THE LIVER MEETING ISSUE

This year’s American Association for the Study of Liver Disease (AASLD)—The Liver Meeting is packed with a ton of information. Check out Lucinda K. Porter, RN AASLD article and Matthew Zielske’s article on research in this newsletter.

THE FIVE: AASLD PART 1

In Part 1 of The Five I have picked five abstracts that I believe can have larger implications for the treatment and management of hepatitis C. These summaries include alcohol and Hep C treatment, the incidence of HBV reactivation during interferon-based and direct-acting antiviral therapies, measuring fatigue (my favorite abstract), HCV treatment and diabetes control, and how hepatitis C can be treated for under $100.00.

1. Source: Abstract # 911
Alcohol use and hepatitis C virus treatment outcomes among 15,151 patients receiving direct antiviral agents—J Tsui et. al

Alcohol and hepatitis C treatment has always been a thorny issue. The current study examined the association between alcohol use and antiviral treatment. The study was conducted in the Veterans Affairs (VA) healthcare system during January 01, 2014 through June 30, 2015. The tool used to screen for alcohol consumption was the Alcohol Use Disorder Identification Consumption (AUDIT-C) questionnaire within the one-year before starting treatment. During the study period, 17,487 Veterans initiated DAA therapy. Of those 15,151 (87%) had completed the

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AUDIT-C questionnaire within one year. The antiviral therapies included sofosbuvir, sofosbuvir/ledipasvir (Harvoni) or Vikiera-Pak.

AUDIT-C scores categorized as follows: 0 (abstinence), 1-3 (low-level drinking) and 4-12 (unhealthy drinking) in men or 0, 1-2 and 3-12 in women.

The patient population was mostly male (96.7%), 28.9% were black, 30% had cirrhosis, mean age was 61 ±7 years and the distribution of HCV genotypes was 1 (79.8%), 2 (12.5%), 3 (7.0%) and 4 (0.8%).

Alcohol abstinence was reported in 10,387 (68.5%) patients, low-level drinking in 3422 (22.6%) patients, and unhealthy drinking in 1342 (8.9%) patients.

**Conclusion:** The SVR/cure rate was: abstinent group: 91%; low-level group: 93%; unhealthy drinking 91%. Additionally, HCV genotype, cirrhosis, or HIV status was not associated with SVR. Alcohol use had no effect on cure rates in the people who used alcohol or in those who did not.

**Editorial Comments:** This study is a large population-based study that proves that drinking alcohol does not lower the chances of achieving an SVR/CURE. For this reason, people with hepatitis C should not be denied treatment just because they consume alcohol. It’s as simple as that, and we should take out the moral judgment that frequently taints the decision-making process of who receives treatment and who doesn’t. (For related content, see Lucinda K. Porter’s coverage of abstract #17691)

### 2. Source: Abstract # 918:
Hepatitis B reactivation after interferon-based therapy versus pan-oral direct acting antiviral agents in chronic hepatitis C patients co-infected with hepatitis B virus: a systematic review and meta-analysis—C Wang et. al

The Food and Drug Administration (FDA) recently issued a Boxed Warning to test for hepatitis B (HBV) before starting treatment of hepatitis C with direct-acting antiviral medications. The authors of the current study conducted a meta-analysis (search) of literature from January 01, 1990 to December 31, 2015, in Pubmed Embase, Ovid, and Cochrane databases in March 2016. The searches were conducted to find the rate of HBV reactivation during or after hepatitis C therapy (interferon-based therapy (INF) or direct-acting antiviral (DAA) therapy).

**Conclusion:** Twenty-two studies reported hepatitis (inflammation of the liver) due to hepatitis B reactivation. The HCV SVR/cure rate was 47% in the hepatitis B/HCV coinfected groups—43% in the IFN treatment group and 100% in the DAA group. The overall hepatitis B reactivation rate was 12.3%, but the rate of hepatitis was 0.3% (0-1.1% in patients treated with interferon vs. 0.2-33.2%) in patients treated with DAAs. What was interesting was hepatitis B reactivation occurred in the post-treatment interferon groups (3 to 72 months) compared to DAA groups (4 to 11 week during treatment).

