On June 28, 2016, Epclusa (ep-Kloo-suh)—a combination of two drugs—sofosbuvir, a polymerase inhibitor, and velpatasvir, an NS5A inhibitor, was approved by the Food and Drug Administration (FDA) to treat adults infected with chronic hepatitis C (HCV) genotype 1, 2, 3, 4, 5 and 6. It is taken with and without ribavirin. It is combined into one pill taken once-a-day. It can be taken with and without food. Epclusa is manufactured by Gilead Sciences INC. The treatment duration is 12 weeks.

FIRST-IN-CLASS

All genotypes - Epclusa is the first HCV medication that can successfully treat all six genotypes.

No ribavirin for most people - the cure rates are from 97% to 100% in those without cirrhosis or with compensated cirrhosis. Ribavirin is still needed for those with decompensated cirrhosis, but the treatment duration is the same and the cure rates are 85% to 100%.

Genotype testing - Epclusa cures all HCV genotypes at very high rates and for the same durations. This eliminates the need for expensive genotype testing.

High cure rates for genotype 3 - The clinical trials of people without cirrhosis or compensated cirrhosis achieved cure rates of 95%. In people with decompensated cirrhosis the addition of ribavirin to Epclusa produced 85% cure rates. Previous therapies produced suboptimal cure rates and treatment duration was 24 weeks especially for people with cirrhosis.

Genotype 2 - in clinical trials of Epclusa (without ribavirin) people without cirrhosis or with compensated cirrhosis the cure rate was 100%. In people with decompensated cirrhosis the addition of ribavirin increased the cure rate to 100%. Previously, treatment for all genotype 2 patients included ribavirin for everyone with genotype 2 and the cure rates were not as high.
Listed below are the cure rates for genotypes 1, 2, 3, 4, 5 and 6. The results below included patients who were treatment naive and treatment experienced.

### Epclusa for 12 weeks – no ribavirin in patients without cirrhosis or with compensated cirrhosis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Cure Rate</th>
<th>(pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>98% * (323/328)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>99.5% (237/238)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>95% (528/553)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>100% (116/116)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>97% (34/35)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>100% (41/41)</td>
<td></td>
</tr>
</tbody>
</table>

*Genotype 1a cure rate = 98% (206 of 210 patients); Genotype 1b cure rate = 99% (117 of 118 patients)*

### Epclusa plus ribavirin for 12 weeks in patients with decompensated cirrhosis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Cure Rate</th>
<th>(pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>94% (51/54)</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>100% (14/14)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>100% (4/4)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>85% (11/13)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>100% (2/2)</td>
<td></td>
</tr>
</tbody>
</table>

Note: no genotype 5 or 6 patients were included in the above study of decompensated cirrhosis patients.

Pregnancy: There are no studies of Epclusa in pregnant women. Ribavirin can cause birth defects and miscarriages. If you are a male taking ribavirin, you and your female sexual partner must use two types of effective birth control. Your female sexual partner will have to take a pregnancy test before and during treatment and 6 months after treatment ends. If you are a female taking ribavirin, you and your male sexual partner must use two types of effective birth control. Additionally, women have to take a pregnancy test before, during and 6 months after treatment ends.

---

Lower cost - The wholesale acquisition cost (WAC) for Epclusa is $74,760.00 for a 12-week course of treatment. It is too soon to tell if insurance companies, Medicaid and Medicare will cover it since it was just approved, but since it is lower than the price of Sovaldi and Harvoni there may be more of a chance of coverage when the prices are negotiated.


Side Effects: The most common side effects of Epclusa that occurred in more than 10% of patients in the clinical trials were headache and fatigue.


Note: at the beginning of the article I wrote that Epclusa could treat all genotypes. You might have wondered why I didn’t include information about genotype 7. Genotype 7 was discovered a few years ago and only a handful of people have been identified. Come to find out in the clinical trials of Epclusa one
patient who was enrolled in Gilead’s Astral 1 trial who was incorrectly identified as genotype 2, but was later retested as genotype 7. The patient was treated with Epclusa for 12 weeks and was cured. So Epclusa does cure all genotypes.

Check out our new HCV Medication Blog for information about all of the direct-acting antiviral medications approved by the Food and Drug Administration (FDA) to treat chronic hepatitis C.

