There was much news in 2015 about hepatitis C (HCV), but most of the news was driven by the high cost of HCV medications—specifically the market leader—Gilead’s Harvoni to treat HCV genotype 1. In 2015, there was another interferon-free HCV Drug approved—AbbVie’s Viekira-Pak. Viekira-Pak carried a high price tag, but it was a little less than Harvoni. The other news tied to the high cost of the medications included the access (or lack of) to the drugs, exclusivity deals, and generic versions of the new HCV drugs. The other news that I will discuss includes the approval of Daklinza and Technivie, safety warnings, a new cell culture, the advocacy community and my wish list for 2016.

Gilead, AbbVie & The Price Tag
The Food and Drug Administration (FDA) approved Harvoni in the third quarter of 2014. It carried a hefty price tag—up to $90,000 for a 12-week course of...
treatment—the standard treatment duration for most people with HCV genotype 1. The side effects are considered low especially compared to the previous therapies that contained interferon. It was a breakthrough in the treatment of hepatitis C for people with genotype 1—an all-oral treatment that consisted of a combination of sofosbuvir and ledipasvir combined into one pill taken once-a-day that cures up to 100% of people who take the combination. Truly Harvoni is a miracle drug. It is hard to say with certainty the exact price of Harvoni since the price has been negotiated with various payers, but regardless the price is high. There has been much negative press, congressional hearings, protests and more attention paid to the cost than any other medicine this year. In November 2015, the FDA approved a new indication for Harvoni for the treatment of genotype 4,5,6 and those coinfected with HIV. Also, the new indication includes treatment with ribavirin for genotype 1 treatment-experienced patients with cirrhosis.

Viekira-Pak was approved December 2014, and the price tag was a little under Harvoni—$84,200. It did not generate as much negative press or sale of prescriptions. They did, however, have an excellent community education/navigation program.

Restrictions

The price of the drugs set the stage for a tug of war between patients, and medical insurance coverage of the drug and Medicaid. Many insurance companies and almost all state Medicaid programs were only approving coverage for people with the most severe HCV disease (severe fibrosis, cirrhosis). At first, Gilead was picking up the gap in insurance coverage with their patient assistance program, but after awhile, Gilead stopped covering the denials deciding that insurance companies and state Medicaid programs needed to start covering the medications.

Exclusivity Deals

Another issue with the price was the exclusivity deals between the pharmaceutical companies (Gilead/AbbVie) and insurance companies/payers to reduce the costs of the medications. The good news is that it lowered the cost of the drugs. However, it set a precedent to have treatment decisions made by corporations rather than a trained medical provider who has years of medical experience to guide an important healthcare decision.

In all of this guess who loses?
Patients of course!

Medicaid and CMS

There is some promising news—towards year-end, the Centers for Medicare and Medicaid Services (CMS) issued a notice to state Medicaid programs that they were breaking the law and should lift the restrictions placed on access to HCV medications. The restrictions limited access to HCV medications to only those who had severe fibrosis or cirrhosis or those with a serious condition such as diabetes, cryoglobulinemia, and other types of extrahepatic manifestations. It is too soon to tell what overall effect the CMS notice will have, but some states are starting to comply.

Lawsuits

The denials by insurance companies and Medicaid lead to many lawsuits in 2015. As of the date of this publication there have not been any judgments made but 2016 should provide some news.

Generic Sofosbuvir

Gilead has licensed sofosbuvir and ledipasvir to some countries (India, Pakistan and Egypt) to make a generic version. Daclatasvir is another drug that is produced
as a generic drug. The countries that manufacture the
generic drugs are responsible for making sure the qual-
ity is chemically the same. There are other sources of
generic sofosbuvir, ledipasvir, and daclatasvir, but there
may be quality assurance issuances. Be sure to do your
research — there are some websites and blogs that verify
the accuracy of the chemical makeup of the generic
drugs—the old saying applies here: buyer beware, or
buyer be careful. Generic drugs are going to be one of
the most important strategies to eliminate HCV worldwide.
There will be a need for drugs that are much cheaper to
treat it especially in developing countries.

Updated AASLD/IDSA Guidance

Finally, the American Association for the Study of Liver
Disease and Infectious Disease Society of America
has issued guidance that “evidence clearly supports
treatment for all HCV infected persons, except those
with limited life expectancy (less than 12 months) due to
non–liver-related comorbid conditions.”

...the old saying applies here: buyer
beware, or buyer be careful.