**Editorial Comments:** As the meta-analysis reports the chances of reactivation of hepatitis B are high, but the rate of hepatitis damage is relatively low. This should reinforce the need to test for hepatitis B before HCV treatment and if hepatitis B is negative to...
vaccinate before HCV treatment. If someone is positive for hepatitis B or if they have been previously infected and cleared of acute hepatitis B infection, they should be carefully monitored during and after treatment for hepatitis B reactivation. The careful monitoring will prevent liver damage and possible death by treating hepatitis B with antiviral medications as needed. For more information about the FDA warning visit our blog for the announcement or our new Easy C fact sheet.

HEP C TREATMENT WARNING: Beware of Hepatitis B

3. Source: Abstract # 1639: Fatigue & Hepatitis C: A Focus Group Study—S K Afdhal et. al

Up to 97% of people with hepatitis C report fatigue with 88% reporting some form of fatigue every day. The current study sought to understand the degree of fatigue by a qualitative—describing the fatigue—focus group approach. The study enrolled patients who would describe their experiences of fatigue and how it influenced their lives. There were three focus groups with 3-7 hepatitis C patients in each group—a total of 16 patients were enrolled. The study was approved by Institutional Review Board—this is standard practice in clinical trials. The patient characteristics were ~58 years old, 56% female, and 50% Caucasian. The patients were asked to focus on their experiences of fatigue and to describe their symptoms. Their responses were audio recorded and analyzed by two independent researchers.

Conclusion: The researchers broke down the experiences into two first measurements of fatigue: capacity and engagement. The subcategories (italics) with patient responses for examples.

Capacity: access “e.g. I don’t have a lack of energy; I have an inability to access that energy. It’s like a car that won’t start,” depletion: “e.g. If I got up today and worked a whole eight hour day, I wouldn’t make it tomorrow.”

Engagement: initiation: “(e.g. “My mental self can see myself getting up but my physical self can’t do it. Frustrating because I want to.”) and personal satisfaction: (e.g. “Affects activity schedule because I have to balance activity and can’t do all the things I want to do”).”

The authors concluded that these domains need to be incorporated to validate future studies of fatigue in people infected with chronic hepatitis C.

Editorial Comments: Fatigue is very hard to measure since it is self-reported. To my knowledge, few self-reported scales accurately measure fatigue. I well remember fatigue when I had chronic hepatitis C. The descriptions reported by patients ring true to me. I will be interested if others with hepatitis C feel the same.

4. Source: Abstract # 964: Viral response to hepatitis C direct-acting antivirals significantly improves diabetes control—S B LeCler et. al

Insulin resistance is believed to be caused by the hepatitis C virus. But diabetes is not believed to cause diabetes. But does successful treatment help to reduce some measurements of the disease? This is what the study examined. The study looked at the effect of direct-acting antiviral (DAA) treatment on diabetic medications. The authors identified studies from February 1, 2014 through October 1, 2015 that included 131 patients who received DAA treatment and who also received diabetes medications.

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The majority of the patients were male (98%), the average age was 63, and the majority of patients were black (59%) and had advanced fibrosis (53%).

Conclusions: Of the 122 patients who achieved a cure 27% (33 of 122 patients) lowered their diabetic medications from baseline measurement to 3 months post-treatment compared to 11% (1 of 9 patients) of the HCV DAA replasers who did not. Of the available data on A1C—A1C is an average measurement of glucose over a three-month period—there was a significant decrease of 0.63% percentage points.

Editorial Comments: This is a small but interesting study. It needs to be replicated in much larger studies to confirm the results. Anecdotally, I hear from many people that being cured has helped to improve their blood sugar levels. Patients would certainly benefit from monitoring their blood sugar levels after being cured and working with their medical providers to find out if their diabetes medications need to be adjusted.

5. Source: Abstract # 955: Hepatitis C could now be cured for under US $100 per person: analysis of mass generic production of Direct Acting Antivirals—A M Hill et al.

The aim of this study was to calculate the cost of generic drugs to treat hepatitis C. The HCV medications evaluated were sofosbuvir, daclatasvir, ledipasvir and velpatasvir. The cost per pill was combined with formulation (chemical synthesis, raw materials, inactive ingredients). A profit margin of 50% was added.

Conclusion: The 12-week treatment for sofosbuvir is $62; daclatasvir $14; sofosbuvir plus ledipasvir $96; velpatasvir $119-154. The prices include a 50% profit margin for the generic suppliers.

