EASL 2013: DAAs Look Good, but Challenges Remain—Part 2

—Liz Highleyman

INTERFERON ADD-ONS

For people who can wait a bit longer, several studies at EASL showed good outcomes when adding more effective and better-tolerated second-generation DAAs to interferon-based therapy.

Focusing on genotype 1, the Phase 3 STARTVerso trial (abstract 1416) evaluated the HCV protease inhibitor faldaprevir (formerly BI 201335) plus pegylated interferon/ribavirin in 656 previously untreated patients. Two-thirds had subtype 1b, about 60% had unfavorable IL28B patterns, and 6% had cirrhosis. They were randomly allocated to receive 120 mg or 240 mg once-daily faldaprevir for 12 or 24 weeks, with pegylated interferon/ribavirin continued for 24 or 48 weeks based on early treatment success, or else interferon/ribavirin alone for 48 weeks.

In an intent-to-treat analysis, 79% of patients taking 120 mg faldaprevir and 80% taking 240 mg achieved SVR12, compared with 52% in the control arm. Most (88%) had early treatment success and stopped all treatment at week 24; of these, 86% and 89% achieved SVR12. People with HCV 1a did not respond as well as those with 1b due to more relapses (69% vs 84% taking 120 mg, 76% vs 83% taking 240 mg). Patients with favorable IL28B also did better. Treatment was generally safe and well-tolerated, with 4% to 5% discontinuing therapy due to adverse events. While the two faldaprevir doses had similar overall efficacy, the lower dose was better tolerated and caused less bilirubin elevation.

The Phase 3 QUEST-2 trial in Europe (abstract 1413) evaluated once-daily simeprevir added to pegylated interferon/ribavirin in 391 treatment-naive patients; 40% had subtype 1a, 30% had the favorable IL28B CC pattern, and 8% had cirrhosis. The study found that 81% of simeprevir recipients achieved SVR12, compared with 50% of those using interferon/ribavirin alone. Most (91%) met response-guided therapy criteria allowing them to finish treatment at 24 weeks. The simeprevir SVR12 rate reached 96% for patients with favorable IL28B, but fell to 65% for people with cirrhosis.

The parallel QUEST-1 trial in the U.S. (abstract 1425) showed similar response rates, but more difference between HCV subtypes 1a and 1b (71% vs 90%). Adverse event and discontinuation rates were similar with both regimens, indicating that simeprevir does not reduce the tolerability of interferon-based therapy.

Adding sofosbuvir to pegylated interferon/ribavirin also improved response in the Phase 3 NEUTRINO trial (abstract 1411), which enrolled 327 previously untreated patients with HCV genotypes 1 (89%), 4 (9%), 5, or 6. Most (70%) had unfavorable IL28B variants and 17% had cirrhosis. Everyone was treated for 12 weeks with no response-guided therapy.

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**Article:** The Negative Impact of the War on Drugs on Public Health: The Hidden Hepatitis C Epidemic.

*Source: Report of the Global Commission on Drug Policy, May 2013*

A global commission on drug policy, chaired by George Shultz (former U.S. Secretary of State), included Kofi Annan, (former Secretary General of the United Nations), Richard Branson (Virgin Group founder), seven former presidents, and other highly-regarded world leaders. The report is a scathing indictment of how the “war on drugs” and repressive drug policies are failing to lower hepatitis C transmission rates.

This report is a call to action to reform governmental drug policy. Recommendations include the decriminalization of drug use, and implementation of programs that provide access to safe drug programs that reduce hepatitis C transmission.

**The Bottom Line:** This is best captured with an excerpt from the report’s executive summary: “The silence about the harms of repressive drug policies has been broken – they are ineffective, violate basic human rights, generate violence, and expose individuals and communities to unnecessary risks. Hepatitis C is one of these harms – yet it is both preventable and curable when public health is the focus of the drug response. Now is the time to reform.”

