More of Lucinda’s Highlights from the 2018 International Liver Congress

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Last month, Alan Franciscus and I highlighted some of our favorite presentations from the 2018 International Liver Congress, hosted by the European Association for the Study of the Liver. Since there were many interesting presentations, we are summarizing more this month. Note: Conference posters and presentations are preliminary investigations, and are not conclusive until the data are published in a peer-reviewed journal.

**STUDY**

Abstract: THU-099 Lowering the upper limit of serum alanine aminotransferase levels may detect significant liver disease in the elderly – H. Schmilovitz-Weiss, et al.

**Study Aims and Results:** A common first blood test used to assess liver injury is measuring serum alanine aminotransferase (ALT), which is a liver enzyme. Some experts believe that the current normal ranges for ALT may be too high. If so, one may have liver injury despite the test result being technically normal.

In this study, researchers compared normal ALT results between previous normal ranges and newly suggested ranges of 49,634 individuals aged ≥ 65 years. The standard normal ranges were 42–45 IU/l for men and 26–34 IU/l for women. The newly...
suggested normal ranges were 15–42 IU/L for men and 10–26 IU/L for women.

Using the standard ranges, researchers found that people whose ALTs were on the high side of the normal range had higher rates of chronic liver disease. They identified 2022 people with chronic liver disease although they had normal ALT levels; 366 had cirrhosis.

Conclusions: These researchers concluded that lowering the current normal ranges of serum ALT might help to identify significant liver disease in the elderly.

Editorial Comments: If your liver enzymes consistently fall in the upper range of normal, talk to your health care provider. Ask if you need to be referred to a liver specialist.

STUDY
Abstract: THU-100 Hepatitis C patients with HIV co-infection demonstrate unique liver-related complications and health behaviors compared to HCV mono-infected patients – M. Lu, et al.

This study gathered data on 14,545 hepatitis C-positive (HCV) people, of which 584 (4%) were co-infected with HIV. The coinfected individuals were significantly younger and more likely to be male, African American, low-income, and publicly insured than those who had HCV monoinfection. The HIV/HCV individuals were less likely to see a liver specialist, receive HCV treatment, and had more comorbidities, fibrosis/cirrhosis, hepatocellular carcinoma (liver cancer), and increased mortality. Among 5008 survey respondents (4885 HCV and 123 HIV/HCV), coinfected individuals were more likely to report substance use and sex with multiple partners.

Conclusions: People who are coinfected with HIV/HCV are more at risk of multiple types of health problems than those with HCV monoinfection.

Editorial Comments: People with HIV/HCV coinfection face serious medical complications and may be falling through cracks in the health care system. This large study identifies key issues that need to be addressed in the public and private health care sectors.

STUDY

Study Aims and Results: The purpose of this study was to investigate the impact of HIV on clinical characteristics and mental health in hepatitis C-positive patients.

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More of Lucinda’s Highlights from the 2018 International Liver Congress — CONTINUED FROM PAGE 2

Researchers looked at 11 years of data (1993–2014) collected from 2,318 people (37% of them HIV/HCV coinfected). More than half died from lymphoma, with no significant differences observed between HIV monoinfected and HIV/HCV coinfected. The survival rate was better for HL than NHL (86.6% after 2 years of diagnosis vs 32.5%).

Conclusions: The incidence of lymphoma (Hodgkin and non-Hodgkin) was up to 15 times higher among people with HIV monoinfection and HIV/HCV coinfected compared with the general population. The researchers hypothesize that HCV treatment will have an important role in reducing risk of lymphoma.

Editorial Comments: Since there was no significant differences between HIV monoinfected and HIV/HCV coinfected, I am not sure how the researcher came to the conclusion that HCV treatment will have an important role in reducing risk of lymphoma. Intuitively, it makes sense, but we need more data.

STUDY


Study Aims and Results: This Spanish study evaluated the incidence of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) in people coinfected with HIV/HCV, and compared them with the general population. Researchers looked at 11 years of data (1993–2014) collected from 2,318 people (37% of them HIV/HCV coinfected). More than half died from lymphoma, with no significant differences observed between HIV monoinfected and HIV/HCV coinfected. The survival rate was better for HL than NHL (86.6% after 2 years of diagnosis vs 32.5%).

Conclusions: There is a clear association between HCV and risk of extrahepatic manifestations. These researchers recommend HCV treatment in order to reduce EHM risk.

