CROI 2018
Conference on Retroviruses and Opportunistic Infections

Hepatitis Research at CROI

The annual Conference on Retroviruses and Opportunistic Infections (CROI) was last week. CROI is a gathering of top researchers from around the world who share the latest studies, important developments, and best research methods in the ongoing battle against HIV/AIDS and related infectious diseases. Below are short summaries of some of the presentations pertinent to hepatitis C virus infection (HCV) that I found most interesting. Note that conference posters are preliminary investigations, and are not conclusive until the data are published in a peer-reviewed journal.

Abstract #600 Increasing Incidence of Denial of DAA Therapy for Chronic HCV by Insurance Type - Charitha Gowda, et al.

Study Aims and Results: When HCV direct-acting antivirals (DAAs) were first approved, insurers restricted access because of the high cost of medications. Looking for information about current practices, this prospective study analyzed access to HCV treatment between January 1, 2016 and April 30, 2017. Using a national specialty pharmacy, researchers collected data from 9,025 people from 45 states who were prescribed a DAA regimen (4,702 covered by Medicaid; 1,821 by Medicare; 2,502 by commercial insurance). There were 3,200 (35.5%) absolute denials. Absolute denial was more common among patients covered by commercial insurance (52.4%) than by Medicaid (34.5%) or Medicare (14.7%). Analyzing quarterly data, denial of treatment increased per quarter from 27.7% in the first quarter to 43.8% in the last quarter.

Conclusions: Despite the fact that HCV has a high cure rate, treatment denials are high and appear to be increasing.

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Editorial Comments: This is outrageous and inhumane. The only way HCV can be eliminated is to improve access to care. Click here to read the entire abstract and view the poster.

Abstract #606 High Efficacy of 8 Weeks of Ledipasvir/Sofosbuvir in African Americans with HCV - Whitney Nichols, et al.

Study Aims and Results: Current HCV guidelines (www.hcvguidelines.org) recommend that African Americans with genotype 1 HCV receive 12 weeks of ledipasvir/sofosbuvir (LDV/SOF), even if they meet criteria for 8 weeks. Research shows conflicting results of treatment outcomes in this group. This retrospective study evaluated the efficacy of 8 weeks of LDV/SOF in African Americans in a real-world setting.

Using data from 2014 to 2017, researchers analyzed data from 59 participants, comparing age, fibrosis level, gender, genotype, medication/treatment adherence, and use of acid-reducing medicines. When comparing 8 weeks to 12 weeks of treatment, they found no significant differences between groups regarding age, genotype, medication and appointment adherence and acid-reducing medication use. However, there were more females, earlier liver fibrosis, and lower baseline viral loads in the 8-week group.

Conclusions: In a real-world setting, 8 weeks of HCV treatment showed good results in African Americans.

Editorial Comments: This study is small and retrospective. I would not rely on these findings to make treatment decisions. I hope we see some large prospective research on this subject. Click here to read the entire abstract and view the poster.


Study Aims and Results: HCV antigen testing is a less expensive alternative to viral load testing. However, antigen testing has difficulty detecting very low viral loads (≤ 3,000 IU/ml). This Swiss study assessed the prevalence and analyzed predictors of very low viral loads (VLVL) in 2,460 treatment-naïve participants. Overall, 5.3% had at least one VLVL. The factors most associated with VLVL are ≤ 40 years old. Gender, HCV genotype and intravenous drug use were not associated with VLVL. Participants with VLVL had a higher rate of spontaneous clearance than those without VLVL. There were 24 cases of cirrhosis, all with either excessive alcohol consumption, HIV coinfection, organ transplantation or other immunosuppressive conditions. The mortality rate was comparable to those without VLVL.

Conclusions: The occurrence of very low viral loads is low. Although the rate of spontaneous clearance is better than expected, the incidence of cirrhosis is disturbing. The use of the HCV antigen assay is questionable as a single tool for HCV detection.

Editorial Comments: Although HCV antigen testing is not the standard assay used in the U.S., this research about very low viral loads is important. Click here to read the entire abstract and view the poster.


