without hepatitis C? I do feel that I will live a longer life, but more importantly, I feel that I will not have to suffer with the severe fatigue or the other symptoms of hepatitis C. For me, the decreased quality of life and suffering was worse than the idea that I might die from hepatitis C.

My advice to someone who is thinking about treatment is to research hepatitis C treatment medications. If you decide to start treatment, set up personal and medical support well in advance of starting treatment. Another strategy that helped was finding something that I enjoyed, which distracted me from the side effects. Probably the best advice I can give is to take treatment one day at a time.

"But let us remember, we cannot wait for others to tell our stories. We must remain visible, vocal, and unified."

— *Yvette Sangster and Ed Kramer*

HCV Advocate February 2006



Liver Transplantation: Part 2

Liz Highleyman

The last issue of *HCV Advocate* discussed the lack of available livers for transplantation and new techniques – including split liver and living donor transplants – that could help relieve the shortage. This article looks at HCV recurrence after liver transplantation in people with hepatitis C.

A large body of research has shown that in untreated liver transplant recipients with chronic hepatitis C, HCV almost always infects the new liver within weeks, and sometimes in as little as 24 hours. Some – but not all – studies suggest that patients with hepatitis C fare less well after liver transplantation than HCV negative individuals. As reported in the June 27, 2004 issue of *Transplantation*, for example, Ergun Velidedeoglu, MD, and colleagues analyzed more than 13,000 patients in the United Network for Organ Sharing (UNOS) database, 57% of whom had hepatitis C. They found that the five-year survival rate was 74.6% for HCV positive patients, compared with 83.5% for HCV negative individuals. Indeed, liver failure due to recurrent hepatitis C is a leading cause of death among liver transplant recipients.

Some experts have gone so far as to describe post-transplant HCV recurrence as “universal,” but here again, data are mixed. It is evident that many patients who achieve sustained virological response (SVR) with interferon-based therapy prior to transplantation still experience viral recurrence. This indicates that a low level of HCV genetic material remains in the body waiting to “seed” the new liver, even if it is undetectable using standard tests. As reported in the January 2006 *Journal of Hepatology*, for example, Martina Gerotto and colleagues found that 26 of 208 hepatitis C patients (12.5%) who had repeatedly undetectable HCV viral load at the end of treatment using common polymerase chain reaction (PCR) technology still had residual detectable HCV RNA using a more sensitive transcription-mediated amplification (TMA) assay.

Based on research to date, the natural history and prognosis for post-transplant HCV recurrence remain uncertain, as studies have yielded conflicting data. In a forum on liver transplantation and hepatitis C in the April 2005 *Journal of Hepatology*, Greg Everson, MD, described three patterns of recurrence. While a small proportion of patients experience severe cholestatic hepatitis, recurrent HCV infection most often becomes chronic and evolves in a manner similar to that seen in nontransplant patients – but typically more rapidly and with a higher viral load set point. Everson estimated that approximately 25% of transplant recipients develop cirrhosis in the grafted liver within 5-10 years (compared with 10-40

years in nontransplant patients). Various studies have revealed a number of factors associated with rapid fibrosis progression, including genotype 1 (especially 1b) or 4 HCV, non-Caucasian race/ethnicity, donor and recipient age, and ischemia time (period without oxygen between removal from the donor and insertion into the recipient); surprisingly, female sex has also been linked to worse progression, since among non-transplant patients, women usually fare better than men.

Accelerated HCV-related disease progression is thought to be the result of impaired immunity due to immunosuppressive drugs used to prevent organ rejection. Some studies have shown that administration of a large dose (bolus) of corticosteroids to treat acute rejection can worsen HCV disease severity. Conversely, other research suggests that avoiding corticosteroids altogether may be beneficial. On the other hand, there is also evidence that rapid reduction of corticosteroid dosages may exacerbate HCV disease progression. Data on the risks and benefits of other types of immunosuppressive therapy, including mycophenolate mofetil and azathioprine, has also been inconsistent. Thus, for now, the best approach remains open to debate. According to Everson, it is likely that “the interplay between the immune system and the virus,” along with recipient genetic factors and the quality of the liver graft, influences post-transplant outcomes. Recent experience has shown that HIV positive transplant recipients have survival rates similar to those seen among HIV negative recipients, as long as they have well-controlled (ideally undetectable) HIV and relatively intact immune systems (e.g., CD4 cell counts of at least 200 cells/mm³); however, HIV/HCV coinfecting patients fare more poorly than HIV positive people receiving liver transplants for other reasons.