**Drug Pipeline**

There has been some exciting news on drugs in development. The majority of the trials listed below are ‘active, but not recruiting’ meaning that the clinical trials have been registered and approved by the Food and Drug Administration (FDA) but have not yet started. A word to the wise—keep an eye on them — hepatitis C clinical trials are few and far between. If you are interested in a trial jump on it.

**AbbVie**

AbbVie’s combination of ABT-493 (protease inhibitor) and ABT-530 (NS5A inhibitor) is entering into phase 3 clinical trials. In phase 2 studies the combination to treat genotype 1, 2 and 3 cured 85% to 100% in 12 weeks. I can not find any open sites in the United States.

If you are interested in this study, you can go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and type in “ABT-493” AND “ABT-530” and look for phase 3 under clinical trial phase. The bottom of the page will include registered clinical trial sites.

**Gilead**

Gilead’s salvage therapy sofosbuvir, velpatasvir and voxilaprevir (GS-9857 – protease inhibitor) is entering into phase 3 studies. A salvage therapy is used to treat people who have been previously treated but have not been cured. In phase 2 studies the combination cured 89% to 100% of genotype 1 treatment experience patients with 8 weeks of treatments. In genotype 3 patients, they cured 100% of patients.

If you are interested in this study, you can go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov), type in “sofosbuvir” “velpatasvir” AND “GS-9857” and look for phase 3 under the clinical trial phase.

**Regulus Therapeutic Inc.**

Now the bad news—in June it was reported by Regulus that the Food and Drug Administration (FDA) put their clinical trial of RG-101 on hold due to safety concerns. The safety issue was due to a second serious case of jaundice. Regulus’ press release states that they would work with the FDA to resolve the safety concerns.

Don’t forget to check out the HCV Drug Pipeline at the end of this issue of the HCV Advocate newsletter.
Epclusa, the newest hepatitis C treatment, was approved in June. New medications to treat hepatitis C virus (HCV) infection are rolling out quickly, and Epclusa is the most exciting treatment so far. If you haven’t had a chance to take in the full significance of Epclusa, look at the newly revised HCV Guidelines, provided by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA), in collaboration with the International Antiviral Society–USA (IAS–USA). Peginterferon is not recommended for anyone now, and there are quite a few ribavirin-free treatments.

Epclusa has the highest cure rates, and can be used by nearly everyone, so one would think that treating hepatitis C would be straightforward. Unfortunately, it isn’t. First, there is the problem of which drug is on your insurance formulary. Epclusa may not be covered. In fact, you may find out that your insurance company will only cover Viekira or Zepatier, drugs that are a bit more complicated to take than Epclusa.

The other problem is that there are still issues with some private and state insurance plans refusing to pay for treatment. Most weeks I get an email similar to this one, “I have hepatitis C and my insurance denied coverage for treatment.” This is usually followed by, “I don’t know what to do. I feel like I’ve been sentenced to death,” or “I am thinking about ordering overseas generic hep C drugs. Is this safe?”

My response to either of these two scenarios is always the same: “Did you appeal the denial, and are you working with a patient assistance program (PAP)?” The response is always the same, “No.” That “no” is usually good news, because between working with a PAP and appealing the insurance denial, people are often able to get coverage for treatment.

Before you start searching the web for generic drugs, try these tips for getting hepatitis C medications:

- Know what the HCV Recommendations are, “Treatment is recommended for all patients with chronic HCV infection (emphasis mine), except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.”
When possible, try to work with a provider who has experience with getting drug approvals. The GI practice in my small mountain town works with a specialty pharmacy with a great success record.

Work with a patient assistance program (PAP). The HCV Advocate provides a resource list with reliable PAPs. My current favorite is the Patient Advocate Foundation’s Hepatitis C CareLine. They will also work with your medical provider, so it is worth mentioning to your doctor that the CareLine offers case management services.

If the treatment your doctor prescribed for you isn’t on your plan’s formulary, consider changing insurance plans during the next open enrollment period. The Patient Advocate Foundation’s Hepatitis C CareLine keeps track of formulary changes, and will provide that information to you.

Check out the National Viral Hepatitis Roundtable’s (NVHR) Hepatitis C Treatment Access page. NVHR provides templates for letters of appeal that your provider can use, as well as links to helpful resources.

Document everything. Write down who you talked to and when.