Study Aims and Results: This retrospective study sought to identify factors involved in the lack of sustained viral response (SVR) following DAA treatment among people living with HIV (PLWH). Data from the U.S., Spain, and Italy were gathered from 2014 to 2017. Researchers analyzed 450 PLWH looking at: demographics, HIV regimen, CD4, and viral load,
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HCV-genotype (GT), prior treatment history, and DAA used, fibrosis stage, cirrhosis, and prior liver decompensation. They also looked at comorbidities, active alcohol, illicit drug use, unstable housing and active psychiatric illness.

Overall, 415 patients (92.2%) achieved SVR. Of the 35 failures, 23 were HCV relapses, 9 were lost to follow-up, 2 discontinued DAA therapy due to side effects, and 1 stopped due to a severe comorbidity. Active psychiatric illness was associated with lack of SVR.

Conclusions: Among PLWH, active psychiatric illness was independently associated with lack of SVR to DAA. The researchers recommend exploring the role of drug adherence and/or drug interactions in this population.

Editorial Comments: People with psychiatric illnesses are often left out of studies. I particularly appreciate the researchers’ recommendations about exploring

the role of drug adherence and/or drug interactions in people with psychiatric illness. Click here to read the entire abstract and view the poster.

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Abstract #163 The Opioid Epidemic and Infectious Diseases: A Public Health Crisis - Sally Hodder

Summary: In the United States in 2016, there were more than 60,000 drug overdose deaths plus nearly 20,000 additional deaths from viral hepatitis. The number of acute hepatitis C cases has increased nearly 3-fold from 2010 to 2015; acute hepatitis B has increased 20%. Opioid-related infections are emerging at epidemic proportions.

Editorial Comments: This last abstract was more of a data review and call to action than a study. I included it because these days, hepatitis C will not be eliminated without addressing the opioid crisis. Click here to read the entire abstract.

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When hepatitis C makes the headlines, it is usually bad news. However, an article in Forbes had good news indeed. “The VA Will Eliminate Hepatitis C in Veterans by Year-End,” wrote John LaMattina on March 1, 2018. This isn’t just good news for the tens of thousands of U.S. veterans who were infected with hepatitis C; its good news for everyone. If we can eliminate hepatitis C in veterans using the VA health care system, we can eliminate hepatitis C in the rest of the U.S. I can’t think of a better place to start than with the women and men who serve this country.

Click here to read this article in its entirety.


Study Aims and Results
To review and compare the rate of opioid injection drug use with the rate of acute hepatitis C (HCV) infections. This analysis included the type of injection drug (heroin vs. prescription opioid drug), patient characteristics (male/female), and race. The annual surveillance records from 2004 to 2014 were analyzed from drug treatment centers and compared to reported cases of acute HCV.

The rate of acute HCV infection increased more than 2-fold from 2004 to 2014—a 133% increase. Admissions to drug treatment centers due to any injection drug use increased 76%. Admissions for heroin injection use increased 85%, and prescription opioid drug injection use increased 258%.

Conclusions
The findings correlate with the increase of acute HCV infections, the opioid epidemic, and admissions to drug treatment centers.

Editorial Comments
This study provides additional evidence that the opioid epidemic and the second HCV epidemic are linked. To control these twin epidemics more resources will be needed on a local, state and national level.

Article: Sofosbuvir-Based Direct-Acting Antiviral Therapies for HCV in People Receiving Opioid Substitution Therapy: An Analysis of Phase 3 Studies—J. Grebely, et. al.

SOURCE: Open Forum Infectious Diseases, Volume 5, Issue 2, 1 February 2018, ofy001, https://doi.org/10.1093/ofid/ofy001

Study Aims and Results
This study analyzed phase 3 treatment data of sofosbuvir-containing therapies to understand the outcomes among people who received opioid substitution therapy (OST) compared to people who did not receive OST. The study included HCV genotypes 1 through 6. There was a total of 4,743 people in the phase 3 studies of sofosbuvir-based therapies (interferon-free) who received OST—194 (4%) received either methadone (113 patients), buprenorphine (75 pts) or neither (6 pts). The OST patients were somewhat younger, and more likely to be male, treatment naïve, genotype 3, and cirrhotic. The treatment period was 8 to 24 weeks.

