Last month, Lucinda K. Porter, Matthew Zielske, and I highlighted some presentations delivered to the International Liver Congress (ILC). Hosted by the European Association for the Study of the Liver (EASL), the ILC provides top-notch liver-related research. This month we provide more of the best from ILC 2017.

**SOURCE**

GS-007 ENDURANCE-3: safety and efficacy of glecaprevir/pibrentasvir compared to sofosbuvir plus daclatasvir in treatment-naïve HCV genotype 3-infected patients without cirrhosis—G. R. Foster et al.

**Study Aims and Results:** The aim of the ENDURANCE-3 study was three-fold—treat genotype 3 patients with glecaprevir plus pibrentasvir (one pill/once a day) for (a) 8 weeks, (b) 12 weeks, and compare it to the (c) 12 weeks of treatment of sofosbuvir plus daclatasvir. The study was a non-inferiority treatment study— that is the challenge was to find out if the new drug combination was as effective as sofosbuvir/daclatasvir.

**Note:** Genotype 3 is one of the most common genotypes worldwide and has been one of the most difficult to treat with direct-acting antiviral medications (DAAs). The majority of patients in the trial were males (52%);
White (88%); with mild liver disease—no cirrhosis (F0-F1—83%) and relatively younger (~47 yo).

**Conclusions:** The cure rates were as follows:

Glecaprevir plus pibrentasvir:
- a) 8 week treatment arm: 95% (149 of 157 patients)
- b) 12 week treatment arm: 95% (222 of 233 patients)

Sofosbuvir plus daclatasvir:
- c) 12 week treatment arm: 97% (111 of 115 patients)

The study met the non-inferiority goal (and more) of the study.

There were two discontinuations in the 12 week arms. The most side effects were headache, fatigue and nausea.

**Editorial Comments:** In clinical trials AbbVie’s new drug combination continues to shine. This study is great news for people with hepatitis C genotype 3 who have had limited treatment options especially because of the high cost of the combination of sofosbuvir and daclatasvir.

This data shows promise to reduce the treatment period for people with HCV genotype 3 who have little or no liver disease damage to a 8-week course of therapy.

This combination is expected to be approved by the Food and Drug Administration (FDA) this year.

**SOURCE**

Abstract # PS-159 Safety and efficacy of the fixed-dose combination regimen of MK-3682/grazoprevir/ruzasvir in cirrhotic or non-cirrhotic patients with chronic HCV GT1 infection who previously failed a direct acting antiviral regimen (C-SURGE)—H. Wedemeyer et al.

**Study Aims and Results:** There is little guidance for patients and medical providers to understand how to treat people who have relapsed on a previous course of direct-acting antiviral treatment. The phase 2 study looked at two approaches to understand the best way to treat people with hepatitis C who are in need of re-treatment. Both treatment arms included MK-3682, grazoprevir/ruzasvir—one-a-day with and without ribavirin. Treatment duration was 16 weeks with ribavirin (arm a) or 24 weeks without ribavirin (arm b). The patient characteristics were genotype 1(1a (80 pts)/1b (14 pts)), no cirrhosis (56%); compensated cirrhosis (43%) and 1% unknown cirrhosis status.

There was a high percentage of resistant-associated substitutions (RASs)—formally named resistant-associated variants (RAVs).

**Conclusions:** The cure rates were as follows:
- • 16 week treatment period with ribavirin – 98% (43 of 44 pts)
- • 24 week treatment period without ribavirin – 100% (49 of 49 pts)

*Note: one patient withdrew from the study.*

There were no treatment discontinuations. The most common side effects were fatigue, pruritus, rash and decreased red blood cell count (hemoglobin) in the ribavirin arm.

**Editorial Comments:** The study included patients with difficult re-treatment characteristics—compensated cirrhosis, genotype 1a, and single and multiple RASs. It produced good if not almost near perfect cure rates. I will be interested to see this combination in larger phase 3 clinical trials.
Abstract # THU-248 No impact of RASs on the high efficacy of SOF/VEL/VOX for 12 weeks in DAA-experienced patients: an integrated resistance analysis of the POLARIS-1 and POLARIS-4 studies—C. Sarrazin et al.

