The authors found that one-third of HIV/HCV positive men shed HCV into their semen.

Study Aims and Results
Hepatitis C is transmitted by blood-to-blood contact. In the current study the authors examined the HCV RNA (viral load) of semen and blood specimens from 33 HIV positive men. The authors found that one-third of HIV/HCV positive men shed HCV into their semen. The average ejaculate (come) would deliver up to 6,630 IU HCV RNA (viral load) into the rectum of the person receiving sex.

The authors pointed out that the rectum tissue of HIV-positive men is generally more susceptible to infection because of a weakened immune system.

Editorial Comments
At the 2015 American Association for the Study of Liver Disease (AASLD) a study reported that of blood and rectal fluid specimens obtained that HCV was detected in 20 of 43 specimens of the rectal fluid. The current study provides more proof that HCV can be transmitted through sex among men who have sex with men.

The pre-exposure prophylaxis to prevent HIV is an important strategy to prevent HIV infection, but people still need to practice safer sex to prevent the transmission of HIV, sexually transmitted diseases and hepatitis C.
Study Aims and Results
The aim of the study was to examine the risk of hepatocellular carcinoma or liver cancer after successful treatment of hepatitis C.

The study reviewed records from the Veterans Administration Hepatitis C Clinical Case Registry. The records analyzed included HCV positive patients in the registry between October 1999 and August 2009. The follow-up period was through December 2010.

The study group identified 33,005 HCV people who had received interferon with and without ribavirin treatment—10,817 were cured. The risk of developing liver cancer was greatly reduced after being cured of hepatitis C.

However, a total of 100 people who were cured later developed liver cancer. This calculated to a .33% (.0033) annual risk of developing liver cancer per year. The annual risk of liver cancer was much higher in patients with cirrhosis (1.39%) and those being cured after age 64 (0.95%). The risk was also higher in patients with diabetes and genotype 3.

Editorial Comments
In the past it was always important to monitor people with cirrhosis even if they had been cured of hepatitis C. This study tells us that certain populations of people should be followed long-term even if they don’t have cirrhosis. More studies are definitely needed to understand why these patient groups need to be followed and if there are other groups that should be included. My understanding is that most people who have been cured are followed with their primary provider. People are usually followed with annual liver function tests. If the tests are elevated further monitoring is warranted. However, this study warrants vigilant monitoring of people who are cured and have the following factors at the beginning of treatment:

• Cirrhosis
• 64 years old
• Genotype 3
• Diabetes

At the risk of sounding like a broken record, this study should reinforce the need to treat people as early as possible and cure them before some of these factors can influence the development of liver cancer.
Dear Alan,

I feel compelled to comment on your recent Editorial Comment in the Mid-month re the VA approval to treat all Veterans with HCV. It is not entirely accurate. You stated, “In general, we do not treat our Veterans very well... this is a good first step”. In reality, our Veterans are treated very well, and they will be the first ones to tell you that, for the most part. Incredible services and benefits are afforded to them, in a multitude of specialties, especially in Mental Health, Substance Abuse, Polytrauma, Homeless Outreach, and in the treatment of GI/ Liver disease. And, those “first steps” were taken long ago and in many ways, our care surpasses what is available in the private sector or at the County/State level. I know that the VA has gotten a lot of negative press in the past, especially in the past 12-18 months, and is sadly deserved in some cases. But, having worked as a nurse practitioner for the VA in Palo Alto for the past 3 years (with 25 years in the private sector prior), I can tell you that we treat our Veterans well. Our Veterans in the Palo Alto system, who live as far away as Redding, Monterey (even Fresno) cannot say enough positive things about the good care they receive and are upset by all the negativity. Whereas you are right, that they initially had to deny HCV treatment to those with minimal disease (just like the private insurances), unfortunately, that made the best economic sense at the time. Now, we can’t treat HCV patients fast enough, which is a great step forward. However, many Veterans do not make themselves available for the treatment, by repeatedly canceling appointments or not showing up for appointments (which then doesn’t allow us to treat another deserving Veteran in that spot) or they completely ignore our earnest attempts to reach out to them and provide them care. The press does not tell that side of the story.