**Editorial Comment:** It is hard not to get emotional about this, but fortunately, the merits of this report need not be judged by feelings and opinions. Data support that the “war on drugs” doesn’t work and sensible humanitarian practices do. If you feel a call to act, work on your local level to change public drug policy. *The Harm Reduction Coalition* is a good source for more information.

**Article:** Knowledge and Attitudes about Hepatitis C Virus (HCV) Infection and Its Treatment in HCV Mono-Infected and HCV/HIV Co-Infected Adults – E.Y. Chen et al.

*Source: Journal of Viral Hepatitis published online April 2013*

This cross-sectional study surveyed 292 people to assess the relationship between HCV knowledge and attitudes towards HCV in patients from an urban, indigent population with HCV and HIV/HCV co-infection. The study also surveyed 87 people who took part in educational sessions before and after participation to assess changes in knowledge and attitudes.

In the cross-sectional survey, the mean knowledge of HCV was low (<50% of the total possible score). Attitudes and knowledge gaps were similar in those who were mono-infected and co-infected. Common attitudes of patients were: 57% feared the consequences of HCV on their life, 37% felt HCV was not fatal, 27% did not believe they needed HCV medication, 21% felt ashamed of having HCV and 16% felt HCV treatment was not important. Those who participated in the education session had improved knowledge but their attitude scores remained unchanged.

**The Bottom Line:** There is a clear need to find ways to effectively change attitudes towards HCV infection and treatment.

**Editorial Comment:** This study underscores the need for continued education. I’d be interested in surveying attitudes after patients participated in an HCV support group or engaged in HCV advocacy, helping others.

**Article:** Hepatitis C in the United States – S. D. Holmberg et al.

*Source: New England Journal of Medicine May 16, 2013; Pages 1859-1861*

Epidemiologists at the Centers for Disease Control and Prevention’s (CDC) Division of Viral Hepatitis wrote this article, using data collected by the CDC from two large HCV studies for the
Technically Speaking: Apps and Hepatitis C

—Lucinda K. Porter, RN

Hepatitis C (HCV) and brain fog go together like sunburn and blistering—you can have one without the other, but when you have both, it is frustrating. Add in HCV treatment, and brain fog gets so thick it would depress the Dalai Lama. Living with HCV and going through three treatments has taught me a few things about brain fog.

1) Acceptance makes brain fog more tolerable; resistance makes it worse.

2) Physical activity, meditation, adequate sleep, good nutrition, pleasure and humor improve thinking ability.

3) Memory devices and tools help us stay organized and can act like memory back-ups.

I recently finished HCV treatment and my brain feels like it is coming back. During therapy, trying to remember things was like trying to push a car uphill on ice; I just couldn’t do it. I’d forget important things, like taking my pills. Sometimes I’d take my pills and then in the seconds between taking them and recording it, I’d wonder if I had taken my pills. I’d have to count the remaining pills in the bottle, and if there were a lot of pills, I’d have to count several times. Even a weekly pill container wasn’t foolproof; once I took my PM pills in the morning.

Acceptance helped, but so did electronic devices. This month I review some of my favorite mobile device apps (applications). Before I do, let me say the following:

- Not everyone uses a smart phone or a tablet; I apologize to those who feel left out this month.
- The apps I reviewed were tested on my iPhone/iPad (iOS). Whenever possible, I tried to find apps that were available on other devices, but most of these are iOS apps.
- I only tested free apps. For a small price, many apps offer additional features and are advertisement-free.
- I don’t receive any benefits, monetarily or otherwise from the products mentioned here.
- I am not a nerd; I am a “woman of a certain age,” and if I can use apps on my mobile devices, anyone can.
- Some people experience increased stress when using electronic devices, alarms, and other aids that are supposed to make our lives easier. If this is you, keep life simple and find equivalent memory tricks that work best for you. There is nothing wrong with pencil and paper.

Apps number in the hundreds of thousands; I only review a handful. If you want to look at other choices, I suggest searching by ratings. Find one or two you like. Read the reviews, both the best and the worst. Download one or two and try them out. You can always uninstall an app if it doesn’t meet your needs.

