In this issue of HCV Drugs, I will discuss some very good news about the 2016 budget for treating Veterans with hepatitis C, a refresher on AbbVie/Enanta’s phase 2 clinical trial data from The Liver Meeting 2015 and Benitec’s clinical trial termination.

Department of Veterans Affairs
The Department of Veterans Affairs recently posted a memo on their website providing information about treating all Veterans with hepatitis C. The additional money ($1.5 billion) was allotted by Congress to the VA and was earmarked for HCV medications. It was not to be used for additional staffing or laboratory testing.

Listed below is section 2 of the memorandum.

“2. Expansion of eligibility for HCV treatment within VA:
a. Effective immediately, for the rest of FY 2016, all Veterans with HCV may receive treatment within VA facilities without regard to stage of liver disease: the use of prioritization protocol to determine eligibility for treatment within VA is no longer in effect. We have received funding from Congress to support a more aggressive roll-out for treatment of Veterans who are infected with HCV.
b. Even though we are not limiting treatment, facilities should manage resources to ensure that patients with more advanced disease receive treatment as

CONTINUED ON PAGE 2
soon as possible and continue outreach to such patients to offer them treatment.

c. Facility managers should take immediate steps to ramp up treatment to the maximum possible capacity. Managers should ensure that adequate clinical resources (staffing, clinical pharmacists, laboratory testing, psychosocial support, etc.) are allocated to clinics providing HCV treatment to allow full utilization of funding of HCV treatment.”

**Editorial Comments**

This is exciting news for Veterans and their loved ones. In general, we do not treat our Veterans very well. We should be supporting our Veterans in every way possible. This is a good first step.

The entire memorandum can be viewed at http://www.hepatitis.va.gov/pdf/choice-prioritization-update.pdf

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**AbbVie/ENANTA**

ABT-493 (protease inhibitor) plus ABT-530 (NS5A inhibitor) co-formulated into one pill, taken once-a-day is currently in phase 3 clinical trials to treat genotypes 1 through 6. The treatment duration for most of the people in the study below was 12 weeks, but a subset of patients were treated for 8 weeks.

The SURVEYOR-I AND SURVEYOR-II phase 2 clinical information is listed in the table below from an ENANTA company press release.

**Overview of SURVEYOR-I and SURVEYOR-II Clinical Data Presented at AASLD:**

<table>
<thead>
<tr>
<th>Number of Patients (n)/ Patient Population</th>
<th>Duration of Treatment</th>
<th>Treatment Arm</th>
<th>Treatment Regimen</th>
<th>SVR12 Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=40 Treatment-naïve=63% PegIFN/RBV null responders=37%</td>
<td>12 Weeks</td>
<td>Arm A</td>
<td>ABT-493 (200mg) + ABT-530 (120mg) once daily</td>
<td>100% (n=40/40)</td>
</tr>
<tr>
<td>n=39 Treatment-naïve=64% PegIFN/RBV null responders=36%</td>
<td>12 Weeks</td>
<td>Arm B</td>
<td>ABT-493 (200mg) + ABT-530 (40mg) once daily</td>
<td>97% (n=38/39)</td>
</tr>
<tr>
<td>n=34 Treatment-naïve=85% PegIFN/RBV treatment experienced=15%</td>
<td>8 weeks</td>
<td>Arm K (n=34)</td>
<td>ABT-493 (300mg) + ABT-530 (120mg) once daily</td>
<td>97% (n=33/34)</td>
</tr>
</tbody>
</table>

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[CONTINUED ON PAGE 3]
### SURVEYOR-II (Genotype 2, Non-cirrhotic)

