At the end of every year, I poll our staff to compile a list of the top news stories. Every year it always amazes us how much news occurs in the wonderful world of hepatitis C (HCV or Hep C for short). To compound the news of Hep C in 2016 was this year’s crazy election. This year I am going to take a different approach in detailing the top news stories—I will write up a brief overview of the news with a footnote at the bottom of the article that will provide a link to our blog. To those who receive our printed version of the newsletter, the entire website address is included. If you do not have a computer or mobile device you can visit your local library or read back issues of the HCV Advocate newsletter. Most of the news items are included in our newsletter. The news below is in no particular order but high on my list are improved HCV treatment and treatment access.

HCV Medications: Current Standard of Care: The medications to cure hepatitis C just keep getting better. Starting in 2016 Harvoni (Genotypes 1, 4, 5, and 6) and Viekira Pak (genotype 1) were the most likely prescribed HCV medications. In 2016 Zepatier (genotype 1 and 4), Viekira XR (genotype 1), Technivie (genotype 4) and Epclusa (genotypes 1 through 6) were approved by the Food and Drug Administration (FDA) to treat hepatitis C.

It should be noted that Epclusa is the first HCV pan-genotypic medication that was approved by the FDA.

--- CONTINUED ON PAGE 2 ---
and it has very high cure rates (95% to 100%) across all genotypes. A remarkable achievement!

Drugs in Development: It’s hard to believe that there are drugs in development to improve the already extremely high cure rates as seen in the current Hep C drugs! Gilead’s salvage therapy—sofosbuvir, velpatasvir and voxilaprevir to treat people who had failed previous therapies and to provide higher cure rates for those who had not been previously treated (genotypes 1 through 6). The cure rates in phase 3 clinical trials were 95% to 98%. The combination received the FDA Breakthrough Therapy Designation for patients who failed a previous course of therapy with direct-acting antiviral therapy—this designation speeds up the FDA approval process. In December 2016 Gilead submitted the triple drug combination to the FDA for marketing approval.

AbbVie’s glecaprevir plus pibrentasvir to treat previously treated patients and patients who had not been treated (genotypes 1 through 6) produced phase 3 clinical trial cure rates of 97% to 99% cure rates. The combination received the FDA’s Breakthrough Therapy Designation for patients who failed a previous course of therapy with direct-acting antiviral therapy—this designation speeds up the FDA approval process. In December 2016 AbbVie submitted their data to the FDA for marketing approval.

Merck’s combination of MK-3682B (MK-3682/grazoprevir/ruzasvir) with and without ribavirin to treat genotypes 1, 2 and 3 in phase 2 clinical trials produced cure rates of 86% to 100%.

Regulus Therapeutics Inc.’s RG-101 plus a direct-acting antiviral medication ledipasvir/sofosbuvir (group 1), simeprevir (group 2), or daclatasvir (group 3) had SVR12/cure rates of 100%, 96% and 92% respectively. However, the trial is on clinical hold due to a second serious adverse event of jaundice.

Janssen’s odalasvir, AL-335, and simeprevir in phase 2 clinical studies to treat genotype 1 treatment naïve patients achieved 90% to 100% cure rates. Additionally, Janssen (J&J), Achillion and Alios have many different combinations of drugs in clinical trials to treat hepatitis C.

Note: Some of the medications above are covered in more detail in the AASLD Part 2 article in this newsletter.

Treating Veterans: The Best News of the Year Award goes to Congress that allocated money so that the Department of Veterans Affairs can treat all eligible veterans infected with chronic hepatitis C. It is estimated that all Vets with hepatitis C can be cured of hepatitis C within 3 years—Amazing! You know what is also amazing? Congress worked together!

Hepatitis C-Positive Kidneys and Livers for hepatitis C negative persons: Transplanted kidneys and livers from a hepatitis C-positive donor to a hepatitis C negative person. After the transplant, the person was treated with HCV medications. We are living in amazing times.

Needle Exchange: In January the federal ban on needle exchange funding was lifted. Needle exchange sites continue to expand across the country especially in areas such as Indiana, Kentucky and Ohio that are experiencing increasing rates of new infections of hepatitis C among people who inject drugs.