The good news is that some patients experience minimal liver disease progression several years after transplantation. Certain individuals show no evidence of HCV recurrence or damage to the new liver even after 10 years. Because hepatitis C normally progresses so slowly, even if fibrosis advances at a similar or moderately accelerated rate in original and newly transplanted livers, this can buy recipients 10-20 or more years of good liver function and the associated improvement in quality of life.

While data on the ubiquity of post-transplant HCV recurrence may appear grim, there is ample evidence that the lower one's HCV viral load at the time of

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Liver Transplantation: Part 2 (continued)

transplantation, the less chance of recurrence – and the less chance of severe disease and rapid progression if the virus does come back. In some studies, more than half of patients achieving SVR with pretransplant interferon-based therapy did not experience HCV recurrence. Yet individuals awaiting transplants typically are quite ill and often have difficulty tolerating the side effects of interferon and/or ribavirin. Looking at the debate over whether to treat hepatitis C patients on the liver waiting list, Everson noted that while tolerability of therapy remains a serious concern, it is often worth pursuing since pretransplant treatment currently prevents post-transplant recurrence in as many as 25% of cases. And even therapy that does not eradicate the virus may still help prevent fibrosis progression.

If pretransplant treatment is the first line of defense, commencing hepatitis C therapy immediately after transplantation – a sort of post-exposure prophylaxis – may also help prevent recurrence by inhibiting the rapid viral replication that typically occurs in the hours and days following the operation. Though post-transplant SVR rates are lower than those seen in nontransplant patients – largely due to the inability to tolerate therapy – roughly 25% achieve long-term undetectable HCV RNA. Here, too, interferon may help stave off liver damage even if viral load remains detectable. But, as Isabelle Morard and Francesco Negro, MD, explained in the *Journal of Hepatology* forum, post-transplant disease progression varies widely among patients, and it is not clear whether immediate preemptive therapy – which would subject some patients unnecessarily to adverse side effects – is preferable to waiting until evidence of damage to the new liver becomes apparent. (For more on post-transplant hepatitis C treatment, see the [September 2004 HCV Advocate](#).)

In addition to hepatitis C therapy, liver selection and transplant procedures can also make a difference. Since HCV patients are at greater risk for poor post-transplant outcomes, they may derive more benefit from receiving livers from younger donors. As Yasuhiko Sugawara, MD, and Masatoshi Makuuchi, MD, discussed in the *Journal of Hepatology* forum, some research indicates that HCV patients experience faster viral recurrence and more severe and rapid liver disease progression after living donor, compared with cadaver donor, transplants. The reasons for this phenomenon are not yet known, but may be related to heightened HCV replication as the liver section from a living donor regenerates in the recipient. On the other hand, success rates for living donor transplants have increased in recent years, and the apparent detriment seen in earlier studies may have been attributable to lack of experience with the procedure.

As treatment for hepatitis C improves – ideally becoming both easier to tolerate and more effective at suppressing the virus – more HCV positive individuals may truly eradicate the virus before or immediately after transplantation, thus minimizing the risk that HCV will invade their new livers.

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HCV Advocate February 2006

Misinformation in HIV/AIDS Care

There's more than one way to skin a virus

By Matt Sharp

The advances made in HIV therapy have obviously saved thousands of lives.

But now, almost 20 years since the first HIV medication came on the market, the number of possible drug combinations can be overwhelming. The intricacy of treating HIV cannot be overstated, causing overall care to be problematic and sometimes substandard.

Few HIV practitioners have the time or wherewithal to keep up with the latest cache of information. People with HIV themselves cannot possibly stay completely informed. Pitfalls abound.

Doctor problems

Docs often practice by their clinical experience or lack of experience, rather than following the latest treatment information based on large randomized controlled clinical trials. Rural doctors have much less access to other HIV providers and treatment forums. Obviously, some doctors are better at keeping up with the information than others. The best HIV treater has been in practice a long time and gets continuing HIV provider education.

Doctors are also rushed, locked into the time constraints of managed care. They also have more patients, since the field of HIV medicine is getting smaller due to competition and market forces.

In some cases, unfortunately, there is complacency and less concern for the whole person that results in a lack of optimal care. There is such a focus on the virus that sometimes the host is forgotten. STD infection, re-infection, depression, substance use and co-infection are some pressing concerns and issues with HIV-positive people.