Acute Outbreaks of HCV 2015

Outbreaks of acute hepatitis C among people who
inject drugs continues to spread. The highest hit ar-
areas were the Appalachian areas in the U.S. The last
report (2013) from the Centers for Disease Control and
Prevention (CDC) listed acute cases as 29,700 (range
23,500 – 101,400). A study titled “Underascertain-
ement of Acute Hepatitis C Virus Infections in the U.S.
Surveillance System: A Case Series and Chart Review,”
by S Onofrey, MPH et. al., published in the Annals of
Internal Medicine, estimated that only 1% of the real
number is reported to the CDC. Needle exchange was
mostly established after the outbreaks. If only needle
exchange were established beforehand it would have
prevented the outbreaks in the first place!

2015 FDA Approval

Daklinza (daclatasvir) in combination with sofosbuvir
was approved by the Food and Drug Administration to
treat HCV genotype 3. Both drugs are taken once-a-
day for 12 weeks. In clinical trials, the cure rates were
98% for treatment naive patients without cirrhosis; 58%
for treatment naive patients with cirrhosis. In
treatment-experienced patients without cirrhosis, the
cure rate was 92%; in treatment-experienced patients
with cirrhosis, the cure rate was 69%.

Technivie (ombitasvir, paritaprevir, and ritonavir) plus
ribavirin to treat treatment naive genotype 4 patients
was approved by the FDA. The cure rates are up to
100%.

2016 FDA Approvals

Some good news! Next year—actually the end of
January Merck’s combination of elbasvir and grazo-
previr—brand name Zepatier will be approved by
the FDA. The cure rates are up to 99% in genotype
1,4 and 6. Merck applied to the FDA for marketing
approval earlier in the year.

Phase 3 clinical trials sofosbuvir plus velpatasvir were
completed, and Gilead applied for marketing approval
to the FDA later in 2015. The cure rates for patients
treated with sofosbuvir plus velpatasvir (GS-5816)
with genotypes 1 through 6 were up to 97% to 100%.
Gilead has applied for marketing approval to the FDA.
The combination will be approved in 2016. This is
good news for all genotypes but especially those with
genotype 3 who had cirrhosis the cure rate was 91%.

Resistance-associated Variants (RAVs)

RAVs occur naturally, during treatment (viral break-
through) and after treatment (relapse) with direct
acting antiviral medications (DAA—protease, poly-
merase, NS5A inhibitors). RAVs may lead to treatment
of a DAA medication not working. The guidelines for testing vary, but the AASLD/IDSA Guidance has guidelines for testing for RAVs before retreatment. Treating with a combination of different DAA drugs that include a one or more pan-genotypic drugs is also an effective strategy.

**Pan-genotypic Drugs**

Drugs that have antiviral properties against all of the genotypes are called pan-genotypic. These types of drugs have come into prominence this year and will continue to be highly sought after to treat hepatitis C. Pan-genotypic drugs, when developed to be highly effective against all genotypes, may eliminate the need for the expensive genotype test, treat people with multiple genotypes and help treat people with resistance-associated variants (RAVs).

**Drug Warnings**

The FDA issued a warning this year that Viekira Pak and Technivie can cause severe liver injury in patients with advanced liver disease. As a result, AbbVie has added new information to their package label. If you are a patient taking the one of the AbbVie combinations, talk to your medical provider if you have any concerns.

**New Cell Culture**

The Journal Nature released a study by led by scientists from The Rockefeller University who identified a human cell that can replicate the hepatitis C virus. This will help science understand the hepatitis C virus and optimize hepatitis C treatment including treating people who develop RAVs.

**Advocates**

2015 has brought a lot of good times for people with hepatitis C – at least, those who were treated and cured. If you fall into the group of individuals who were denied HCV treatment by insurance companies or Medicaid it has been a frustrating and depressing year.

What has been very positive this year for me in advocacy is to see so many advocates working for patients. You may not hear or see them, but they are out there working tirelessly to help people with hepatitis C. Many are working for access to treatment. HCV Advocacy is finally coming of age, and it is reassuring to see so many new people in HCV advocacy. There are also a large number of individuals who work in HIV who are turning their energies to HCV advocacy.

So if you think no one has your back know that there are hundreds of people who are working hard to try to get you access to treatment and other services. If you see them, or they contact you ---thank them. Most people who work in advocacy don’t expect it and ‘thank you’ sure feels good when gratitude comes their way.