Calculated target prices and current prices for 12-week DAA treatment courses (below)

<table>
<thead>
<tr>
<th>Drug</th>
<th>June 2016 API cost/kg</th>
<th>Target price per 12-week treatment</th>
<th>Current global lowest price per 12-week treatment</th>
<th>Current US price per 12-week treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir</td>
<td>$1,094</td>
<td>$62</td>
<td>$324</td>
<td>$49,860-84,000</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>$998</td>
<td>$14</td>
<td>$153</td>
<td>$50,653-83,000</td>
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<tr>
<td>Ledipasvir</td>
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<td>$34</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>SOF+LDV</td>
<td>N/A</td>
<td>$96</td>
<td>$507</td>
<td>$56,700-94,500</td>
</tr>
<tr>
<td>Velpatasvir</td>
<td>$8,900-11,700</td>
<td>$119-154</td>
<td>unknown</td>
<td>unknown</td>
</tr>
</tbody>
</table>

Editorial Comments: It is unlikely that hepatitis C will be eradicated worldwide at least in our lifetime. Access to generic drugs will help, but basic services are lacking in many countries including preventive services that are the key to eradicating HCV. Even in the United States—a resource rich country—we are not providing treatment and little preventive services to the most common group that is affected by hepatitis C — people who inject drugs. We are very far from eradicating hepatitis C.

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.

1: http://hcvadvocate.org/hepatitis/easyfacts/Easy_C_Beware%20of%20Hepatitis%20B.pdf
It’s that time of the year when the HCV Advocate highlights the latest research from the annual meeting of the American Association for the Study of Liver Diseases. Alan Franciscus and I divide the task; he focuses on hepatitis C treatment-related research and I cover non-treatment-related findings. The 2016 Liver Meeting was late this year, so for more information, be sure to check out future issues of the HCV Advocate and the News and Pipeline Blog.

There were more than 2100 accepted submissions to this year’s meeting. The breadth of research was amazing, and quite a bit was patient-centered. Sadly, there continues to be a lack of pediatric research. There were two adolescent treatment studies; a genotype 1 trial using sofosbuvir/ledipasvir, and a genotype 2/3 study using sofosbuvir/ribavirin. I realize that hepatitis C virus infection (HCV) is not as common in kids as it is in adults, but children need better treatment options.

Here are my favorite posters. Note that conference posters are preliminary investigations, and need to be published in a peer-reviewed journal before data can be considered conclusive.


Insurance denials for hepatitis C treatment are preventing access to care for some people. The purpose of this retrospective study was to see if there were more barriers to treatment among specific types of payers. The study enrolled medical center patients who were prescribed HCV treatment using DAAs between October 2014 and April 2016. Treatment was prescribed regardless of known payer restrictions and the study used a designated pharmacist familiar with payer criteria. Note that this center was in a state that opted out of Medicaid expansion under the Affordable Care Act.

Beginning with initial prior authorizations, 794 cases were approved and 206 were denied. Medicaid had the highest rate of denials (nearly 39%) compared to commercial payers (25%), Medicare (12%) or MPAP (2%). Of those initially denied, 146 were appealed of which 115 were eventually approved. Medicare had the highest approval rate; Medicaid had the lowest, and both had the most successful appeals at around 93%. Appeals had a nearly 72% success rate for commercial plans.

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The most common reasons for denial were mild liver damage (<F2 fibrosis), not meeting criteria, non-formulary/plan exclusions and missing info. However, all but the mild fibrosis level denials had successful appeals above 90%. Patients with <F2 fibrosis were only able to gain access to DAAs about 47.6% of the time.

**Conclusion:** Around 90% of cases eventually had access to DAAs. Those with the most success were patients insured by Medicare and non-insured patients who used the Manufacturer Patient Assistance Programs. Medicaid is still problematic in that the denial rates are high and appeals are not all being submitted. There is still a problem with treatment access for patients with mild fibrosis.

**Editorial Comments:** There are no excuses for these denials. Plain and simple, approvals should be 100%. The next abstract is one of many studies showing why we need to offer HCV treatment to people at all stages of fibrosis.

**Abstract #1757 Impact of Pre-Existing Liver Disease on Treatment and Outcomes of Breast Cancer – Robert Griffiths, et al.**

The goal of this study was to explore the impact of pre-existing liver disease on the treatment and outcomes of breast cancer. Researchers identified 940 female subjects, average age 66 with mild to severe liver disease who were later diagnosed with breast cancer. Subjects were followed for up to a year during cancer treatment, and up to seven years for all forms of cancer and other mortality causes.