Cherokee Nation Elimination Project: An initiative between Cherokee Nation Health Service (CNHS) and various private and public organizations to cure all of the native peoples in the Cherokee Nation Health Service was initiated in 2016.

Revisionist History: People infected with hepatitis C carry a huge burden of stigma that prevents people from seeking medical care and can affect almost every area of their lives. In a study released earlier
this year it was found that the hepatitis C epidemic peaked around 1950. That means that the majority of infections were 15 years earlier than previously believed and the most common transmission routes at that time were from unsafe medical practices and unscreened blood products and blood transfusions. This study should go a long way to help reduce the stigma of hepatitis C.

Harm Reduction: For the first time, the Surgeon General has recommended harm reduction—“Harm reduction programs provide public health-oriented, evidence-based, and cost-effective services.” The endorsement of harm reduction will help to bring about more services, funding and better care to all of the many who will benefit from it.

Vietnam Memorial Wall: Jim McGough a 19-year old infantry soldier who served in the Vietnam War had his name etched in the Vietnam Veterans Memorial Wall. Mr. McGough was wounded in Vietnam and received a blood transfusion. He found out later that the blood contained the hepatitis C virus. Mr. McGough is the first person to die of hepatitis C to have his name added to the Memorial.

Treatment Access: In 2016 more and more people with hepatitis C were able to access hepatitis C treatment and cure. Most commercial insurance carriers are now covering the medications to treat hepatitis C — at least the larger ones. Slowly Medicaid is also starting to remove some restrictions mainly due to lawsuits and from being nudged from Centers for Medicare and Medicaid Services (CMS) in 2015. Additionally, Health and Human Services estimated that 20 million Americans gained health insurance because of the Affordable Care Act (ACA) in 2016. The ACA is helping people with Hep C access health care and treatment.

We still have a slow climb ahead of us before everyone with hepatitis C is screened and has access to medical care, treatment and cure. But we are getting there.

HCV Epidemic in Appalachia: The steady rise in HCV (and HIV) infections in Appalachia continues. There is some work being done, but many more services (needle exchange, social services, HCV treatment) are needed to stem the rising tide of the second hepatitis C epidemic. The second epidemic is not just confined to the Appalachia region of the U.S.—it is occurring all over the country and it seems to be happening unabated. SAD because we could be doing such a better job and learn from the past.

Lasker Awards: Drs. Bartenschlager and Rice made discoveries to grow the hepatitis C virus in a laboratory. Their discovery led to the development of direct-acting antiviral medications. Dr. Sofia and collaborators of Pharmasset developed sofosbuvir —the first effective direct-acting antiviral drug that is the backbone of Gilead’s many HCV therapies. These three distinguished scientists received the Lasker Awards.

Jacques Chambers: Sadly, we lost a member of the HCV Advocate family—Jacques Chambers. Jacques was an excellent HIV and HCV advocate for many years. Jacques started out as a volunteer for HCV Advocate and subsequently worked for us for 12 years. We have yet to find a replacement—his shoes are hard to fill. We still miss him for his invaluable work and his keen sense of humor.

Elimination of Hepatitis B and C: Many national and international organizations issued hepatitis B and C elimination strategies in 2016. It is a lofty goal. Lucinda K. Porter, RN discusses this in this month’s HealthWise column.
Moving Forward in 2017: My wish list for this year include:

- A better job of identifying everyone with hepatitis C
- Lower the cost of medications to treat hepatitis C
- Remove the treatment access restrictions
- Fund needle exchange and provide health services at needle exchange sites
- Treat persons who inject drugs and extend services that will help prevent re-infection

2017 will bring a lot of challenges to people living with hepatitis C. The potential of reduced services, loss of medical care and social services can be overwhelming for anyone. For people who are already living on the edge of poverty, it can be devastating.

We are all going to have to work together to demand services so that people can all live healthy and productive lives with dignity and respect.