Myths and complacency

Some people with HIV today are less informed because the desperation around illness and death may not be an issue anymore. They also may have become apathetic and not want the latest treatment information, or they may not have access to it, or know how to access it. They also may ask for a medication they have heard about through an urban myth or advertisement, or want to stop a medication, not understanding that there may be effective ways to deal with side effects. On the other hand, some want a drug simply because they have seen positive effects with it out in the community.

Guidelines

The Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents (aidsinfo.nih.gov) can help providers. But treatment guidelines are only that, a guide for treating, not a prescription.

Nevertheless, the guidelines are the best amalgam of HIV treatment information we have and can be helpful, especially for the inexperienced medical provider. They are continually updated to keep up with the current information.

Drug ads

The HIV drug market is big and getting bigger, and competition is fierce. New regulations have allowed for less restrictive pharmaceutical advertising, so we are now bombarded with ads and aggressive visits from pharmaceutical sales representatives, sometimes prejudicing our overall treatment opinions. It's easier to remember a subliminal new drug ad campaign rather than read up on its side effects in the latest medical journal or treatment newsletter.

Balance must be weighed by staying current with the actual research and staying unbiased despite the aggressive marketing.

Treatment stories

As a treatment activist and educator, I have heard many stories about mistakes in care and treatment. Some of the stories I hear would make your hair curl. Others are just common misunderstandings or mistakes.

Among the questions I get asked are the following: What is the best drug combination for starting initial therapy? Which drugs are less likely to cause lipodystrophy? What drugs are safest and which will interact and be cross-resistant? Should I take a newer once-daily drug or stick to my old twice-daily regimen? Should I boost my protease inhibitor? Are the new drugs necessarily better? Safer? Can I stop my treatments now that I am doing so well?

Misinformation in HIV/AIDS Care (continued)

Switching drugs

One common story I hear is about switching therapies.

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Misinformation in HIV/AIDS Care (continued)

Lou is a long-term treatment experienced man who approached me about his concern over his low CD4 count and his high viral load. Knowing he had a few options, he had asked his Chicago doctor to switch drugs, to no avail.

I asked if the doctor had spoken to him about Fuzeon or the new protease inhibitors he had not tried yet. My concern was that there may have been reluctance in prescribing the twice-daily injectable Fuzeon. Whatever the case, I saw that Lou had lost a lot of weight and with all I knew, was willing and ready to switch to some new options that would most likely benefit him.

As a treatment activist and educator, I have heard many stories about mistakes in care and treatment. Some of the stories I hear would make your hair curl. Others are just common misunderstandings or mistakes.

There has been great impact in treating late stage HIV in the past years with new classes and drugs that are not cross-resistant with each other. It is worrisome that less aggressive doctors would hold off these new options for someone like Lou unless there is some other medical condition or drug interaction issue. I urged him to force the issue with his doctor.

On the other hand I have heard from people that doctors have wanted to switch to a new drug when according to them, it appeared there was no need to. Most of the time these people were very stable and doing well, with undetectable viral loads, stable CD4 levels and no sign of side effects. They had no indication of why their docs wanted them to switch. Many patients for various reasons will not refuse a doctor's wishes.

Reyataz & lipids

Many docs are unnecessarily prescribing Reyataz as a switch therapy. It has shown benefit in not raising lipid levels, but no proof in reducing fat redistribution. Unless there is clear benefit to switching a drug, rocking the boat may actually do harm. We need more head-to-head comparison studies to show one drug is superior to another before switching. As the old adage goes, "If it ain't broke, don't fix it."

On the other hand, with rising lipids that haven't been brought under control, and especially with other cardiac risk factors, switching to Reyataz might be a good strategy to try.

Drug data, adherence, & Trizivir

Prescribing an initial regimen should be based on the individual with back-up information from clinical trials.

One would hope that doctors understand that the first regimen is the most important and that the patient's understanding of adherence is crucial to maintaining effectiveness.

Providers also must not assume that because a patient is a substance user or person of color that they are any less likely to adhere to their medications.

One e-mail response I received was about a doctor incorrectly prescribing Trizivir for a treatment-experienced person with documented drug resistance. While I understand the need and desire for treatment simplification, at what expense should that be done? Are doctors at ease knowing that their patients are on a sub-optimal regimen simply because they are comfortable that they can adhere to it? Are treaters too busy to work with their patients on treatment adherence? Or again, do they just not have time?