Study Aims and Results: The study was a combination of two studies (POLARIS-1 & 4) looking at treating HCV genotype 1 through 6 (pan-genotypic) direct-acting treatment experienced patients with a combination of sofosbuvir, velpatasvir and voxilaprevir. A total of 445 patients were treated for 12 weeks with the 3-drug combination. Thirty-one percent did not have resistant-associated substitutions (RASs) and the remainder had either one RASs or multiple RASs.

Conclusions: The overall cure rates were 97 to 100% regardless of genotype, cirrhosis/no cirrhosis, type of prior treatment failure or RASs. The 12-week treatment of this combination yields very high cure rates for people who have been previously treated with a direct-acting antiviral medication and who have single or single or double RASs.

Editorial Comments: This is good news for patients and medical providers. The triple combination of sofosbuvir, velpatasvir and voxilaprevir in a once-a-day dose is scheduled to be approved by the Food and Drug Administration (FDA) later this year.

PS-035 Among Cirrhotic Patients with a Hepatitis C Sustained Viral Response, the Risk of De-novo Hepatocellular Carcinoma Relates to Baseline Factors and Not the Use of Direct Acting Antivirals: Results from a Nationwide Cohort—H. Innes et al.

Study Aims and Results: The current study is a retrospective study (looking back over time) from the period of 1997 to 2017. Importantly, there were no cases of liver cancer prior to treatment in the patients. The patients in the study were treated previously with interferon-based therapies (585 pts) or direct-acting antiviral therapies (272 pts). The patient characteristics included mostly white (92%), male (75%), current smokers (73%), history of IDU (70%) and heavy alcohol users (44%). Nine percent of the interferon-based group and 30% of the interferon-free group had moderate to severe cirrhosis.

Conclusions: The number of people who developed liver cancer in the interferon-based group was 34 (5.8%) and 12 (4.4%) in the direct-acting antiviral (DAA) group. The study didn’t find a difference in the occurrence of liver cancer rates after achieving a cure with an interferon-based therapy or a direct-acting antiviral medication. It is still important that people who are cured and have cirrhosis are followed closely after being cured because liver disease can progress.

Editorial Comments: There are many studies that are looking at disease progression and liver cancer occurrence and reoccurrence after being cured of hepatitis C. Most studies have found that being cured of hepatitis C reduces the risk of serious disease progression, liver cancer and death. Some studies...
Abstract #PS-097 Sustained virological response for 94% of people treated with low-cost, legally imported generic direct acting antivirals for hepatitis C: analysis of 1087 patients in 4 treatment programmes—J. Freeman, et al.

**Study Aims and Results**
Direct-acting antivirals (DAAs) are extremely expensive in most countries, and the cost has created a barrier to treatment for those with hepatitis C virus (HCV). This study evaluated the efficacy of generic sofosbuvir (SOF), ledipasvir (LDV), and daclatasvir (DCV) obtained from India, Bangladesh, Egypt and China. Data were obtained from 1,087 patients undergoing treatment in hospitals, private doctors and clinics in 42 countries worldwide. Treatment length, choice of DAA, and use of ribavirin (RBV) were based on HCV genotype and fibrosis level. Response rates (SVR12) for patients taking SOF/RBV = 91%; SOF/LDV +/- RBV = 92%; SOF/DCV = 86%.

**Conclusion**
HCV treatment using equivalent generic medications is a feasible, economic treatment choice, especially when considering limited access to non-generics.

**Editorial Comments**
James Freeman and colleagues provide an excellent, evidence-based service to the hepatitis C community. Note that the generics provided in this study have been quality tested. I strongly suggest avoiding the purchase of generic drugs from any source that has not been properly vetted.

"Direct-acting antivirals (DAAs) are extremely expensive in most countries, and the cost has created a barrier to treatment for those with hepatitis C virus (HCV). "

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
“If you are coinfected, be sure your medical provider tests for current or prior hep B infection by measuring hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc), prior to starting hepatitis C treatment with the commonly used DAAs.”

