



## 41<sup>st</sup> EASL Coverage



Liz Highleyman

The 41<sup>st</sup> annual European Association for the Study of the Liver (EASL) meeting took place April 26-30 in Vienna, Austria. The hepatitis C abstracts that generated the most interest were mainly in two areas: refinements of standard therapy and novel experimental agents.

### TREATMENT REFINEMENT

J.G. McHutchison and colleagues (*abstract 744*) reported that patients who achieve sustained virological response (SVR) – undetectable HCV viral load six months after the end of treatment – are very unlikely to relapse in the future. After five years of follow-up, 98% of nearly 500 patients in six clinical trials who achieved SVR with interferon (with or without ribavirin) still had undetectable HCV RNA. The authors concluded that SVR at six months “is an excellent predictor of long-term clearance of the virus” – further evidence that a “cure” for hepatitis C is possible.

In an attempt to reduce the side effects and costs associated with hepatitis C therapy, researchers have increasingly focused on individualized regimens using lower doses or shorter courses of therapy. Long-term data from

the WIN-R study, presented by R. Brown and colleagues (*abstract 41*), confirmed that a 24-week course of therapy is adequate for patients with genotypes 2 or 3 HCV. In this study, more than 1800 participants with these genotypes were randomly assigned to receive pegylated interferon-alpha 2b (Peg-Intron) plus either fixed-dose or weight-based ribavirin for 24 or 48 weeks. Among patients who achieved an end-of-treatment response, 6-10% in the 24-week arm relapsed during the post-treatment follow-up period, similar to the 5-12% seen in patients treated for 48 weeks; discontinuation rates were also similar.

But further shortening treatment to 16 weeks is not advisable, according to data from the 1469-person ACCELERATE trial, presented by M. Shiffman and colleagues (*abstract 734*). In this study, 24 weeks of pegylated interferon-alpha 2a (Pegasys) plus ribavirin was more effective than 16 weeks for patients with HCV genotypes 2 or 3. While both groups responded well at the end of treatment, the extra eight weeks reduced the risk of relapse: 76% in the 24-week arm achieved SVR, compared with 65% in the 16-week arm. “This study shows that genotypes 2 and 3 patients really do need 24 weeks

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of treatment for optimal results,” Shiffman said.

Research has consistently shown that early response predicts ultimate treatment success. P. Ferenci and colleagues (*abstract 8*) reported that shorter therapy may be effective for so-called “super-responders” who achieve undetectable HCV viral load by week 4. In this study, 106 “super-responders” out of more than 400 total participants with “hard to treat” genotype 1 or 4 HCV were randomly assigned to receive standard-dose Pegasys plus ribavirin for 24 weeks (rather than the usual 48 weeks for these genotypes). Using an intent-to-treat analysis, 75% achieved SVR at the end of follow-up – higher than the overall SVR rate for all genotype 1 patients observed in most studies using 48 weeks of therapy.

Lowering the dose of ribavirin is another approach that has been proposed for reducing side effects. Ferenci and colleagues (*abstract 82*) also reported that reduced

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doses of ribavirin produced similar SVR rates, while improving tolerability in patients with genotype 2 or 3 HCV. More than 200 patients (most with genotype 3) were randomly assigned to receive either 800 or 400 mg daily ribavirin plus standard-dose Pegasys for 24 weeks. At the end of follow-up, 74% and 80%, respectively, achieved SVR. Hemoglobin levels (a measure of anemia, a common side effect of ribavirin) remained higher in the patients who received the lower ribavirin dose, leading the authors to conclude that reduced dosing provides “tolerability benefits.”

### TREATMENT OF NON-RESPONDERS

Another important area of research is management of individuals who did not respond to their first course of therapy. P. Marcellin and colleagues (*abstract 11*) reported data from the REPEAT trial, in which 950 participants who did not respond to prior treatment with Peg-Intron plus ribavirin were retreated with either a standard dose (180 mcg) or a higher induction dose (360 mcg) of Pegasys plus weight-based ribavirin. After 12 weeks, 45% in the standard-dose arm achieved early virological response (at least a 2 log decrease in HCV RNA), compared with 62% in the induction arm. In a separate presentation, D. Jensen and colleagues (*abstract 583*) reported that while the rate of side effects was similar in both arms, more patients in the induction arm required dose reduction.

