Drug Approval
July and August are very important months in hepatitis C treatment for patients. On July 18, 2017 the Food and Drug Administration (FDA) approved Gilead’s sofosbuvir/velpatasvir/voxilaprevir—brand name Vosevi—to re-treat adults with hepatitis C. In August 2017 the FDA is expected to approve AbbVie’s glecaprevir/pibrentasvir—brand name Maviret. The July and August approvals will push hepatitis C cure rates up to nearly 100%!

Vosevi
Gilead’s three drug combination is a pan-genotypic HCV medication co-formulated into one pill, taken once-a-day. The FDA stipulates that Vosevi is approved to treat people who have previously been treated with a DAA but who did not achieve a cure. The treatment period is 12 weeks is considered a salvage therapy—a term used for people who have failed another DAA therapy.

For the people who were treated prior with DAAs but who did not achieve a cure, 12 weeks of treatment cured up to 100% of patients.

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

This is very good news for the 5% to 10% of people who have failed prior DAA therapy who had few treatment options until now.

Be sure to check out our Hep C Medications Blog for more detailed information about Vosevi and the other HCV medications approved to treat hepatitis C. http://hepatitismedications.hcvadvocate.org/

Maviret
AbbVie’s two drug combination is also a pan-genotypic (genotypes 1 through 6) co-formulated into one pill, once-a-day treatment for people with hepatitis C and compensated cirrhosis. The treatment period is 8 weeks and cure rates in the clinical trials were 95% to 99%.

The most common side effects were fatigue and headache.

Once Maviret is approved I will update and post the FDA information in a condensed form to our Hep C Medications Blog http://hepatitismedications.hcvadvocate.org/
IN THE PATIENTS WHO TOOK THE SOFOSBUVIR-BASED THERAPY GROUP, 23 OF THE 26 PATIENTS WHO INITIALLY HAD ACUTE KIDNEY DISEASE, KIDNEY FUNCTION RETURNED TO NORMAL—THIS WAS THE NUMBER OF PEOPLE WHO WERE AVAILABLE DURING THE FOLLOW-UP PERIOD.

CONCLUSION
Sofosbuvir-based therapies to treat hepatitis C in people without pre-existing kidney disease can produce acute kidney disease in a minority of people. However, in the available follow-up data, kidney function returned to normal.

EDITORIAL COMMENTS
For people with acute kidney disease while on sofosbuvir-based therapies, the absence of long-term danger is reassuring. Of course, any acute disease should be followed carefully. It is also reassuring that we have moved on from telaprevir and boceprevir!

Did you know that NSAIDs account for 100,000 hospitalizations and 16,000 deaths each year in the United States.*

* http://emedicine.medscape.com/article/816117-overview#a6
Study Aims and Results
People who inject drugs (PWID) are usually denied HCV treatment because of preconceived attitudes that they will not adhere to treatment. The aim of the current study was to assess adherence of PWID over a period of 10 years. There were 1000 patients treated with pegylated interferon plus ribavirin. The group was divided into two groups—608 former injection drugs users (no injection drug use for 6 months of therapy) and 85 recent (injecting drug use within 6 months), and 307 non-drug users. The non-adherence was 8.4% in the people who injected drugs; 6.8% in the people who did not inject drugs. The cure rates were also similar—64% in the people who injected drugs; 61% in the people who did not inject drugs.

Conclusion
The adherence and cure rates were similar between the two groups—those who injected drugs and those who did not inject drugs.

Editorial Comments
This long-term study has proven that people who inject drugs can adhere as well as people who do not inject drugs. This is even more impressive with the severe side effects of pegylated interferon and ribavirin.

The bottom line is that people who inject drugs can adhere to treatment as well as people who do not inject drugs.

“People who inject drugs (PWID) are usually denied HCV treatment because of preconceived attitudes that they will not adhere to treatment.”

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

—By Lucinda K. Porter, RN

Your hepatitis C virus (HCV) is gone. You went through treatment, and you are cured. You won’t ever have to think about it again, right? Wrong. You may have to think about it, depending on the condition of your liver at the time treatment ended. This article explores life after hepatitis C.