**Conclusion:** Basically, they found no differences in the treatment and breast cancer outcomes between patients with or without pre-existing liver disease. However, patients with pre-existing liver disease were more likely to die from other causes, specifically those diagnosed with stage II disease.

**Editorial Comments:** Multiple studies report an increased mortality rate in patients with liver disease, and specifically with viral hepatitis. Common sense tells us to treat a disease as early as possible, and hepatitis C is no exception.

**Abstract #64 Hepatitis C Virus Reactivation in Patients with Cancer: A Prospective Observational Study of 91 Patients – Harrys A. Torres, et al.**

There have been reports of possible reactivation of HCV in cancer patients receiving chemotherapy. Up until now, the data are from retrospective studies. This prospective study enrolled 91 HCV-infected cancer patients. Those with liver cancer were excluded. The study looked for signs of HCV reactivation defined as an increase in HCV RNA ≥1 log10IU/mL over baseline and a hepatitis flare defined as liver enzymes (ALT) to >170 IU/mL.

**Conclusion:** Among those receiving cancer treatments, HCV reactivation occurred in 21% of patients, but only half of them (9 total) had a hepatitis flare. None had liver failure. The researchers concluded that most cancer treatments are safe in HCV+ pts, but advised monitoring those receiving rituximab or high-dose steroids.
Editorial Comments: I have two problems with this study. First, I think the study would have been better if they enrolled cancer patients who were cured of hep C. Second, I wish the study had been blinded. Chemotherapy and steroids can cause an increase in ALT levels, and comparing HCV-negative cancer patients to HCV-positive cancer patients seems like good science.

Abstract #1769 Alcohol Use Disorder Among Chronic Hepatitis C Patients: Prevalence and Treatment Outcome, CHeCS, 2006-2013 – Eyasu H. Teshale

People with hep C are advised to avoid alcohol use. Alcohol increases the risk of liver damage, and it may create HCV treatment-related barriers. This study examines the prevalence of alcohol use and subsequent treatment barriers in HCV patients. Data were collected from 11,636 HCV patients seen at four large U.S. healthcare systems from 2006-2013. Note that these dates are before the approval of highly effective, all oral DAA regimens.

Approximately 40% of subjects received HCV treatment. Approximately 30% of HCV patients had one or more alcohol-related diagnoses, but only 50% of those with alcohol-related liver disease received treatment. The treatment rate dropped to 30% among those who were diagnosed with alcohol abuse. Treatment response rates (SVRs) were 41.6% overall, 44.7% for those with alcohol abuse, and 28.4% for those with alcohol-related liver disease.

Conclusion: Controlling for age, gender, race, and household income, persons with alcohol abuse were less likely to receive HCV treatment. Those with alcohol-related liver disease were more likely to receive treatment than those with no alcohol use disorder. The use of direct acting antiviral therapy may improve the likelihood of treatment and outcomes among all patients, including those with an alcohol use disorder.

Editorial Comments: Alcohol and drug use should not be barriers to HCV treatment. In fact, the only reason to deny HCV treatment is if someone is likely to die within a year from a disease unrelated to hepatitis C. (For related content, see Alan Franciscus’s coverage of #911.)

Abstract #1446 The Fatigue of Chronic Liver Disease is Associated with Altered Circadian Rhythm of Cortisol – Michele M. Tana, et al.

Fatigue is a common complaint for patients with liver disease, and researchers don’t completely know the cause of this. Scientists noticed that patients with chronic liver disease (CLD) had various signs and symptoms associated with circadian rhythms, also known as sleep-wake patterns. Were these problems caused by the brain’s master clock or in the liver’s clock?

This prospective study enrolled 12 subjects with CLD; six had fatigue and six did not. They took blood samples at various times while evaluating fatigue level.

“The use of direct acting antiviral therapy may improve the likelihood of treatment and outcomes among all patients, including those with an alcohol use disorder.”
Conclusion: Looking at various factors, they found that the circadian rhythms of cortisol were “significantly disrupted in CLD patients with fatigue.” The researchers recommend more studies examining the hypothalamic-pituitary-adrenal axis in the brain to help us find ways to improve fatigue in CLD patients.

Editorial Comments: This study only looked at the broader picture of liver disease. People who have hepatitis C may have additional factors that contribute to fatigue.

Abstract #1766 Hepatitis A and B Vaccination Rates in Patients with Chronic Liver Disease: A Quality Improvement Project – Mooz Sial, et al.