Footnotes:
1: Hep C Medications Blog
6: AHF Applauds Congress for Restoring Federal Money for Syringe Exchange Programs Partial lifting of the decades-long ban still does not allow federal funds to directly purchase needles; AHF calls on state and local governments to provide clean syringes for programs: http://hepatitisc.hcvadvocate.org/2016/01/ahf-applauds-congress-for-restoring.html
10: Vietnam Veteran Who Died Of Hepatitis Added To Memorial Wall By Michelle Andrews http://hcvadvocate.org/?s=vet+added+to+memorial
12: Affordable Care Act: https://www.hhs.gov/about/news/2016/03/03/20-million-people-have-gained-health-insurance-coverage-because-affordable-care-act-new-estimates
13: Scientists honored for research toward hepatitis C therapies http://hepatitisc.hcvadvocate.org/?s=lasker+

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
What does it mean to be an advocate? What’s the right way, or the best way, to advocate for something or someone? Well, truthfully, depending on who you ask you’ll get different answers. For me, there isn’t so much a right way as there is an honest way. That honest way begins with a person’s character. John Wooden is quoted as saying, “The true test of a man’s character is what he does when no one is watching.”

I believe advocacy is the same. It’s not about column inches, headlines or newspaper quotes. It’s not about money accrued, or credit given (or taken). It’s about honesty and sacrifice. It’s understanding that advocating for something, or someone, doesn’t necessarily mean you have to have the illness, disease, sexual orientation, gender, skin color or any other identifier that a particular person or group has. Because being an advocate is not about any single person being better or stronger than another and having something to give. It’s about seeing and embracing that we are all the same.

John Donne put it best when he began one of his most well-known poems with, “No man is an island entire of itself; every man is a piece of the continent, a part of the main.” And ended it with, “And therefore never send to know for whom the bell tolls; it tolls for thee.”

Being an advocate is about hearing the bell toll and asking not for whom it tolls, but doing everything you can, in whatever way you can, for however long you can, to make the bell ring out one less time.

One of my favorite books is The Alchemist, by Paulo Coelho. Throughout the book there are a lot of subtle life lessons. Arguably, the best one comes while the books protagonist Santiago, a Shepard boy from Andalusia, is listening to a story about a boy who visits a Wiseman and asks him the secret to happiness.
The Art of Seeing — CONTINUED FROM PAGE 5

To find the answer the Wiseman tells the boy to walk throughout his grounds while making sure not to spill a teaspoon of oil. When the boy returns, he is happy to have not spilled the oil, but becomes sad when asked about all the beauty throughout the palace. The boy admits he didn’t see any of it because he wasn’t looking. Having heard this the Wiseman tells him to go again as he did before, but this time as he makes his way throughout the gardens and grounds to look at all the beauty he comes across.

When the boy returns to the Wiseman to tell him what he saw his spoon is empty, save for a few drops of oil. The Wiseman looks at the boy and says, “The secret of happiness is to see all the marvels of the world, and never forget the drops of oil on the spoon.”

For me, it’s easy to get caught up in advocacy, in reading research and in general focusing on work that addresses hepatitis C and harm reduction. This became especially difficult after returning from Scott County. At times I’ve become obsessed with trying to figure out how to make the bell toll one less time, with making sure not a single drop of oil spills from that spoon.

Thankfully, folks like Alan remind me of the need to look up from the spoon. Because when I do I see not only the marvels that result from advocacy, but those in my personal life. My loving and incredibly understanding girlfriend, Jenna, who deals with my obsession and late nights more than most. And our always energetic, cuddly toy poodle Zsa Zsa.

When I pressed send and set sail across the digital sea, “The Perfect Storm,” to land on the shores of Alan’s inbox, I wasn’t sure what would be next. I simply trusted and believed. By all accounts I’m an advocate. But like most, it’s less a role I’ve chosen and more one that I simply exist in. One that I believe is a responsibility, because none of us are islands unto ourselves.

The truth is, regardless of where we have come from, how little money we’ve made (and for how long we’ve made it), how much we’ve sacrificed, or what we’ve been through, as advocates we are owed nothing. I am owed nothing. Our payment is simple. It comes in the form of one less toll of the bell. Of one more person helped, empowered, cured, stood beside and not in front of. And nothing should ever ring louder than that. Those few remaining drops of oil are why we work, and the marvels we see are those that we create together as we move forward. And of all the reasons we do this and for all those things that result from it, that is the only thing that matters.