So, in closing, I just wanted to share this slightly different perspective on your Editorial comment. Sorry to have been so verbose, but I feel we need to be as positive as we can be for our Veterans and the general public by reflecting that which is accurate.

Respectfully,

Ginny Morrow
Dear Ginny,

Thank you for your thoughtful response. My comment was a knee jerk reaction to the larger issue of how we have treated our veterans. My response goes back to the Vietnam War. I witnessed our armed forces returning from the Vietnam War being treated with the utmost disrespect.

In regards to hepatitis C care, the general services for Veterans over the years have varied depending on the location of the Veteran Center—at least according to some older published studies from the Veterans Administrations (VA) and from Veterans who have contacted me. I understand that every VA medical center is different and, in general, the hepatitis C care provided now at the VA is good.

A part of the comment was also directed at the Veterans Administration medical care due to the backlog in access to care for all veterans. I understand that the VA is aggressively taking action to correct the backlog.

I hope that every VA center is providing the excellence of care that your center is providing. Personally, I have met many VA medical providers over the years that provide excellent care to their hepatitis C patients.

At the same time, I think it’s important that every American should advocate to make sure our Veterans receive the best possible care and services. That’s the least we owe our Veterans for serving our country.

Sincerely,

Alan Franciscus

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
The Perfect Storm
A reflective essay on the Scott County HIV outbreak and the current state of HIV/Hepatitis C prevention in Southern Indiana

—By Matthew Zielske

Situated an eyelash above sea level, in the southern pocket of a state mostly known for basketball and the Indy 500, rests lazily in an oxbow of the Ohio River the enigmatic city of Evansville. It’s the 3rd largest city in Indiana and synonymous with economic stability and a generous cost of living. A college town of millennials and XXYzer’s is anchored by a well-established generation of baby boomers. This diversity gives way to a tapestry of voices, interests and opinions stitched together to create the social fabric of the city.

In recent years the Franklin Street Events Association and the Haynie’s Corner Arts District has transformed sections of the city into vibrant pockets of restaurants, bars, and nightlife hotspots. Streets, neighborhoods and subdivisions are peppered with reincarnated bohemian souls and well-dressed political elites who have beaten, through sheer will, energy and economic opportunity back into old neighborhoods and parks.

We should appreciate and celebrate these achievements as a positive sign of civic engagement. At the same time we must be cognizant of the fact that Evansville exists as part of a state fast becoming known for heroin overdose, opiate addiction and one of the worst HIV outbreaks in the last 30 years. No city is immune to the ravenous nature of substance use, and the public health crises that follow, not even Evansville.

Vanderburgh County, of which Evansville is the seat, ranks 77 out of 92 counties for over-all health outcomes in Indiana. The county has higher than state average rates of sexually transmitted infections, teen pregnancy and chemical overdose deaths. In addition, 25% of children live in poverty and 41% of households are single parent. I want to be clear that I’m not inferring single parent households are bad households, or that single parents are representative of something that needs to be fixed, but rather, the statistic is important to keep in mind when we consider those households are more likely to have limited resources.

This may result in those households, and the youth living in them, having less access to health care, preventative services and healthy nutrition information. Recognizing these social determinants of health, as well as many others, is imperative as they are indicators of areas where higher incidence rates of HIV/hepatitis C (HCV) may occur.

Also consider that in 2015 the HCV+ rate increased 800 percent for the whole of Indiana. Vanderburgh County has also seen a significant increase in HCV incidence. This sharp increase in HIV/HCV is a direct result of the rise in injection drug use, combined with limited to no access to preventative services for persons who inject drugs (PWID) where they can obtain sterile syringes and comprehensive health education.

— CONTINUED ON PAGE 6
To better understand the precarious position that Evansville and surrounding rural counties are in I need explain why the very thing that is a sign of economic success for Indiana, and the city of Evansville, is also the mechanism that makes us vulnerable to continued HIV/HCV health crises.