In promising news for non-responders, S. Kaiser and colleagues

(*abstract 584*) presented further data showing that long-term maintenance therapy with low-dose Peg-Intron can improve liver histology. In this study of 240 previous non-responders with advanced fibrosis or cirrhosis, those receiving the maintenance regimen (0.5 mg/kg weekly for 36 months) were significantly more likely than untreated control subjects to experience reduced liver fibrosis and decreased necroinflammatory score, although the latter was temporary and rose again after maintenance therapy was discontinued. No adverse side effects were reported, leading the researchers to conclude that interferon maintenance may be used as “salvage therapy.”

### SIDE EFFECTS

Traditionally, healthcare providers have discouraged hepatitis C treatment for patients with pre-existing psychiatric conditions due to the higher risk of side effects. J. Lang and colleagues (*abstract 591*) reported data from a study of nearly 2000 French patients, 22% of whom had a history of psychiatric disorders including depression, suicide attempts, or psychiatric hospitalization. Patients with a psychiatric history were four times more likely to stop treatment (16% vs 4%); however, the overall rate of treatment discontinuation for any reason was similar in patients with and without a psychiatric diagnosis (36% vs 30%). These results suggest that such patients should not automatically be excluded from treatment, since a majority can tolerate therapy.

Thrombocytopenia – a low level of platelets in the blood, which can lead to easy bruising and bleeding is common in patients with hepatitis C, and is a potential side effect of interferon. McHutchison and col-

leagues (*abstract 745*) reported that a new medication called eltrombopag is a safe and effective treatment for this condition. Eltrombopag stimulates the proliferation and maturation of platelet precursor cells called megakaryocytes. In this interim analysis of data from a Phase II placebo-controlled trial, eltrombopag increased platelet counts in 67-90% of 28 patients; response rates increased with higher doses (30, 50, or 75 mg daily). There were no serious side effects, and platelet counts increased enough to allow all treated patients to start interferon.

### EXPERIMENTAL THERAPIES

The latest trial data for several new hepatitis C agents was presented at EASL. Valeant Pharmaceuticals’ viramidine is a pro-drug of ribavirin that works primarily in the liver, and thus is less likely to cause anemia. Y. Benhamou and colleagues (*abstract 751*) reported data from the Phase III VISER1 trial comparing fixed-dose viramidine (9600 mg twice daily) to weight-based ribavirin (500-600 mg twice daily), both with Peg-Intron. In this study, which included 970 treatment-naïve patients, anemia rates were significantly lower in the viramidine arm compared with the ribavirin arm (5% vs 24%). However, in an intent-to-treat analysis, viramidine was not shown to be “non-inferior” to ribavirin, with SVR rates of 38% vs 52%, respectively. Viramidine did work as well as ribavirin in younger patients (under 45 years) and lighter-weight individuals, suggesting that weight-based dosing may be preferable.

One of the novel anti-HCV agents furthest along in the development pipeline is the oral polymerase inhibitor valopicitabine

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# HealthWise:

## *Healthy Living with HCV Series*

### *Part 2: Physical Fitness*



Lucinda K. Porter, RN

Anyone over the age of 50 might remember one of my favorite weight loss commercials. The ad featured a vibrating belt, strapped around the user's hips. The hype professed that fat could be jiggled off without any exercise. The notion was ridiculous, but the device sold well.

Here we are, more than half way through the first decade of the new millennium and guess what? Vibrating weight loss belts are popular again. Does this mean they work? Absolutely not. Think about this: if we could vibrate off unwanted pounds, then anyone who uses a jackhammer or rides the New York subway would be thin. Models and movie stars would be trading personal trainers for personal tremblers.

Yet in spite of the quackery, people are buying vibrating belts. This is probably because exercise involves effort, commitment and time. For those who do not like it, exercise is especially hard work. Having our fat pulsed off sounds appealing, especially if it involves minimal effort.

