Interferon and ribavirin; although it’s been many years since my hepatitis C treatment, these two words still strike a nerve in my body. Interferon and ribavirin were the backbone of hepatitis C treatment for decades. These drugs caused so many side effects it led to my writing two books to help patients through hep C treatment. It was grueling to take those drugs, especially for those who had to take them for a long time or more than once.

Patients’ experiences are much different now that we have new hep C medications known as direct-acting antivirals (DAAs). Peginterferon is hardly used in the U.S. except perhaps for genotype 3 patients. Ribavirin is used less too, and when it is used, treatment lengths are far shorter, making the overall treatment experience more tolerable. Soon my books will be obsolete, and I am happy about it.

Compared to the old days, current treatment is a cakewalk. I thought that when DAAs were available that the need for patient support would diminish. I figured people would take their pills, be cured, and move on to freedom from hepatitis C. I was wrong on so many levels. I was naïve, misguided, and showed a serious lack of understanding in human nature.

I thought that because hepatitis C treatment is easier, people would just naturally want to do it. I overlooked the simple fact that taking any pill is scary when there is a risk of side effects. I don’t care if you are going to take an aspirin or chemo, no one wants a side effect.

— CONTINUED ON PAGE 2
Some people are more concerned about side effects than others are, and perhaps with good reason. Research has shown that some people appear to metabolize some medicines differently, suggesting that some are more sensitive than others are. We saw this in a recent study about statins, showing proof of sensitivity in some patients. DNA research is slowly uncovering evidence of genetic differences in drug metabolism. In short, science is leading us closer to understanding why some people report adverse effects from drugs, while others don’t.

Why do we have anxiety about side effects? Why don’t we just take the medication and see what happens? I don’t know the answer, but I wonder if we are hardwired with the instinct to protect ourselves from harm. For instance, would you use something that had the following side effects?

...Upset stomach, vomiting, diarrhea; elevated liver enzymes, liver damage; drowsiness, impaired judgment, cognitive problems, bouts of amnesia, decreased perception/coordination, speech difficulties, distorted vision/hearing, depression, hallucination, headaches, anemia, breathing difficulties, unconsciousness, coma, and death...

I asked some people if they would take this, and they said no. These sound awful except these are the side effects of alcohol, enjoyed by many people (hopefully none with hep C). Yet wouldn’t you think twice about taking this if these side effects were listed for a medication? I would, and I think it’s because taking a chemical scares me more than the thought of drinking fermented grapes did. Still, I suspect that most of the current hep C medicines are safer than alcohol is. (Again, I am NOT endorsing alcohol use for people with a history of liver disease.)

Plus, alcohol never cured hep C. It really comes down to a risk/benefit analysis. Do the potential benefits of medication exceed the potential risks? Here’s an example: I’ve always had dry eyes. Last year my doctor prescribed Restasis. When I went to the pharmacy, I was shocked by the sticker price of $70 for a month of drops. I declined the prescription, went home and read about Restasis. In clinical trials over a period of six months, 15 percent of subjects improved versus 5 percent in the control group. It would cost me $420 to find out if I was one of the lucky 15 percent. Those are terrible odds. My dry eye condition cleared up on its own.
Compare this to a better than 90 percent chance of being cured of hep C, typically after 12 weeks of treatment. If I tried treatment, there was a risk of mild side effects. If I didn’t try treatment, I risked living with an infectious disease that could cause liver cancer, lymphoma, cirrhosis, depression, sleep difficulties, premature death, and so on.

Actually, it isn’t fair to say that the downside is merely having potential side effects, since in fact, many side effects can be managed and minimized. Good side effects management is a delicate balance that relies on good communication between the patient and his/her medical team. Here are some tips:

• Report side effects early. It’s easier to fix a side effect when it is a small problem than wait until it’s a big problem.

