Lucinda’s Highlights from the 2017 International Liver Congress
Lucinda K. Porter, RN

Every April, experts from around the world meet in Europe to learn about the latest in liver research. The meeting is called the International Liver Congress (ILC) and it is hosted by the European Association for the Study of the Liver (EASL). This April, Matthew Zielske and Alan Franciscus and I highlight some of our favorite presentations from ILC 2017.

SOURCE
Abstract #THU-451 History of marijuana use does not affect outcomes on the liver transplant waitlist—P. Kotwani, et al.

Study Aims and Results: The goal of this study was to also determine the prevalence and factors associated with marijuana use by people on the liver transplant waitlist. Additionally, researchers sought to evaluate the risk of waitlist death, delisting, and receiving of transplants among current and prior marijuana users. This two-year retrospective study of 884 adults found marijuana use was 48%; 7% were current users and 41% prior users. The incidence of death/delisting or receiving transplant was the same among marijuana users and non-users.

— CONTINUED ON PAGE 2
Conclusions: History of marijuana use was not associated with worse outcomes on the liver transplant waitlist. Based on these data, the researchers concluded that marijuana use alone may not warrant contraindication or disqualification from transplant listing.

Editorial Comments: More than half the states in the U.S. have legalized the use of medical marijuana, but that doesn’t mean you can use it if you are on the transplant list. Alcohol is legal in all states but drinking it disqualifies you from receiving a liver transplant, since alcohol damages the liver. Research on marijuana’s effect on the liver is long overdue.

SOURCE

Study Aims and Results: The current U.S. guidelines recommend one-time hepatitis C virus (HCV) testing for all people born 1945–1965, targeted testing of high-risk persons. This study simulated 4 HCV testing and treatment strategies in the U.S.:

1. Current standard of care
2. Routine testing for all persons aged ≥40
3. Testing people aged ≥30 years
4. Testing people aged ≥18 years

The expanded age-based testing strategies identified approximately 5% more people with an increased cure rate of 6%.

Conclusions: This study found that testing all adults for HCV is an economically sound strategy.

Editorial Comments: It feels uncomfortable when the value of healthcare is reduced to cost-effectiveness, however, sometimes that is an argument that catches the most attention. This year’s EASL presentations have at least 4 abstracts that show the gains that can be made when HCV testing and treating includes more people in the U.S. For more information about this, see:

- Abstract #FRI-179 Integrated healthcare system implementation of one time hepatitis C virus testing for patients born between 1945 and 1965 with linkage to care (J.M. Levin, et al.)
- Abstract #FRI-458 The Cost-effectiveness of a one time hepatitis C virus antibody test followed by treatment for all Americans ages 18 and older as compared to current testing recommendations in the United States (D.B. Rein, et al.)
- Abstract #FRI-478 An alternative screening strategy for hepatitis C virus infection among Americans not belonging in the baby boomer birth cohort (P. Udompap, et al.)

Alcohol is legal in all states but drinking it disqualifies you from receiving a liver transplant, since alcohol damages the liver. Research on marijuana’s effect on the liver is long overdue.

SOURCE
Abstract# SAT-218 Health-related quality of life in children with hepatitis C viral (HCV) infection treated with sofosbuvir and ribavirin—Z.M. Younossi, et al.

Study Aims and Results: This phase 2 study assessed quality of life outcomes in 50 HCV-positive adolescents treated with sofosbuvir and ribavirin. Treatment success rates were 100% of patients with HCV genotype 2 and 95% with genotype 3.

Conclusions: This study found that adolescents treated with sofosbuvir and ribavirin did not report
decreased quality of life during treatment, and had significant improvement in social and school function after responding to HCV treatment.

**Editorial Comments:** Sadly, there are too few pediatric hepatitis C studies. Another pediatric study highlighted the need to treat children early to prevent progression of liver disease. (THU-286 Chronic hepatitis C in children in the Russian Federation—G.V. Volynets et al.) It’s time to step up pediatric HCV research.