Words of Advice: 1) Be sure to password protect your information. My mobile devices are all password protected. 2) Some other apps require signing in using email or Facebook account. Facebook knows enough about me, and I limit what I use through that account.

MEDICATION REMINDERS

The current treatment for hepatitis C involves multiple pills at varying times. Most computers and cell phone clocks can be programmed to remind you to take medications, making an app unnecessary. However, medication reminder apps have more features than just a clock, and can be quite helpful.

My favorite is GenieMD. It has a good drug database and
you can upload information to your medication reminder. If you are taking drugs that may interact, this app alerts you. Although it does include over-the-counter drugs in its database, it does not include herbs and supplements. For instance, St. John’s wort may interact with Incivek and Victrelis, and it wasn’t listed.

GenieMD is much more than a medication reminder. It can remind you about medical appointments, prescription refills, to drink more water, to take your blood pressure, and to exercise. This app is packed with patient information, although I was not thrilled with some of the hepatitis C information. It was too simplistic and potentially misleading. Otherwise, this app is fabulous.

Other features of GenieMD include:

- Personal health record-keeping. The user can load all personal information into this app and always have it on hand for medical appointments. Be sure to password-protect your information.
- Drug leaflets; food interaction information
- Symptom checker
- Discharge instructions
- Detailed information about medical procedures
- Guides to healthy living. You can calculate your Body Mass Index, get a UV Index, forecast pollen levels, and much more.

RxmindMe Prescription for iOS is another good app. It can be programmed for medication reminders, doctor appointments, and any other items you want to remember. Using the FDA drug database, you can download your medication information, add the Rx number, pharmacy, and set up an alert to request a prescription renewal. You can even take a picture of a pill or the prescription label. I love the photo feature because although we are always supposed to leave our pills in their original containers, let’s face it, sometimes we don’t. If you forget what the pill looks like, the photo will help.

"Words of Advice:

1. Be sure to password-protect your information. My mobile devices are all password protected.
2. Some offer apps require signing in using email or Facebook account. Facebook knows enough about me, and I limit what I use through that account."

The only problem I have with RxmindMe is that Incivek and Victrelis were not listed in the database at the time I tested this app. These drugs have been out for two years and should be in the database. However, these drugs can be manually added.

You can track when you took your pills, and this extra step really helped me remember that I took my medications. RxmindMe is compatible with Apple’s VoiceOver screen reader. I downloaded the iPhone version to my iPad and it worked well, especially after I enlarged the screen.

Another worthwhile app is Epocrates Rx. The information is thorough, current and easy to access. It has a great drug interaction checker and pill identifier. It is also available for Android and Blackberry.

One of my favorite apps was the Hepatology Animated Pocket Dictionary. Unfortunately, the free version lists liver diseases beginning with the letter “A” and stops at biliary atresia. The full version is $6.99. Alternatively, there are free animations on YouTube. To see how HCV replicates, visit Hepatitis C Lifecycle.

For healthcare providers and those who say they are, the Viral Hepatitis app offers great hepatology education modules. For those on liver transplant lists, there are free, easy to use, MELD calculator apps.

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**Healthwise**

**MEDICAL HISTORY**

For Android and iOS users, there is iTriage. This app is packed with info. It has some of the same features as GenieMD, but offers some other options. The medical content is reliable, but the hepatitis C information was minimal. The other downsides are it is missing a medication reminder, and Incivek and Victrelis were not listed in the drug database.

iTriage has decision support tools to research problems and helps answer the two most common medical questions: “What could be wrong?” and “Where can I go?”. If you need medical support, it directs you to nearby facilities. You can sort facilities by distance or ratings, and locate them on maps. iTriage offers a pharmacy discount program.

**WATER REMINDER**

The Daily Water app reminds you to drink water and tracks it for you. The manufacturer of Daily Water makes other good apps worth checking, such as fitness apps and those that monitor other medical conditions.

**GENERAL MEDICAL**

My favorite is WebMD. This app is beautifully designed and easy to use. It is also available for Android & Kindle Fire. The HCV information is better than on other apps I tried. The drug information is current. The app can be personalized, although there is no drug reminder or interactions checker. I am a bit nervous about info that can be tracked and there is lots of advertising on this app.