SOURCE
Abstract #PS-098 Ledipasvir/sofosbuvir for 12 weeks is safe and effective in patients with chronic hepatitis C and hepatitis B coinfection: A phase 3 study in Taiwan C—J. Liu, et al.

Study Aims and Results
Compared to people who have either hepatitis B or C, patients who are coinfected with both have more rapid liver disease. This study evaluated the safety and efficacy of treatment using ledipasvir (LDV)/sofosbuvir (SOF) for 12 weeks in patients with chronic HCV and HBV coinfection in Taiwan, which has a high prevalence of HCV/HBV coinfection. The main goal was to measure SVR12 while monitoring HBV DNA during treatment and for 2 years post-treatment. At the time of this presentation, SVR4 rate was 100% based on 111 patients. Although most patients experienced an increase in HBV DNA during treatment, this was not associated with ALT elevations ≥2 × baseline, and no patients started HBV therapy to date.

Conclusions
LDV/SOF was well tolerated, and is a potential treatment option for HCV/HBV coinfected patients.

Editorial Comments
Hepatitis C direct-acting antivirals (DAAs) carry a black box warning, stating that there is a risk of hepatitis B virus reactivation in patients coinfected with hepatitis C and B virus. The FDA reported at least 24 cases of hepatitis B reactivation from 2013-2016. Of these, two patients died; one required a liver transplant. The FDA believes that there may be additional unreported cases of hepatitis B reactivation that occurred with DAA treatment for hepatitis C.

This study is entirely too small and too preliminary to draw conclusions about the safety of HCV treatment using DAAs in coinfected patients, albeit it is a good study. If you are coinfected, be sure your medical provider tests for current or prior hep B infection by measuring hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc), prior to starting hepatitis C treatment with the commonly used DAAs, Click here to read the entire FDA Hepatitis Update.

SOURCE
Abstract #PS-101 Ledipasvir/sofosbuvir ± ribavirin for 12 or 24 weeks is safe and effective in children 6–11 years old with chronic hepatitis C infection—K.F. Murray, et al.

Study Aims and Results
The U.S. Food and Drug Administration (FDA recently expanded the use of Sovaldi (sofosbuvir) and Harvoni (sofosbuvir/ledipasvir) to adolescents 12 years and older who have hepatitis C virus (HCV). However, the only FDA-approved hep C treatment for children under age 12 is peginterferon plus ribavirin, a combination that has many side effects and poor response rates when compared to the new DAAs. This ledipasvir/sofosbuvir +/- ribavirin study enrolled 90 HCV+ children, ages 6–11 years old. The SVR4 rate among the 88 patients who completed the post-treatment Week 4 visit was 99%; one GT1a patient relapsed after 12 weeks.
Study Aims & Results: Chronic hepatitis C is associated with increased risk of developing cardiovascular disease. Physical inactivity and poor aerobic fitness are also well-known predictors of heart disease. This study assessed physical activity and cardiorespiratory fitness in 94 individuals living with chronic hepatitis C. Most of the participants had poor aerobic capacity and were not adequately physically active.

Conclusion: These results suggest that low levels of physical activity and aerobic capacity are factors that may need to be addressed when profiling the cardiovascular risk associated with chronic hepatitis C.

Editorial Comments: This is a proverbial chicken/egg problem. Hepatitis C causes fatigue, inflammation and body aches, making it difficult to be physically active. On the other hand, being physically active helps to reduce fatigue, inflammation and body aches. Studies show us that successful hepatitis C treatment leads to improved quality of life. (See May Healthwise: Abstract # 215 Risk of cardiovascular and cerebrovascular events in hepatitis C patients following completion of direct-acting antiviral therapy—A.W. Singer, et al. and PS-032 HCV eradication reduces the occurrence of major adverse cardiovascular events in hepatitis C cirrhotic patients—P. Cacoub, et al)

Hepatitis C is a monumental health threat, and we need to eliminate it. Universal access to hepatitis C treatment is a right; it’s time to make this a reality.