<table>
<thead>
<tr>
<th>Number of Patients (n)/ Patient Population</th>
<th>Duration of Treatment</th>
<th>Treatment Arm</th>
<th>Treatment Regimen</th>
<th>SVR Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=74</td>
<td>12 Weeks</td>
<td>Arm A (n=25)</td>
<td>ABT-493 (300mg) + ABT-530 (120mg) once daily</td>
<td>96% (n=24/25)</td>
</tr>
<tr>
<td>Treatment-naïve=88%</td>
<td></td>
<td>Arm B (n=24)</td>
<td>ABT-493 (200mg) + ABT-530 (120mg) once daily</td>
<td>100% (n=24/24)</td>
</tr>
<tr>
<td>pegIFN/RBV treatment experienced=12%</td>
<td></td>
<td>Arm C (n=25)</td>
<td>ABT-493 (200mg) + ABT-530 (120mg) once daily + RBV (weight-based, 1000 or 1200mg) twice daily</td>
<td>100% (n=25/25)</td>
</tr>
</tbody>
</table>

### SURVEYOR-II (Genotype 3, Non-cirrhotic)

<table>
<thead>
<tr>
<th>Number of Patients (n)/ Patient Population</th>
<th>Duration of Treatment</th>
<th>Treatment Arm</th>
<th>Treatment Regimen</th>
<th>SVR Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=30</td>
<td>12 Weeks</td>
<td>Arm D</td>
<td>ABT-493 (300mg) + ABT-530 (120mg) once daily</td>
<td>93% (n=28/30)</td>
</tr>
<tr>
<td>Treatment-naïve=90%</td>
<td></td>
<td>Arm E</td>
<td>ABT-493 (200mg) + ABT-530 (120mg) once daily</td>
<td>93% (n=28/30)</td>
</tr>
<tr>
<td>pegIFN/RBV treatment experienced=10%</td>
<td></td>
<td>Arm F</td>
<td>ABT-493 (200mg) + ABT-530 (120mg) once daily + RBV (weight-based, 1000 or 1200mg) twice daily</td>
<td>94% (n=29/31)</td>
</tr>
<tr>
<td>n=30</td>
<td></td>
<td>Arm G</td>
<td>ABT-493 (200mg) + ABT-530 (40mg) once daily</td>
<td>83% (n=25/30)</td>
</tr>
<tr>
<td>Treatment-naïve=93%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pegIFN/RBV treatment experienced=7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The phase 3 studies are underway without ribavirin. To find out more about the phase 3 studies go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov) – type in ABT-493 phase 3
Benitech

Benitech Biopharma announced on February 26, 2016, that it was winding down and will terminate their hepatitis C program as soon as the patients complete cohort 4 in the Phase I/IIa clinical trial for TT-034. The decision to discontinue the development of TT-034 was due to the landscape of current therapies to treat hepatitis C because they have such high success rates (cure rates/low side effects/short treatment duration).

We have updated our HCV Drug Pipeline for the HCV Advocate Mid-Month edition (attached to the newsletter). In the past, the HCV drug pipeline used to contain a large number of drugs in development. Now there is only a handful. To develop a new HCV medication and become commercially viable, it would have to have similar or a higher cure rate, once-a-day dosing, similar or lower side effect profile, and similar or shorter treatment durations. There is another area that would help, and that would be a lower price. 

**SNAPSHOTS**

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**Article:** Concordance of sustained virologic response at weeks 4, 12 and 24 post-treatment of hepatitis c in the era of new oral direct-acting antivirals: A concise review—S V Burgess et al.

*Source: Annual of Hepatology Concise Review March – April, Vol. 15 No. 2, 2016: 154-159*

**Study Aims and Results**

The aim of the study was to find out the primary end-point of HCV therapy at week 12—SVR12—(sustained virological response / cure) with direct-acting antivirals (DAA) is the same as the end-point of the older 24 weeks (SVR 24). The comparator was studies of pegylated interferon plus ribavirin (PEG/RBV) HCV therapies.

The authors compared six direct studies of each type therapy (DAA vs. PEG/RBV).

**Conclusion**

The data from the current analysis supports SVR12 to replace SVR 24 with the use of direct-acting antiviral medications. It was pointed out that the “long-term durability of SVR12 is still needed.”