The analysis revealed that there were no or very little differences in the groups who received OST and those who did not: treatment completion rates (97% vs 99%), cure rates (94% vs 97%), relapse rate (0.5% vs 2.1%), side effects (78% vs 77%), or serious side effects (3.6% vs 2.4%). Additionally, the cure rates were similar for those with cirrhosis (99% vs 95%) and HCV genotype 3 (95% vs 95%).

Conclusions
Treatment with sofosbuvir-based therapies is safe and effective in people with HCV taking OST.

Editorial Comments
The current analysis provides additional evidence that people who receive OST can be successfully treated with DAA-based therapies.

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The Adverse Effects of Interferon-Free Regimens in 149,816 Chronic Hepatitis C Treated Egyptian Patients—D. Attia, et. al.


Study Aims and Results
This study was conducted to understand the rates of side effects during and after treatment with direct-acting antiviral (DAA) therapy among Egyptian patients. In this retrospective study, a total of 149,816 patients received DAA treatment. The breakdown of type of DAA treatment received included sofosbuvir plus ribavirin (21,835 patients), sofosbuvir plus simeprevir (24,215 pts), sofosbuvir plus daclatasvir (58,477 pts), sofosbuvir, daclatasvir plus ribavirin (45,188), and paritaprevir, ombitasvir plus ribavirin (101 pts). The treatment period was 12 to 24 weeks. The majority of patients treated were male (53%), HCV genotype 4 (90%), and the mean age was 54 years old.

In the analysis, a total of 1.7% of the 149,816 patients treated reported side effects. Of these, 68% were serious which means that slightly more than 1% had serious side effects. The majority of the serious side effects were anemia (low red blood cells) and hyperbilirubinemia (high levels of bilirubin). The two serious side effects were in the patients treated with sofosbuvir plus ribavirin. The combination of sofosbuvir plus daclatasvir had the lowest rate of side effects.

There were 0.02% of people in the analysis treated who developed liver cancer, and .06% died after treatment completion. Patients with cirrhosis showed the highest risk for serious side effects and death.

Conclusions
In this large group of patients treated with various combinations of direct-acting antiviral (DAA) medications the reported side effects were very low. The most common side effects reported were in the group treated with sofosbuvir plus ribavirin.

Editorial Comments
This very large study reaffirms that DAA medications have relatively few side effects with a couple of important caveats:

1. The highest rates of side effects were in the therapies that included ribavirin. Anemia is a well-documented side effect of ribavirin. Now, the vast majority of HCV treatment does not include ribavirin.

2. The current study reinforces the need to closely monitor people with cirrhosis while they are receiving HCV treatment (and afterward).
Imagine that you have a thirty-something year-old daughter or son. Your adult child is the parent of your grandchild, who is the love of your life. Tragedy has struck. Your adult child is a heavy drinker, and is now in the intensive care unit, fighting to live. Your child needs a liver transplant, and will die without one, leaving your grandchild minus a parent.

The heartbreaking reality is that your son or daughter might not receive a liver. For as long as liver transplants have been performed, most U.S. transplant centers require people with alcohol-related liver injuries to be sober for 6 months before they are listed as a candidate. The rationale for this is to avoid risking scarce organs on alcoholics who might relapse and harm the transplanted liver.

It’s complicated from both a medical and ethical standpoint. Although alcoholism is a medical diagnosis, alcohol use is perceived as a behavioral problem. Heavy alcohol use doesn’t necessarily mean that one is an alcoholic. Let’s say in this fictitious case, the adult child is your daughter. She recently had a baby, and is battling postpartum depression. Although alcohol is a depressant, she uses it to cope. The situation is complicated because as a female, her body doesn’t metabolize alcohol as well as most men’s bodies do. She binges, and is now in a hospital with acute alcoholic hepatitis.

There is no doubt in my mind about what I’d hope for: I’d want a transplant for my child, even if he or she isn’t sober. I believe in mercy.

Now imagine the same scenario, except this time your adult child was the victim of a motor vehicle accident. Life support will be stopped after all vital organs are removed. Your child is technically dead, but his or her organs will give life to others. One of the potential recipients may be dying of alcoholic hepatitis. How do you feel about that? How would you feel about it if your child’s death was caused by a drunk driver?

In this situation, my belief in mercy is tested. Fortunately, decisions about cadaver organ allocations are not left up to donors or recipients. Decisions are based on evidence and ethical standards.