**SOURCE**
FRI-245 Total cholesterol and low-density lipoprotein increases after treatment with direct-acting antiviral agents – Implications in the future? J Carvalho, et al.

**Study Aims and Results:** It’s already known that HCV lowers cholesterol levels, and when HCV is eliminated, cholesterol levels rise. The aim of this study was to understand this better, especially with the use of direct-acting antivirals (DAAs).

**Conclusions:** Elimination of HCV was associated with a significant increase in total cholesterol levels with both the new DAAs versus the old treatment regimens using peginterferon/ribavirin (PEG/RBV). LDL levels significantly increase post-DAA treatment, but not with PEG/RBV. However, treatment using PEG/RBV increased triglyceride levels, while DAAs reduced them.

**Editorial Comments:** The increased number of people who are now cured of HCV is providing researchers with more data about post-treatment outcomes. The next abstract offers more information about health benefits following successful HCV treatment.

**SOURCE**
THU-215 Risk of cardiovascular and cerebrovascular events in hepatitis C patients following completion of direct-acting antiviral therapy—A.W. Singer, et al.

**Study Aims and Results:** The purpose of this retrospective research was to compare cardiovascular and cerebrovascular risks of patients completing HCV treatment with DAA regimens compared to untreated HCV patients. The study looked at ten years of data collected from 322,276 adults in the U.S.

**Conclusions:** This research found that the risk of cardiovascular and cerebrovascular events in HCV patients in treatment using DAAs reduces shortly after therapy is completed. The benefits of curative DAA therapy in reducing extrahepatic complications of HCV may be even greater with longer periods of follow-up.

**Editorial Comments:** Now that more people are being successfully treated for HCV, it is easier to evaluate the effect of successful treatment. Another study reported a decreased rate of cardiovascular events in patients with compensated HCV cirrhosis after successful treatment. (PS-032 HCV eradication reduces the occurrence of major adverse cardiovascular events in hepatitis C cirrhotic patients—P. Cacoub, et al)

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Abstract # THU-200 High prevalence of concomitant substance abuse and mental health disorders in an urban underserved FQHC-based hepatitis C virus treatment program—A. Nateras et al.

Study Aims and Results
HCV treatment is seldom offered to injection drug users and people with mental health disorders. This is slowly changing with the availability of direct-acting antivirals (DAA) drugs. The current study describes the prevalence of mental health, substance use, and HCV DAA treatment in an urban underserved primary care network.

Electronic health records from 23 urban community health clinics in San Diego (1/1/12 - 11/17/16) were reviewed that included people with positive HCV antibodies, HCV RNA (viral load), substance use, and mental health diagnoses according to ICD-10 codes (The International Classification of Diseases). All of the patients were treated or awaiting treatment with DAAs.

Conclusion
A total of 3,233 people were HCV RNA (viral load) positive—of these 435 (13%) were already on treatment or had finished treatment. In the total group of HCV RNA positive 891 (28%) had substance use disorders, 403 (12%) had mental health disorders, 1,220 (38%) had both substance use and mental health disorders; 718 (22%) had neither disorder.

In the group of treated people (n=435), 287 (66%) had substance use disorders, 221 (51%) had a mental health disorder, 186 (43%) had both mental health and substance disorders and 93 (21%) had none of the disorders.

The most common type of diagnoses were depression (140 people-32%), drug use disorder in remission (55 people-2%), alcohol remission (45 people-1%). In the treated population the most common diagnosis was a psychotic disorder (58 of 435 people-13%). Of those with a substance disorder—more than half were in remission.

The authors commented that the percentage of patients with substance and mental health disorders was similar between those on and off HCV treatment.

Editorial Comments
As this study points out, there is no reason that people who inject drugs or who have mental health disorders should be denied HCV treatment.

# THU-204 Understanding factors associated with hepatitis C spontaneous viral clearance: a meta-analysis –D. N. Aisyah et al.

Study Aims and Results
The study analyzed the rate of spontaneous or natural clearance of hepatitis C after becoming acutely infected. The authors reviewed various studies (meta-analysis) from several databases (Ovid Embase, Ovid Medline, Pubmed) from 1/1/1994 – 6/30/2015 to understand the time of acute infection to spontaneous clearance and the factors associated with spontaneous clearance. Forty-four studies of 20,409 people were included in the review.