For anyone who has ever driven through Indiana on their way to somewhere else, you’ve likely encountered signs proudly proclaiming we are the “Crossroads of America.” As you traverse the main artery of I-64 that runs from St. Louis to Louisville you are greeted with flat farmlands that subtly give way to rolling landscapes, which eloquently turn into the clay cliffs and the fertile soil of Kentucky. The newly completed I-69 corridor that runs North/South to Indianapolis places the finishing touches on a series of inter and intrastate roadways that converge pointedly through Evansville. If viewed from above you would see Evansville in the middle of a directional cardinal of roadways. This makes the city a nexus point within a state that most people hurriedly pass through.

I-69 affords fast transit to and from cities like Nashville and Indianapolis. This increased traffic through Evansville in turn increases the potential for further economic growth. It supplants the city as a midway stop between the four city giants of Indianapolis, St. Louis, Nashville and Louisville. This is a good time to note that Ohio, Kentucky (both in the top 10) and Indiana (15) all rank in the top 15 states in the U.S. for Heroin/Opiate overdose deaths. When you combine the fact that Ohio and Kentucky are states with similar health crises related to substance use, with the frequent intrastate travel that occurs amongst the three states by way of Indiana and Evansville, increased incidence of HIV/HCV begins to make sense.

Inevitably, the direction of key policy change and resource allocation in Evansville has become focused on placing the city in the best possible situation to ensure economic success. This is a larger discussion of city governance and politics, so I’ll avoid getting too off track. Suffice it to say that suggesting the decision to declare a state of emergency for HIV/HCV isn’t determined by the anticipated economic outcomes would be naïve at best. At worst, such a statement suggests we prefer to remain willfully ignorant and only want businesses to commit to Evansville so that when we are forced to declare a HIV/HCV state of emergency they will find it harder to leave.

This economic mindset helps create an environment where HIV/HCV incidence is much more likely to go unchecked until it’s too late. Such a viewpoint has far reaching implications that I will revisit later, but first, let me tell you about Scott County and the lessons we encountered but seemingly don’t want to use.

In December of 2014, local health department officials and HIV testing counselors in Scott County began to notice something concerning. In Austin, a city of roughly 4,000 people, where newly diagnosed HIV cases were less than 5 per year previously, public health workers had confirmed 27 people as HIV positive, with 10 preliminary, by the middle of February. In March 2015, when I was dispatched to Scott County to assist with HIV/HCV testing, education and outreach, new HIV diagnoses were accelerating with as many as 5 people per day being diagnosed.

As summer was coming to a close approximately 175 people had been diagnosed as HIV+ in Scott County; a figure that would have been 35% of the total HIV diagnoses for Indiana the previous year. For comparison,
in roughly 7 months Indiana had more HIV positive diagnoses that identified injection drug use as a primary risk factor than all of New York City did for the 2014-year. A startling fact when you consider Scott County has a population of 40,000 and New York City has a population of 8 million.

I still vividly recall the first person I screened for HIV/HCV in Scott County. They told me in an exasperated and helpless tone, “When they stopped selling syringes over the counter, we knew they wanted us to get sick.” A heartbreaking statement of despair and hopelessness that would be echoed in the days, weeks and months that followed. Unless you’ve experienced it there isn’t any effective way to describe what happens in the moments after you tell someone they are HIV+.

I was asked once by a newly trained testing counselor what the first thing I said was after telling someone they were HIV+. My response was then, and still is, I don’t usually speak first. I mean what can you really say in those moments that seem to stretch on forever? Nothing really. So, after some time has passed and their breathing has relaxed, if they haven’t spoken, I simply ask them if they want a hug, because the truth is, far too often the compassion of others is what they’re most afraid of losing.