**Editorial Comments**

There have been other studies that have proven that SVR 12 is as reliable a marker as SVR 24. It is even more so with direct-acting antiviral medications because the medications are ‘direct-acting’ and very potent.
That study found that the risk of liver decompensation and death was more than 40% lower for the people who used statins.

HCV DRUGS

**Article:** Atorvastatin and fluvastatin are associated with dose-dependent reductions in cirrhosis and HCC, among patients with HCV Results from ERCHIVES—TG Simon et al.


**Study Aim and Results**

In the last issue of the HCV Advocate newsletter I wrote about a study published in Gastroenterology titled *Statins Are Associated With a Decreased Risk of Decompensation and Death in Veterans with Hepatitis C-Related Compensated Cirrhosis* by A Mohanty et al. That study found that the risk of liver decompensation and death was more than 40% lower for the people who used statins.

In the current study, the authors wanted to understand what type of statin and at what dose would reduce fibrosis progression and liver cancer in persons chronically infected with hepatitis C. The authors used the Electronically Retrieved Cohort of HCV-Infected Veterans (ERCHIVES) database. They identified all the people started on HCV therapy from 2001 to 2014 with cirrhosis and hepatocellular cancer (HCC—liver cancer). Among the 9,135 eligible people, 1,649 had developed cirrhosis, and 239 had developed liver cancer. Importantly, statin use was associated with a 44% reduction in the development of cirrhosis. Mean change in FIB-4 score (cirrhosis) with the statins—atorvastatin (n=944) and fluvastatin (n=34) was -0.17 and -0.13 respectively (p=0.04) after adjustment for baseline FIB-4 score and established predictors of cirrhosis.

Statin use was also associated with a 49% reduction in incident liver cancer (HCC).

**Conclusion**

In people with hepatitis C, the use of statins was associated with a dose-dependent reduction in the incident of cirrhosis and liver cancer. Two statins, in particular, had dose-dependent reductions in cirrhosis and liver cancer—atorvastatin and fluvastatin.

**Editorial Comment**

This is, at least, the second study that has found that statin use can provide reductions in cirrhosis and liver cancer. This would be the time for a medical society to look at providing guidance or sponsor an extensive study to guide medical providers to help their patients with prescribing a statin that would be beneficial to delaying the progression of fibrosis, cirrhosis and possibly liver cancer. It might be a first step to find a statin(s) that is beneficial for other liver conditions such as chronic hepatitis B, fatty liver disease and alcoholic liver disease and many other diseases of the liver.
Article: Prevalence of hepatitis C virus infection among HIV+ men who have sex with men: a systematic review and meta-analysis—AE Jordan et al.

**Study Aim and Results**

The transmission of hepatitis C is blood-to-blood contact. Sharing needles and works is the most common transmission route. Although sexual transmission it is uncommon, it can occur if there is blood involved. A recent study found the hepatitis C virus has been found in rectal fluid—more on that later.

The authors pooled 42 global studies of HIV-positive men who have sex with men (MSM) to determine the prevalence of hepatitis C infection.

Pooled prevalence produced an overall antibody hepatitis C virus prevalence among HIV-positive MSM of 8.1%; active HCV prevalence estimate was 5.3% to 7.3%.

Antibody hepatitis C virus prevalence among injection drug use (40%) and non-injection drug use (6.7%) HIV-positive MSM.

**Conclusion**

The significant decrease in HCV infections among injection drug users. The moderate increase in sexual transmission.

**Editorial Comment**

- Significant decrease among people who inject drugs – good news! We should be increasing prevention measures to reduce it even more.

- A moderate increase in sexual transmission is alarming. We should be providing additional prevention tools and incorporating messages about preventing sexual transmission of hepatitis C and providing information rectal shedding of hepatitis C:

Of concern is the sexual transmission component of the study and a recent study from The Liver Conference 2015—abstract # 89 titled Rectal Shedding of HCV in HCV/HIV Coinfected Men by authors Andrew L. Foster et al. The Foster study found that although blood was not detected, the hepatitis C virus was detected in 20 of 43 of the specimens of rectal fluids of HCV/HIV-positive men who have sex with men (MSM).