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
January seems like a good time to examine big ideas, such as the present state of hepatitis C. Knowing what we know, can hepatitis C be eradicated?

According to the Centers for Disease Control and Prevention, chronic hepatitis C virus infection (HCV) kills more Americans annually than all 60 reportable infectious diseases combined. Experts don’t know how many Americans are living with this virus, because the ways in which we calculate chronic HCV infections is inadequate largely because of insufficient funding. The range seems to be between 3 and 4 million people in the United States have chronic hepatitis C infection.

Fortunately, there is a cure for hep C. This cure is so effective that it is stirring a global conversation. Can we eliminate hepatitis C the way we did to small pox? Experts think we can, and many believe we can also eradicate hepatitis B.

In the October 2016 issue of Hepatology, four major global liver organizations issued a joint statement calling for the elimination of viral hepatitis. The organizations are the Latin American Association for the Study of the Liver, the European Association for the Study of the Liver, the Asian Pacific Association for the Study of the Liver, and the American Association for the Study of Liver Disease (AASLD). These societies add their names to the list of other organizations calling for an end to viral hepatitis, including the World Health Organization (WHO) and the World Hepatitis Alliance. WHO has set a goal to eliminate the threat of viral hepatitis by 2030.
Here is the rationale for this joint statement:

- The World Health Organization (WHO) estimates that as many as 400 million people worldwide are living with chronic hepatitis viral infection. (Note: 130 to 150 million of these are HCV.)
- More than one million people die of cirrhosis, mostly caused by viral hepatitis.
- More than 500,000 people die every year from hepatocellular carcinoma (the most common form of liver cancer). It is the third leading cause of cancer deaths.
- Vaccination makes hepatitis B preventable. Chronic hepatitis B infection is manageable, especially with early diagnosis and intervention.
- Hepatitis C is curable; early diagnosis and intervention are key in order to prevent cirrhosis.

Setting goals to eradicate HCV are also occurring in the United States. In April 2016, the National Academies of Sciences, Engineering, and Medicine published, “Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One Report,” which examines the feasibility of eliminating hep B and C as a goal. The phase two report will be released in 2017, proposing a strategy to reach the goals identified in the first report.

Efforts to eradicate hep C are occurring on a slightly smaller scale in the Veterans Affairs (VA) healthcare system. At AASLD’s 2016 Liver Meeting, Andrew Moon and colleagues presented data showing the impact of direct antiviral agents (DAAs) on HCV cure rates in the VA. (Towards Eradication of Hepatitis C Virus Infection in the Veterans Affairs National Healthcare System: A Study of 107,079 Antiviral Treatment Regimens Administered from 1999-2015)

Researchers in this study identified all HCV treatment regimens prescribed in the national VA system during the 17-year period from 1/1/1999 to 12/31/2015. The treatment rates were low during the interferon days (1999-2011) at 1989 to 7196 cases per year.

When the first DAAs using boceprevir and telaprevir were approved (2011-2013), the treatment rates stayed about the same at 2943 to 5207 treatments per year. The number of veterans who were treated jumped when simeprevir (Olysio) and sofosbuvir (Sovaldi) was approved in 2013, followed by ledipasvir/sofosbuvir (Harvoni) and paritaprevir/ombitasvir/ ritonavir/daasabuvir (Viekira) in 2014. In 2014, 9,180 veterans were treated; the following year that number was 31,028.

The cure rates (sustained virologic response or SVR) progressed at impressive rates from nearly 23 percent in 1999 to over 91 percent in 2015. As good as that looks, it gets better. Just looking at the first half of 2015, approximately 800 veterans were treated every month. When funding for HCV treatment increased, the number of veterans who received treatment jumped to 7000 later that year. The researchers concluded that the VA has the capacity to cure most HCV-infected veterans who use the VA system within the next 2 to 3 years.

