In this month’s HCV Drugs there is excellent news about drugs to treat hepatitis C and encouraging news on some insurance companies easing restrictions on access to HCV medications.

**Sofosbuvir plus Velpatasvir**

On January 4, 2016, Gilead issued a press release to announce that the U.S. Food and Drug Administration (FDA) granted priority review to sofosbuvir (polymerase inhibitor) plus velpatasvir (a pan-genotypic NS5A inhibitor). Gilead stated that FDA approval is expected on June 28, 2016.

Below is a brief overview of study results from articles published in the New England Journal of Medicine (vol. 373 no.27 December 31, 2015).

**Genotype 1, 2, 4, 5 and 6 (ASTRAL Studies)**

In the group of patients with genotype 1, 2, 4, 5, and 6 (624 patients) the cure rates were 99% across all the genotypes. Less than 1% of patients discontinued treatment due to side effects. The most common side effects were headache, fatigue, sore throat, runny nose, and nausea.

“For people who have been denied claims, it just might be a good time to check-in with your medical provider or you insurance company to find out the status of your claim.”
Genotype 2 and 3 (ASTRAL 2 & 3 Study)

**ASTRAL 2:** The results from the Phase 3 clinical trial for the treatment of 134 patients with genotype 2 who were treated with sofosbuvir plus velpatasvir for 12 weeks resulted in a cure rate of 99%.

**ASTRAL 3:** In the Phase 3 clinical trial of 277 genotype 3 patients the overall cure rate was 95%. 

- **Treatment naïve:** In the group of patients without cirrhosis the cure rate was 98% (160 of 163 pts); in the group of patients with cirrhosis the cure rate was 93% (40 of 43 pts).
- **Treatment-experienced:** In patients without cirrhosis the cure rate was 91% (31 of 34 pts); in patients with cirrhosis the cure rate was 89% (33 of 37 pts).

The ASTRAL 2 and 3 studies had comparator arms that included 132 genotype 2 patients and 275 patients genotype 3 patients who received sofosbuvir plus ribavirin. The patients who received sofosbuvir plus velpatasvir had higher cure rates and less side effects.

The most common side effects in sofosbuvir plus velpatasvir groups were fatigue, headache, nausea and insomnia.

**Viekira Pak**

On January 7, 2015, AbbVie issued a press release that the FDA had granted Viekira Pak without ribavirin a priority review status for the treatment of hepatitis C genotype 1b in people with compensated cirrhosis. AbbVie did not provide details on an expected FDA approval date.

AbbVie submitted data to the FDA based on the Phase IIIb TURQUOISE-III study of 60 genotype 1b patients treated with Viekira Pak (ombitasvir, paritaprevir/ritonavir, dasabuvir) for a treatment duration of 12 weeks. The cure rates were 100% (60 of 60 pts). The most common side effects were fatigue, diarrhea, headache and joint pain.

**Merck’s Drug Approval**

The FDA is expected to approve Merck’s two drug combination of elbasvir plus grazoprevir—brand name Zepatier—one pill, once-a-day by the end of this month. Zepatier’s treatment duration is 12 weeks to treat genotype 1, 4, and 6.

**Easing Insurance Restrictions**

There have been reports that insurance companies are easing some of the strict fibrosis/cirrhosis restrictions that have prevented many people from accessing HCV treatment. Personally, a friend who had been denied multiple times by her insurance company for HCV medications was notified that she had been approved for treatment. Since that time I have heard from other patients and other advocates that insurance companies have dropped some of the more severe restrictions. These restrictions included having to have severe liver disease progression—severe fibrosis/cirrhosis (F3/F4). For people who have been denied claims, it just might be a good time to check-in with your medical provider or your insurance company to find out the status of your claim.

“2016 will likely be an exciting year for patients and medical providers that will offer more choices and better access to treatment.”
Article: Hepatitis C virus infection in inclusion body myositis: A case-control study—A Uruha et al.