• Don’t try to be your own doctor by assuming that just because you are on a medication that the symptoms you are having is a side effect. Two days after I started ribavirin, I developed a hideous rash. I assumed it was caused by ribavirin. I waited five days before abandoning self-treatment and sought help. It was poison oak.

• Once diagnosed, work with your doctor by being informed about things you can do to help with side effects. The HCV Advocate website offers many fact sheets and guides on side effects management. www.hcvadvocate.org/publications/fact-sheets

• Join a support group. Even if you don’t have a single side effect, treatment is still a journey into the unknown, and better endured with others. My favorite is the HEP Forum at http://forums.hepmag.com

Finally, consider reporting side effects to the FDA, especially ones that aren’t listed in the prescribing information. It’s frustrating when you think you have a side effect and your doctor says, “It’s not listed.” That can feel dismissive, as if your doctor thinks your complaints are in your head. Reporting side effects may help other patients. You can report suspected adverse reactions to the FDA (800) FDA-1088 www.fda.gov/Safety/MedWatch/HowToReport/ucm053074.htm

These days, most people can expect a fairly easy hep C treatment, and in the end walk away cured. Bring along a good attitude and some support, and before you realize it, you are free from hepatitis C.”

Lucinda K. Porter, RN, is a long-time contributor to the HCV Advocate and author of Free from Hepatitis C and Hepatitis C One Step at a Time. She blogs at www.LucindaPorterRN.com and HepMag.com
This year’s International Liver Congress was held in Barcelona, Spain on April 13–17, 2016. In year’s past the conference had hundreds of presentations about drugs in development to treat hepatitis C. This year’s conference had much less. This is a trend that will continue because the medications to treat hepatitis C have cure rates of to 90% and higher. The push now is to find drugs that work in people who have failed a previous course of direct-acting antiviral medications (DAAs), people with cirrhosis and those with resistant associated variants (RAVs) and pan-genotypic drugs.

In this article, I have picked out what I think are the most interesting and important studies from the International Liver Congress meeting. I will discuss the use of pan-genotypic drugs, the use of DAAs for treatment-experienced patients, the results from the first study of DAAs in the treatment of children with chronic hepatitis C, a Veterans Administration review of treating HIV/HCV coinfected veterans with DAAs, treating acute hepatitis C, and a very interesting clinical study using generic DAAs.

1. DRUGS IN DEVELOPMENT - ADULTS

AbbVie presented data on a new once-daily pan-genotypic therapy of ABT-493 (protease inhibitor) and ABT-530 (NS5A inhibitor)-once daily.*

The top-line cure rates — non-cirrhotic patients — 8 weeks of treatment:

- Genotype 1: 85% were treatment naive; 15% were pegylated interferon (PEG)/ribavirin (RBV) experienced, cure rates—97% (33 of 34 patients)
- Genotype 2: 87% were treatment naive: 87% were PEG/RBV treatment experienced: cure rate—98% (53 of 54 pts)
- Genotype 3: 100% were treatment naive: cure rate—97% (28 of 29 pts)

The top-line cure rates — 12 weeks of treatment:

- Cirrhotic treatment naive patients, genotype 3 — cure rate —100% (24 of 24 patients)

Non-cirrhotic treatment naïve patients (85%), PEG/RBV (15%); genotype 4 (22 pts), genotype 5 (1 pt), genotype 6 (11 pts)—cure rate—100% (34 of 34 pts)

Editorial comment

This trial produced excellent results. I am interested to see the results from the upcoming phase 3 study and if these results can be replicated. If so, this would be another excellent choice for treatment.

*I did not include the results of the arms that included ribavirin because the cure rates were similar between the arms that included ribavirin and the arms that did not include ribavirin.