However, exercise is more than a weight management technique – much more. Physical activity helps fight fatigue and depression. It is the cornerstone for managing high blood pressure, high cholesterol and diabetes. There is evidence that physical activity reduces the risk of cancer and may boost the immune system. Experts recommend exercise to reduce the risk of stroke and heart attack. Movement can reduce the symptoms of back pain, arthritis and other muscle and joint aches. It may lower the risk of osteoporosis and dementia.

Insurance companies and employers promote physical fitness because ultimately it is good for business. Fitness programs can improve flexibility, balance, tone, strength and stamina. Exercise can clear the head and body of worry and anxiety. Being physically active may improve sleep, reduce food cravings, and help us feel more energetic.

The following recommendations for minimum fit-

ness goals are from the Centers for Disease Control (CDC):

- Adults should engage in **moderate-intensity** physical activities for at least 30 minutes on 5 or more days of the week. Moderate intensity exercise is defined as an increase in breathing or heart rate; the effort a healthy individual might use while walking briskly, mowing the lawn, dancing, swimming, or bicycling on level ground; any activity that burns 3.5 to 7 calories per minute (kcal/min)

–American College of Sports Medicine

OR

- Adults should engage in **vigorous-intensity** physical activity 3 or more days per week for 20 or more minutes per occasion. Vigorous-intensity physical activity may be intense enough to represent a substantial challenge to an individual and refers to a level of effort in which a person should experience: large increase in breathing or heart rate; the effort a healthy individual might expend while jogging, mowing the lawn with a nonmotorized pushmower, participating in high-impact aerobic dancing, swimming continuous laps, or bicycling uphill, carrying more than 25 lbs up a flight of stairs, standing or walking with more than 50 lbs; any activity that burns more than 7 kcal/ min

– Healthy People 2010

Many of us already engage in moderately intense activities. Examples are most household and home repair chores, grocery shopping, gardening, and waxing a car. The rule of thumb for vigorous activity is you should be able to talk but not sing during the activity. I tried this yesterday and attracted a lot of attention. I do not know if this was due to my singing or my running style.

Most of us know that we are supposed to exercise, but there can be a huge gap between what we do and

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## PHYSICAL FITNESS

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what we wish we could do. People living with hepatitis C (HCV) know this more than most. People with HCV report fatigue, muscle and joint aches. Depression, weight gain, and mental “fogginess” can also create obstacles. Exercise is still harder for those undergoing HCV treatment. For them, climbing the stairs may feel like climbing Mt Everest.

If this is true, then how do we get moving? The key may be the way we perceive exercise. If we view exercise as a chore or something that creates pain, then physical activity may feel like an obstacle. Perhaps the first step is as simple as replacing the words “exercise” and “fitness” with “play” and “fun.” When exercise is an act of recreation or play, we are more willing to engage in it.

Willingness to act is a good first step, but then what? Consult your medical provider. There may be medical reasons to limit or modify a fitness program. This is especially true if you are older or live with disabilities. A physical fitness plan should be safe and fit your needs. Identify what you need most. Is it strength, flexibility, balance, aerobic endurance or a combination of these? What type of program does your provider recommend?

For those new to exercise, a reasonable beginning regimen might be to walk a few minutes, stretch, and stop for the day. Always allow a day of rest between weight training workouts. Some fitness trainers recommend a day of active rest every week. Active rest means taking a break from a regular fitness regimen but does not mean spending it on the couch.

Start small and gradually work up to a goal. If the long-term goal

is to walk 30 minutes five days a week, then start with 5 minute walks 3 days a week until you can do this effortlessly. Do not overdo it. Too much exercise may lower your immune function.

Be sensible about exercise. Remember to drink water, apply sunscreen and avoid injuries. Pain is NOT gain. However, sore muscles may occur. Heat, cold packs, and stretching may be beneficial. Remember to consult a doctor for injuries and discuss a back-up fitness plan for common injuries. Avoid exercise when ill.

Sometimes a successful fitness program is just a matter of finding the right one. Fortunately, there are many from which to choose. Walking, hiking, swimming, dancing, bicycling and weightlifting are some common recreational activities. Yoga, Tai Chi, Pilates, gardening and playing with children are forms of exercise.