Let’s begin with some basic information about hepatitis C. Being cured from hepatitis C means you don’t have the virus any more. You are a free from it, and you can’t infect anyone else. If you don’t get a new hepatitis C infection, you are cured for life. However, this is a virologic cure. The virus is gone, but if you have cirrhosis, your liver disease isn’t cured. Sometimes, the liver will regenerate. If the liver returns to its beautiful, original condition, these lucky individuals have both a virologic cure and a disease cure. If there is still cirrhosis, or near-cirrhosis, the patient needs medical follow-up.

The experts at the HCV Guidelines recommend quantitative HCV viral load testing at 12 weeks following completion of therapy. The guidelines recommend testing viral load using a sensitive polymerase chain reaction (PCR) assay.

When people are cured of hepatitis C, their tests results show an undetectable viral load (HCV RNA) at 12 weeks after completion of treatment with direct-acting antivirals (DAAs). We call this a sustained virologic response (SVR), also known as a virological cure. Note that some doctors wait for 24 weeks following treatment completion before declaring someone has had an SVR, particularly for genotype 3 patients.

As for monitoring people who have successfully completed hepatitis C treatment, the critical factor is determined by the degree of liver damage you had. The HCV Guidelines recommend that the follow-up for patients who do not have advanced fibrosis (stage F0-F2) is the same as if they were never infected with HCV.

For those with stage F-3 or F4 who achieve an SVR, twice-yearly ultrasound examination is recommended. This is because people with cirrhosis (or near-cirrhosis) are at risk for developing hepatocellular carcinoma. If cirrhosis is present, a baseline upper endoscopy is recommended. The purpose of this is to screen for varices, which are swollen vessels in the digestive tract, usually in the esophagus and upper stomach. These can hemorrhage, which can be life threatening.
Patients in whom varices are found should be treated and followed as indicated.

**Note** that just because we are cured doesn’t mean we can’t get another hepatitis C infection. And hepatitis C isn’t the only liver disease we can get. If we have any indication of a liver problem, a quantitative viral load test is recommended. This is especially important for people with an ongoing risk for another hepatitis C infection.

**For those who want another opinion on the matter,** three experts published their recommendations in the May 2017 issue of Gastroenterology. (American Gastroenterological Association Institute Clinical Practice Update—Expert Review: Care of Patients Who Have Achieved a Sustained Virologic Response after Antiviral Therapy for Chronic Hepatitis C Infection — Ira Jacobsen, et al.) Their recommendations are the same as those in the HCV Guidelines, but they also recommend the following:

- In addition to the 12-week post-treatment viral load, they advise a routine confirmation of SVR at 48 weeks following completion of HCV treatment. A viral load may be performed 24 weeks following treatment. They do not recommend routine viral load testing beyond 48 weeks unless there are risk factors for reinfection.

- Twice-yearly surveillance for hepatocellular carcinoma (liver cancer) for patients with stage 3 fibrosis or liver cirrhosis post-SVR. The screening tests that Jacobsen and colleagues recommend using are liver imaging with or without a blood test measuring alpha-fetoprotein (AFP).

- These researchers are specific in their endoscopic screening recommendations, advising them for cirrhotic patients every 2 to 3 years if no varices or small varices are identified on initial screening examination. These can be stopped if no varices are found and there are no risk factors for progressive cirrhosis.

- Noninvasive tools, such as liver elastography, can be used to assess for interval fibrosis progression or regression to guide clinical management.

We don’t have long-term data evaluating liver-related outcomes in patients post-SVR with oral DAA regimens. However, hepatitis C or no hepatitis C, there are other types of liver disease, such as fatty liver disease or alcoholic liver disease. Talk to your health care provider about how to maintain a healthy liver. Alcohol, poor diet, lack of physical activity, diabetes, some medications, and toxins can injure the liver. Vaccination will protect you from hepatitis A and B.

There is one more thing you can do if you have a healthy liver: register to be an organ donor. Hopefully you will live a long and healthy life and die of natural causes when you are old. But just in case, consider organ donation.

Hepatitis C in Children

—By Alan Franciscus

Introduction
In this article, I will discuss the various aspects of hepatitis C (HCV) in children including what we know and what we don’t know! The topics I will cover are mother-to-child transmission, hepatitis C transmission among children, HCV disease progression in children, which tests to monitor children with hepatitis C, and the newly approved medications to treat children. The outlook for children with hepatitis C is looking better now that we have direct-acting antiviral medications to treat children with hepatitis C but we first have to identify, manage and treat them.