In both groups HCV positive men access to testing, treatment and cure should be provided to stop the spread of hepatitis C and increase a persons quality of life.

*Although sexual transmission it is uncommon, it can occur if there is blood involved.*
Undetectable” is a story about Kim Goldberg’s journey through hepatitis C treatment. It may muddy the waters to say that this tightly written book parallels a 17th century travel diary written by Matsuo Basho. But trust me, it works. *Undetectable* is part memoir, part poetry, and part journey into the interior of the self. Gathering images from nature, Kim weaves history and social issues into a story that is everyone’s story.

Told with achingly raw truth, Kim taunts us to look deeper, but applies a balm of humor just in case the reader decides to take Kim too seriously. Kim’s journey can’t be pigeon-holed. You don’t need to have hepatitis C or any illness for this book to be relevant. You just need to be human, and this book invites us to be fully that.

Spoiler alert: the title is deceptive. The story won’t be ruined by saying the treatment cures Kim, since she reveals in the preface. What you will have to discover for yourself is that this book is not just about hepatitis C treatment; “undetectable” refers to more than her final viral load.

*Undetectable* is published by Pig Squash Press, is 159 pages, and sells for $19.00. If you love words and storytelling, the book is a bargain.

Reviewed by Lucinda K. Porter, RN, a long-time contributor to the HCV Advocate and author of *Free from Hepatitis C* and *Hepatitis C One Step at a Time*. She blogs at [www.LucindaPorterRN.com](http://www.LucindaPorterRN.com) and [HepMag.com](http://HepMag.com).
The current drugs to treat hepatitis C have high cure rates and minimal side effects (compared to the older therapies). This has created a dilemma for drug developers who must develop new drugs that somehow improve upon the current drugs. This is a difficult task, but not impossible. Probably the biggest achievement will be shorter treatment duration and lower cost. There is a percentage of patients who are the more difficult to treat, such as those with genotype 3 who have cirrhosis and have not achieved a cure with a previous course of therapy. The race is on for new, better and cheaper therapies—this is very good news for people living with chronic hepatitis C.

You will see below that the need for these new therapies has narrowed the pharmaceutical companies to a number that you can count on your fingers! As a result I have decided to rework our pipeline and list it by the pharmaceutical company. I am also just listing the major studies. This is also a new pipeline that will grow as information is released. The pipeline is a brief overview. More extensive information is listed in our newsletters and in our blog.

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 Mid-Month Newsletter

**Genotype (s):** This lists the drugs or combination of drugs and the particular genotype or genotypes that the drug is active against. I am not going to name the particular drug that works against one or all of the genotypes

**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:** Many of the drugs listed below have been updated with the latest information from the Liver Meeting 2015 and news reports as of 1/28/2016. More detailed information about drugs in development is available in our blog reported in the HCV Advocate newsletters.

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### AbbVie

<table>
<thead>
<tr>
<th>Genotype 1b</th>
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</thead>
</table>

**COMMENTS:**

**Genotype 1b - Phase 3b Study:** On January 7, 2016 the FDA granted Viekira Pak without ribavirin priority review status for people with compensated cirrhosis. The clinical trial to support the pending approval enrolled 60 patients and after 12 weeks of treatment the cure rate was 100%. The most common side effects were fatigue, diarrhea, headache and joint pain.
### AbbVie

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

**COMMENTS:**

**Genotype 1 – Phase 2 Study:** ABT-493 (protease inhibitor) plus ABT-530 (NS5A inhibitor) with and without ribavirin in non-cirrhotic patients were treated for 12 weeks. The cure rates were 97-100% in genotype 1 patients; 96-100% in genotype 2 patients; 83-94% in genotype 3 patients. In a separate study of ABT-493 plus ABT-530 the cure rate was 97% in genotype 1 non-cirrhotic patients treated for 8 weeks. The combination of ABT-493 plus ABT-530 is currently in Phase 3 studies. For a breakdown of the phase 2 clinical trial results click here.