Editorial Comments: I am curious about the finding that non-Hodgkin’s lymphoma and diabetes were not more prevalent among people with untreated HCV. This isn’t consistent with earlier studies. For more about lymphoma, see the next abstract (THU-418). The abstract after that (FRI-368) discusses more about HCV-associated cryoglobulinemia.
More of Lucinda’s Highlights from the 2018 International Liver Congress  — CONTINUED FROM PAGE 3

**STUDY**


Study Aims and Results: The goal of this Spanish study was to evaluate the long-term impact of direct-acting antiviral (DAAs) in patients with HCV-related symptomatic or asymptomatic cryoglobulinemia (cryo). This study enrolled 94 patients, of which 50 had symptomatic and 44 had asymptomatic cryo.

Conclusions: Although this study found that patients who were treated for HCV experienced significant improvements in both clinical and immunological response, cryo persisted in more than 20% of patients for 2 years after HCV elimination. Cryo relapses also occurred. No patients with asymptomatic cryo developed symptomatic cryo during follow-up. Researchers recommended a longer monitoring period for these patients.

Editorial Comments: Although this is a small study, I think it is valuable. Approximately 40% to 60% of patients with chronic HCV have circulating cryoglobulins, symptomatic cryo (vasculitis) is only observed in about 10% of HCV patients. Two features of this study stand out:

- No one with asymptomatic cryo developed symptomatic cryo during follow-up. This adds more evidence to the long-term benefits of HCV treatment.
- Perhaps this study offers insight into why some patients continue to have medical problems after HCV treatment. I hope we see more research on this subject.

**STUDY**

Abstract: THU-412 Among 1945–1965 birth cohort patients with at least one additional hepatitis C virus risk factor, one in eight were positive for HCV antibody: an underserved safety-net population experience – G. Hirode, et al.

Study Aims and Results: This study conducted in an urban hospital (Oakland, CA) evaluated a pilot program that integrated HCV screening into an outpatient endoscopy unit. Using the U.S. Preventative Services Task Force’s HCV screening guidelines, this study screened adults undergoing outpatient endoscopy from 2015 to 2017. None of the 1,752 adults evaluated were previously tested for HCV, of which 67% were found eligible.

Conclusions: Among those who completed HCV testing, the prevalence of HCV antibody-positive results was 3.4%. The highest occurrence of positive HCV-antibody results occurred in baby boomers (born — CONTINUED ON PAGE 5
1945–1965) who had other risk factors (HIV positive, hepatitis B virus positive, history of intravenous drug use, previously incarcerated, or blood transfusion pre-1992). HCV prevalence was 12.5% in baby boomers with other HCV risk factors; the prevalence was nearly 27% in U.S.-born baby boomers with other HCV risk factors.

Editorial Comments: The part of this study that I find most noteworthy is the high number of adults who had not been previously screened for HCV. This shows the value of creating safety-net programs in order to identify people who meet HCV screening criteria, and might not otherwise be screened.

STUDY


Study Aims and Results: There is strong evidence of HCV transmission in HIV-positive men having sex with men (MSM), especially those engaging in at-risk sexual practices such as chemsex (use of stimulants to enhance sexual experience), or other practices that may cause mucosal trauma (tissue damage). This French study sought to assess the risk in HIV-negative MSM.

Data were collected from 86 MSM (63 HIV+, 23 HIV-) between 2014 and 2017, identifying 92 acute HCV infections (71 first infections, 21 reinfections). The HCV risk factors included IV drug use (34%), nasal drug use (31%), sex party (66%), fisting (22%), and any drug or sexual risk (83%).

Conclusions: There was a significant increase in the number of cases of sexually transmitted HCV infections in MSM, both in HIV-positive and in HIV-negative.

Editorial Comments: These findings underscore the importance of education and harm reduction, screening of people at risk for HCV and other infectious diseases, and increasing efforts to enable access to care and HCV treatment. By doing so, we keep progressing toward the goal of eliminating viral hepatitis, as well as to help those affected by hep B and C.

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More of Alan’s Highlights from the 2018 International Liver Congress

STUDY

Abstract: GS-018 Long-term follow-up of patients with chronic HCV infection and compensated or decompensated cirrhosis following treatment with sofosbuvir-based regimens - A. Mangia, et al.

Study Aims and Results: The study followed patients treated with sofosbuvir-based therapies to understand how treatment and cure affect liver-related health and the risk of further liver disease progression and death.

As of October 5, 2017, 1,564 cirrhotic patients with sofosbuvir-containing therapies were cured and enrolled in the study.

In the long-term – 99.9% of the patients remained cured. The majority of patients with compensated and decompensated cirrhosis showed an improvement in their liver-related disease. So far, there have been 20 liver transplantations and five liver-related deaths. There were 55 cases of liver cancer that mostly occurred in the patients with decompensated cirrhosis. The majority of cirrhotic patients showed improvement in their liver disease.

Conclusion: In this registry of people cured with sofosbuvir-based regimens, the long-term outcomes show improvement in liver-related outcomes. However, people with more advanced liver disease before treatment had liver disease progression even after being cured of HCV.