Physical fitness is more likely to be successful if it is portable, not dependent on the weather, and fits any budget. Water bottles are good hand weights. Put the radio on your favorite oldies station and dance to your heart’s content. Take a walk in a park.

Staying fit does not have to be an all or nothing proposition and can fit into the busiest schedules. Some ways to do this include gardening, using the stairs, choosing a parking spot on the outskirts of the lot, getting off the bus before the scheduled stop and walking the rest of the way, window shopping, sweeping the floor, and mowing the lawn. Replace power tools with manual tools. Trade a motorized lawnmower for a nonmotorized one. Walk rather than drive. Do not use the remote control when watching TV. Stretch, do leg exercises or lift light weights while talking on the phone or watching television. Any

opportunity to be active helps us to stay in shape.

Make sure you reward yourself. Reward efforts, not results. Choose healthy rewards, such as new exercise clothes, like socks or a warm-up jacket; exercise gadgets such as a pedometer, heart rate monitor; and additional time for relaxation or engaging in a favorite activity.

Just as in life, variety is an important aspect of exercise. If you walk, add activities at various intervals that increase your heart rate and use other muscles. Examples of this: Every 5 minutes of walking, try skipping for a minute, or do 4 lunges, or 2 minutes of speed walking. If you use weights for toning, try a session using light weights with 20 to 30 repetitions, and another session using heavy weights and perhaps only 5 or 6 repetitions. You can also vary the speed of your workout. Lifting weights at a very slow rate can be incredibly challenging.

Here are some other suggestions, especially when it is hard to maintain a fitness program:

- Schedule your exercise. Mark it on a calendar. Stick to your schedule.
- Make it regular. This is how good habits are formed.
- Suit up and show up. Some people find the act of putting on sneakers and starting the activity helps overcome mental resistance.
- Find a fitness buddy. We are less likely to cancel out on a friend than we are on ourselves.
- Join a group or class.
- Keep a log. Watch your progress.
- Use the Internet and other motivation tools. (See *Resources* for more information.)

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# Alcohol and the Liver



Alan Franciscus, Editor-in-Chief

One of the best strategies to keep the liver healthy for people living with hepatitis C is to stop drinking alcohol or to greatly reduce the amount of alcohol consumed. In addition to the harmful effects alcohol has on the liver, alcohol also poses other problems for people with hepatitis C. Consuming alcohol (especially in large quantities) can:

- Lower the immune response in people with hepatitis C
- Help the hepatitis C virus replicate or make more copies of itself
- Lower HCV treatment response
- Add to the emergence of HCV quasi-species
- Increase the level of iron stored in the liver
- Increase fat accumulation in liver cells

When all of these factors are considered, it is no wonder that people are advised to abstain from alcohol. But how is alcohol actually metabolized by the body? This article will focus on how alcohol is absorbed and metabolized throughout the body and also on some of the effects of prolonged alcohol use.

- When alcohol is consumed it reaches the stomach then the small intestine where it passes into the blood stream. About 20% is absorbed through the stomach and about 80% is absorbed through the small intes-

tines. Once the alcohol enters the blood stream it is sent to and processed by the liver. After one drink of alcohol the concentration of alcohol in the blood peaks in about 30 to 45 minutes and drops back to normal in about an hour if no further alcohol is consumed.

The liver is responsible for converting the alcohol into a substance that is safe for the body. There may be a small quantity of alcohol that does not reach the liver – this is excreted in the urine and breath. That's why breath analyzers are able to measure the amount of alcohol someone has consumed.

## LIVER

There are two liver enzymes that are responsible for converting alcohol into a safe substance: alcohol dehydrogenase (ADH) and cytochrome P450IIE1 (CYP2E1). ADH is the main enzyme responsible for converting alcohol. CYP2E1 is another enzyme that is involved in the process of metabolizing alcohol. In people who are chronic alcohol drinkers the liver will make more CYP2E1 in an effort for the body to compensate for excess alcohol consumed. Unfortunately, the extra production of CYP2E1 does not stabilize the effects of long term alcohol use or the damage that is caused to the liver.