Source: Company press release

Gilead presented data on GS-9857 (protease inhibitor) combined with sofosbuvir (polymerase inhibitor) and velpatasvir (NS5A inhibitor) to treat genotype 1 through 6
with and without cirrhosis. The information presented is from their phase 2 clinical studies. * In the group of treatment naïve patients treated for 6 weeks the cure rate was 79% (53 of 67 pts); the treatment naïve group that was treated for 8 weeks the cure rate was 96% (95 of 99 pts)

In another study presented with the same combination to treat treatment experienced genotype 1 through 6 and who had been treated with a previous course treatment—prior NS5A experienced (27%); non-NS5A experience (52%), direct-acting antiviral experienced (DAA (52%)), and 21% that failed an interferon based therapy without a DAA. The cure rate was 99% (127 of 128 pts).

In yet another study GS-9857 with sofosbuvir/velpatasvir was tested to treat DAA experienced genotype 1 patients with cirrhosis. The treatment period was 12 weeks. The cure rate was 100% (24 of 24 pts).

The most common side effects were headache, fatigue, diarrhea and nausea.

The fixed dose combination of sofosbuvir, velpatasvir and GS-9857 is currently in 4 phase 3 clinical trials (POLARIS 1, 2, 3 and 4). The Food and Drug Administration has granted the combination as Breakthrough Therapy for those who have previously failed an NS5A inhibitor-containing regimen.

**Editorial Comments**

The Gilead studies produced excellent results and show great promise. The need for treatment of people who are cirrhotic, have failed prior therapy, or have developed RAVs are some of the most important obstacles left in the treatment landscape. That is unless you count access to HCV medications.

*I did not include the results of the arms that included ribavirin because the cure rates were similar between the arms that included ribavirin and the arms that did not include ribavirin.*

Source: Company press release

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**COMMONLY USED TERMS**

- **Acute Infection:** rapid-onset, short-term initial stage of a disease.
- **Breakthrough Therapy Designation:** assigned by the Food and Drug Administration (FDA) to a drug if it can treat a serious or life threatening disease or condition. The designation can accelerate FDA approval.
- **Cure:** also call sustained virological response (SVR) – HCV RNA (viral load) is undetectable at week 12 after treatment ends. Also called viral cure.
- **Direct-acting antiviral medication (DAAs):** also called HCV inhibitors - there are 4 categories of direct antivirals medications—protease inhibitors, polymerase inhibitors (nucleoside and non-nucleoside inhibitors) and NS5a inhibitors. DAAs target and inhibit viral enzymes that are important for replication of hepatitis C.
- **Pan-genotypic drugs:** Drugs that have some activity against all of the genotypes of the hepatitis C virus.
- **Resistance-associated variants (RAVs):** hepatitis C virus mutations that form resistant strains that occur naturally, during treatment breakthrough or after treatment relapse.
- **Treatment Naïve:** people who have never been treated.
- **Treatment Experienced:** people who have been treated but have not been cured.
Regulus Therapeutic Inc.
The study included 79 treatment naïve genotype 1 and 4 patients. RG-101 is a GalNAc-conjugated anti-miR targeting miR-122, a host factor for HCV infection. It is an injectable medication given at Day 1 and Day 29 plus 4 weeks of a once-a-day direct-acting antiviral medication—Harvoni (27 patients), Olysio (27 patients), Daklinza (25 patients).

Sixty-four of the patients were evaluated through week 8 of follow-up, 41 reached 12 weeks post treatment. The cure rate was 97% (40 of 41 pts). The most common side effects included fatigue, headache and injection site reaction.

“...It has been very frustrating to have these life-saving drugs available but out of reach for many patients because of the exorbitant prices.”

Editorial Comment
To tell the truth I was very doubtful this drug would fulfil its promise when it was first introduced. I am glad I was proven wrong. I am very eager to see this drug commence phase 3 clinical trials and learn the final results. If the phase 3 study results are as excellent as these results and the drug is priced appropriately it just might be a viable future treatment option.