Vaccination against hepatitis A and B is recommended for people with chronic liver disease (CLD). This retrospective study examined medical records of 300 people with CLD from 2013 through 2014. They identified patients who did not appear to be immune to hep A and/or hep B. Hep A vaccine was recommended in 35%; hepatitis B vaccine in 36% patients. Of these, 12% forgot to get it, 33% didn’t recall being advised, and 55% gave no specific reason as to why they didn’t get vaccinated.

Conclusion: The rate of hepatitis A and B immunization in patients with chronic liver disease needs to be improved.

Editorial Comments: Immunization is a basic, cost-effective, and necessary way to protect people from diseases. It’s discouraging to think that people with CLD aren’t getting their hep A and B vaccinations.

Abstract #57 Poor Adherence to Hepatocellular Carcinoma (HCC) Surveillance in a U.S. Cohort of 2376 Patients with Chronic Hepatitis C (CHC) and Cirrhosis – Sally A. Tran, et al.

Abstract #1768 Identifying Barriers to Hepatocellular Carcinoma Surveillance in a National Sample of Patients With Cirrhosis – David S. Goldberg, et al.

Abstract #1762 Lack of Compliance to Hepatocellular Carcinoma (HCC) Screening Guidelines in Hepatitis B (HBV) or C (HCV) Virus Co-Infected HIV Patients with Cirrhosis – Sophie Willemse (Netherlands)

The incidence of liver cancer is rising. Several studies looked at how effective the medical profession is doing at screening for hepatocellular carcinoma (HCC).

Conclusion: These three large studies (two in the U.S. and one in the Netherlands) concluded that surveillance is poor.

Editorial Comments: If you have cirrhosis or hepatitis B (with/without cirrhosis), talk to your doctor about HCC screening recommendations. In the U.S., screening includes imaging (ultrasound, CT, or MRI) every 6 months.

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

1: http://hepatitisc.hcvadvocate.org
Each of us is a natural researcher. From the moment we are born we begin asking questions about the space around us, and watching other people as they move through the world. Being curious about the world is an opportunity to learn to how to avoid mistakes, improve on something we are doing, or find patterns that can explain why things happen in a certain way. We accomplish this by observing and asking questions about why and how things work. This curiosity and inquisitiveness is the foundation of research and rigorous inquiry.

I’m learning the hard way that engaging in research is like Sisyphus pushing the bolder up the hill. At the end of the difficult and exhausting road to earn my Master’s in Communications degree I had two choices. 1) I could take comprehensive exams that are long form essays which I verbally defend. Or 2) I could write a Master’s thesis that would require approval from the institutional review board, intense data collection, a lot of sleepless nights and ultimately a verbal defense in front of a committee.

There are pros and cons for choosing either, and one isn’t necessarily better than the other. I chose option 2, and although it’s been incredibly frustrating at times, with each interview I carry out I’m reminded why I chose this path in the first place.

When I embarked on this journey I chose to look at connections between knowledge, communication and HCV regarding the success, or willingness, to access medical care. Throughout the process I’ve sat with many people who are living with hepatitis C who didn’t know the ways that HCV can be transmitted, or that there is a cure, and most of whom haven’t accessed healthcare.

As a communication scholar, I am interested in the pathways of how information is delivered and what barriers may be present to accessing healthcare from lack of information, poor communication or miscommunication. Although my research isn’t finished quite yet, I can share some non identifying, anecdotal and unofficial observations about HCV and access to education that I’m noticing. One of the questions I ask during the research session is, in the opinion of the participant, what types of places that currently don’t have HCV education or information should have them.

Some of the responses I’ve gotten are:
- Post offices
- Grocery stores
- Bus stops
- Public libraries

Some of these may surprise you and others may not. For me, the take away is to realize that the places we think of having HCV education is too narrow. Part of reducing, or erasing, the stigma associated with HCV is accomplished by increasing awareness of, and access to, relevant education and information.

The conversations I’ve had with people when they’ve agreed to sit down with me are fun, insightful and at times frustrating and disheartening. There are a lot of challenges that you encounter when carrying out research with a stigmatized or marginalized population, especially if they are affected by a stigmatized illness. Challenges such as an unwillingness to be audio recorded despite the utmost assurance of confidentiality (I keep all audio recorded interviews, and research data, — CONTINUED ON PAGE 10
on an encrypted hard drive at my home that requires two unique passwords to access.), fear of speaking about how or when they contracted HCV, uncertainty of who I am, or what I’m going to use the information for, and a busy work and home schedule that doesn’t always allow someone to take 90 minutes and talk with me.