It is essential that we have a fair system for the sharing of organs. The Organ Procurement and Transplantation Network (OPTN) brings together medical professionals, transplant recipients and donor families to develop our national policy. The U.S. organ transplant system is managed by the United Network for Organ Sharing (UNOS).

Years ago, UNOS opted not to recommend an exact timeframe for alcohol abstinence before liver transplants.
transplantation. Although specific guidelines determine who will be eligible for the next liver, the actual eligibility requirements differ among transplant centers. Some centers in the U.S. are now considering transplanting people with acute alcoholic hepatitis, and are relaxing their six-month abstinence from alcohol requirement.

**Second Chances** I said I wasn’t sure about how I’d feel if my child was the donor for someone in alcohol-related liver failure. I hope I’d feel generous, especially since I was once in a similar situation. In 1988, beaten by 20 years of severe clinical depression and post-traumatic stress syndrome, I attempted suicide. I was abusing alcohol and added a near lethal overdose of pills to the mix. The initial result was multi-organ failure. My liver failed, with enzymes above 18,000. My kidneys failed, and my heart was following. The transplant team was not keen about giving me a liver, and quite frankly, they were justified. I was 35 years old and had a 3-year-old daughter. I was told to say my good-byes, as I would not live another 24 hours.

In the end, I didn’t need the transplant. However, I did need multiple blood transfusions. That beautiful donated blood saved my life and gave me hepatitis C. I am grateful to those who donated the blood that gave me a second chance. I hope our organ allocation system continues to give second chances to others, despite the challenging situations they may find themselves in.

**Some Facts About Liver Transplantation** The liver transplant waitlist in the U.S. is increasing annually, growing by 7.6 percent in 2016. There are nearly 14,000 people waiting for a liver; roughly half will receive one.

For nearly two decades, hepatitis C-related complications were the leading indication for liver transplantation. Hepatitis C treatment using direct-acting antivirals (DAAs) is changing this. In 2016, alcoholic liver disease (ALD) took the lead, with non-alcoholic steatohepatitis (NASH) following closely behind. Transplant for hepatitis C declined 18 percent in 2016.[1]

**Ways You Can Make a Difference** Two awareness events that occur in April are Alcohol Awareness Month and National Donate Life Month. Learn the signs of alcohol abuse and how to help others. Increase the organ donor pool by being an organ donor. Urge families and friends to participate. **If you can, donate blood as often as you are eligible to.**

### References and Resources

- Alcohol Awareness Month [www.ncadd.org/about-ncadd/events-awards/alcohol-awareness-month](http://www.ncadd.org/about-ncadd/events-awards/alcohol-awareness-month)
- Donate Life America [www.donatelife.net](http://www.donatelife.net)
- National Donate Life Month [www.organdonor.gov](http://www.organdonor.gov)
- National Council on Alcohol and Drug Abuse [www.ncadd.org](http://www.ncadd.org)
- Organ Procurement and Transplantation Network [https://optn.transplant.hrsa.gov/](https://optn.transplant.hrsa.gov/)
- United Network for Organ Sharing (UNOS) [www.unos.org](http://www.unos.org)
Diarrhea

Do you have diarrhea? It may be as simple as altering eating and drinking habits.

Avoid spicy, greasy, and deep-fried foods.

• Avoid trigger foods and odors.

Nausea and vomiting. It may be as simple as altering eating and drinking habits.

• Unpleasant sensation at the back of the throat from general queasiness to a strong urge to vomit.

• Retching (vomit like contractions but no contents expelled).

Maintaining a Positive Attitude

• Use the tools and guides we send you to track your progress.

Don’t forget to check out the PackHealth – a free resource to help patients navigate their HCV treatment journey from applying for treatment to cure!

Do you have hepatitis C? Get support. Get answers.

• Get a personal Health Advisor to coach you on your journey.

• Develop a personalized plan – you set the goals, we’ll help you get there.

• Find answers and accountability to get the results you want.

• Use the tools and guides we send you to track your progress.

Enroll online: packhealth.com/hcv

As easy as 1-2-3!

1. Enter your contact info

2. Use promo code: HCV2017

3. Get 3 months of membership free!

Questions? Call us at 888-355-2362

8am-5pm | Monday-Friday


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