In people without liver disease, chronic drinking will lead to the deposit of fat in the liver cell, leading to inflammation and

cell death. After a time the cell death will cause light scarring of the liver and after years of chronic drinking the liver can develop cirrhosis. If you combine the efforts of alcohol and with another factor such as hepatitis C the time it takes to cause damage is much shorter.

There are differences in what causes intoxication in people. Some factors that influence the degree of absorption and, therefore, intoxication include:

- The amount of alcohol consumed – the liver can only metabolize a certain amount of alcohol per hour
- The rate of metabolism differs depending on the amount of ADH enzyme in the liver and this differs by gender.
- Food can affect the amount of alcohol absorbed by the body. If there is food in the stomach it can slow down the absorption of alcohol. Foods high in carbohydrates and fat help to slow down the process of the stomach pushing the food (and alcohol absorbed) into the small intestine. Mixing alcohol with beverages can also affect the absorption of alcohol – alcohol mixed with fruit juice or water is absorbed more slowly than alcohol mixed with carbonated beverages.

- Muscle tissue contains more water than fat tissue so the more muscle tissue a person has the more diluted the alcohol will be.

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## ALCOHOL

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### GENDER DIFFERENCES

There are differences in the way alcohol affects men and women. The amount of body water affects the rate at which alcohol is absorbed. The more body water a person has the less the amount of alcohol that is absorbed. In general, women have higher body fat composition (less body water); men have a higher body composition of muscle (more body water). For this reason women will achieve higher concentrations of alcohol in their bodies than men who consume equal amounts of alcohol. In addition to gender differences, total body water composition decreases as people age so a person over 60 years old has less total body water than someone under 40 years old.

Another reason women metabolize alcohol differently is that women have less of the enzyme (ADH) that metabolizes alcohol than men. This means that women who drink the same amount of alcohol as men will achieve a higher concentration of alcohol in the blood.

Because of these gender differences the amount of alcohol for a healthy adult (without liver disease) differs for women and men – women should not drink more than 1 alcoholic drink a day and men should not drink more than 2 alcoholic drinks per day.

### EXCESS ALCOHOL

The liver can only absorb and metabolize so much alcohol. The excess is distributed to other areas of the body. If the alcohol can not be processed by the liver it can greatly affect other organs in the

body and a person's psychological well being. Excess alcohol use can cause a variety of problems including:

- Hypertension (high blood pressure)
- Irritation of the gastrointestinal system causing ulcers, gastritis, and inadequate absorption of nutrients
- Central nervous system disorders, including brain disorders, vitamin B deficiency, and peripheral neuropathy
- Male and female impotence
- Depression and anxiety as well as many social problems

If you are a person living with hepatitis C, the message is clear: mixing alcohol and hepatitis C will decrease the way the body is able to control hepatitis C and lead to faster liver disease progression. If you can not stop drinking consider seeking help from family, friends and medical providers. Alcoholism is an insidious disease that affects millions of Americans and destroys many lives. Resources listed below can offer help and guidance to stop drinking.

### Resources

- HCSP Factsheet: *Alcohol and HCV*
- HCSP Factsheet: *Tips for Staying Alcohol-Free at Social Events*
- [www.alcoholics-anonymous.org](http://www.alcoholics-anonymous.org)
- [www.hcvanonymous.com](http://www.hcvanonymous.com)



## PHYSICAL FITNESS

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Get a good coach. We have unlimited access to one – the coach we carry with us. Be a supportive coach. Skip the criticism. Show up, suit up and keep a positive attitude. The effort is worth it, especially when fitness becomes fun.

*Next month: Weight Management*

### Resources

*Note: These websites are recommended for the quality of information. Although some sites have advertising, these products and services are not endorsed by HCSP or the author.*