### Gilead sofosbuvir, velpatasvir, and GS-9857

**Genotype 1,2,3,4,5,6, (Pan-Genotypic)**

**COMMENTS:**

- **Genotype 1 – Phase 3:** Sofosbuvir plus velpatasvir (GS-5816) In Phase 3 clinical trials (ASTRAL-1-4), the cure rates in genotypes 1 through 6 ranged 97% to 100%. Gilead has applied for marketing approval to the Food and Drug Administration, (FDA) and approval is expected in 2016. The most common side effects were headache, fatigue, sore throat, runny nose, and nausea. In January 2016 the combination received priority review status and Gilead stated that FDA approval is expected by June 28, 2016. To view the Phase 3 data go here: [http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate0116_mid.pdf](http://hcvadvocate.org/news/NewsUpdates_pdf/Advocate_2016/advocate0116_mid.pdf)

- **Genotype 1 and 3 – Phase 2:** The combination of sofosbuvir, velpatasvir, and GS-9857 given to genotype 1 and 3 patients for 4, 6, and 8 weeks. Unfortunately, 4 weeks of treatment did not work. The optimal responses included:
  - 6 weeks of the combination to treat treatment naïve non-cirrhotic genotype 1 patients produced 93% cure rates
  - 8 weeks of the combination to treat treatment experienced cirrhotic genotype 1 and 3 patients produced 100% cure rates

This combination is now in phase 3 studies.
### Janssen (Achillion/Alios) vs Genotype 1,2,3,4,5,6

**COMMENTS:**

- **Genotype 1 – Phase 1:** In a small study of samatasvir, it was found to be safe and have antiviral properties against genotype 1, 2, 3 and 4. There is now a phase 2 study of samatasvir plus Olysio (simeprevir) in treatment-naive (never been treated) patients with genotype 1b or 4.

- **Genotype 1:** Janssen (Alios Pharma) has initiated a phase 2a study of AL-335, odalasvir, and simeprevir to treat HCV genotype 1 treatment naïve patients. There will be 60 patients divided into three treatment arms who are treated for 4, 6 or 8 weeks.

- **Genotype 1 – Phase 2 Study:** ACH-3422 and Odalasvir (ACH-3102) and Sovaprevir are in studies with various combinations. Recently, Johnson & Johnson Innovation – JJDC, INC (Janssen) made an investment in Achillion for co-development and distribution. **See Janssen for a new study that features odalasvir.**

- **Genotype 1 – Phase 2 Study:** Odalasvir plus sofosbuvir (used as a proxy drug) to treat genotype 1 patients for 6 weeks achieved 100% (12 of 12 patients) cure rates. A proxy drug is a drug used to stand in for another drug. Sofosbuvir is a polymerase inhibitor so it is assumed that odalasvir plus a polymerase inhibitor that is being developed by Achillion will produce similar cure rates.

### Merck vs Genotype 1, 2, 3, 4, 6

**COMMENTS:**

- **Phase 2**—There were two studies – Part A: grazoprevir plus MK-3682 or elbasvir plus MK-3682 the cure rates for genotype 1a/b was 98%; Genotype 2 was 60-71%, but one group who received grazoprevir/MK-3682/MK-8408 had a 91% cure rate; Genotype 3 cure rate across all of the arms was 91%.
WHAT’S UP!

CRYOglobulinemia
Fact Sheet

We have updated our fact sheet about cryoglobulinemia that appeared as an article in last month’s HCV Advocate newsletter with additional information and resources.

A BRIEF HISTORY OF HCV FACT SHEET

Learn about hepatitis C from the early beginnings to the latest information about the newest treatments that can cure most people infected with hepatitis C.

EASY C TREATMENT GUIDES

The new guides have the latest information about the drugs to treat hepatitis C by HCV genotype. Check it out.

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