Conclusions
Approximately 1/5 of those who cleared hepatitis C did so within 3 months, 1/3 did so in 6 months and over
1/3 did so in 12 months. If people did not clear the virus by 12 months they were unlikely to clear the virus.

The groups that were less likely to spontaneously clear the virus early in the acute phase included males, those who did not have a hepatitis B co-infection, who lacked hepatitis C symptoms, black race, non-genotype 1, older age, those with alcohol or drug use and people with HIV.

Editorial Comments
There are two important outcomes from this study:

1. It clearly shows that 12 months establishes the time period needed to ascertain the time to spontaneously clear the hepatitis C virus from the body in most people acutely infected with hepatitis C. But it is important to take note of the exceptions listed above. (see the abstract below to treat acute HCV in people with HIV for an example of why it’s important to treat sooner than the above date range.)

2. It gives a better understanding of who and when to treat with direct-acting antiviral therapy for those who have been recently infected with the hepatitis C virus.

Releasing prisoners cured of hepatitis C into the general population means that we can stop the spread of hepatitis C. It is a public health issue and a humane one.

Study Aims and Results
Prior studies to treat acute hepatitis C in people with HIV for 6 weeks with Harvoni (sofosbuvir/ledipsavir) did not achieve favorable results. The aim of this study was to find out if extending the treatment period to 8 weeks improved the cure rates. The inclusion criteria was elevated ALT levels (liver enzymes), documented recent exposure to the hepatitis C virus (HCV antibody and HCV RNA (viral load)) or re-infection after a spontaneous, natural clearance or treatment cure.

Twenty-six HIV positive men who acquired hepatitis C from sexual contact (21 primary infection; 5 re-infection) were enrolled in the study between August 2014 and March 2016. Active drug use was common during this period—mostly methamphetamines. Five men had spontaneous clearance during this period before treatment could be started. The characteristics of the remaining 21 people treated was a median age of 37 yo; 14 (58%) black or Hispanic, twenty (95%) were genotype 1 and one person was a genotype 4.

Treatment was started at a medium of 18 weeks after a diagnosis of acute hepatitis C. Nineteen men received 8 weeks of treatment, one received 6 weeks and one was extended to 12 weeks.

Conclusion
All of the men who were treated were cured. The authors commented that a better understanding of the best timeline to treat acute hepatitis C in people infected with HIV.

Editorial Comments
A meta-analysis review of acute HCV in people with HIV would be helpful. This will narrow down the optimal timeframe to treat. Still, the cure rates are very encouraging!
Abstract # FRI-186 Treatment of chronic hepatitis C virus (HCV) infections with Direct Acting Antivirals in the New Mexico State Prison System using the Project ECHO Model—K. Thornton et al.

Study Aims & Results: Approximately 1/3 of people infected with hepatitis C in the United States pass through the jail and prison system each year. This abstract is about treating prisoners with the aid of telemedicine. Although prisons would be a perfect place to test and treat people with hepatitis C there are many barriers to treating people in prisons such as the cost of HCV medications and lack of medical providers available to provide care and treatment for the thousands of hepatitis C positive persons in prisons.

Project Echo (Extension for Community Health Outcomes) model has been providing telemedicine to people with hepatitis C and other conditions for more than a decade. It is the basis for this study that took place in New Mexico. New Mexico has a prevalence of 43% of hepatitis C on intake into the state prison system. Project ECHO uses multipoint videoconferencing to guide New Mexico Correction medical providers to treat inmates with hepatitis C.

Fifty-six TeleECHO clinics were held with 115 patients (96% male; 57% genotype 1; 39% genotype 3; 4% genotype other). By October 31, 2016 –77 patients started treatment and 56 patients completed treatment with post-treatment follow-up. The average age was 49yo; 82% had cirrhosis. The reason for treatment in the non-cirrhotic patients was coinfection with HIV/HCV coinfection.