Prevalence
The prevalence of hepatitis C (HCV) in children is estimated at .05% to 0.36%. This number is likely an underestimate for several reasons:

• Screening of pregnant women for hepatitis C is based on risk factor assessment so it’s likely we may be missing some children with hepatitis C.

• The current opioid crisis in America is among young female and male injection drug users. The most frequent age of the people who are affected by the recent opioid crisis are ages 20 YO to 29 YO and equally female and male. Women in this age group are in their childbearing years.

• Women who are pregnant are not routinely tested for hepatitis C. Pregnant women must acknowledge a risk factor such as injection drug use before they are tested for hepatitis C. This is a problem because once they acknowledge their drug use, they face stigma and more importantly, the state may take their baby away from them.

We do know that some of the rates among pregnant women in the rural and Appalachian counties have reached a record high. In West Virginia, 1 in 50 newborns were exposed to the hepatitis C virus. In 2014, Tennessee had the highest rate with 10.1 hepatitis C infections per 1,000 live births. The increased rates of mother-to-child transmission reached a 15-year high across the U.S. Yet, we do not really have a handle on the true rate of hepatitis C mother-to-child transmission since some states may not report it to the Centers for Disease Control and Prevention.

Mother-to-Child Transmission
The risk of mother-to-child transmission is approximately 4-6%. There are some factors that may increase the likelihood of transmission from mother to child such as fetal scalp monitoring, birth by caesarean, high viral load (HCV RNA), and coinfection with HIV. At this time there have not been any studies in hepatitis C direct-acting drugs that could prevent the transmission of hepatitis C from mother-to-child.
Hopefully, future studies (without ribavirin) will be conducted to find out whether HCV treatment is safe and effective in preventing mother-to-child transmission of HCV.

Testing
A baby born to a mother who is hepatitis C positive will receive the mother’s HCV antibodies. The HCV antibodies will remain in the infant’s blood for a year or longer. For this reason, it is recommended that the baby should not be tested for HCV antibodies for at least 18 months. However, an HCV RNA (viral load) test can be given after two months, but the baby should be re-tested again 12 months later to confirm if the baby is still HCV positive. The reason for re-testing is that many infants naturally clear the virus out of their body—this is called spontaneous viral clearance. If the viral load comes back negative, the test is repeated twice—at least six months apart. Twenty-five percent to forty percent of babies will naturally clear HCV six months after birth.

Interestingly, another 6% to 12% of children will spontaneously clear the virus before reaching adulthood.

Childhood Transmission and Prevention
The most common transmission of hepatitis C in children is injection drug use. Sexual transmission is another possible risk factor but is unlikely unless children are having unprotected sex with multiple sexual partners or having sex with trauma. Another possible route is getting a tattoo in an unlicensed tattoo parlor where attention to safety is not practiced.

Disease Progression
In general, most children have a slow disease progression during the acute phase and chronic phase of hepatitis C. In a minority of children chronic hepatitis C disease progression may be more aggressive. As a child ages, the disease progression process can accelerate. For this reason, all children with hepatitis C should be monitored on a regular basis. There are factors that increase the likelihood of a more serious disease progression such as coinfection with HIV, or hepatitis B, having cancer, or anemia.

Homelessness and incarceration can also increase HCV disease progression of hepatitis C in children.

To keep a child healthy and prevent liver disease progression in children, the same advice that is given to adults should be followed by children. This includes avoiding alcohol and recreational drugs, eating a healthy diet and regular exercise.

Children who do have a more serious case of disease progression should be evaluated for treatment. There may be some thought to treat children before disease progression occurs especially since we now have newer therapies available.
Disease Monitoring
Children should be monitored on a regular basis. It is recommended that they have yearly visits to their medical provider and consultations with a liver specialist.

Children should receive regular vaccinations including hepatitis A and B if not already immune. Other childhood vaccines should be given as advised by a medical provider.

There are various tests to monitor the liver functioning such as the aminotransferase—a non-specific marker of liver inflammation. Another test is the Fibroscan—vibration-controlled transient elastography that can estimate the amount of scarring in the liver.

Treatment
Recently, two drugs by Gilead were approved by the Food and Drug Administration (FDA) to treat children aged 12 and over:

- Harvoni (ledipasvir plus sofosbuvir) for pediatric patients 12 years of age and older or weighing at least 35 kg (77.16 lbs) to treat genotype 1, 4, 5, or 6 without cirrhosis or with compensated cirrhosis. The cure rates in the clinical trials were 98% to 100%,

- Sovaldi (sofosbuvir) for pediatric patients 12 years of age and older weighing at least 35 kg (77.16 lbs) to treat genotype 2 or 3 chronic HCV infection without cirrhosis or with compensated cirrhosis in combination with ribavirin (dosed by weight). The cure rates in the clinical trials were 97% to 100%.