Keep trying. Each time there is a lawsuit, insurance companies and state Medicaid programs are confronted with the reality that if they don’t change their restrictive policies, they may be sued. As a result, there have been quite a few revisions to hepatitis C treatment requirements.

If you have trouble accessing treatment through your state Medicaid program, report this to NVHR.

Don’t despair. Despair serves no one. It will steal all the life out of you and will not help you get your hepatitis C medications. The “system” may deny your hepatitis C treatment, but don’t let them also have your precious joy.

If you have it in you, consider a lawsuit. A number of people have won their suits, opening the door to access to hepatitis C treatment for others. NVHR has a webinar about some of these successes. Read Valerie Green’s story, a woman who was instrumental in getting the state of Delaware to change its restrictive Medicaid policy.

“Don’t despair. Despair serves no one. It will steal all the life out of you and will not help you get your hepatitis C medications.”

Join a support group. The appeals process can be frustrating. A support group can help keep you fortified and focused.

The reason I am so adamant about fighting for coverage is that if everyone gives up, the situation will not change. If insurance companies have to pay for hepatitis C treatment, they will complain about the price to the drug companies. If insurance companies keep denying treatment, the drug companies won’t sell their drugs. Either way, the price is likely to drop, and access to treatment may improve.

Even more important, we have to fight because our lives depend on it. To borrow words from the late Elie Wiesel, “There may be times when we are powerless to prevent injustice, but there must never be a time when we fail to protest.”

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
Health literacy (HL) is the ability of a person to understand and use written, spoken and numerical information to make better decisions about their health. The ability to read a prescription bottle and understand how often to take medicine, what it may interact with and whether or not to eat a meal (and how much) when taking it are some examples of numeracy or numeric HL. The readability of a brochure given to a patient by a doctor, or information found online, is an example of written HL, and lastly, the words used when having a conversation about an illness, or during a medical appointment is an example of oral HL.

In 2003 the National Assessment of Adult Literacy (NAAL) found that roughly one third of Americans had low HL. In the 13 years since the NAAL study was published more focus has been placed on the improvement of health literacy through creating materials that are easy to understand. To help with this the U.S. Government released the Federal Plain Language Guidelines as a resource for individuals and organizations.

People with low levels of HL are more likely to avoid health care, have lower levels of formal education, and have worse overall health outcomes than those with average or above average HL. Meaningful delivery of health information has the best chance of success when we are present in the relationships with our clients and the populations we are trying to educate.

We need to have conversations with people who use health information on a daily basis so they can give input on ways to make it more user friendly. Having low HL can result in shame and avoidance, especially if people are spoken to by others in a condescending tone. This means talking about HL concerns requires the health care worker and patient to be on equal footing.

I think all of us have experienced situations where health information was difficult to understand or not completely clear. This common shared experience can be used to dispel the myth that low HL is a problem exclusive to people who lack higher education. The truth is HL like all literacy isn’t fixed. If I wake up tomorrow and diagnosed with a chronic illness that I am unfamiliar with my HL in relation to it will be low. I might be able to learn information about it quickly, but I wouldn’t be inherently better off at the start than anyone else who is also new to it.

Health literacy plays an important role in the hepatitis C treatment cascade. The information currently available on topics such as the liver, long term progression, diagnosis, treatment and prevention is complex, conflicting and sometimes not even made readily available. A real world example I encounter is the difference of acute and chronic hepatitis C. When I first start my job I used to explain their differences in group sessions by going through their definitions, but overtime I’ve found I have more success getting my point across by saying sudden or short term and long term or lasting. This isn’t a big change but it’s one my clients led me to and has helped.
Health Literacy and Hepatitis C — CONTINUED FROM PAGE 6

The difference between hepatitis C antibodies and hepatitis C RNA is also an area where HL and simple language can play a role. When we talk about the fact that people will always carry hepatitis C antibodies if they are cured how well we explain it will either reduce anxiety or increase it. If we combine this with other conversations like, “your liver isn’t bad enough yet, come back in 2 months,” or “eat well, drink alcohol moderately & maintain a good weight,” then you can begin to see that improvement of HL is more than making written information simple. It’s also being more specific with suggestions and less condescending with the assumption that a person should know the meaning of a vague statement. If that sounds like something I’ve said before it’s because I covered it extensively in a recent article on unique hurdles to healthcare, and it’s also because it’s a point that can’t be stressed enough.