Treatment included Harvoni or Zepatier for genotype 1 and daclatasvir plus sofosbuvir plus ribavirin for genotype 3.

Conclusion: The cure rates for genotype 1 was 91%; 89% for genotype 3. In the 5 patients who were not cured three relapsed while on treatment, one patient died and one patient was re-infected, 1 patient relapsed 12 weeks post-treatment with a different genotype.

Editorial Comments: I would like to see this study replicated in other prisons. It seems to be a good model that can be effectively replicated.

Eliminating hepatitis C means that we have to treat and cure everyone with hepatitis C including prisoners. Prison is an optimal place to treat inmates and telemedicine can help achieve this goal. Releasing prisoners cured of hepatitis C into the general population means that we can stop the spread of hepatitis C. It is a public health issue and a humane one.
SOURCE

Abstract # THU-238 Feasibility and acceptability of a group medical visit intervention to improve hepatitis C virus treatment uptake among persons who inject drugs (PWID) in a primary care setting—B. Norton et al.

Study Aims and Results: This study focuses on an inventive intervention called, HCV Group Evaluation and Treatment Uptake (HCV GET-UP).

In this study patients were recruited from a primary care clinic in the Bronx, NY. Group visits with a physician took place over the course of four weeks. During the group visits, hep C related health care evaluations, education support and skill building took place. The likelihood of this study being successful was assessed through recruitment, retention rates and acceptability by means of a short post group survey which was laid out as a 5-point Likert scale (not helpful to very helpful).

Phone contact was made with 27 (67.5%) of the 40 people initially eligible. There were 13 (48.1%) people of those 27 who agreed to be screened with seven deciding to enroll. The demographic breakdown is as follows; most were male, all were African American or Latino and their median age was 55. Almost all of them were being treated for opioids and three of them were actively using drugs at their initial visit.

Conclusion: Of the 6 people that initially attended one group visit, 5 attended a follow up HCV treatment appointment and 4 have begun treatment. The average of the survey results was; evaluation: 5, education: 4.8, skill building: 5, group activity or support: 5

Editorial Comments: A meta-analysis review of acute HCV in people with HIV would be helpful. This will narrow down the optimal timeframe to treat. Still, the cure rates are very encouraging! Although the study is promising in its approach to engaging and retaining hepatitis C positive people who inject drugs in healthcare only 4 of the 40 antibody positive patients began treatment. Of the 7 who enrolled this is a great result but more needs to be done to increase the number of those who willingly begin the process. The fact that three people who were actively using drugs were included is also very promising and shows the healthcare model can and is willing to change.

SOURCE

Abstract # THU-225 Four weeks of Ledipasvir/Sofosbuvir + Ribavirin with or without pegylated interferon gives very high and sustained cure rates in difficult to reach but easy to treat injecting drug users with chronic hepatitis C: final results of the 4WIDUC study— A.L.H. Oevrehus et al.

Study Aims and Results: Researchers in this study looked at sustained virologic response (SVR) outcomes of treatment naïve patients on opioid substitution therapy (OST) 12 and 24 weeks after a 4-week treatment cycle. There was an equal number of patients who received Harvoni + Ribavirin with and without interferon. Harvoni is only approved to treat genotypes 1, 4, 5 and 6.

Although people with any genotype could be considered for this study, only those who were treatment
naïve, on OST, under the age of 50, weighed less than 220lbs and had a viral load under 2 million IU/ml were accepted.

**Conclusion:** Over the course of a year 32 of 48 people screened began treatment. Of those 32 people, 6 failed to move further into the study because of a high viral load. In the SVR 12 group all but one person with genotype 2 reached SVR. Among those in the SVR 24 population 92% reached SVR when interferon was included and 69% reached SVR when interferon wasn’t included. Causes for failure among those in the SVR 24 group were early relapse, probably reinfection/late relapse, treatment unrelated suicide and dropout before end of treatment.