Now, here’s my wish list for 2016:

- 2-4 new therapies approved in 2016
- More drug competition
- Lower drug prices
- Treating everyone with hepatitis C
- Identify everyone with hepatitis C

If you think this is grandiose, you should see my New Year’s resolutions!
Highlights from the 2015 Liver Meeting

This month, I highlight some of the latest research presented at AASLD’s 2015 Liver Meeting. Note that conference posters are preliminary investigations, and need to be published in a peer-reviewed journal before data can be considered conclusive.

Abstract #1885: Safety and Efficacy of Interferon/Ribavirin-Free Therapy in Septuagenarians and Octogenarians with Chronic Hepatitis C - Rafael Stern, et al.

Elderly people with chronic hepatitis C virus (HCV) infections are generally not included in clinical trials. This study enrolled 44 healthy subjects over 70 years old. The majority had cirrhosis (n=32); the rest had stage 3 fibrosis (n=12). Most had genotype 1b (n=34) and were treated with sofosbuvir (SOF) combined either with daclatasvir (DCV), simeprevir (SMV), or ledipasvir (LPV) for 12 to 24 weeks.

No one dropped out of the study; 37 completed treatment, and 7 were still on treatment at the time of this presentation. At the week 12 follow-up, 14 of 16 subjects achieved a sustained virologic response (SVR). Treatment was well tolerated, and no severe adverse events were observed.

Conclusion: Interferon/ribavirin-free treatments are safe and effective in elderly chronic hepatitis C patients with advanced liver disease.

Editorial Comments: Other research on elderly people with chronic liver disease presented at the meeting included abstract #528: Geriatrics and Cirrhosis: Changing Epidemiology of Chronic Liver Disease among the Elderly, 2004-2013. Michael Hagan and colleagues concluded that older subjects had more comorbidities, more complicated liver disease, needed more procedures, and had substantial inpatient mortality. They also found a higher prevalence of fatty liver disease (NAFLD) rather than viral hepatitis. The researchers urged aggressive management of chronic liver disease. The approval of HCV direct-acting antivirals (DAAs) may help with this goal.

Abstract #1878: Repeated Biopsies within 23 Years Showed Increased Frequency of HCV Infections and Suggested a 3-Year Median Monitoring to Allocate Fibrosis Progressions - Shaul Yaari, et al.

When the cost of HCV drugs skyrocketed, many health insurance payers began requiring fibrosis levels prior to authorizing HCV treatment. However, little is known about the fibrosis progression rate among those with minimal liver damage. Further, there aren’t clear guidelines on the frequency of liver biopsies. This study analyzed data from 885 HCV patients who underwent 1440 liver biopsies from 1991 to 2014.

“The elderly people with chronic hepatitis C virus (HCV) infections are generally not included in clinical trials.”

The distribution of fibrosis levels were: 30% with F0, 11% with F1, 27% with F2, 17% with F3, and 15% with F4. Long-term follow-up of 249 subjects who had repeated biopsies revealed that 28% of those with...
baseline F0-1 progressed to F3-4 in 5 years (range from 0.01 to 20.95 years, with median of 3.1 years). Of 36 cases with baseline F2, 36% progressed to F3-4 at a slightly faster rate (range from 0.05 to 17.11 years, with median of 4.3 years).

**Conclusion:** The researchers recommended three-year monitoring intervals for HCV patients with F0-F2 who had no previous treatment or who had not achieved an SVR.

**Editorial Comments:** Similar research was presented in abstract #1841: Fibrosis Progression in Patients with Chronic Hepatitis C Virus Infection - Marija Zeremski, et al. This study found that fibrosis progression rates are influenced by the inflammation grade and high ALT levels. Patients with low initial fibrosis who had at least one ALT flare (above 200) were more likely to have rapid fibrosis progression. Patients infected with HCV genotype 3 were more likely to develop cirrhosis.

**Abstract # 1884:** Does Pregnancy Protect Against Fibrosis or Promote SVR in HCV Infected Women? - Christine Pocha, et al.

There are differences between men and women with liver disease. Women are more likely to clear HCV spontaneously and have higher HCV treatment response rates; cirrhotic women are less likely to decompensate. Evidence suggests that a pregnancy hormone (relaxin) may have antifibrotic qualities. This study evaluated the influence of past pregnancies on the rate of liver fibrosis progression and sustained virologic response (SVR) in women.

Data were examined from 2001 and included 1669 women, of whom 1121 reported at least one pregnancy. Overall 39% of women received at least one HCV treatment with improvement or no change in fibrosis score.

**Conclusion:** Pregnancy was associated with an 18% risk reduction of cirrhosis. The influence of pregnancy on HCV treatment was non-conclusive. However, a history of pregnancy was associated with higher likelihood of achieving SVR with interferon-based HCV treatment.