Austin is the unfortunate example of how isolated you can be as a community despite being perfectly situated between the two cities of Indianapolis and Louisville. The majority of those diagnosed as HIV positive were PWIDs, who were also co-infected with HCV. What unfolded in Scott County, and in many ways is still unfolding, is unfortunate and saddening because we allowed it to happen. It doesn’t have to be all for naught though. If we look close enough we will find information that allows us to predict where HIV/HCV is going and carry out effective disease prevention to try and avoid what happened in Scott County occurring again.

I didn’t know it at the time, but I was witnessing a shift in the organic trajectory of HIV prevention. In the 35 years since the HIV pandemic began we have learned a lot about the virus and how to treat it. People are living longer and healthier than ever before. AIDs diagnoses both nationally and on a state level are decreasing, a direct result of advanced antiretroviral therapy.

Unfortunately, new HIV infections are increasing among certain populations. Being outpaced by HCV incidence that a few years ago would have seemed inconceivable. A recent snapshot of Epidemiology data for 2015 from the Indiana State Department of Health shows that 32% of all new HIV infections were among PWIDs, and 40% were among 20-29 year olds. A sign that in our certainty of how to handle HIV we became overly confident and forgot about its pernicious nature and determination to adapt.

The HIV outbreak in Scott County didn’t suddenly manifest out of thin air. For some time the social determinants of health were working to make an environment conducive to large scale HIV/HCV transmission. We simply didn’t notice them, in part because we weren’t looking, but also because we weren’t encouraged to look.

Epidemiology is a complex field that is vital to tracking the progression of communicable disease while also giving us a trove of data to reference when allocating and...
maximizing resources. As with all tools, epidemiology data is only as effective as the ways it’s used and by the people who use it.

As I see it, the danger of epidemiology data is twofold. First, it can reinforce tunnel vision and limit innovation in the field of HIV/HCV prevention. This occurs most often when viewing culture through a singular lens as a static variable, using macro data trends on a micro level, and as a direct result of only going where the numbers lead.

As an example, if the national incidence and prevalence data on HIV infection tell us that we should be focusing on young men who have sex with men and African Americans, then we tend to do so because our grants are constructed in ways that force our hand.

Yet, allowing this epidemiology data to take precedence and ignoring local demographic and risk information simply does not make sense. If the racial composition of Evansville is 86% white, with a high prevalence of persons who inject drugs, this would suggest, and encourage, that those are the populations we direct the bulk of resources to. Ignoring that information because it doesn’t fit the messages of national health campaigns is reckless and lazy.

HIV/HCV does not disproportionately affect populations simply because of their cultural variable.

I would hope this goes without saying, but by chance that isn’t the case let me explain. African Americans are not disproportionately affected by HIV incidence simply by proxy of being African American. Rather, they exist within structural systems of policy and social norms that limit their agency and lead to social determinants of health that indirectly increase risk. The same can be said for men who have sex with men. In prevention we have a phrase you may be familiar with, “It’s not who you are, it’s what you do,” a nice sentiment that we don’t truly let guide us as often as it should.

This distinction is important because the narrative that is projected through health campaigns inadvertently leads the general public to ignore their risk as a result of “othering.” If the highest risk group is men who have sex with men and African Americans, then what health information would regularly be encountered to lead heterosexual women to be aware their risk of contracting HIV/HCV is also high? None. Not until you tell them that over 50% of all new HIV infections are among heterosexual women. There is a very real possibility that targeted outreach and health information as a direct result of macro epidemiology data contributes to a cycle of HIV/HCV incidence by way of limiting peripheral vision.

The second danger of epidemiology data is that it takes a while to verify and compile. Rightly so, we want this data to be valid and statistically significant. Yet, this is all the more reason to keep in mind most publicly available epidemiology data is a year old.

Which means, more often than not, we are working on an information delay. So when people present the argument to me that, “we need the numbers,” to support the declaration of an HIV/HCV state of emergency, my response is usually an exasperated one.

You see, we can only get the data if there are large numbers of people infected with HIV/HCV, which is what the entire field of prevention is trying to avoid. In addition, the subtle message that accompanies such a statement is that in order to take action there
is only one statistic that will allow it. Again, this ignores the possibility of using peripheral epidemiology data such as other social determinants of health to predict the possible occurrence of an increase in HIV/HCV incidence.