Videx/Viread—& other drug interactions

Drug interactions discovered shortly after drug approval have become an important treatment issue.

The Videx/Viread interaction was discovered after this backbone combination was in widespread use, the thrill being that they are both once-a-day drugs. I heard about these interactions through the grapevine before the news was out. Even today I hear of some doctors not warning of potential problems with Videx/Viread.

Zerit and Retrovir, & side effects

What do people know about potential side effects with prescribed drugs? Today there is a better understanding of metabolic issues and lipodystrophy.

It baffles me that there are people still using Zerit even though we know it is one of the causes behind lipodystrophy. Even Retrovir has been correlated with lipoatrophy, but docs are used to prescribing it rather than newer, safer, less toxic drugs.

There are also ways to manage elevated lipids besides use of statins, but once again docs rely upon a pharmaceutical intervention rather than having a discussion about exercise, nutrition, and complementary therapies.

Norvir

Norvir, one of the most commonly used protease inhibitors, is in widespread use now as a boosting agent to increase levels of other protease inhibitors, making them more potent. There are more drug interactions with Norvir than any AIDS drug, even though the boosting dose is lower. Many people still don't realize that Kaletra has Norvir in it.

Aptivus

There were also several drug interactions discovered before Aptivus, the newest protease inhibitor (PI) on the block, became approved. It lowers levels of other protease inhibitors, so they can't be taken together. Using a dual PI combo is one treatment strategy that's not available with Aptivus.

Street drugs

Unfortunately, we still do not know much about the interactions of recreational drugs with antiretroviral drugs, and we may never know until people overdose.

Drugs, drugs, drugs

These issues highlight just a few of the growing number of possible drug interactions and their complexities. Interactions can impact effectiveness and drug resistance, and even be dangerous and fatal.

Treatment activists are now demanding that pharmaceutical companies perform interaction studies with all antiretroviral drugs and concomitant medicines used by people with HIV, long before approval.

Study us!

Unfortunately, many doctors do not offer clinical trial information to their patients. In many cases, joining a trial is the best way to provide a treatment either because of access issues or due to the patient's need for new compounds not yet approved.

Some doctors may not want to "lose" their patients to a clinical trial, but a study should never be a substitute for good clinical care.

My survival is based on the availability of new treatments through clinical trials and it is known that research institutions are clamoring for new recruits. Minority populations also protest there are not enough minorities enrolling in clinical trials. Recruitment by all people affected by HIV is vital for ongoing treatment success and scientific breakthroughs.

Stopping therapy

Structured treatment interruptions (STIs) are an area of important continuing research. I hear of people who do not have the complete picture and are interrupting their HIV medications.

While it may be necessary to stop medications due to toxicity, the word is not final on interrupting HIV meds, and we will not know more for at least another year. I continue to speak to people who stop their meds out of the blue.

The best way to stop therapies is to enroll in a STI clinical trial where monitoring is frequent.

Ask the pharmacist

Less and less time is spent describing new drug information to a person with HIV. All the relevant information a person may need versus the time the doctor has to spend explaining it is becoming a bigger issue as the information becomes more cumbersome and complex.

Patients need to know that they should also discuss any new treatment with their pharmacist or any other medical provider, such as the Physician's Assistant or Nurse Practitioner.

We're all human

I remind clients here in TPAN's TEAM program (Treatment Education Advocacy Management) that doctors are only human and they make mistakes. It is, needless to say, challenging to treat a long-term chronic and incurable disease.

There are countless variables to misinformation in HIV treatment and this article certainly cannot address everything. However, the point here is to get people with HIV and doctors to communicate with each other and to do their homework. Stay current, and stay informed.

As always, it is time to take stock of all the HIV treatment advances, look at what has worked and what hasn't, evaluate what can be changed and advocate for better research, as well as patient and provider education and support. Providers and patients should acknowledge and face the gaps in understanding and work together as a team to attain optimal health in 2006 and beyond. The question becomes: how can we all do a better job with keeping up with all the changes and work as a team to stay as healthy as possible!

Reference: Positively Aware, January/February 2006

READERS NOTE: The issue of Positively Aware that contains this article also contains one chart listing some side effects and another chart listing some drug interactions. These charts are not shown.