Editorial Comments: This study is notable because it adds to our knowledge that successful direct-acting antiviral(DAA) treatment has beneficial long-term outcomes.

STUDY

Abstract: LBO-008 A phase 3b, open-label, randomized, pragmatic study of glecaprevir/pibrentasvir +/- ribavirin (RBV) for HCV genotype 1 subjects who previously failed an NS5A inhibitor + sofosbuvir (SOF) therapy - A. Lok, et al.

Study Aims and Results: To find out if re-treatment with glecaprevir plus pibrentasvir (Mavyret) provided a cure for genotype 1 patients previously treated with an NS5a—an HCV containing inhibitor—plus sofosbuvir (plus/minus ribavirin) treatment regime but who did not achieve a cure. This is an ongoing study. There are four arms in this study; two non-cirrhotic and two cirrhotic arms. Each arm has a 12 and 16-week arm, but one arm of

There were 55 cases of liver cancer that mostly occurred in the patients with decompensated cirrhosis. The majority of cirrhotic patients showed improvement in their liver disease.
the cirrhotic group received ribavirin. There was a high rate of resistant-associated variants in all of the re-treatment arms.

The undetectable HCV RNA results at 4-week post-treatment was 95% (132 of 139 patients). However, the 4-week post-treatment result was 86% in the arm that included ribavirin.

**Conclusion:** 12- and 16-week re-treatment using Mavyret on patients who previously failed treatment using an NS5a plus sofosbuvir produced high 4-week post-treatment HCV RNA undetectable rates. The addition of ribavirin did not add additional benefits. These are preliminary results.

**Editorial comments:** These results are encouraging and I am looking forward to the entire clinical trial results. However, adding a different DAA has been shown to be more effective to treat drug resistance treatment failures. Also, including ribavirin to re-treatment does not appeal to the majority of patients if there is an effective alternative.

**STUDY**

Abstract: THU-121 Track, Trace & Treat: Results from a retrieval strategy to identify lost to follow-up chronic hepatitis c patients - I. Munsterman, et al.

**Study Aim and Results:** A chart review was conducted to identify patients lost to follow-up in Netherland’s Nijmegen Medical Center.

There were 104 patients identified that needed follow-up care including viral load testing or treatment initiation.

**Conclusion:** A follow-up chart review identified patients lost to follow-up and who were re-engaged into medical care.

**These results are encouraging and I am looking forward to the entire clinical trial results. However, adding a different DAA has been shown to be more effective to treat drug resistance treatment failures.**

**Editorial Comments:** This is an encouraging study that shows reviewing records and contacting patients resulted in getting people back into medical care and treatment. It is common that some patients are lost to care in practices and clinical studies. Finding and re-engaging patients is an important strategy to eliminate HCV.

**STUDY**

Abstract: LBP-0231 The percentage of patients with HCV infection in need of a liver transplant is rapidly declining while their survival after transplantation is improving: a study based on European Liver Transplant Registry – G. Perricone, et al.

**Study Aims and Results:** The objective of the study was to understand the effect of direct-acting antiviral (DAA) treatment on the hepatitis C (HCV) liver transplants and improved outcomes post-transplant. The study reviewed 36,000 liver transplantations for hepatitis B (HBV), alcoholic liver disease (ALD) or non-alcoholic steatohepatitis (NASH). The study reviewed the European Liver Transplant Registry between January 2007 – June 2017. I am only including the second-generation period of the DAA period (2014 – June 2017).

Liver transplantations for HCV decreased by 21% during the first half of 2014 to 11% during the first
More of Alan’s Highlights from the 2018 International Liver Congress — CONTINUED FROM PAGE 7

half of 2017. The survival of HCV patients with HCV post-transplants improved and was comparable to post-transplant HBV patients.

NASH transplants increased from 1% to 6% and transplants due to ALD remained the same.

Conclusion: In Europe, the number of liver transplants has declined since the introduction of DAA therapy.

Editorial Comments: More good news about the widespread use and effectiveness of DAA therapy.

STUDY


Study Aims and Results: To understand the transplant outcomes of Hispanics compared to whites. The study analyzed data from the United Network for Organ Sharing (UNOS). Included in the transplant data were 19,217 Hispanics, 92,892 whites, 11,534 African Americans, 5,914 Asians and 1,638 people listed as “others.”

Transplantation waitlist removal was 26% higher for Hispanics due to death or deterioration of health. Transplantation rates for Hispanics were 22% lower compared to whites. The 1-year and 5-year survival were similar for Hispanics and whites. As reported in previous studies, African Americans had the lowest post-transplant survival.

Conclusions: Hispanics had a higher removal rate from transplantation waitlists compared to other races. The good news is that their 1- and 5-year survival rates were similar to whites.