Source
Abstract #THU-184 An assessment of physical activity levels and cardiorespiratory fitness in individuals living with hepatitis C—A.M. Monaghan, et al.

“Chronic hepatitis C is associated with increased risk of developing cardiovascular disease. Physical inactivity and poor aerobic fitness are also well-known predictors of heart disease.”
Abstract #SAT-206 Field evaluation of Xpert® HCV Viral Load point-of-care test for detection of hepatitis C virus infection by venipuncture-collected and finger-stick capillary whole-blood samples—J. Grebely, et al.

**Study Aims and Results:** Improving HCV testing, diagnosis and linkage to care is a continuing challenge. Current point-of-care testing allows for easy and quick delivery of HCV antibody results. Developing a similar HCV RNA point-of-care test will allow for the diagnosis of active infection at the same time. This study evaluates the Xpert® HCV Viral Load assay using samples collected by venipuncture and finger stick capillary whole-blood. The needed samples were collected from people in a study where they were observed receiving services in Australia. Xpert® HCV Viral Load assay’s reliability and accuracy was compared to the current “gold standard”, Abbott Real Time HCV Viral Load assay. There were 150 participants in the study. The median age was 44 years, 87% were male and 65% reported a history of injection drug use. There were 45 HCV RNA positive people. The reliability and accuracy of the Xpert® HCV Viral Load assay for HCV RNA detection in blood draw samples was 100% and 99.1%. In the one instance where the Abbott Real Time HCV RNA was undetectable and the Xpert® HCV RNA was detectable HCV RNA was confirmed with a RT-PCR HCV RNA assay. This confirmation determined the Xpert® was false positive. The reliability and accuracy of the Xpert assay for HCV RNA detection in finger stick samples was 95.5% and 98.1%.

**Conclusion:** The study showed that the Xpert® HCV Viral Load assay had comparatively reliable results to the Abbott Real Time HCV RNA Viral Load assay in terms of reliability and accuracy.

**Editorial Comments:** The reliability of the Xpert® HCV Viral Load assay when compared to the Abbott Real Time HCV RNA Viral Load assay is promising. The inability to provide on-site HCV RNA confirmation for the existing OraQuick HCV Antibody point-of-care test has shown to be unable to improve the HCV Treatment Cascade issues of client confirmation. Providing an HCV antibody result is important but if we are unable to confirm active infection providing a positive antibody assay runs the potential of increasing anxiety without providing concrete answers. The Xpert® HCV Viral Load assay looks to be a promising step towards improving that.

“Improving HCV testing, diagnosis and linkage to care is a continuing challenge. Current point-of-care testing allows for easy and quick delivery of HCV antibody results. Developing a similar HCV RNA point-of-care test will allow for the diagnosis of active infection at the same time.”
Matthew’s International Liver Congress Part 2 — CONTINUED FROM PAGE 7

**SOURCE**

Abstract #SAT-201 Gender differences on long-term outcomes in patients with dual chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infection—S. Shah, et al.

**Study Aims and Results:** Male gender is a proven risk factor among those with chronic mono HCV infection to develop end-stage liver disease and liver cancer (hepatocellular carcinoma or HCC). What is unclear is if any gender differences persistently exist among patients with dual HBV/HCV infection. This study investigated the occurrence of cirrhosis, hepatic decompensation and HCC in HBV/HCV dual infected individuals. 239 men and 120 women with HBV/HCV infection that were seen from 1999 through 2015 at U.S. tertiary care centers were evaluated for this study. Subject’s medical records yielded laboratory values, imaging results and necessary treatment information. The main outcomes were the 10-year occurrence of cirrhosis, hepatic decompensation and HCC. The demographic breakdown is as follows: 41% White, 31% Asian, 15% Hispanic and 13% identified as Other. The mean age was 55.2 with a plus or minus of 10.9 years among men and 56.8 with a plus or minus of 13.1 among women. There was no baseline gender difference in HCV viral load or level of liver scarring, however, men did have higher rates of alcohol and tobacco use, as well as diabetes, lower number of blood clotting agents and were more likely to present with HCC than women. The 10-year occurrence of cirrhosis in individuals without baseline cirrhosis was high yet similar across genders. Despite this, men were significantly more likely to develop HCC. The occurrence of HCC in men and women was 101.6 (men) and 57.8 (women) per 1,000 person years. This means that 101.6 and 57.8 cases would be be expected in a given year among HBV/HCV dual infected people. The 10-year total HCC occurrence was 37% among men and 17% among women. Men also showed a higher total trend of a 10-year occurrence in hepatic decompensation than women.