One of our technical reviewers made reference to the following web sites as containing helpful information on HIV drugs:

Aegis. Org
Aidsmeds.com
Medscape.com

(Continued from page 1)

Hepatitis C Combination Therapies in Pill Form Move Nearer (continued)

Percentages achieving early virological response (at least a 2-log reduction in hepatitis C virus RNA at twelve weeks) were 5%, 41%, 54%, 71%, and 63%, respectively ($p < 0.001$ for the latter two arms compared with pegylated interferon/ribavirin). In the 400-800 and 800mg valopicitabine combination arms, 21% achieved at least a 4-log drop in hepatitis C virus RNA compared with 6% in the pegylated interferon/ribavirin arm ($p=0.05$). Valopicitabine was safe and generally well tolerated, with no dose-limiting adverse events. Among the 50 participants observed for six months, no viral breakthrough or resistance has been detected. "These are promising results, particularly for the many treatment-refractory patients in urgent need of new therapeutic options," O'Brien concluded.

SCH503034

Stefan Zeuzem from Saarland University Hospital in Homburg, Germany, reported on a Phase Ib study of Schering-Plough's NS3 serine protease inhibitor, SCH503034. In this international multicentre trial, 61 patients were randomly assigned to receive one of four different schedules of SCH503034 (100, 200, or 400mg twice daily or 400mg three times daily), or placebo, for 14 days. Baseline characteristics were similar across the arms, with a mean age of about 50 years. All patients were non-responders to prior treatment with pegylated interferon plus ribavirin (less than 2-log reduction in hepatitis C virus RNA after twelve weeks of treatment) and had genotype 1 hepatitis C. Participants had baseline hepatitis C viral loads of at least 30,000 copies/mL, mean ALT levels of 82-112 IU/L, and compensated liver disease.

SCH503034 was rapidly absorbed, reaching a maximum concentration at 1-2 hours post-dosing. The most pronounced reduction in hepatitis C viral load was seen in the 400mg three times daily arm, with a mean maximum decline of 2.06 \log_{10} copies/ml from baseline (range 1.1-2.7 \log_{10} copies/ml). The magnitude of hepatitis C viral load reduction was positively correlated with SCH503034 trough level. Participants in all three twice-daily arms experienced smaller hepatitis C viral load decreases than seen in the three times daily group, but still did better than the placebo arm. Sixty percent of patients in the 400mg three times daily arm achieved a maximum hepatitis C viral load reduction of more than 2 \log_{10} copies/ml, compared with 18%, 17%, and 8%, respectively, in the 400mg, 200mg, and 100mg twice daily arms. Conversely, no patient in the 400mg three times daily group had less than a 1-log viral load decrease, compared with 18%, 50%, and 67%, respectively, in the

400mg, 200mg, and 100mg twice daily arms. ALT reduction corresponded with viral load decreases.

Zeuzem also presented data from a second small trial showing that SCH503034 exhibited promising antiviral activity when combined with pegylated interferon in previous non-responders. In this open-label crossover study, all participants received 200 or 400mg SCH503034 monotherapy for seven days, pegylated interferon alpha-2b (Peg-Intron) 1.5 mcg/kg/week for 14 days, and SCH503034 plus pegylated interferon for 14 days, but in different orders (i.e., some started with SCH503034 alone, some with pegylated interferon alone, and some with the combination). The mean hepatitis C viral load decrease was more than 2 \log_{10} copies/ml in both the 200mg and 400mg SCH503034 combination arms, compared with 1 \log_{10} copies/ml in the pegylated interferon monotherapy arm; 40% of patients (4 out of 10) in the 400mg arm achieved undetectable hepatitis C viral load, compared with none of those receiving only pegylated interferon. Zeuzem concluded that combination therapy produced at least an additive decline in HCV RNA.

In both studies, SCH503034 appeared self and well-tolerated at all dose levels. In the monotherapy study, adverse events were mild and similar in the SCH503034 and placebo arms. The adverse event profiles in the second study were similar in the SCH503034 and combination therapy arms, consisting mostly of well-known pegylated interferon side effects. Importantly, in animal and human studies to date, researchers have seen no clinical or histopathological evidence of the type of cardiac toxicity that led to the discontinuation of an earlier hepatitis C protease inhibitor, BILN-2061. While one patient did develop the V170A mutation (shown to cause resistance to SCH503034 in laboratory studies), no phenotypic resistance was observed and no viral rebound was seen during treatment in the 400mg three times daily arm. Phase II studies assessing 24 and 48 week VX-950/pegylated interferon combination therapy are underway.