Other apps to try are Urgent Care - Doctors and Nurse Standing by 24/7 (available on Android) and Everyday First Aid Lite. The free lab values reference apps were all disappointing. The best I could find was Mayo Clinic’s Mayo Medical Laboratory, tailored more for the medical provider than for the consumer.

**SLEEP**

I was disappointed with the sleep-related apps I tried. Alarm Clock Sleep Sounds, Sleep Machine Lite and Sleep Pillow Sounds were okay.

**RELAXATION, INSPIRATION, MOTIVATION**

Personally, I think using an app to relax misses the point. However, hepatitis C treatment creates an unusual state of mind, and sometimes we just can’t settle down. My favorite is Pandora, which provides music for multiple devices. The Deep Relax app and the Relax Melodies Oriental app are worth checking out. I also liked the Grateful (available for Android) and Inspiring Quotes 5000 apps.

There are many other types of apps that will support good health. You name it; there is probably an app for it. The fitness apps are too numerous to list. There are interval trainers, sit-up reminders, apps for yoga, tai chi, etc. If you have a fitness goal, find an app that fits your needs.

There are humor apps, nutrition apps, and apps to entertain. YouTube provides a fountain of information and distraction, and is available on all mobile devices.

Memory Aid apps such as password keepers are indispensable. I use SecureSafe, which is available on Android. I also have the Find iPhone app on my iPad and iPhone because if I lose one, I lose my memory. I don’t know what I would do if I lost both.

My final advice is for those taking ribavirin. Be sure not to use computers and mobile devices when feeling short-tempered. Hammers should never be within reach of any electronic device.

Lucinda K. Porter, RN, is a long-time contributor to the HCV Advocate and author of Free from Hepatitis C and Hepatitis C One Step at a Time (September 2013). Her blog is http://lucindaporterrn.com
SVR12 rates were 89% for genotype 1, 96% for genotype 4, and 100% for the seven patients with genotypes 5 or 6. Cirrhosis, unfavourable IL28B, and higher baseline viral load predicted poorer response, but all achieved SVR12 rates of at least 80%, which presenter Eric Lawitz noted “is the highest reported in cirrhosis yet.” Treatment was safe and well-tolerated with only 1% reporting serious adverse events.

Further back in the pipeline, Merck’s second-generation protease inhibitor MK-5172 increased sustained response rates in a Phase 2 study of 332 previously untreated genotype 1 patients without cirrhosis (abstract 66). About 60% had subtype 1a and 73% had unfavorable IL28B patterns. Participants were randomly assigned to receive once-daily MK-5172 at doses of 100, 200, 400, or 800 mg with pegylated interferon/ribavirin for 12 weeks, continuing pegylated interferon/ribavirin alone through week 24 or 48 depending on early response. The control group received the latest standard-of-care, boceprevir plus pegylated interferon/ribavirin.

SVR24 rates in the MK-5172 arms ranged from 86% to 92%, with no clear dose-response effect, compared with 54% in the control group (many of whom were still undergoing follow-up). Focusing on the 100 mg dose selected for further development, 91% of recipients were eligible for shorter response-guided therapy, and in this group 90% achieved SVR24. IL28B genotype had a minimal effect and HCV subtype had a small influence. Rates of serious adverse events were similar in the combined MK-5172 arms and the boceprevir arm (9% vs 8%), but MK-5172 recipients were half as likely to discontinue therapy due to adverse events (7% vs 14%). Some patients taking MK-5172 developed elevated bilirubin or transaminase levels, and a data safety board recommended that people in the 400 and 800 mg arms lower their dose for this reason.