I’ve learned from my clients that the information given to them by health care workers isn’t always easy to get. At times they have to ask, which can be embarrassing because hepatitis C is associated with a certain type of person (e.g. people who inject drugs) and if information is offered to them, it often comes with a judgmental tone. Their conversations with providers are often short, dismissive and end in anxiety instead of feeling better about their health and future.

Health literacy is a constantly changing field and still in its infancy. There are debates over how to best measure it and even over how to best define it. These conversations are important to have, but until we can reach an agreement on the ways of how to find and address low HL, it can be difficult to know where to begin.

I think an easy place to start is by making a conscious effort to write and deliver health information less like we are trying to remind people we are experts and more like we are having a friendly chat with friends over dinner. We need to always be trying to improve how we deliver health information by working together with the people who we want to access it.

We are not here to impress with how much we know. We are here to empower with what we can give. Information isn’t a privilege but sometimes we make it seem that way.

Matthew Zielske currently works as a HIV/HCV special populations prevention specialist at an HIV services organization. He utilizes a harm reduction model in his work with the substance use population focusing pointedly on persons who inject drugs. He is currently conducting research on Health Literacy and hepatitis C for his Master's Thesis in Communications. www.umbrellaway.org
Article: Treatment of Chronic Hepatitis C in the Aged - Does It Impact Life Expectancy? A Decision Analysis—YU Maor et al.


Study Aims and Results
Studies on the aged population infected with the hepatitis C virus are lacking. The current study estimated the number of life years and quality-adjusted life years (disease burden, medical burden, future medical intervention) gained with the treatment of Harvoni (sofosbuvir plus ledipasvir) in treatment naïve patients. The data was extracted from published studies and expert opinion. The Markov model was used to estimate HCV disease progression toward advanced liver disease. The Markov model is a standardized model that estimates a possible eventual outcome (long-term disease outcome) based on predetermined factors (current disease state, cure).

Conclusions
The Markov model predicted that life years and the quality adjusted life years “gradually decreased with advancing age but the rate of decline was slower with more advanced fibrosis stage.” In those with F1, F2, F3 life years gained was below 6 months if treated by 55, 65 or 70 years old.

The authors concluded that “the quality of life years gained for treated over untreated elderly were reasonably high even for those treated at early fibrosis state.” The authors also concluded that there is significant life expectancy benefit to HCV treatment in patients up to age 75 with advanced stage fibrosis.

Editorial Comments
There is a significant life expectancy and monetary benefit to HCV treatment in patients up to age 75 with advanced-stage fibrosis. HCV treatment is now easier to tolerate and the cure rates are very high. We should be testing every ‘Baby Boomer’ (and perhaps those even born 5 to 10 years earlier than ‘Baby Boomers’) and those at-risk for hepatitis C and treating everyone infected with hepatitis C. This would decrease the disease progression, the medical burden and importantly increase the quality of life for everyone with hepatitis C including those who are up to and beyond age 75 year old.

“HCV treatment is now easier to tolerate and the cure rates are very high.”
Article: Pharmacokinetics, safety and efficacy of a full dose sofosbuvir-based regimen given daily in hemodialysis patients with chronic hepatitis C—A Desnoyer et al.

Study Aims and Results
The study sought to understand the effects of treatment with sofosbuvir-containing therapies on people requiring hemodialysis. Hemodialysis is a process of filtering the blood of a person when the kidneys are not working normally. This was a prospective study. Patients received sofosbuvir once daily (7 patients) or 3 times a week (5 patients) after hemodialysis treatment. Sofosbuvir was given with either simeprevir, daclatasvir, ledipasvir or ribavirin.

It was found that all of the patients tolerated the medications. Two relapses occurred in the 3 times a week group but no one relapse in the daily group.

Conclusions
It was found that sofosbuvir could be safely administered but that close monitoring should be given to hemodialysis patients. They also noted that more data is needed to safely and effectively treat hemodialysis patients.

Editorial Comments
HCV liver disease progression can increase the risk of severe kidney disease progression. It is important to have effective therapies to treat hepatitis C that are safe for people with severe kidney disease. In clinical trials, Zepatier was shown to be safe and effective in people with kidney disease and hepatitis C. Until more clinical studies are conducted on sofosbuvir containing therapies, Zepatier is a safe alternative to sofosbuvir containing therapies for people on hemodialysis.