VX-950

Finally, Henk Reesink from the Academic Medical Centre in Amsterdam reported data from a Phase Ib dose-ranging trial of a second hepatitis C protease inhibitor, VX-950 (Vertex Pharmaceuticals). This study included 36 individuals with genotype 1 hepatitis C, mostly prior non-responders, but also a few treatment-naïve patients. Participants were assigned to receive either placebo or an oral suspension of VX-950 as monotherapy, 450 or 750mg every 8 hours (three times daily) or 1250mg every twelve hours (twice daily), for 14 days. Here, too, baseline characteristics were generally similar across the study arms.

Participants in all VX-950 dose groups showed steep declines in hepatitis C during the first two-to-three days of treatment. All patients receiving VX-950 experienced at least a 2-log viral load decrease from baseline. Most individuals in the three VX-950 arms (26 out of 28) had a maximum hepatitis C viral load decrease of at least 3 log₁₀ copies/ml, and four patients had a greater than 5-log decrease. The 750mg three times daily dose produced the highest VX-950 trough levels and the largest mean HCV RNA decrease: 4.4 log₁₀ copies/ml, or a 25,000-fold reduction. Four patients in this arm had undetectable viral load (below 30 IU/mL) at the end of the treatment period. Hepatitis C viral load also decreased in the other two dose groups, but started to climb again after seven days. VX-950 appeared to work as well in prior non-responders as in naive patients. ALT levels declined during treatment in all dose groups. There were no severe adverse events, dose reductions, or treatment discontinuations. The most commonly reported side effects (headache and diarrhoea) occurred with similar frequency in the VX-950 and placebo arms. As with SCH503034, no cardiotoxicity was observed.

In a companion resistance study presented by Christoph Sarrazin, also from Homburg, researchers sequenced the HCV NS3 gene from 34 patients at baseline, day 14, and day 21-24. Several variants were seen with reduced sensitivity to VX-950, at amino acid positions 36, 54, 155, and 156. A single V36 change conferred minimal resistance, while A156V/T was associated with high-level resistance. These mutations were detected in patients who experienced hepatitis C viral load rebound or plateau rather than continued decline. Variants with reduced sensitivity to VX-950 also had decreased replicative fitness, allowing wild-type hepatitis C virus to re-emerge after treatment discontinuation.

According to Reesink, VX-950 produced "the most rapid and dramatic response" seen to date with a single agent. Based on viral kinetic analysis, he suggested that the drug may reduce hepatitis C to undetectable levels in approximately 12 weeks - substantially shorter than the standard 48 week therapy for genotype 1 hepatitis C. Based on data collected so far, Vertex filed an investigational new drug application with the U.S. Food and Drug Administration on November 11. A 14-day Phase Ib study of a new tablet formulation of VX-950 in combination with pegylated interferon is underway in Europe, and a 12 week combination study is planned for next year.

While all three of these experimental agents look promising, it is too soon to say whether they will ultimately produce sustained virological response. Nevertheless, based on research to date, many experts believe antiviral drugs - potentially in combination regimens consisting entirely of oral agents - are the wave of the future

for hepatitis C therapy.

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AIDS Map News
Friday, November 18, 2005

(Continued from page 5)

Stigma: Living with the Labels of Others (cont.)

¹For more information about the double stigma associated with injection drug use and HCV, see *Stigma: Hepatitis C and Drug Abuse*, by Janetta Astone-Twerell, Ph. D. Shiela M. Strauss, Ph.D. and Corrine Munoz-Plaza, M.PH. This article is part of the "Medical Writers' Circle" series at www.hcvadvocate.org.

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Living with the Label of HCV (continued)

- ☞ Visualize health, not illness. Visualization is a powerful tool for self-transformation.
- ☞ Practice gratitude. Make it a habit to find things for which you are grateful.
- ☞ Learn what you can control and what you cannot. There are things you cannot control, such as the fact that you have HCV. However, there are things you can control, such as your attitude and what you say to yourself about having HCV.
- ☞ Learn from HCV. Ask yourself what HCV can teach you about living.
- ☞ Get support. Being with others who are dealing with

the same issues can bring encouragement and hope. See if there is an HCV support group in your area.

- ☞ Help others. When it comes to stepping outside of ourselves, probably nothing works as well as reaching out to others who are also struggling.