A good portion of the people who have completed a research session with me have noted they only did so because they recognized my name.

Someone having a history of substance use, or a bad experience when sharing their HCV status, are common reasons for being hesitant to “go on the record” with me or anyone.

When folks did agree to sit down with me, a few common things I’ve heard regarding HCV education and healthcare are:

• They are often treated like they are “stupid.”
• When their history of substance use is discovered they are treated differently in terms of body language and nonverbal communication.
• They are often sent to many different physicians or health centers for different types of tests (e.g. A RNA confirmatory at one place, a PCR/Viral Load or Genotype test at another).
• Many give up trying to access care because the barriers or “hoops” they have to jump through discourage and exhaust their willingness to improve their health.
• They were very careful about who they disclosed their status to because HCV is often associated with injection drug use, which carries stigma all its own.

Many of these conversations discourage and frustrate me. Being made to feel “stupid” or ashamed is unacceptable. And adding barriers to being able to get a confirmatory test, or genotype test, because of whatever reasons (insurance, organizational capacity, poor communication, etc.) is a weak excuse at best and at worst is irresponsible, lazy and I would argue unethical. Even the most dedicated and informed people will become discouraged and give up if they continually meet resistance, poor attitudes, cold shoulders and condescension.

There is good news though. I have also heard a handful of stories from people giving praise and credit to doctors and healthcare providers who took the time to sit down and clearly explain HCV to them. Overwhelmingly, people say that these positive experiences encourage and motivate them to improve their health and seek treatment.

A good measure of successful research is often publication and conference presentation, but more than that my hopes with this research is to illuminate common struggles regarding HCV, education and treatment access as they exist in Southern Indiana, while also providing recommendations that are generated by the affected population so that we can improve treatment access, uptake and overall health outcomes.

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
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 [here](http://hcvadvocate.org/publications/newsletter/2016-2/) and our blog [here](http://hepatitisc.hcvadvocate.org/)

If you are interested in finding out about clinical trials visit HCV Advocate Clinical Trial Reference Guide [here](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>
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</thead>
</table>

**COMMENTS:**
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:

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Patient Population</th>
<th>Treatment Duration</th>
<th>Treatment Regimen</th>
<th>SVR12 Rates</th>
</tr>
</thead>
<tbody>
<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>
<td>8 week</td>
<td>G/P</td>
<td>99% (348 of 351 pts)</td>
</tr>
<tr>
<td>ENDURANCE-3</td>
<td>GT3 without cirrhosis, new to treatment</td>
<td>8 week</td>
<td>G/P</td>
<td>95% (149 of 157 pts)</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>
<td>8 week</td>
<td>G/P</td>
<td>97% (196 of 203 pts)</td>
</tr>
</tbody>
</table>

*pegINF = pegylated interferon; RBV= ribavirin; SOF=sofosbuvir; AbbVie expects to file for marketing approval in early 2017*
**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*

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.

Gilead is expected to apply to the FDA for marketing approval of this triple combination in the fourth quarter of 2016.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Genotype</th>
<th>Treatment</th>
<th>Duration</th>
<th>SVR12 Rates</th>
</tr>
</thead>
<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>
</tr>
<tr>
<td></td>
<td>41 percent (172/415) had cirrhosis</td>
<td></td>
<td>Placebo</td>
<td>12 Weeks</td>
<td>0% (0/152)</td>
</tr>
<tr>
<td></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>
</tr>
<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>
</tr>
<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>
</tr>
<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></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>
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:** 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%.

<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.
WE HAVE TWO NEW EASY C FACT SHEETS AND AN UPDATED HCSP FACT SHEET:

EASY C Facts

EASY C Treatment: What Are RAVs?¹
The resistant-associated variates can affect treatment and retreatment of chronic hepatitis C. Learn about these mutations of hepatitis C.

EASY C Adherence: Taking HCV Meds²
Learn about why taking all of the medications to treat hepatitis C are so important and some helpful tips to stay on course.

HCSP FACT SHEET

Adherence to HCV Therapy³

COMING NEXT MONTH

• The Top News Stories of 2016
• A New Fact Sheet Series: Harm Reduction

3: http://hcvadvocate.org/hepatitis/factsheets_pdf/AdherenceToHCVTherapy.pdf

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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