“It was found that sofosbuvir could be safely administered but that close monitoring should be given to hemodialysis patients.”

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
The PROP UP study is a prospective, observational study that is evaluating patient-reported outcomes associated with the treatment of chronic hepatitis C infection and benefits of viral cure. PROP UP was funded by the Patient Centered Outcomes Research Institute (PCORI) last August and the study is actively recruiting patients. The outcomes the study is evaluating hepatitis C treatment-related side effects, adherence to the treatment medications, the cost that patients have to pay out-of-pocket, long-term benefits of cure, and the potential harms of treatment. The study will also evaluate whether hepatitis C symptoms and patient functioning improve after treatment. The study will continue to track side effects and toxicities that may occur up to 1 year after treatment ends. The patient reported outcomes will be compared between the various hepatitis C medications.

Patient Centered
The study will answer certain questions in a “real world” setting. This is different than past studies conducted by pharmaceutical companies. The study was designed by investigators at the University of North Carolina: lead investigator, Donna M. Evon Ph. D, and co-investigators, Michael W. Fried, MD and Carol E. Golin, MD., along with a patient engagement group. The patient engagement group includes people who have had hepatitis C with a wide variety of experiences. They have been involved in every step of designing PROP UP, since 2013 when the original proposal was submitted.

Patients with HCV helped to decide which outcomes were important to evaluate, and how we would measure them. I am part of the patient engagement group and The Hepatitis C Support Project / HCV Advocate is the patient advocacy group who will help to disseminate the study’s findings to the larger HCV Community. We are all still involved in the ongoing collaboration.

The study will enroll 1,600 people nationwide. People can earn up to $155.00 for participating in the study. The surveys take about 20-minutes over email or on the phone. There are a total of 5 surveys over a period of 15 to 20 months that covers how patients feel before, during and up to 1 year after treatment ends.

You may be eligible if you are prescribed treatment for hepatitis C by your doctor and have not started treatment yet. The study is enrolling patients with all genotypes and five major oral treatments.

I hope that people with hepatitis C who are thinking about starting HCV treatment will be eager to enroll in this study. It is a way to give back to the hepatitis C community. It will help countless others in the future who may not have to deal with the same issues that many of us have had to face. The best outcome of this study is that patients and providers will be able to make educated health care choices—that is the ultimate outcome of clinical studies. We will also find out answers to other important issues that are vital to each and everyone one of us.

For more information about this study:
Call Shani Alston, PROP UP Project Director at 919-966-4847
http://propup.web.unc.edu/
The PROP UP Study — CONTINUED FROM PAGE 10

Patients are being enrolled at the following 9 medical centers. If you are being treated at the following liver centers and you are interested in the study, please contact the research coordinator listed below. Please note: the study is only recruiting patients who have not yet started their treatment.

<table>
<thead>
<tr>
<th>Clinic</th>
<th>Research Coordinator</th>
<th>Phone</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of North Carolina</td>
<td>Shani Alston</td>
<td>919-966-4847</td>
<td><a href="mailto:shani_alston@med.unc.edu">shani_alston@med.unc.edu</a></td>
</tr>
<tr>
<td>Chapel Hill</td>
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<tr>
<td>Yale University</td>
<td>Claudia Bertuccio</td>
<td>203 785-2204</td>
<td><a href="mailto:hong.chau@yale.edu">hong.chau@yale.edu</a></td>
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<tr>
<td>Saint Louis University</td>
<td>Theresa Cattoor</td>
<td>314-977-9335</td>
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<tr>
<td>University of Michigan</td>
<td>Elizabeth Wu</td>
<td>734-647-0236</td>
<td><a href="mailto:elizwu@med.umich.edu">elizwu@med.umich.edu</a></td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Kelly Borges</td>
<td>215-615-3755</td>
<td><a href="mailto:Kelly.Borges@uphs.upenn.edu">Kelly.Borges@uphs.upenn.edu</a></td>
</tr>
<tr>
<td>University of Florida</td>
<td>Patrick Horne</td>
<td>352-273-9464</td>
<td><a href="mailto:Patrick.horne@medicine.ufl.edu">Patrick.horne@medicine.ufl.edu</a></td>
</tr>
<tr>
<td>Virginia Commonwealth</td>
<td>Christian Ammons</td>
<td>804-828-9154</td>
<td><a href="mailto:Christian.ammons@vcuhealth.edu">Christian.ammons@vcuhealth.edu</a></td>
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<td>University</td>
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<tr>
<td>Rush University</td>
<td>Lelani Fetrow</td>
<td>312.942.1372</td>
<td><a href="mailto:Lelani_C_Fetrow@rush.edu">Lelani_C_Fetrow@rush.edu</a></td>
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<tr>
<td>UC Davis</td>
<td>Wendy Smith</td>
<td>916-703-4372</td>
<td><a href="mailto:wksmith@ucdavis.edu">wksmith@ucdavis.edu</a></td>
</tr>
</tbody>
</table>