Results
The hepatitis C virus is known to cause many extra-hepatic manifestations such as fatigue, muscle and joint pain, insomnia and cryoglobulemia just to name a few. The current study was to test to see if there was a link between the hepatitis C virus and inclusion body myositis (IBM). IBM is a progressive group of muscle diseases. IBM usually occurs (but not always) in people who are over 60 years old. The researchers studied 114 patients with hepatitis C and IBM and 44 age-matched patients with polymyositis (disease of the muscle fibers) diagnosed from 2002 to 2012. Muscle biopsies were taken and compared between the two groups.

Conclusions
The authors found that 28% of the patients with IBM had HCV antibodies compared to 4.5% of patients with polymyositis who had HCV antibodies and 3.4% of Japanese patients in their 60’s with polymyositis. The authors also did not find a difference in the disease characteristics of IBM in both groups leading them to conclude that both diseases were the same (non-HCV and HCV IBM groups).

Editorial Comment
The same authors had published a smaller study in 2013 on inclusion body myositis (IBM) and HCV and came to the same conclusion. While this does not prove that hepatitis C causes IBM, it does suggest an association. More studies are needed to find out if hepatitis C causes IBM and if treatment can arrest or reverse it.

For more information about IBM visit: www.mda.org/disease/inclusion-body-myositis/overview

Article: Improvement of platelets after SVR among patients with chronic HCV infection and advanced hepatic fibrosis—A J van der Meer et al
Source: Journal of Gastroenterology and Hepatology doi: 10.1111/jgh.13252

Study Aim and Results
One of the consequences of advanced fibrosis and cirrhosis is low platelets and enlarged spleen. Platelets help the blood to clot and the spleen stores blood cells including platelets. In this study, the authors reviewed studies conducted between 1990 and 2003—platelet counts of 464 patients were measured six months before treatment and 24 weeks following the end of treatment. Of the 464 patients evaluated 353 (75%) had cirrhosis, and 187 (40%) were cured.

Conclusions
Among the patients who were cured the platelet counts increased and the spleen size decreased—all postive signs of improvements of liver functioning. In those who did not achieve a cure, the platelet counts decreased, and the spleen size increased — signs that the liver functioning was worsening. The authors commented that the results of this study suggested
that curing hepatitis C reduces portal hypertension, increased platelet counts and reduced the size of the spleen.

**Editorial Comment**
The study supports treating (and curing) people with advanced hepatitis C. Curing persons with advanced hepatitis C can improve symptoms and quality of life, and improves long-term survival. It is critical to remember, however, that HCV disease progression still occurs, and lifelong monitoring is still needed. This is why we need to treat people BEFORE their disease reaches this critical stage.

**Article: Functional impairment in older liver transplantation candidates: From the functional assessment in liver transplantation study—C W Wang et al.**

*Source: Liver Transplantation, Volume 21, Issue 12 December 2015*

**Study Aim and Results**
Patients 65 years old and older typically have poorer liver transplant outcomes than younger patients. The authors in the current study wanted to understand what factors could predict better outcomes in these patients other than the health issue criteria used for the Model for End-Stage Liver Disease (MELD) score to assess patients for eligibility to receive a liver transplant. The authors used an additional battery of tests called the short physical performance battery (SPPB) test. They tested and divided the patients into two groups—younger (under 65 years old) and older (65 years old and older). The SPPB measures gait speed (how quickly someone could walk), chair stands (standing up from a sitting position), and balance (various balancing exercises such as standing on one foot) and graded the patients on scales as either impaired or robust.

**Conclusions**
The SPPB impaired scores at any age were more likely to die while waiting for a liver transplant. There was no significant difference between the younger and older robust patients when it came to the risk of dying while waiting for a liver transplant.

**Editorial Comment**
The logical outcome of this study is that people with physical performance problems as listed in the SPPB should be given physical therapy instructions to improve their conditions and increase long-term survival.