Sometimes I like to think of myself as a weatherman. I’m not as crazy as that sentence reads. Just hear me out. Instead of looking at humidity, weather patterns and air streams to predict storms, I look at social determinants of health to predict spikes in HIV/HCV incidence before they happen. I have found this process to be further complicated by the differences of importance people place on chronic HCV incidence versus acute HCV incidence. There appears to be a persistent mindset that chronic HCV numbers are the only ones that matter.

Roughly 75% of people who are exposed to HCV develop chronic infection, liver complications and are likely to require treatment. The other 25% of people will virally suppress HCV on their own resulting in no long-term complications or need for treatment.

This focus on chronic HCV likely comes from the cost of treatment. In 2016 the Medicare system will incur costs of 9 billion dollars to treat all U.S. persons living with chronic HCV. Some economic models predict the cost to treat all chronic HCV persons living in the U.S. would exceed 300 billion dollars.

These economic projections are all the more reason to pay close attention to acute HCV incidence rates. Ultimately, acute cases of HCV are signs of risk occurrence. They indicate the sharing of injection equipment and continued exposure to possible HIV contraction. They indirectly tell us where we need to be. Ignoring them simply doesn’t make sense. Epidemiology data is crucial; vital in fact, but we should not, and cannot, allow that data to limit our creativity and innovation in prevention.

Prevention is about limiting, slowing, or eradicating the incidence, morbidity and prevalence of illness. In order to do this effectively we need to be predictive, not reactive. I understand, and support, the need for statistically valid data to be successful with grant funding and policy change. I am not refuting the necessity of it.

The truth is, however, that even though epidemiology data is sound in methodology and objective in the information it reveals, how it is used can be highly subjective when trying to advocate for policy change. My issue isn’t with the tool, but with the arguably intentionally incorrect fashion by which that tool is used.

There is no better example I can think of to highlight the consequences of improperly using epidemiology data than what can occur in the process of Senate Bill 461 (SB 461). SB 461 is a law signed & approved by Indiana Governor Mike Pence that authorizes an emergency syringe exchange program (SEP) in Scott County. Additionally, the law allows individual counties within Indiana to approve and operate an SEP as long as they complete required steps.

The approval of SB 461 was intended to project a sense of urgency and empathy for those affected by the HIV outbreak while pragmatically addressing the health crisis. A message that I could have gotten on board
“Some would say that at least SB 461 is a step in the right direction, and that we are making progress. I agree with that sentiment, in part…”

with had the legislation not been signed until well into the HIV outbreak. If we are being honest, Governor Pence more than likely signed SB 461 at the behest of the CDC than his own volition.

I’m sure somewhere in the hallowed halls of a dysfunctional Indiana legislature feelings of urgency and empathy can be found. Keep in mind, however, that over the course of the previous few years this is a State Government that has shown a lack of emotional intelligence and flexibility in regard to broader social concerns. A lack of self awareness that has landed it in the national spotlight on more than one occasion. I would never suggest a part is representative of the whole, I know Indiana government officials and policy makers can be found who are rational, pragmatic and emphatic of the HIV/Hepatitis C and substance use epidemic. I’ve talked to them myself. I am grateful that they’ve fought hard, and continue to fight, for an effective and comprehensive approach to this growing public health concern.

The truth is though, SB 461 is really just a half measure designed to placate the public and abdicate responsibility, more than pragmatically address the crisis. Ultimately, the legislation gives the appearance of autonomy for individual counties to approve a SEP, but in reality the law is laden with a key barrier that can make it difficult to get approval.

Some would say that at least SB 461 is a step in the right direction, and that we are making progress. I agree with that sentiment, in part, but in the time that elapses while counties try and navigate the process of approving SB 461, people are still contracting HIV/HCV at a unprecedented rates. It is true that the door has been unlocked for us, but an unlocked door is only as advantageous as the person standing in front of it.