According to the Centers for Disease Control and Prevention, chronic hepatitis C virus infection (HCV) kills more Americans annually than all 60 reportable infectious diseases combined.
You may be thinking, “What about the high cost of hep C treatment? Surely we can’t treat everyone?” Presenting data at the 2016 Liver Meeting, Andrew Hill and colleagues suggest that hep C treatment could cost under $100 per person (Hepatitis C Could Now Be Cured for Under US $100 per Person: Analysis of Mass Generic Production of Direct Acting Antivirals). Researchers analyzed production costs for generic HCV treatments from India. The cost of 12 weeks of treatment using sofosbuvir and daclatasvir can be manufactured for around $76; sofosbuvir/ledipasvir priced at $96. Velpatasvir was more expensive at $119 to $154. These prices included a 50 percent profit margin for generic suppliers.

Granted, that is not how we do business in the United States. But eventually we will find our way to make this happen. Patents expire. Insurance companies find ways to negotiate better drug prices. Generics are imported for personal use. Medical tourism attracts global travelers. We keep protesting the high costs and eventually common sense prevails. The seemingly insurmountable becomes real. In the meantime, you can be a part of the global campaign to eradicate viral hepatitis. Here’s how:

• Be immunized against hepatitis A and B.
• If you have viral hepatitis, get treated. Hep C is curable; hep B is manageable.
• Urge others to get tested, immunized, and treated.
• Get active. Join an advocacy group such as the National Viral Hepatitis Roundtable (NVHR).
• Don’t quit until the world is free of viral hepatitis.

“The seemingly insurmountable becomes real. In the meantime, you can be a part of the global campaign to eradicate viral hepatitis.”

Resources Used for This Article

American Association for the Study of Liver Disease
www.aasld.org

Asian Pacific Association for the Study of the Liver
www.apasl.info

Centers for Disease Control and Prevention
www.cdc.gov/hepatitis/hcv/index.htm

European Association for the Study of the Liver
www.easl.eu

Latin American Association for the Study of the Liver
aleh2016.com/wp

National Academies of Sciences, Engineering, and Medicine

National Viral Hepatitis Roundtable
nvhr.org

World Health Organization
www.who.int/hepatitis/en

World Hepatitis Alliance
www.worldhepatitisalliance.org
This is the second of our two part coverage of the American Association of the Study of Liver Disease 2016 Liver Conference. The Hepatitis Debrief has been my go-to for the best summation of the conference. This year the Debrief was presented by Dr. Robert S. Brown. I am summarizing his presentation on Merck’s, and Abbvie’s clinical trials and a study about screening for liver cancer. The last summary is from Jason Grebely’s presentation on treatment of HCV in people who inject drugs. If you have access to the Liver Meeting I highly recommend watching these excellent presentations. I left out Gilead’s Polaris trial results since I covered it in detail in the November 2016 HCV Advocate. It is also listed in the HCV Advocate Drug Pipeline in our newsletter.

**Merck: C-Crest:** The trial was a phase 2 study of a 3-drug co-formulation of MK-3682 (polymerase inhibitor), grazoprevir (protease inhibitor) plus ruzasvir (NS5A inhibitor) with and without ribavirin to treat HCV genotypes 1, 2 and 3. The treatment period was 8, 12 or 16 weeks. In the people who were previously treated with pegylated interferon plus ribavirin the SVR12/cure rates were 95% to 100% in genotype 1a, 1b and 3. In people with genotype 2 the cure rate was 87% in the 8-week group and a 100% rate in the 12 week group and 96% to 98% in the 16 week groups. There was very little difference in cure rates between the groups who had cirrhosis, and who did/did not receive ribavirin.

**C-Surge:** An on-going phase 2 study to treat people with genotype 1 who had failed a previous course of a direct-acting antiviral therapy (Harvoni or Zepatier) using MK-3682, grazoprevir and ruzasvir with and without ribavirin. In the group that received ribavirin the treatment duration was 16 weeks; in the group that did not receive ribavirin the treatment duration was 24 weeks. The SVR 8 results were 98% in the 16 week group that received ribavirin and 100% in the 24 week group that did not receive ribavirin.

**AbbVie: Phase 3 Clinical Trials:** Four studies of AbbVie’s two drug combination—glecaprevir (protease inhibitor) and pibrentasvir (NS5A inhibitor) were presented. **Endurance 1:** 703 genotype 1 non-cirrhotic treatment naïve and treatment experience patients. The patients were treated for 8 or 12 weeks. No ribavirin was used in the study. The cure rates were 99% to 100% across all treatment groups. **Endurance 2:** 199 genotype 2 non-cirrhotic treatment-naïve and treatment-experience patients treated for 12 weeks achieved 99% to 100%.