Another Merck protease inhibitor, vaniprevir (formerly MK-7009), also increased pegylated interferon/ribavirin cure rates for a more challenging group, previously treated genotype 1 patients with compensated cirrhosis (abstract 106). The cirrhotic cohort in this Phase 2b study had 74 patients, including 25% prior null responders, 42% with subtype 1a, and 80% with unfavorable IL28B. They were randomly allocated to five treatment arms, receiving 300 mg or 600 mg twice-daily vaniprevir plus pegylated interferon/ribavirin for 24 or 48 weeks, or pegylated interferon/ribavirin alone for 48 weeks.

Vaniprevir SVR24 rates ranged from 53% to 77%, compared with just 14% in the control arm. These were somewhat lower than the 67% to 84% seen in a previous cohort of non-cirrhotic patients. The lower vaniprevir dose and shorter treatment duration were less effective. HCV subtype had a notable effect, with 83% of 1b patients but just 50% of 1a patients achieving SVR24 in the combined vaniprevir 600 mg arms. Vaniprevir was generally safe and well-tolerated, with 4% to 7% experiencing serious adverse events, comparable to the frequency in the control arm.

Turning to genotypes 2 and 3, the COMMAND trial (abstract 1418) evaluated adding once-daily daclatasvir to pegylated interferon and fixed-dose ribavirin for 12 or 16 weeks in 151 treatment-naive patients. One-third of genotype 2 patients and 40% with genotype 3 had the favorable IL28B CC pattern, and nearly 25% of genotype 3 patients (but only one with genotype 2) had cirrhosis.

Here too, people with genotype 2 responded better than those with genotype 3. In the genotype 2 group, 83% in both the 12-week and 16-week arms achieved SVR24, compared with 63% who received pegylated interferon/ribavirin alone for 24 weeks. In the genotype 3 group, however, more patients relapsed, resulting in SVR24 rates of 69%, 67%, and 59%, respectively. Adding daclatasvir was generally safe and well-tolerated, with few serious adverse events or early discontinuations for this reason.

In summary, several next-generation DAAs added to pegylated interferon produce cure rates in the 80% to 90% range, can often shorten treatment to three to six months (down from six months to a year), and generally do not cause more side effects than pegylated interferon and ribavirin alone.

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Myths about Weight Loss

—Alan Franciscus, Editor-in-Chief

It is well-known that nutrition is one of the best strategies for staying healthy (in general) and especially for people living with hepatitis C. We also know that obesity can increase the rate of HCV disease progression and the development of steatosis or fatty liver. Both obesity and steatosis have been linked to lower HCV treatment response, so in order to optimize treatment outcome, eating a healthy diet and being physically active should be a priority for everyone living with hepatitis C.

Healthy eating is difficult especially with all the misinformation out there. But finally we have some good solid scientific data from a well-known and credible resource that exposes many of the myths and presumptions about weight loss and obesity. The article “Myths, Presumptions and Facts about Obesity” by K. Casazza and colleagues was published in the New England Journal of Medicine earlier this year (June 6, 2013 Vol. 368 No. 23).

The authors conducted searches on the internet which included media and scientific literature. Next, the myths were compared to what scientific evidence was available. The authors identified six myths, six presumptions and nine facts supported by scientific evidence to help formulate “sound public health, policy, or clinical recommendations,” to help everyone trying to eat healthily and lose weight. This article will focus on the 6 myths identified and the actual facts:

1. **Myth:** Small changes over a long period of time will result in a large weight loss. **Example:** walking a mile a day will lead to losing about 50 lbs. in a 5 year period.
   **Fact:** Walking a mile a day would only lead to about a 10 lb. weight loss. But that would only happen if there was no increase in number of calories consumed. I wonder if walking 5 miles a day would do it if you didn’t eat more food?

2. **Myth:** Set realistic weight loss goals. **Example:** Set a modest goal rather than unrealistic goals and you will be more successful.
   **Fact:** Studies have actually found that mixing realistic and unrealistic goals were found to be associated with more weight loss. The take home message—dream big, but try to keep the goals somewhat realistic.

3. **Myth:** Slow, gradual weight loss will result in more weight loss in the long term compared to rapid weight loss. **Example:** It is better to lose 1-2 lbs. a week than say 5 lbs. a week.
   **Fact:** Long-term follow-up found that those who had slow gradual weight loss had similar overall results to those who had rapid weight loss.