**Conclusion:** The occurrence of cirrhosis and HCC was high in both men and women with HBV/HCV dual infection. Still, men showed a significantly higher risk for HCC. There also were no gender differences in the occurrence of cirrhosis development.

**Editorial Comments:** This study showed the importance of early antiviral therapy among HBV/HCV dual infected individuals. An approach of early treatment intervention among this group will help prevent long-term complications. A focus on those who are at a higher risk is especially important. Testing for HBV upon HCV diagnosis is key to this approach as well. This study shows the potentially negative outcomes of failing to address HBV/HCV dual infection among both men and women while underscoring the significant risk posed to men who go untreated.
**HCV Advocate**

**Monthly Pipeline Update**

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 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</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;
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](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</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>POLARIS-4</td>
<td>DAA-experienced (No NS5A inhibitor)</td>
<td>1, 2, 3, 4</td>
<td>SOF/VEL/VOX</td>
<td>12 Weeks</td>
<td>97% (177/182)</td>
</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>POLARIS-3</td>
<td>DAA-naïve</td>
<td>3</td>
<td>SOF/VEL/VOX</td>
<td>8 Weeks</td>
<td>96% (106/110)</td>
</tr>
<tr>
<td></td>
<td>All had cirrhosis</td>
<td></td>
<td>SOF/VEL</td>
<td>12 Weeks</td>
<td>96% (105/109)</td>
</tr>
</tbody>
</table>

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

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

In December 2016 Gilead applied to the FDA to market and treat all HCV genotypes with the combination listed above—combined into one pill taken once-a-day.
Janssen (Achillion/Alios)           Genotype(s) 1,2,3,4,5,6 (Pan-genotypic)

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

<table>
<thead>
<tr>
<th>Dose</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>AL-335 (mg QD)</td>
<td>50 QD</td>
<td>100</td>
<td>1</td>
<td>8</td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>400</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></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 2 studies.
Merck

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

COMMENTS:

- **Phase 2- AASLD 2016:**
  
  **C-Crest:** The trial was a phase 2 study of a 3-drug co-formulation of MK-3682 (polymerase inhibitor), grazoprevir (protease inhibitor) plus ruzasvir (NS5A inhibitor) with and without ribavirin to treat HCV genotypes 1, 2 and 3. The treatment period was 8, 12 or 16 weeks. In the people who were previously treated with pegylated interferon plus ribavirin the SVR12/cure rates were 95% to 100% in genotype 1a, 1b and 3. In people with genotype 2 the cure rate was 87% in the 8-week group and a 100% rate in the 12 week group and 96% to 98% in the 16 week groups. There was very little difference in cure rates between the groups who had cirrhosis, and who did/did not receive ribavirin.

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

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.

<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.
WHAT’S UP!

We have added voiceover to some of our most popular Easy C fact sheets. See below:

EASY C’S (TREATMENT) – WITH VOICEOVER

Easy C Facts – Treatment.

These fact sheets are easy to understand, one-page fact sheets related to hepatitis C and come with a voice over reading. After downloading and saving the file to your computer, open in Adobe Reader and click the play icon at the top of the fact sheet to open play, pause and stop controls.

If you have any comments or would like more voiceover fact sheets please contact Alan Franciscus at sfhepcat@msn.com with what types of information future voiceovers should cover.

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