Sources:
- Hepatitis C Virus Infection in Children and Adolescents, Hepatology Communications, VOL. 1, NO. 2, 2017—J.E. Squires et. al.

Conclusion
The hepatitis C epidemic is continuing in the general population because of a decade-long surge in injection drug use across the United States and among the Baby Boomer population. This now affects and will continue to affect children. I wrote that we have HCV treatment that is very effective for children who have HCV disease progression. But since we have highly effective direct-acting antiviral medications with very few side effects maybe we should think about treating every child with hepatitis C.

As we work towards eliminating hepatitis C there should be no question that the first population that we aim to eradicate this disease should be our most vulnerable population—our children.
Over the last year, the opioid epidemic has gone from dominating the well-known areas of public health and the justice system into less known ones like foster care and high schools. Hepatitis C comes along as heroin and opiate use/overdose climb dramatically. Access to medicine and treatment continue to be challenges despite high curative success. To end the opiate crisis and eliminate hepatitis C, we will need to be persistent, thorough and creative. Because so many different areas need to be addressed, there are opportunities for almost anyone to help. Areas of screening, epidemiology and pharmacology are vital. Equally as vital are education, peer support, health disparities and achieving health equity. The Hepatitis C Support Project focuses on many of those things and that’s why I love working with the team as we relaunch the Train-the-Trainer program. As you can imagine such an undertaking can be very challenging, especially when many of the people who work at the HCSP work remotely.

All the challenges and road bumps have been, and will continue to be, worth it. So far, I’ve been to a handful of cities like Cincinnati, OH, Franklin, NC, Indianapolis, IN, Birmingham and Montgomery, AL. Throughout the months of August, September and October I’ll be going to roughly 20 more trainings. From now until the end of the year I want to use my articles, when possible, to highlight some of my experiences on those trips. I won’t be revealing anyone’s information or identity; it will just be my account of the trip (both training and free time). In the short time I’ve been doing this; I’ve come to discover what we all know intuitively. The U.S. is a diverse community of beliefs and culture. I have always said that I learn just as much from the participants as they learn from me. I believe there is incredible value by standing in a room of other people and communicating face to face instead of on a webinar or online course. Not necessarily more, but different and effective. Standing among a room of people who have sometimes driven hours across their state to learn, discuss and create a plan to end hepatitis C, is just flat out fun for me. Below are just a few things that stuck out to me at each of the previous sites so far. Each state has its own challenges with funding and access, so there is often a nice range of topics across training sites.

— CONTINUED ON PAGE 10
Columbus, OH – One of the topics that came up the most was access to vaccines. A recommendation for HCV+ people to be vaccinated against HBV can be challenging without resources. These resource challenges continue into the areas of surveillance and screening. Funding restrictions prevent many from being able to do adequate testing.

Indianapolis, IN – I was excited to visit some of the people I worked with for so long in HIV prevention around the state. I was excited to see what the participants’ perspectives were after having gone through the HIV outbreak that garnered so much attention. The main barriers discussed were treatment access regarding METAVIR score and sobriety restrictions as well as syringe exchange implementation. The CDC is currently working on a few great projects with the Indiana State Department of Health to improve access to testing materials and surveillance.

Franklin, NC – Tucked nicely between mountain ranges, Franklin is a key stop on the Appalachia trail that hikers try to complete every year. A bit of a homecoming for me, as it was the first time I had been to North Carolina since I was about 6 months old. Key challenges here were transportation, access to treatment, insurance and testing kits. North Carolina is making great progress. It is home to both harm reduction and HIV/HCV centered organizations. I thought it was interesting that dialects could change drastically from one side of a mountain to the next.

Birmingham/Montgomery, AL – My first time to Alabama was a great one. The distance between the two cities was a short 1.5-hour drive and are home to many historical sites. Challenges were similar among the two sites although they had different attendees from different parts of the state. Confirmatory testing/follow up were talked about as well as ways to collaborate on education and how to start a support group.