**Surveyor-II Part 3 Phase 2/3:** In genotype 3 patients who were cirrhotic and treatment experienced but who had not been previously treated with a NS5A inhibitor were treated with glecaprevir plus pibrentasvir. Those treated for 12 weeks achieved 91% to 98% cure rates and those treated for 16 weeks achieved 96% cure rates. This treatment was particularly effective for people with end-stage kidney disease.

**Surveyor-II Part 4:** In genotype 2, 4, 5 or 6 patients without cirrhosis. There were a total of 203 patients—both treatment naïve and treatment experienced (no NS5A treatment experienced). The treatment period was 8 weeks. The cure rates were 98% for genotype 2; 93% for genotype 4; 100% for genotype 5 and 90% for genotype 6—although the number of patients in the genotype 5 and 6 groups were very small.

**Expedition-IV:** The goal of the study was to treat patients with renal impairment. There were 104 genotype 1 through 6 patients enrolled. The majority of the patients had severe renal impairment, and 82% were on dialysis (filtering of the blood because the kidneys...
are impaired. The patients were treatment naïve and treatment experienced (no NS5A experienced). The cure rate was 99% (103 of 104)—one patient discontinued treatment before the trial ended.

Liver Cancer and Hepatitis C: It is recommended that people who have cirrhosis should be screened for liver cancer every 6 months. It is known that curing hepatitis C greatly reduces the risk of developing liver cancer in people with cirrhosis, but disease progression and liver cancer can still occur. This is why it is important that people with cirrhosis are screened.

But what is the actual practice of screening patients for liver cancer? A study out of Stanford University found that the actual rate of liver cancer monitoring is alarming. Of 2,916 patients that should be screened every 6 months only 18.9% were screened every 6 months; 17.0% were every 6 to 12 months; 18.6% were every 12 to 24 months; 21.1% were screened every 24 months or over a longer period of time, and 24.5% patients were never screened. The people who were most frequently monitored were those who came into the clinic and those who had decompensated cirrhosis.

Not surprisingly, patients with less frequent screening were diagnosed with more severe liver disease that led to complications that included:

- Portal vein thrombosis (blockage of the vein that carries blood from the intestines to the liver). Portal vein thrombosis excludes people from obtaining a liver transplant.
- Patients were less likely to meet the Milan or University of California of San Francisco criteria for receiving a liver transplant.

People who Inject Drugs (PWIDs) and who are infected with hepatitis C are not generally considered for hepatitis C treatment except in clinical trials. This is troubling because PWIDs are now the largest group of people who are at risk of acquiring hepatitis C. Additionally, a strategy to eliminate hepatitis C has to include a strategy to treat the most at-risk population. This year’s Conference included a presentation “Treatment of HCV in People Who Inject Drugs” by Jason Grebely. I am only going to cover the cure rates and re-infection rates from Dr. Grebely’s presentation.

Treatment: In various phase 3 clinical trials of people on HCV direct-acting antiviral medications the cure rates were 92% to 96% in people on opioid substitution therapy vs. 95% to 98% in people who were not on opioid substitution therapy (OST). In one of the largest clinical trials of people who inject drugs—C-EDGE Co-STAR (elbasvir/grazoprevir), genotypes 1, 4 and 6, treatment naïve patients, fibrosis stage F0 through F4, 12 week treatment duration the cure rate was genotype 1a: 96% (146 of 152 pts); genotype 1b: 97% (28 of 29 pts); genotype 4: 100% (11 of 11 pts); genotype 6: 60% (3 of 5 pts). The adherence in the group was 96%.

In other clinical trials of ‘real world’ study of people who inject drugs (heroin 66%; cocaine 62%; other stimulants 46%; OST 40%) and treated with different direct-acting antiviral medications the overall cure rate was 95%.