**Editorial Comments:** This was a very interesting look at the potential for shortened treatment. Although the number of participants was small, the results of reaching SVR when incorporating pegylated interferon seem to indicate a distinct difference in treatment success. More research needs to be done with a larger group of people, but this is a promising exploration into finding successful ways to treat hard to reach populations. The drawbacks to the study are many people do not want to take pegylated interferon and it’s not to be used with people who have mental health issues.

**SOURCE**
Abstract # FRI-454 The evaluation of homelessness on HCV treatment outcomes among current and former people who inject—A. Singh et al.

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**Study Aims and Results**
This study focuses on figuring out the impact homelessness has on HCV + people who inject drugs successfully reaching and maintaining SVR among. The location of this study was the Vancouver Infectious Diseases Center (VIDC) program, which provides care to address medical, psychological, social and addiction related needs. Homelessness was self-declared, Patients were followed up with every 6 months after SVR and more frequently if reinfection was believed to be a concern. In situations where reinfection happened treatment was also considered a failure.

**Conclusion**
Of the 74 people who participated in the study, 58% of them were homeless and 88% of those homeless reached SVR. In comparison, 97% of those with stable housing reached SVR. The two occurrences of reinfection were among people who identified as homeless.

**Editorial Comments**
This study is promising because of its focus on the role of homelessness both reinfection and successfully reaching SVR. I recently worked with someone who was living under a bridge and keeping his Harvoni in a backpack and successfully reached SVR. But challenges are numerous and this study shows that even while being homeless 88% can reach and maintain SVR. This is a remarkable achievement in some of the most challenging conditions.
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/) and in the HJCV Advocate Hepatitis C Drug Pipeline & Conference Coverage Site hcvdrugs.com For EASL coverage see 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>
</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>

*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.
**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>
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</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-naive 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-naive 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-naive 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

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

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Regulus

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

<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 weeks 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.
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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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HCSP Train-the-Trainer Workshops:
Monday June 5th • Vestavia, Alabama
Wednesday June 7th • Montgomery, Alabama

The Hepatitis C Support Project presents
Hepatitis C Train-the-Trainer

Monday, June 5th
Check in at 9:00 am. Training begins at 9:30 am to 2:00 pm.
Vestavia Hills Library in the Forest
1221 Montgomery Highway
Vestavia Hills, AL 35216

Goals and Objectives
At the conclusion of this workshop, participants will be able to:
• Explain transmission, prevention, symptoms and treatments for HCV.
• Explain basic information regarding hepatitis C.
• Contrast between acute and chronic hepatitis C and describe possible long-term liver damage.
• Identify various methods helpful in managing hepatitis C.
• Describe current medical treatments and the side effects.
• Communicate a plan of action of how to educate and support others in your community about hepatitis C.
• Learn about local resources.

This training is funded by unrestricted funds from Gilead Sciences and Fibrosure.

Email registration to:
ronada.anderson@adph.state.al.us
Registration closes May 29th

The Hepatitis C Support Project presents
Hepatitis C Train-the-Trainer

Wednesday, June 7th
Check in at 9:00 am. Training begins at 9:30 am to 2:00 pm.
Alabama Public Library Service
6030 Monticello Drive
Montgomery, AL 36130

Goals and Objectives
At the conclusion of this workshop, participants will be able to:
• Explain transmission, prevention, symptoms and treatments for HCV.
• Explain basic information regarding hepatitis C.
• Contrast between acute and chronic hepatitis C and describe possible long-term liver damage.
• Identify various methods helpful in managing hepatitis C.
• Describe current medical treatments and the side effects.
• Communicate a plan of action of how to educate and support others in your community about hepatitis C.
• Learn about local resources.

This training is being sponsored by Fibrosure.

Email registration to:
ronada.anderson@adph.state.al.us
Registration closes May 31st

Check out the following Updated fact sheets

HCSP FACTS: ACUTE HEPATITIS C¹

EASY C FACTS: METHADONE AND HCV TREATMENT²

¹http://hcvadvocate.org/hepatitis/factsheets_pdf/Acute_HCV.pdf
²http://hcvadvocate.org/hepatitis/easyfacts/Methadone_and_Treatment.pdf