All the sites I’ve been to so far have been coordinated and attended by amazing people who care deeply about their communities whether rural, urban or semi-urban. The conversations were always civil and new ideas/partnerships were formed by those who attended. In one way or another I always tell participants that all the information we cover, the slides, facts, statistics, our fact sheets, guides, manuals and the treatment rates, are accessible once they leave. The information is important, and learning it is key to being certified, but the most valuable thing that cannot be replicated is the unique chance we all have at that moment to be together, face to face and side by side, learning and challenging in an engaging way that hopefully changes all our perspectives a little.

“Each state has its own challenges with funding and access...”

“The U.S. is a diverse community of beliefs and culture.”

Matthew Zielske is the Training Manager for the Hepatitis C Support Project’s Train-the-Trainer workshop.

He has a Master’s in Communication with a focus on health communication and health literacy.

You can read his blog at 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 (http://hcvadvocate.org/publications/newsletter/) and our blog (http://hepatitisc.hcvadvocate.org/) and in the HCV Advocate Hepatitis C Drug Pipeline & Conference Coverage site hcvdrugs.com

For EASL coverage see www.hcvdrugs.com

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>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>
</tr>
<tr>
<td><strong>Study Name</strong></td>
<td><strong>Patient Population</strong></td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------</td>
</tr>
<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>
</table>

*pegIFN = 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. On February 02, 2017 the FDA granted AbbVie Priority review for this combination.
Gilead – Sofosbuvir, Velpatasvir& 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>
</tr>
</thead>
<tbody>
<tr>
<td>POLARIS-1</td>
<td>NS5A inhibitor-experienced 41 percent (172/415) had cirrhosis</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></td>
<td></td>
<td>Placebo</td>
<td>12 Weeks</td>
<td>0% (0/152)</td>
</tr>
<tr>
<td>POLARIS-4</td>
<td>DAA-experienced (No NS5A inhibitor) 46 percent (153/333) had cirrhosis</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></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 18 percent (174/941) had cirrhosis</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></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 All had cirrhosis</td>
<td>3</td>
<td>SOF/VEL/VOX</td>
<td>8 Weeks</td>
<td>96% (106/110)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SOF/VEL</td>
<td>12 Weeks</td>
<td>96% (105/109)</td>
</tr>
</tbody>
</table>

Vosevi approved in August 2017!

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.
EASL 2017: The results of the phase 2 study results of JNJ-4178 are included in the table below:

<table>
<thead>
<tr>
<th>AL-335 (mg QD)</th>
<th>ODV (mg)</th>
<th>SMV (mg QD)</th>
<th>HCV Genotype</th>
<th>Dosing Duration (weeks)</th>
<th>Number (%) with undetectable HCV RNA at SVR24*</th>
</tr>
</thead>
<tbody>
<tr>
<td>400</td>
<td>50 QD</td>
<td>100</td>
<td>1</td>
<td>8</td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>75</td>
<td>1</td>
<td>8</td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>75</td>
<td>1</td>
<td>6</td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>—</td>
<td>1</td>
<td>8</td>
<td>21/25 (84%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>—</td>
<td>1</td>
<td>12</td>
<td>7/8 (88%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>75</td>
<td>3</td>
<td>8</td>
<td>0/5 (0%)</td>
</tr>
<tr>
<td>800</td>
<td>50 QOD</td>
<td>75</td>
<td>3</td>
<td>12</td>
<td>10/13 (77%)**</td>
</tr>
</tbody>
</table>

QD: every day; QOD: every other day; RNA: ribonucleic acid; SVR: sustained virologic response. *All results SVR24, with the exception of genotype 3 which is SVR12 **One patient did not attend SVR12 follow-up.

Note: The two drug combination of odalasvir and AL-335 for a treatment duration of 8 weeks will not proceed into phase 3 clinical trials. Clinical trial development of the combinations to treat HCV genotype 3 will also not move forward.

The combinations were generally safe and well-tolerated.

The next phase of development is to study these combinations in phase 2B studies.
**Merck**

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

**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 cure rates were 98% (43 of 44 pts) in the 16 week group that received ribavirin and 100% (49 of 49 pts) in the 24 week group that did not receive ribavirin.

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**Regulus**

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

**COMMENTS:**

**Regulus has permanently canceled the development of RG-101.**

**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.

<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.*
**WHAT’S UP!**

More new Harm Reduction Fact Sheets by Matthew Zielske!

These five fact sheets are all about drug use and drug treatment interaction with HCV.

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