An overview of reinfection rates after being cured of hepatitis C among PWID were 2% to 3% in people who had a history of reinfection, 6% per year in people who injected drugs after achieving a cure and in one study presented at AASLD 4% per year in people on OST. There was no information given about prevention education—the most important component when treating people who are actively using drugs.
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:** There is more detailed information about the drugs in development in our newsletter (http://hcvadvocate.org/publications/newsletter/2016-2/) and our blog (http://hepatitisc.hcvadvocate.org/)

If you are interested in finding out about clinical trials visit HCV Advocate Clinical Trial Reference Guide (http://hcvclinical.hcvadvocate.org/) for a list of trials that are currently recruiting patients.

<table>
<thead>
<tr>
<th>AbbVie</th>
<th>Genotype(s): 1, 2, 3, 4, 5, 6 (Pan-genotypic)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMMENTS:</strong></td>
<td></td>
</tr>
<tr>
<td>The combination of glecaprevir (ABT-493) plus pibrentasvir (ABT-530) to treat genotype 1, 3, 4, 5, 6 for a treatment duration of 8 weeks. The sustained virological results (SVR12/cure) released on 11/12/2016 are listed below:</td>
<td></td>
</tr>
<tr>
<td><strong>Study Name</strong></td>
<td><strong>Patient Population</strong></td>
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<tr>
<td>ENDURANCE-1</td>
<td>GT1 without cirrhosis, new to treatment or not cured with previous IFN-based treatments (pegIFN +/- RBV or SOF/RBV +/- pegIFN), and patients co-infected with HIV-1</td>
</tr>
<tr>
<td>ENDURANCE-3</td>
<td>GT3 without cirrhosis, new to treatment</td>
</tr>
<tr>
<td>SURVEYOR-2 (Part 4)</td>
<td>GT2, 4, 5, or 6 without cirrhosis, new to treatment or not cured with previous IFN-based treatments (pegIFN, SOF/RBV or pegIFN/SOF)</td>
</tr>
</tbody>
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*pegINF = pegylated interferon; RBV = ribavirin; SOF = sofosbuvir; This combination was granted Breakthrough Therapy designation by the Food and Drug Administration (FDA) for those with HCV genotype 1 who had failed a previous course of therapy that contained a NS5A inhibitor. In December 2016 AbbVie applied to the FDA to market and treat all HCV genotypes with the combination listed above.
Gilead – Sofosbuvir, Valpatasvir & Voxilaprevir (GS-9857) | Genotype(s) 1, 2, 3, 4, 6, (Pan-genotypic)

**COMMENTS:**

Gilead released the results of four phase 3 studies (POLARIS) of the triple combination of sofosbuvir (polymerase inhibitor), velpatasvir (NS5A inhibitor), and voxilaprevir (protease inhibitor). The study included 1,056 patients who received the triple combination (sofosbuvir (SOF), velpatasvir (VEL), plus voxilaprevir (VOX)—611 were treatment naïve and 455 were treatment experienced.

*Note: I am only listing the results from the triple therapy below – you will note that the percentage and numbers include all the patients treated. For a complete breakdown of all treatment regimens see November 2016 newsletter: http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate1116.pdf*

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Genotype</th>
<th>Treatment</th>
<th>Duration</th>
<th>SVR12 Rates</th>
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<tbody>
<tr>
<td>POLARIS-1</td>
<td>NS5A inhibitor-experienced</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>SOF/VEL/VOX</td>
<td>12 Weeks</td>
<td>96% (253/263)</td>
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<td></td>
<td>41 percent (172/415) had cirrhosis</td>
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<td>Placebo</td>
<td>12 Weeks</td>
<td>0% (0/152)</td>
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<td>POLARIS-4</td>
<td>DAA-experienced (No NS5A inhibitor)</td>
<td>1, 2, 3, 4</td>
<td>SOF/VEL/VOX</td>
<td>12 Weeks</td>
<td>97% (177/182)</td>
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<tr>
<td></td>
<td>46 percent (153/333) had cirrhosis</td>
<td></td>
<td>SOF/VEL</td>
<td>12 Weeks</td>
<td>90% (136/151)</td>
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<tr>
<td>POLARIS-2</td>
<td>DAA-naïve</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>SOF/VEL/VOX</td>
<td>8 Weeks</td>
<td>95% (476/501)</td>
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<tr>
<td></td>
<td>18 percent (174/941) had cirrhosis</td>
<td></td>
<td>SOF/VEL</td>
<td>12 Weeks</td>
<td>98% (432/440)</td>
</tr>
<tr>
<td>POLARIS-3</td>
<td>DAA-naïve</td>
<td>3</td>
<td>SOF/VEL/VOX</td>
<td>8 Weeks</td>
<td>96% (106/110)</td>
</tr>
<tr>
<td></td>
<td>All had cirrhosis</td>
<td></td>
<td>SOF/VEL</td>
<td>12 Weeks</td>
<td>96% (105/109)</td>
</tr>
</tbody>
</table>