PROP UP is also listed on www.clinicaltrials.gov at https://clinicaltrials.gov/ct2/show/NCT02601820?term=prop+up&rank=1

The HCV Advocate gets recognized for The HCV Advocate News and Pipeline Blog.

We post the latest news items about hepatitis C, HIV/HCV coinfection and hepatitis B on a daily basis.

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WE HAVE UPDATED THE FOLLOWING HCSP FACT SHEETS:

HCV Acute Hepatitis C
HCV Genotype, Quasispecies & Subtype

CHECK OUT OUR NEW HCV MEDICATIONS BLOG
We have all of the direct-acting HCV medications to treat hepatitis C and the Patient assistance programs including resources to help people access the medications.
http://hepatitiscmedications.hcvadvocate.org/

REGISTERED TO VOTE?
The upcoming election is one of the most important elections of our lifetime. If you are not registered, Goggle has made it easy to register or to find out if you are registered. Check it out

BTW...
I was a Poll Worker in the recent primary election.
It was a very interesting experience and personally rewarding. The election offices are always looking for poll workers. If you are interested, call you local elections officer.

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The current drugs to treat hepatitis C have 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 HCV Advocate Newsletter

**Genotype (s):** This lists the drugs or combination of drugs and the particular genotype or genotypes that the drug is active against.

**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 the International Liver Congress 2016. More detailed information about drugs in development is available in our blog and reported in the HCV Advocate newsletters.
## AbbVie

<table>
<thead>
<tr>
<th>Genotype(s): 1, 2, 3, 4, 5, 6 (Pan-genotypic)</th>
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**COMMENTS:**  
**Genotype 1 – Phase 2 Study:** Information from the International Liver Congress 2016: AbbVie’s once-daily therapy of ABT-493 (protease inhibitor) and ABT-530 (NS5A inhibitor).

**Non-cirrhotic patients Treatment period - 8 weeks:**  
- Genotype 1: 85% were treatment-naive; 15% were pegylated interferon/ribavirin (PEG/RBV) experienced, cure rates—97% (33 of 34 patients)  
- Genotype 2: 87% were treatment-naive; 15% 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)

**Treatment period 12 weeks:**  
Cirrhotic treatment-naive patients, genotype 3 – cure rate —100% (24 of 24 patients)  
Non-cirrhotic treatment-naive patients (85%), PEG/RBV (15%); genotype 4 (22 pts), genotype 5 (1 pt), genotype 6 (11 pts)—cure rate—100% (34 of 34 pts)

**Bottom line:** cure rates were 97% to 100%. **Now in Phase 3 clinical trials**

## Gilead

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<thead>
<tr>
<th>Genotype 1,2,3,4,5,6, (Pan-genotypic)</th>
</tr>
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</table>

**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%. In January 2016 the combination received priority review status and Gilead stated that FDA approval is expected by June 28, 2016. To view the Phase 3 data go here: [http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate0116_mid.pdf](http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate0116_mid.pdf)  

**Epclusa approved in June 2016**  
The results from a phase 2 study of sofosbuvir, velpatasvir and voxilaprevir are listed below.