**Note:** If you are older (or possibly of a younger age) and have SPPB issues it makes sense to be evaluated by a medical provider and take the appropriate action. SPPB issues (especially balance issues) are one of the most common reasons that older people fall and have severe injuries that can be life-threatening. There are some very easy exercises that anyone can do to improve balance issues. If balance issues are more advanced talk with a medical provider, who can send you to a physical therapist who can instruct you on exercises to increase your strength and balance. The key is to start early.
Editorial Comment

I saw this study abstract a couple of months ago, but I wanted to find out more about the study before I wrote about it. The story was recently picked up by many news outlets, which, of course, made the study results even scarier.

It is important to remember this study proves that there is an association but does not prove causation. In other words—while this is a well-designed study it shows an association between hepatitis C and Parkinson’s disease. The study does not prove that hepatitis C causes Parkinson’s disease. More studies are needed with hepatitis C. However, until this is proven (or not), it is critical that everyone with hepatitis C is treated and cured of HCV and the associated extrahepatic manifestations that just may include Parkinson disease. 😊

**Study Aim and Results**

The study was to find out if hepatitis C is a risk factor for developing Parkinson’s disease. The researchers searched the Taiwan National Health Insurance Research Database for the period 2000 to 2010. There were 49,967 people with viral hepatitis (hepatitis B and hepatitis C) patients included in their analysis and 199,868 patients without viral hepatitis were included for comparison.

**Conclusions**

The analysis found that there was a significant increase risk for Parkinson’s disease for those with HCV, but not those with hepatitis B. The increase occurred even after the researchers adjusted for age, sex and other conditions or diseases that patients with hepatitis C may have had.

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**HealthWise**

**Hepatitis C: A Waiting Exercise**

Hepatitis C patients spend a lot of time waiting. We wait for medical appointments, for lab test results, for insurance companies to approve our treatment, and for the medications to arrive. If treatment doesn’t cure us, we wait for the next treatment, and again for the appointments, insurance decisions, and so on. For those needing a liver transplant, the process of waiting takes on new meaning.

When I worked at Stanford, a patient was on a waiting list, hoping to get hep C treatment. There were

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“Don’t be a slave to waiting. Live life in the present and you live in freedom.”

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unexpected delays and his wait was unusually long. Frustrated, he told me, “I feel like I am sitting around and doing nothing while hepatitis C is eating away at my liver.” This is a powerful image. I am sure others have felt helpless and discouraged and can relate.

His reaction was quite understandable. However, this person assumed he was “doing nothing.” In fact, he was actually doing a great deal. Between maintaining a healthy diet and exercise regimen, he was plowing the way towards a favorable outcome. Now, when I use the term “favorable outcome,” I am not speaking about response to treatment. I am referring to a larger concept. Hepatitis C is only one factor that can hurt our health. There are other conditions, such as heart disease and cancer that may confront us. We are whole entities, not separate organs. It can be emotionally consuming to think that hepatitis C is our major problem. This can cause us to neglect the rest of our needs.

Waiting is an active process. It means gathering data, looking at the truth, and making good decisions. Whether you are waiting for better treatment options, the availability of a particular drug, an insurance decision, or hoping for a liver, you don’t need to be waiting passively. Here are things you can do while you wait:

- **Try to maintain a healthy weight.** Obesity can have a negative impact on the liver, heart, and overall health.
- **Reduce your intake of fat.** In particular, avoid trans-fatty acids and saturated fats. Choose “heart-friendly” oils such as olive and canola. Foods that are high in omega-3 fatty acids are particularly good choices.

- **Increase your intake of fruits and vegetables.** Vary the color of your produce. In other words, eat something green (such as broccoli, greens), orange (cantaloupe, carrot), red (such as tomato or red pepper), etc.
- **Keep moving.** The word “exercise” is limited in its scope. Engage in a daily activity such as walking, bicycling, gardening, dancing, swimming or tennis. Walking is my personal favorite because it is simple.
- **Maintain strong bones.** Resistance exercises, and a healthy diet are the cornerstones for this. Check with your doctor to evaluate if you are at risk for osteoporosis.
- **Avoid alcohol, smoking, and recreational drug use.** We all know this. No lectures are necessary. If you can’t quit, get help.
- **Get sufficient sleep.** The function of sleep is to restore our bodies. Insufficient sleep can negatively affect daily performance and immune function. Sleep deprivation has been linked to traffic accidents.
- **Stay well hydrated, mostly with water.**
- **Wear your seatbelts.**

Finally, replace harmful images with helpful ones. The patient who felt that “hepatitis C was eating away at his liver” was holding on to a very powerful, but unhealthy image. Picturing his immune system defending his liver may be an easier image to live with, especially while one is waiting.