2. DRUGS IN DEVELOPMENT – CHILDREN

The study included 100 adolescents aged 12 to 17 years old treated with ledipasiv/sofosbuvir that is being conducted in the U.S., U.K and Australia at 24 sites. There were 100 adolescents- male (37%); white (90%), genotype 1a (81%); all but one were non-cirrhotic; the transmission route was mostly mother-to-child (84%).

The overall cure rate was 97%. Three patients were lost to follow-up. More than 10% of the adolescents experienced the following side effects: headache, diarrhea, fatigue, nausea, cough, throat pain, and vomiting.

The study is on-going and includes children aged 3 to under 12 years of age.

Editorial Comment
This is an important study. The current standard of care for the treatment of children with chronic hepatitis C is the combination of pegylated interferon plus ribavirin. Most medical providers are reluctant to treat children with this combination unless a child has severe HCV disease progression. Hopefully, this trial will be completed soon and FDA will expedite the approval.

Source: NATAP.com

3. DRUGS IN DEVELOPMENT – GENERICS

An on-going study comparing low-cost generic versions of sofosbuvir, sosbuvir/ledipasvir and daclatasvir to the branded versions was presented by Dr. James Freeman. The generic drugs have been verified with technology using the same means that pharmaceutical and governmental agencies use. The cost of the generic study drugs run between $1400 and $1600 per treatment.

The overall cure rates were 90% for genotype 3 and 96% for genotype 1. The clinical trial is on-going.

Editorial Comment
It has been very frustrating to have these life-saving drugs available but out of reach for many patients because of the exorbitant prices. Generics are a part of the answer. I’ve been very reluctant to embrace and advocate the use of generic DAAs. It’s very reassuring to know that steps are being taken to test the medicines. I support this approach if the generics can be tested.
and assure people they are safe and effective. Generics provide much needed access for some people especially and importantly in resource poor countries. But what we really need is for our government to address the outrageous pricing practices of the pharmaceutical industry. The exception is Merck who has priced their drug—Zepatier—lower than all of their competitors.

Note: This is a very brief overview. For a detailed breakdown of the study results Liz Highleyman wrote an excellent article from an EASL presentation—EASL 2016: Low-Cost Generic Hepatitis C Drugs Match Branded Products in Viral Response article visit: Source: http://hivandhepatitis.com/hcv-policy-advocacy/5687-easl-2016-low-cost-generic-hepatitis-c-drugs-match-branded-products-in-viral-response

Source: HIVandHepatitis.com

Editorial Comment
Most studies have found that DAA therapy has produced similar cure rates in HIV/HCV co-infected and mono-infected people. It’s not surprising the 11% difference when interferon is included in the therapy. I wonder if the 6% is really a difference in the drug therapy or some other factor? More studies are needed to resolve this important issue.

Source: International Liver Congress Press Release

5. ACUTE HCV CURE – 6 WEEKS
Up to 50% of people who are initially infected with hepatitis C naturally clear the infection. The remaining people will go on to have chronic disease and suffer from on-going long-term liver illness. In the current study from Germany, 20 patients were recruited. The risk factors included sexual (11 people), medical procedures/needlestick (5 people), drug use (1 person), nail treatment complications (1 person) and the remaining were listed as unspecified.

All of the patients in the study received Harvoni (sofosbuvir/ledipasvir) for six weeks. The follow-up period was the standard 12 weeks. The cure rate was 100%. The most common side effect was fatigue.

Editorial Comment
This is very good news for treating people with acute hepatitis C. I am not familiar with the surveillance system in Germany, but in this country it is abysmal. It would certainly help if there was more dollars allocated to fund prevention, identify acute infection and to treat acute and chronic infections.

Source: International Liver Congress

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
WE HAVE REVIEWED AND UPDATED THE FOLLOWING…

The Medical Glossary- check it out

The following Easy C fact sheets

Easy C Fact Sheet: Alcohol

Easy C Fact Sheet: What is Stealosis?

Easy C Fact Sheet: Diabetes

Easy C Fact Sheet: Top Ten Healthy Habits

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

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