For a SEP to be approved and operated within an Indiana county a series of steps need to be completed. First, the county has to declare a public health emergency of HIV/HCV. This declaration has to come from the county health commissioner who is likely to make the decision, in part, using epidemiology data that is outdated and/or only representative of chronic HCV incidence. This power of the county health commissioner to turn the first lever can be a very difficult step in the process to navigate. After a state of emergency for HIV/HCV is declared, a vote must take place among the local legislature, and then only after that can a SEP legally operate under SB 461.

The successful navigation of all of those steps, which can take months, only ensures the opportunity to run a SEP. The funding, staffing and housing resources of the operation have to come from somewhere else. These requirements are a tall order to fill, especially in rural parts of Indiana where resources range from limited to nonexistent.

Gauging public opinion and engaging in civil discussion about SEPs so that concerns are addressed, and law enforcement is supportive, is important to the long-term health of individuals who access SEPs. I firmly believe that transparency is key. I also firmly believe that in dire situations like the one we now find ourselves in throughout Southern Indiana and Evansville, the long-term cost we incur by laboring through that process significantly outweighs the benefits. The argument against SEPs cannot be one of their efficacy. On that subject there is little to no debate. We can’t be anymore right on the fact that SEPs are effective at reducing HIV/HCV incidence while also increasing retention in abstinence-based treatment by 5x on average.
According to 2010 estimates, the economic cost of lifetime treatment for HIV infection is around $380,000 per person. That means the lifetime cost to treat the 175 persons who contracted HIV in Scott County is 66 million dollars. Add to that the cost of a Hepatitis C treatment that averages roughly $89,000 for 12 weeks, and you have the recipe for an economic situation that, when put mildly, is crippling.

We have to get to a point where we realize we all want the same thing. We want our communities and families to be loved, healthy and safe. What we spend far too much time arguing about is how to get there.

SEP isn’t the silver bullet to the current HIV/HCV epidemic among persons who inject drugs. It cannot stand-alone. We still need abstinence based treatment facilities, NA/AA meetings, support groups, hospitals and community health organizations. We need law enforcement to carry naloxone and continue addressing the issue of narcotics coming into the city while we also work to keep them safe.

We need social workers and social service agencies to continue creating safe spaces where marginalized groups can come to receive comprehensive services without fear of judgement. We need to lead the advancement of HIV/HCV prevention with innovation and fearlessness by changing the structure within which we all live. We need to take the risk that we may be wrong, because there is no other way to know if we are right.

Above all, we need to remember that behind all the metrics and measurable, behind all the p-values and the 95% confidence intervals stand our brothers and sisters, our mothers and fathers and our significant others. That underneath all the multivariate analysis and the linear regressions is our family, our community, asking for just a little bit of the most inexhaustible resource on earth. Compassion.

Matthew Zielske currently works as a HIV/HCV special populations prevention specialist at an HIV services organization. He utilizes a harm reduction model in his work with the substance use population focusing pointedly on persons who inject drugs. He is currently conducting research on Health Literacy and hepatitis C for his Master's Thesis in Communications.

New data was just released by the Centers for Disease Control and Prevention (CDC) in conjunction with Hepatitis Awareness Month.

**Acute Infections:** It was estimated that there were 30,500 acute or new HCV infections of hepatitis C in 2014. The acute infections are mostly among younger adults who inject drugs. The criteria for reporting acute infections and the surveillance system in the United States lead many people to believe that the true number is much, much higher.

**Chronic Infections:** The estimated number of people in the United States who are chronically infected with hepatitis C is 3.5 million. Again, this number is most likely underestimated since much more testing is needed to reveal the true number of chronic hepatitis C.

**Deaths:** In 2014 there were an estimated 19,659 deaths attributed to hepatitis C. This number is from death certificate information. Hepatitis C may not be listed as a cause of death on the death certificate. Also, hepatitis C may be a contributing factor to a death but not list as cause of death.