<table>
<thead>
<tr>
<th>Genotype 1: 6 - 8 weeks</th>
<th>Treatment-naive no cirrhosis 6 weeks</th>
<th>Treatment-naive cirrhosis 6 weeks</th>
<th>DAA-experienced with &amp; without cirrhosis 6 weeks</th>
<th>PEG-RBV-experienced with cirrhosis 8 weeks</th>
<th>PI-experienced with &amp; without cirrhosis 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure rates</td>
<td>93% (14/15 pts)</td>
<td>87% (13/15 pts)</td>
<td>67% (20/30 pts)</td>
<td>100% (17/17 pts)</td>
<td>89% (25/28 pts)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotype 3: 8 weeks</th>
<th>Treatment-naive with cirrhosis</th>
<th>PEG/RBV-experienced with cirrhosis</th>
<th>DAA experienced cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure rates</td>
<td>83% (15/18 pts)</td>
<td>100% (19/19 pts)</td>
<td>100 (4/4 pts)</td>
</tr>
</tbody>
</table>

**Note:** DAA experienced: direct-acting antiviral treatment-experienced patients; PEG – pegylated interferon; RBV: ribavirin; PI experience: Protease inhibitor treatment-experienced; Treatment-naive: patients who have never been treated

The most common side effects were a headache, nausea, and fatigue. **Now in Phase 3 clinical trials**
Janssen (Achillion/Alios)  |  Genotype 1,2,3,4,5,6 (Pan-genotypic)

**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 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-naive patients. There will be 60 patients divided into three treatment arms who are treated for 4, 6 or 8 weeks.

- **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.

- **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.

- **Genotypes 1 through 6–Phase 2b Study:** Odalasvir, AL-335, and simeprevir in treatment-naïve and treatment-experienced patients with and without cirrhosis. The trial will enroll 400 patients for six or eight weeks. The study will include four arms with different combinations of drugs. The trial will begin in June 2016 and end in July 2017.
**Merck**

<table>
<thead>
<tr>
<th>Genotype 1, 2, 3, 4, 5, 6 (Pan-genotypic)</th>
</tr>
</thead>
</table>

**COMMENTS:**

- **Phase 2**—The study was to evaluate the safety and efficacy of an all-oral therapy. There were three different groups that included treatment-naïve, non-cirrhotic patients. The patient population included 93 genotype 1 patients, 61 genotype 2 patients, and 86 genotype 3 patients. The treatment duration was 8 weeks. All of the treatment groups received MK-3682 (300 mg or 450 mg) combined with grazoprevir/elbasvir or grazoprevir /MK-8408.

Twenty-four percent of genotype 1 patients had resistant associated variants (RAVs): 59% had NS3 (protease) RAVs and 21% had NS5B (polymerase) RAVs.

The overall cure rates were 91 to 100% in the genotype 1 groups; 60 to 94% in the genotype 2, and 86 to 91% in genotype 3. The drugs were well-tolerated with no treatment discontinuations.

Part B of C-CREST 1 and 2 will evaluate the most effective dose to treat prior treatment failures, cirrhotic patients and treatment in people with HIV/HCV coinfection.

**Bottom line:** The most effective dose was associated with cure rates in the 90 to 100%.

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**Regulus**

<table>
<thead>
<tr>
<th>Genotype 1, 2, 3, 4, 6</th>
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</table>

**COMMENTS:**

**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). Regulus issued a press release on June 7, 2016 that reported through 24 weeks of follow-up an additional 4 patients relapsed.

<table>
<thead>
<tr>
<th>Time Since Treatment Completion</th>
<th>RG-101 + Harvoni</th>
<th>RG-101 + Olysio</th>
<th>RG-101 + Daklinza</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 12</td>
<td>27/27 pts (100%)</td>
<td>26/27 pts (96.3%)</td>
<td>22/24 pts (91.7%)*</td>
</tr>
<tr>
<td>Week 16</td>
<td>21/21 pts (100%)</td>
<td>19/20 pts (95.0%)</td>
<td>20/22 pts (90.9%)</td>
</tr>
<tr>
<td>Week 20</td>
<td>14/14 pts (100%)</td>
<td>13/15 pts (86.7%)</td>
<td>13/13 pts (100%)</td>
</tr>
<tr>
<td>Week 24</td>
<td>10/10 pts (100%)</td>
<td>8/10 pts (80.0%)</td>
<td>8/9 pts (88.9%)</td>
</tr>
</tbody>
</table>

* One patient missed the Week 12 visit. Viral load results for this patient at week 8 and 16 were collected and indicate that the patient was a responder at both time points. **This trial is on clinical hold due to safety concerns.**