Don’t be a slave to waiting. Live life in the present and you live in freedom.

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](http://www.LucindaPorterRN.com) and HepMag.com.
The current drugs to treat hepatitis C have such high cure rates and minimal side effects (compared to the older therapies). This has created a dilemma for drug developers who must develop new drugs that somehow improve upon the current drugs. This is a difficult task, but not impossible. Probably the biggest achievement will be shorter treatment duration and lower cost. There is a percentage of patients who are the more difficult to treat, such as those with genotype 3 who have cirrhosis and have not achieved a cure with a previous course of therapy. The race is on for new, better and cheaper therapies—this is very good news for people living with chronic hepatitis C.

You will see below that the need for these new therapies has narrowed the pharmaceutical companies to a number that you can count on your fingers! As a result I have decided to rework our pipeline and list it by the pharmaceutical company. I am also just listing the major studies. This is also a new pipeline that will grow as information is released. The pipeline is a brief overview. More extensive information is listed in our newsletters and in our blog.

A brief overview of how this pipeline is laid out:

**Date:** The Pipeline will be updated on a monthly basis and will be included with the Mid-Month Newsletter

**Genotype (s):** This lists the drugs or combination of drugs and the particular genotype or genotypes that the drug is active against. I am not going to name the particular drug that works against one or all of the genotypes

**Comments:** This section will list the study results. Within this section, I will list the genotype(s) being studied and the phase of the study with a brief recap of the study.

You will note that many of the drugs or combinations of drugs are pan-genotypic—that is they work on many or most of the HCV genotypes. **Note:** Many of the drugs listed below have been updated with the latest information from the Liver Meeting 2015 and news reports as of 1/15/2016. More detailed information about drugs in development is available in our blog reported in the HCV Advocate newsletters.

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**Comments:**

**Genotype 1b - Phase 3b Study:** On January 7, 2016 the FDA granted Viekira Pak without ribavirin priority review status for people with compensated cirrhosis. The clinical trial to support the pending approval enrolled 60 patients and after 12 weeks of treatment the cure rate was 100%. The most common side effects were fatigue, diarrhea, headache and joint pain.
### AbbVie

**Genotype(s):** 1, 2, 3, 4, 5, 6 (Pan-genotypic)

**COMMENTS:**

**Genotype 1 – Phase 2 Study:** ABT-493 (protease inhibitor) plus ABT-530 (NS5A inhibitor) with and without ribavirin in non-cirrhotic patients were treated for 12 weeks. The cure rates were 97-100% in genotype 1 patients; 96-100% in genotype 2 patients; 83-94% in genotype 3 patients. In a separate study of ABT-493 plus ABT-530 the cure rate was 97% in genotype 1 non-cirrhotic patients treated for 8 weeks. The combination of ABT-493 plus ABT-530 is currently in Phase 3 studies.

### Achillion – Johnson & Johnson (Janssen)

**Genotype 1**

**COMMENTS:**

- **Genotype 1 – Phase 2 Study:** ACH-3422 and Odalasvir (ACH-3102) and Sovaprevir are in studies with various combinations. Recently, Johnson & Johnson Innovation – JJDC, INC (Janssen) made an investment in Achillion for co-development and distribution. See Janssen for a new study that features odalasvir.

- **Genotype 1 – Phase 2 Study:** Odalasvir plus sofosbuvir (used as a proxy drug) to treat genotype 1 patients for 6 weeks achieved 100% (12 of 12 patients) cure rates. A proxy drug is a drug used to stand in for another drug. Sofosbuvir is a polymerase inhibitor so it is assumed that odalasvir plus a polymerase inhibitor that is being developed by Achillion will produce similar cure rates.