4. **Myth:** You must be mentally ready before starting a diet for it to be successful. **Example:** Before starting any weight reduction program you must be mentally equipped to stay on and follow through with it.
   **Fact:** What the authors found was that there was very little difference in weight loss between the groups that were mentally ready and those who were not. So perhaps if people are on the fence about starting a weight loss program they should take the plunge.

5. **Myth:** Physical education classes in school reduce the risk of childhood obesity. **Example:** Children who actively participate in schools’ PE programs are less likely to be obese.
   **Fact:** Current PE classes have not been shown to reduce childhood obesity. The key word is ‘current’ programs and this is an example of how current exercise programs are missing the mark. Perhaps a program that combined diet and exercise would be effective to help reduce childhood obesity.

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Snapshots

FROM PAGE 2

past four years. This represents the views of the authors, and is not an official CDC document.

- It is estimated that there are about 3.2 million people in the U.S. with chronic HCV
- Of these, HCV was detected in 1.6 million (50%)
- 1.0–1.2 million (32–38%) were referred to care
- 630,000–750,000 (20–23%) had HCV viral load testing
- 380,000–560,000 (12–18%) underwent liver biopsy
- 220,000–360,000 (7–11%) were treated
- 170,000–200,000 (5–6%) were successfully treated

The Bottom Line: There are many ways we can improve HCV screening and care. Intervention can decrease future HCV-related hospitalizations and deaths.

Editorial Comment: I have some problems with this analysis.

The authors stand by their interpretation of the National Health and Nutrition Examination (NHANES) data. Although this surveyed random noninstitutionalized U.S. civilians, the authors state that people who were institutionalized, incarcerated, or homeless were factored in. They also said that they used unpublished prevalence data from more a recent NHANES (2003 through 2010).

I’d be interested in seeing more documentation on the 7–11% who were treated. In particular, I’d be interested in knowing what percentage of HCV patients underwent retreatment. The treatment success rates seem high (55-77%), particularly since this data was gathered before the approval of triple therapy.
Weight Loss FROM PAGE 7

6. **Myth:** If you are breastfed as a baby it will protect you from becoming obese. **Example:** All those people who were breastfed as babies are skinny as a rail.

**Fact:** Breastfeeding does not confer any anti-obesity properties. BUT it is well-known and proven scientifically that there are many other important benefits to breastfeeding and it should be encouraged.

**Myth:** Having sex will burn between 100 and 300 kcal for each person. **Example:** I don’t think that anyone needs an example of having sex (at least I hope not) and how energetic it can be if people take their time and enjoy themselves.

**Fact:** Sex contributes to a healthy body and mind, but unfortunately this also involves a myth. The authors used the example of a man who weighed 154 lbs. burning about 3.5 kcal per minute and **210 kcal per hour during sex.** This is one myth that deserves some serious myth busting or at least we should all strive to hit that 210 kcal loss in that frame of time.

EASL 2013 FROM PAGE 6

“DAAs are ready for prime time,” EASL Secretary General Mark Thursz said at a press conference kicking off the congress, but “interferon is not dead yet.”

The question on everyone’s mind is whether to treat now with available but poorly tolerated approved DAAs, wait for more effective and better tolerated second-generation add-ons to interferon/ribavirin, or hold out even longer for interferon-free regimens.

“If a patient has early stage [liver disease], lots of physicians are recommending their patients wait,” Thursz explained. “For those with more advanced disease, treating with the standard of care is probably the way to go—unless they have very advanced disease,” in which case they have “significant risk of dying from septic complications” if treated with current triple therapy.

As the new DAAs reach the clinic, twelve weeks of an interferon-based triple regimen will be “tolerable for a large number of patients,” he continued. “Many are perfectly happy with that, and it may be better than waiting another year for a suitable all-oral regimen.” Within two to four years, however, “the pressure to use all-oral regimens will become overwhelming.”

For Part 1 of this article see the June edition of the HCV Advocate.