In *Minding the Body, Mending the Mind*, Joan Borysenko writes: "Adversity is the crucible in which the spirit is forged." A similar expression is "that which does not kill us, makes us stronger." Hepatitis C is an invitation to cherish each day, to live fearlessly and fully. It is the opportunity to wear a new label.

HCV Advocate February 2006

AASLD 2005: Continuation of Part 2

The first four sections of Part 2 are featured in the March 2006 issue

Durability of SVR

A most important question about HCV treatment outcome is whether a sustained virological response (SVR-HCV RNA negative during and six months post treatment) is long lasting. M.G. Swain and colleagues from the University of Calgary, Canada reported (abstract 62232) on follow-up data from an on-going international study of patients treated with Pegasys alone or in combination with Copegus (ribavirin).

To date the follow-up data is available for 901 patients who achieved an SVR. Study participants include chronic hepatitis C patients, patients with normal ALT levels and persons infected with HIV and hepatitis C.

It was found that overall 894 patients (99.2%) of the patients remained HCV RNA negative. In addition, all of the patients who were treated for 48 weeks with Pegasys plus Copegus (ribavirin-1000 or 1200 mg/day) were still HCV negative including the patients with HIV/HCV coinfection, and "normal" ALT levels.

The authors concluded that "[a]n SVR achieved with peginterferon alfa-2a (40KD) (Pegasys), alone or in combination with ribavirin, is durable for up to 5 years after completion of therapy." The authors are currently investigating whether the 7 patients who became HCV RNA positive after treatment were true relapsers or were reinfected after the end of treatment.

Rapid Virological Response

After 12 weeks of therapy with pegylated interferon plus ribavirin therapy, a 2-log drop in viral load or elimination of HCV can help predict whether treatment will be successful or not. The 12 week rule has been a valuable tool in helping patients and their medical providers decide whether or not to continue treatment based on these results. Another potential treatment predictor is looking even earlier at viral load parameters.

At AASLD, D. Jensen and colleagues presented data from a large retrospective study of genotype 1 patients to find out if the data for those who achieved a Rapid Virological Response (RVR) at week 4 (abstract 65969) was predictive of an SVR and if treatment duration for those who achieved an RVR could be reduced from 48 weeks to 24 weeks without compromising treatment outcome.

In this study of patients treated with Pegasys plus Copegus, data from 729 genotype 1 patients with week 4 results were available and analyzed. Of these, 146 patients had an RVR - defined as an HCV RNA (viral load) of less than 50 IU/mL after 4 weeks of treatment - and were subsequently treated for 24 weeks. Of these, 51 (24%) patients achieved an SVR. It was found that 89% of the patients who achieved an RVR and who were treated for 24 weeks achieved an SVR compared to only 19% of the group that did not achieve an RVR. A low baseline HCV RNA (viral) was the only significant and independent factor associated with an SVR.

The authors concluded that "[a]n RVR at week 4 of treatment is the single best predictive factor for SVR," and that "[t]he use of RVR status to guide treatment duration in genotype 1 patients is appealing and should ideally be confirmed by prospective studies." HCV Advocate, December 2005

(Continued from page 10)

It's Not Only About the Pills (continued)

If you take a look back, you may rediscover some coping mechanisms that have slackened off due to lack of use but, with some exercise, can again be relied on to help you deal with this challenge. Below are some ideas you may find useful.

Update Your Knowledge: I often hear that, over time, people's drive to actively gather information has declined when the current medication is doing its job or they've grown to trust their doctors. How long has it been since you updated your knowledge about HIV and the latest treatments? Some clients approach their new regimen with such enthusiasm that they don't want to "jinx" anything by over-analyzing or otherwise questioning the limitations and the benefits of the new regimen. Others avoid knowing too much out of a concern that their worst expectations will only be confirmed. Either way, a new regimen is often the kick in the butt that gets people re-involved in their treatment. Is it time for you to start asking questions again and seeking answers? The HIV medication picture is constantly changing. If you haven't been keeping yourself educated, or have gotten out of the habit, now could be a good time to restart the process. Even a few minutes a week, on a regular basis, can be a step toward staying informed and can give you an outlet for anxiety and frustration you may be experiencing.