### Bristol-Myers Squib (BMS)

**Genotype 1**

**COMMENTS:**

- **Genotype 1 – Phase 3:** Unity-2 Phase 3: The combination of daclatasvir/asunaprevir/beclabuvir to treat 112 treatment-naïve and 90 treatment-experienced patients with compensated cirrhosis (DCV-TRIO) with and without ribavirin for 12 weeks. The average age was ~59 yo; mostly White males, HCV genotype 1a.

  The cure rates were 93% in the DCV-TRIO group (naïve-93%; experienced 87%) and 98% (naïve 98%; experienced 93%) in the DCV-TRIO group plus ribavirin.

  The most common side effects were headache, fatigue, nausea, and diarrhea. As expected the group that received ribavirin had more side effects.
### Gilead

**Genotype 1, 2, 3, 4, 5, 6, (Pan-Genotypic)**

**COMMENTS:**

- **Genotype 1 – Phase 3:** Sofosbuvir plus velpatasvir (GS-5816) In Phase 3 clinical trials (ASTRAL-1-4), the cure rates in genotypes 1 through 6 ranged 97% to 100%. Gilead has applied for marketing approval to the Food and Drug Administration, (FDA) and approval is expected in 2016. In January 2016 the combination received priority review status and Gilead stated that FDA approval is expected by June 28, 2016. The most common side effects were headache, fatigue, sore throat, runny nose, and nausea.

- **Genotype 1 – Phase 2:** The combination of sofosbuvir, (velpatasvir), and GS-9857 given for 6 weeks to treatment naïve (never been treated) people who did not have cirrhosis cured 93% of people. This combination is currently in Phase 3 studies.

### Janssen

**Genotype 1, 2, 3, 4, 5, 6**

**COMMENTS:**

- **Genotype 1 – Phase 1:** In a small study of samatasvir, it was found to be safe and have antiviral properties against genotype 1, 2, 3 and 4. There is now a phase 2 study of samatasvir plus Olysio (simeprevir) in treatment-naïve (never been treated) patients with genotype 1b or 4.

- **Genotype 1:** Janssen (Alios Pharma) has initiated a phase 2a study of AL-335, odalasvir, and simeprevir to treat HCV genotype 1 treatment naïve patients. There will be 60 patients divided into three treatment arms who are treated for 4, 6 or 8 weeks.

### Merck

**Genotype 1, 2, 3, 4, 6**

**COMMENTS:**

- **Genotype 1, 4, and 6 – Phase 3:** The combination of grazoprevir plus elbasvir (combined brand name Zepatier into one pill, once-a-day) to treat genotype 1, 4 and 6 produced cure rates from 92% to 99%. The treatment duration was 12 weeks. The treatment was given Breakthrough Designation by the Food and Drug Administration. **The safety profile was excellent. Grazoprevir plus elbasvir – brand name Zepatier – should be FDA-approved at the end of January 2016.**

- **Phase 2 –** There were two studies – Part A: grazoprevir plus MK-3682 or elbasvir plus MK-3682 the cure rates for genotype 1a/b was 98%; Genotype 2 was 60-71%, but one group who received grazoprevir/MK-3682/MK-8408 had a 91% cure rate; Genotype 3 cure rate across all of the arms was 91%.
WHATS UP!

CHECK OUT OUR HERBAL GLOSSARY.
We have updated the Herbal Glossary to include more information about herbs and supplements. Learn about what specific herbs are used to treat a particular condition, what effect they may have on the liver, which ones are safe and which ones may be unsafe.

EVENTS PAGE
Do you have an event, conference, or meeting? If so, send us the information, and we will post it on our website.

hullabaloo

Don’t forget to check out our hepatitis C and hepatitis B blogs – we will be posting original articles to our blogs during the entire month of January 2016.

SUPPORT GROUPS
With treatment getting shorter and easier for people we are finding that many support groups are closing. If you are aware of any changes in a group near you, please let us know so we can keep our list current. On the other hand, if you know of new support groups please let us know.

Please send us any changes to supportgroup@hcvadvocate.org

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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