- Aetna Intellihealth – [www.intelihealth.com](http://www.intelihealth.com)
- American College of Sports Medicine – [www.acsm.org/AM/Template.cfm?Section=General\\_Public](http://www.acsm.org/AM/Template.cfm?Section=General_Public)
- American Heart Association – [www.justmove.org](http://www.justmove.org)
- Centers for Disease Control – [www.cdc.gov/nccdphp/dnpa/physical/index.htm](http://www.cdc.gov/nccdphp/dnpa/physical/index.htm)
- Mayo Clinic – [www.mayoclinic.com/health/fitness/SM99999](http://www.mayoclinic.com/health/fitness/SM99999)
- National Institute on Aging – [www.niapublications.org/agepages/exercise.asp](http://www.niapublications.org/agepages/exercise.asp)
- Office of Disease Prevention and Health Promotion – [www.healthypeople.gov](http://www.healthypeople.gov)
- The President's Council on Physical Fitness and Sports – <http://www.fitness.gov>
- PrimusWeb.com – [www.primusweb.com/fitnesspartner](http://www.primusweb.com/fitnesspartner)
- StrongWomen.com – [www.strongwomen.com](http://www.strongwomen.com)
- U.S. Department of Health and Human Services – [www.smallstep.gov](http://www.smallstep.gov)



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(NM238) from Idenix Pharmaceuticals. N. Afdhal and colleagues (*abstract 483*) presented interim results from a Phase IIb study that included 190 previous non-responders with genotype 1 HCV. Participants were assigned to one of five arms: 800 mg daily valopicitabine monotherapy, Pegasys plus one of three doses of valopicitabine (400 mg daily, 800 mg daily, or escalating doses from 400 to 800 mg), or continued standard therapy. After 24 weeks, those in the two higher-dose valopicitabine/Pegasys arms responded significantly better (2.99-3.29 log IU/L decrease in HCV RNA) than subjects receiving valopicitabine monotherapy (.046 log IU/L decrease) or standard therapy (2.27 log IU/L decrease). In the combination valopicitabine arms, 12-24% achieved undetectable HCV RNA, compared to 18% in the standard treatment arm and none in the valopicitabine monotherapy arm. Valopicitabine was generally well-tolerated, although mild-to-moderate gastrointestinal (GI) side effects were common, and four patients (3%) discontinued for this reason. Response rates were higher in treatment-naive patients. D. Dieterich and colleagues (*abstract 736*) presented data from another study in which 173 previously untreated genotype 1 patients were randomly assigned to receive Pegasys plus valopicitabine at doses of 200 mg daily, 800 mg daily, or escalating doses from 400 to 800 mg, or else Pegasys monotherapy. In the combination arms, at least

80% achieved early virological response, 45-67% had undetectable HCV RNA at 12 weeks, and median viral load reductions were about 3.9-4.5 log IU/L. Similar early results were seen in the Pegasys monotherapy arm, however, and the question remains whether valopicitabine will produce a more durable response after treatment is completed.

Joining valopicitabine, S. Roberts and colleagues (*abstract 731*) reported the first data from a Phase I study of another HCV polymerase inhibitor, Roche's R1626. Eighteen treatment-naive patients with genotype 1 HCV were randomly assigned to receive either 1500 mg

*"In promising news for non-responders, S. Kaiser and colleagues (abstract 584) presented further data showing that long-term maintenance therapy with low-dose Peg-Intron can improve liver histology."*

or 500 mg twice daily R1626 monotherapy or placebo for 14 days. After 14 days of follow-up, those who received the 1500 mg dose experienced a median 1.2 log IU/L (range 0.5 to 2.5) reduction in HCV RNA. R1626 was well-tolerated, with no serious adverse events or early withdrawals.

S. Zeuzem and colleagues (*abstract 78*) presented data from a study of SCH503034, an HCV protease inhibitor being developed by Schering-Plough. In this open-label crossover study, 26 prior non-responders with genotype 1 HCV were treated with SCH503034 monotherapy (200 or 400 mg three times daily), Peg-Intron mono-

therapy, or the combination (all subjects received all three regimens in differing orders). The 400 mg SCH503034/Peg-Intron combination was most effective, with 40% (4 out of 10 patients) achieving undetectable HCV RNA; the average viral load reduction in this arm was 2.9 log IU/L. The combination regimen was well-tolerated; side effects were generally mild-to-moderate, and mostly attributable to interferon. One patient developed a temporary SCH503034 resistance mutation.