Editorial Comments: This is an alarming study. I need more information to understand the differences. I hope the journal article will shed more information.

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STUDY

ABSTRACT: FRI-374 The impact of sustained virologic response on severe fatigue in patients with chronic hepatitis C: the role of HCV viremia and co-morbidities - Z. Younossi, et. al.

Study Aims and Results: To assess the effect of being cured of HCV on fatigue. Patients enrolled in phase 2 and phase 3 sofosbuvir-based clinical trials were given a FACIT-F instrument fatigue scale test before beginning treatment and at post-treatment week 12. There were 6,113 patients (mean age 53 yo, 56% male, 40% employed, 35% cirrhotic, 28% reported a history of anxiety, 43% had a history of depression, 15% had type 2 diabetes, and 7% were coinfected with HIV). After taking the FACIT-F fatigue scale before treatment, 1,427 of the participants tested for the most severe fatigue.

After cure: In the people who had severe fatigue before treatment, 42% continued to have severe fatigue, 45% of patients improved to moderate fatigue, and 13% improved to minimal or no fatigue. The patients who were more likely to have improved scores were younger, less likely to have cirrhosis and lower rates of depression, anxiety, sleep disorders, diabetes and HIV coinfection.
Conclusion: Being cured of HCV reduced the symptoms of fatigue but managing the other symptoms of the patients is equally important to reducing fatigue post-treatment and cure.

Editorial Comment: Hepatitis C is a disease that affects the entire body, not just the liver. We need to attend to healing the whole body, not just the liver.

BRIEFLY…
What I like about EASL is that it provides a worldview of hepatitis C and liver-related issues. This year’s conference was exceptional. There were thousands of posters and presentations from all over the world. Listed below are three posters I found interesting and provide a glimpse of hepatitis C in countries that are usually not covered in the press.

**STUDY**
Abstract: THU-075 hepatitis C screening within the National Elimination Program in the country of Georgia - A. Gamkrelidze, et. al.

Summary: The country of Georgia is a testing ground for the elimination of hepatitis C (HCV). The prevalence of HCV is 7.7% and the government has started a campaign to identify 90% of people infected with hepatitis C and treat and cure 95%. There are 602 free testing centers across the country.

The testing results were available: as of November 2017, 1.2 million antibody screening tests have been conducted and 9.3% tested HCV antibody positive. The majority (79%) of positive results were among people aged 30-59 years old.

Note: They are also well on their way to treating many Georgians with DAA therapies. I will cover this in a separate HCV Advocate issue.

**STUDY**
Abstract: THU-104 The first result from the general population hepatitis screening in Mongolia: 38% of 40–65-year-olds screened and anti-HCV prevalence of 15.6% among 40–65-year-olds - B. Dashtseren, et. al.

Summary: The goal in Mongolia is to test all Mongolians for HCV by 2018 and eliminate HCV by 2020. The estimated prevalence of HCV in Mongolia is 8.5%. The first stage started in June 2017 to test all adults aged 40-65-years of age. The number of people aged 40-65-years old who tested positive for HCV antibodies was 116,092 (15.9%).

**STUDY**
Abstract: PS-090 Direct-acting antiviral treatment in sub-Saharan Africa: A prospective trial of ledipasvir/sofosbuvir for chronic hepatitis C infection in Rwanda (The SHARED Study) - N. Gupta, et. al.

Summary: The SHARED study was initiated to evaluate the safety and efficacy of ledipasvir/sofosbuvir (Harvoni). 300 adults with HCV genotype 1 and 4 were treated for 12 weeks. The majority of participants were women, and were genotype 4—47 pts (17%) had mixed genotypes 1 and 4. Ten percent were coinfected with HIV.

164 patients have completed treatment and had follow-up data. The cure rate was 87% (142 of 164 patients). The majority of treatment failures were in the people with mixed genotypes and high viral loads.
Hepatitis C in Denver Is Booming, but a Pill That Tells Doctors Whether You’ve Taken it Could Change That

The Denver Post reported about the development of technology that will tell doctors whether a patient took their medicine. Researchers at Denver Health are conducting a study of a pill that contains hepatitis C medicine and a microscopically small sensor that, when it reaches the stomach, it sends a signal to the internet. This signal enables health care providers to see when someone hasn’t taken their medicine, and follow-up with a reminder. Then the sensor dissolves harmlessly.

Genghis Khan’s Mongol Horde Probably Had Rampant Hepatitis B

This past month a story about hepatitis B has been dominating the headlines. A team of German scientists sequenced genomes of hepatitis B virus (HBV) and found that the virus has been circulating Europe for at least 7000 years. A particularly engaging version of this story is speculation that Genghis Khan and his army may have had HBV (reported by ARS Technica). Click here to read this story.
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