**Editorial Comments:** Ribavirin may harm a fetus, and should never be prescribed to a pregnant woman or her partner during HCV treatment. In the U.S., the safety of the new DAAs during pregnancy has not been proven.


The Centers for Disease Control and Prevention and U.S. Preventative Services Task Force have recommended one-time screening for hepatitis C virus (HCV) among adults born between 1945 and 1965. Some experts oppose HCV screening of baby boomers, so this study examined the impact of HCV infection on the U.S. liver transplant (LT) list.

**Conclusion:** Using data from the 1995-2012 registries, there was an increase in HCV baby boomers on the LT waitlist. Baby boomers with HCV undergoing LT doubled to 35% of all LT in 2012 compared to 17% in 1995. The demand for LT among the HCV baby boomer group is continuing to expand. The researchers recommend birth cohort screening as a strategy to diagnose and preemptively treat HCV-infected baby boomers.

“The influence of pregnancy on HCV treatment was non-conclusive.”
Editorial Comments: Another study presented equally compelling data. (Abstract#201 HCV Infection in Aging Baby Boomers is an Independent Predictor of Poor Outcome in Liver Transplant Recipients: An Analysis of the UNOS Database) Andy Liu and team found that chronic HCV infection is an independent predictor of lower overall patient survival following LT in the aging U.S. baby boomer cohort. This study underscored the need for HCV screening of adults born between 1945 and 1965.

Unfortunately, a need for HCV baby boomer testing doesn’t translate into action, as shown in research by Amy Jessop (#547 A Qualitative Assessment of Factors Impacting Adoption and Implementation of USPSTF Age-Based Hepatitis C Virus Screening Guidelines). Physicians’ knowledge of the testing guidelines is low, misinterpreted, and underutilized.

Abstract #1827: Comparative Analysis of Online Patient Education Resources Relating to Hepatitis C - Rishabh Gulati, et al.

It’s recommended that health information for patients be written for a 6th grade level. This study analyzed the readability of online patient hepatitis C literature. They compared text from the American College of Gastroenterology (ACG), Centers for Disease Control & Prevention (CDC), American Liver Foundation (ALF), Mayo Clinic, National Institutes of Health (NIH), Uptodate, HCVAdvocate and WebMD. In general, information about treatment was the most difficult section when compared with other subsections. NIH and WebMD had the lowest readability scores (7th to 8th grade level, respectively). ACG had the highest grade level compared to other websites (grade 17+). HCV Advocate was 6th on the list with grade 11 readability scores.

Conclusion: The researchers urged a greater emphasis on clear and simple language to increase quality and comprehension of online patient education resources.

Editorial Comments: Since I write some of the HCV Advocate literature, I took this study to heart. Although I accept the data and am delighted for the opportunity to improve, it is worth noting that HCV Advocate does offer the Easy C’s series that meets the recommended low readability scores.

As for this article, I flunked the 6th grade level readability test, so I wrote an Easy C version:

Here are some studies from the 2015 Liver Meeting, but read with a grain of salt:

- New drugs are safe and work well in older hep C patients with serious liver disease.
- If you have hep C, talk to your doctor about getting a test every three years to see how your liver is doing.
- Pregnancy may reduce the risk of severe liver disease.
- More baby boomers are on the liver transplant list than ever before.
- Doctors are not following hep C screening advice.
- Patient info may be too hard for some people to understand.

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"The researchers urged a greater emphasis on clear and simple language to increase quality and comprehension of online patient education resources."
JOIN US IN JANUARY 2016 FOR OUR FIRST

HEPATITIS

hullabaloo

synonyms: fuss, commotion, hue and cry, uproar, outcry, clamor, storm, furor, hubbub, ruckus, brouhaha

We will have a plethora of original articles, facts, and more information about hepatitis C, hepatitis B, and viral hepatitis coinfections during the entire month of January. Think you know it all about hepatitis – guess again. Visit us on Facebook, HBV blog and our HCV News and Pipeline Blog to learn everything you need to know and more.

● ANTIBODY TESTING ●

Walgreens is offering free HCV antibody testing at certain locations – If you, a friend, a client or someone at risk for hepatitis C needs to be tested send them to this link for the free test.

● EVENTS PAGE ●

We have updated our Events page for 2016. Also, there is an on-line form you can fill out to list your event.

● MEDICAL GLOSSARY ●

We have updated and expanded our Medical Glossary with relevant definitions. For instance, we just added a definition for the resistance-associated variants (RAVs). To find out about RAVs search our Medical glossary under “R”.

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