Promising data on another new oral HCV protease inhibitor, Vertex's VX-950, were presented by H. Reesink and colleagues (*abstract 737*). In this Phase Ib study, 20 treatment-naive patients with genotype 1 HCV were randomly assigned to receive 750 mg VX-950 monotherapy three times daily, Pegasys monotherapy, or the combination. After 14 days, the combination arm was most effective, with 50% (4 out of 8 patients) achieving undetectable HCV viral load and a median viral load decrease of 5.5 log IU/L, compared

with 4.0 log IU/L in the VX-950 monotherapy arm and 1.0 log IU/L in the Pegasys monotherapy arm. All patients then continued on standard Pegasys plus ribavirin; after 12 more weeks, eight had undetectable HCV RNA. VX-950 was well-tolerated, with no serious adverse events or discontinuations. However, development of drug resistance is a concern with protease inhibitors, especially when used alone. Previously research showed that drug-resistant mutations (A156T, A156V, V36M/A/L, T54A, R155K/T/S/M) can emerge with exposure to VX-750. But, as T. Kieffer and

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**COLORADO ORGAN REGISTRY:**

Worldwide, the first successful liver transplant was performed by Thomas Starzl, M.D. in 1967 at the University of Colorado Health Services Center, Denver, Colorado. A new chapter in medicine began with that event. Colorado residents may continue this legacy by donating their organs upon death. Residents are encouraged to make their wishes known by enrolling in the Colorado donor registry. Coloradoans may also signify their intentions on their state driver's licenses. In this and all other states, it is a good idea to tell your family and loved ones about your donation wishes.

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colleagues (*abstract 12*) reported at EASL, gene sequence analysis showed that “wild-type” (non-resistant) HCV re-emerged as the dominant type within 3-7 months after VX-750 was stopped.

Early data on another new type of experimental agent, Coley Pharmaceutical Group’s toll-like receptor agonist CPG 10101 (Actilon) was reported in two presentations by McHutchison and colleagues. In a Phase 1b study (*abstract 111*), 60 previous non-responders, most with genotype 1, were randomly assigned to receive CPG 10101 in various doses by subcutaneous injection once or twice weekly for four weeks. Patients receiving CPG 10101 experienced reduced HCV viral load, which was associated with improved measures of immune function such as cytokine levels and activation of T-cells, B-cells, and natural killer cells.

The agent was generally well-tolerated, producing flu-like symptoms. Another trial (*abstract 730*) looked at CPG 10101 in combination with pegylated interferon plus ribavirin. Here, 74 genotype 1 patients who relapsed after prior therapy were randomly assigned to receive 0.2 mg/kg once weekly CPG 10101 alone or in various combinations with pegylated interferon, ribavirin, or both, or else standard therapy, for 12 weeks. In this study, 86% (12 out of 14 patients) receiving all three agents achieved early virological response at week 12, compared to 60% (9 out of 15) of those receiving standard therapy; 50% (7 out of 14) and 15% (2 out of 13), respectively, achieved undetectable HCV RNA. Patients receiving CPG 10101 plus either pegylated interferon or ribavirin – but not both

– were less likely to respond (57% and 21% undetectable, respectively); CPG 10101 alone was not effective.

**RITONAVIR BOOSTING**

Finally, D.J. Kempf from Abbott Laboratories and colleagues (*abstract 4*) reported data showing that the antiretroviral drug ritonavir (Norvir) can increase serum concentrations of experimental HCV protease inhibitors. Ritonavir, itself an HIV protease inhibitor, is used at low doses in anti-HIV therapy to “boost” blood levels of other drugs in its class; this works because ritonavir inhibits the activity of cytochrome P450 enzymes, thus slowing clearance of other drugs. In laboratory cell cultures and in rats, ritonavir strongly inhibited metabolism of both VX-950 and SCH 503034. Raising blood levels of HCV protease inhibitors may enhance their efficacy and reduce the development of drug resistance, but may also worsen side effects.

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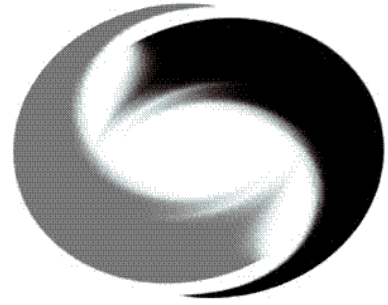
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