The side effects were similar between the placebo (sugar pills) group, sofosbuvir plus velpatasvir, and the sofosbuvir, velpatasvir plus voxilaprevir groups. The most common side effects were headache, fatigue, diarrhea and nausea. Only one patient in the entire study discontinued therapy due to side effects.

This combination was granted Breakthrough Therapy designation by the Food and Drug Administration (FDA) for those with HCV genotype 1 who had failed a previous course of therapy that contained a NS5A inhibitor.

In December 2016 Gilead applied to the FDA to market and treat all HCV genotypes with the combination listed above—combined into one pill taken once-a-day.
Janssen (Achillion/Alios) | Genotype(s) 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 – Phase 2a Study**: Janssen (Alios Pharma) has initiated a 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. The results were listed in the October 2016 HCV Advocate newsletter. [http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate1016.pdf](http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate1016.pdf)

- **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 began in June 2016 and will end in July 2017.
### Merck

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

**COMMENTS:**

- **Phase 2- AASLD 2016:**

  **C-Crest:** The trial was a phase 2 study of a 3-drug co-formulation of MK-3682 (polymerase inhibitor), grazoprevir (protease inhibitor) plus ruzasvir (NS5A inhibitor) with and without ribavirin to treat HCV genotypes 1, 2 and 3. The treatment period was 8, 12 or 16 weeks. In the people who were previously treated with pegylated interferon plus ribavirin the SVR12/cure rates were 95% to 100% in genotype 1a, 1b and 3. In people with genotype 2 the cure rate was 87% in the 8-week group and a 100% rate in the 12 week group and 96% to 98% in the 16 week groups. There was very little difference in cure rates between the groups who had cirrhosis, and who did/did not receive ribavirin.

  **C-Surge:** An on-going phase 2 study to treat people with genotype 1 who had failed a previous course of a direct-acting antiviral therapy (Harvoni or Zepatier) using MK-3682, grazoprevir and ruzasvir with and without ribavirin. In the group that received ribavirin the treatment duration was 16 weeks; in the group that did not receive ribavirin the treatment duration was 24 weeks. The SVR 8 results were 98% in the 16 week group that received ribavirin and 100% in the 24 week group that did not receive ribavirin.

<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.

### Regulus

**Genotype(s)** 1, 2, 3, 4, 6

**COMMENTS:**

**Regulus Therapeutic Inc.**

The study included 79 treatment-naive 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.
**WHAT’S UP!**

**Paper PI** — we have decided to discontinue this service since we provide extensive news coverage on our HCV News and Pipeline Blog. If you want to stay up to date on the latest information you can sign up on this page: [http://hepatitisc.hcvadvocate.org/](http://hepatitisc.hcvadvocate.org/)

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We have launched a new fact sheet series

**HCV & Harm Reduction**
The first in the series is an **Overview of Harm Reduction**¹

[CLICK TO DOWNLOAD]

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**Easy C Fact Sheet**

**Hepatitis B**²

We have revised our fact sheet on hepatitis B treatment reactivation. The reactivation was due to any treatment including the older pegylated interferon treatment and the reactivation was rare.

[CLICK TO DOWNLOAD]

**Easy C Fact Sheet**

**Hep C Prevention in a Household**³

Hepatitis C transmission is uncommon in a household environment. Learn how to reduce the risk even more in this easy to understand fact sheet.

[CLICK TO DOWNLOAD]

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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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