Don't Hesitate to be High Maintenance: Getting involved begins with asking questions. If you haven't asked why a regimen change is recommended, that would be the starting point. While the answer may be obvious to you (for example, if the side effects were becoming intolerable) your physician may still be able to give you additional insights into why the regimen is being changed at this time. What are the risks of changing the regimen in terms of keeping the virus in check? And then there is a whole new set of questions regarding the new regimen. Why this regimen and not one of the other options? And what can you expect in terms of effectiveness? Side effects? It is not uncommon for HIV patients to become complacent in their relationships with their physicians over the years. Patients have told me that they have almost forgotten how to express complaints or concerns to their physicians, and may even feel guilty doing so, as if they are letting their doctors down by no longer acting like model patients. But you shouldn't worry about being "high maintenance"—it's your health at stake.

Keep Records: It may be a long time since you have thought about your medications beyond keeping your prescriptions on hand and taking them on schedule. But a new regimen is going to completely throw off your routine, and if you don't stay conscious of this new routine, you may find yourself taking the new medications at the

wrong time. Until you retrain yourself to follow the new schedule, it can be helpful to carry a small notepad to use to keep track when you took what medication each day. This will save you from having to reconstruct what you were doing earlier in the day. While you are keeping a record of when you took your new medications, you may also want to make brief notes on how you are feeling. Did you experience some nausea one afternoon? Write it down. Dizziness or a headache on another day? Make a note of that too. And what about questions? It can be helpful to keep track of your questions in this same notepad, which you can bring to your next doctor's appointment.

Stay Connected: Because a new regimen can raise some unfamiliar issues and emotions, it can be really helpful to have a place to talk about what you are going through. You may want to connect with a support group through a community center or HIV organization. Here, you are likely to find people who are going through the same situation as you are, and possible with the same regimen, who can offer both emotional support and their own perspectives. If you are involved in a church, or synagogue, or a spiritual group, this may be a time when you want to reach out for support. You may want to consider talking to a counselor who is experienced in dealing with HIV-related concerns. This is not a time to be alone. Find a safe place to talk and strategize with someone who cared about you, understands what you are going through, and who can also be an objective sounding board.

Adhering to Your Regimen: Depending on what you were facing with your most recent regimen, adherence may have become an issue. Consequently, you may be looking forward to an easier schedule with the new regimen, or have other reasons for anticipating the change. Or, as I discussed earlier, the new regimen may look like a steep uphill climb. Either way, you don't need another lecture about adherence. But if you have doubts about your ability or willingness to stay with it, talk to your physician so that he or she can explore whether the regimen is having a biochemical effect on your mood. Talking about your emotions with a support group, friends, or a professional counselor can also be helpful.

A new regimen can unleash a whole range of emotions, some of them a blast from the past, and some of them brand new, and your emotions can impact effectiveness of the new regimen as well as adherence. This is not the time to continue going it alone. Keep a close watch on how you are feeling emotionally, and don't hesitate to ask someone else to watch with you.

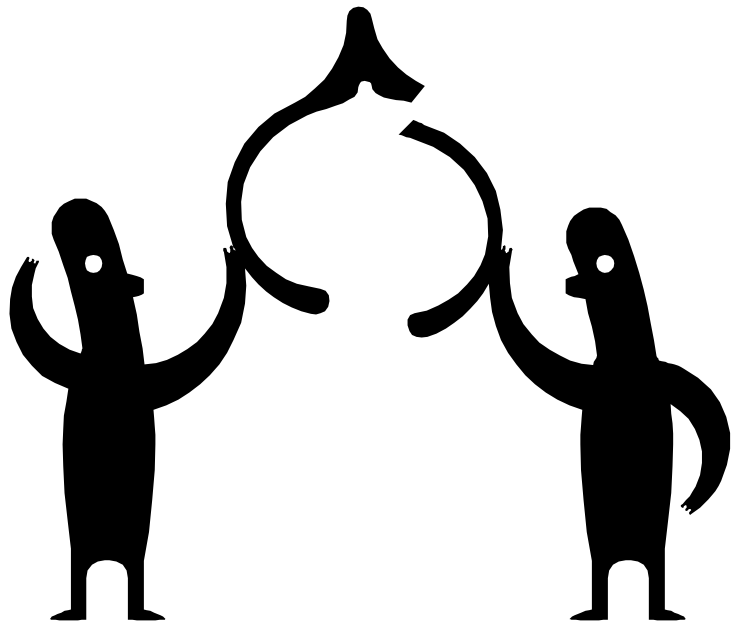
Gary McClain, PhD, is a counselor in New York City. He is developing a Websiet, www.IJustGotDiagnosed.com.

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