Disclaimer: The viewpoints and opinions expressed in this essay are solely those of Matthew Zielske. They do not represent the views of his employer, funding sources or community partners.
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 HCV Advocate Newsletter

**Genotype (s):** This lists the drugs or combination of drugs and the particular genotype or genotypes that the drug is active against.

**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 the International Liver Congress 2016. More detailed information about drugs in development is available in our blog and reported in the HCV Advocate newsletters.

<table>
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<th>AbbVie</th>
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<td><strong>COMMENTS:</strong></td>
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<td><strong>Genotype 1b - Phase 3b Study:</strong> 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. <strong>Approved by the Food and Drug Administration in April 2016.</strong></td>
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**AbbVie**  
**Genotype(s):** 1, 2, 3, 4, 5, 6 (Pan-genotypic)

**COMMENTS:**  
**Genotype 1 – Phase 2 Study:** Information from the International Liver Congress 2016: AbbVie’s once-daily therapy of ABT-493 (protease inhibitor) and ABT-530 (NS5A inhibitor).

**Non-cirrhotic patients Treatment period - 8 weeks:**
- Genotype 1: 85% were treatment-naïve; 15% were pegylated interferon(PEG)/ ribavirin (RBV) experienced, cure rates—97% (33 of 34 patients)
- Genotype 2: 87% were treatment-naïve; 13% were PEG/RBV treatment experienced: cure rate—98% (53 of 54 pts)
- Genotype 3: 100% were treatment-naïve: cure rate—97% (28 of 29 pts)

**Treatment period 12 weeks:**
- Cirrhotic treatment-naïve patients, genotype 3 – cure rate —100% (24 of 24 patients)
- Non-cirrhotic treatment-naïve patients (85%), PEG/RBV (15%); genotype 4 (22 pts), genotype 5 (1 pt), genotype 6 (11 pts)—cure rate—100% (34 of 34 pts)

**Bottom line:** cure rates were 97% to 100%.

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**Gilead**  
**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:** Information from ILC 2016: In the group of treatment-naïve patients treated for 6 weeks the cure rate was 79% (53 of 67 pts); the treatment-naïve group that was treated for 8 weeks the cure rate was 96% (95 of 99 pts)

In another study to treat people who are treatment experienced genotype 1 through 6 and who had been treated with a previous course treatment—prior NS5A-experienced (27%); non-NS5A-experienced (52%), direct-acting antiviral-experienced (DAA (52%), and 21% that failed an interferon-based therapy without a DAA. The cure rate was 99% (127 of 128 pts).

In yet another study GS-9857 with sofosbuvir/velpatasvir was tested to treat DAA experienced genotype 1 patients with cirrhosis. The treatment period was 12 weeks. The cure rate was 100% (24 of 24 pts).

**The bottom line:** the cure rates were in the 79% to 100% in people treated 6 to 12 weeks.

The combination of sofosbuvir, velpatasvir and GS-9857 is currently in phase 3 clinical trial (POLARIS 1,2,3 and 4). The Food and Drug Administration (FDA) has granted the combination as Breakthrough Therapy for those who have previously failed an NS5A Inhibitor-containing regimen.
Janssen (Achillion/Alios)                  Genotype 1,2,3,4,5,6 (Pan-genotypic)

**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-naïve 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-naive 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.

- **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.

- **Genotypes 1 through 6–Phase 2b Study:** Odalasvir, AL-335, and simeprevir in treatment-naïve and treatment-experienced patients with and without cirrhosis. The trial will enroll 400 patients for six or eight weeks. The study will include four arms with different combinations of drugs. The trial will begin in June 2016 and end in July 2017.
**COMMENTS:**

- **Phase 2** - The study was to evaluate the safety and efficacy of all-oral therapy of grazoprevir; MK-3682, and either elbasvir or MK-8408.

In Part A of 2 ongoing clinical trial of 93 genotype 1 patients (46 genotype 1a, 47 genotype 1b), 61 genotype 2 patients, and 86 genotype 3 treatment-naïve, non-cirrhotic patients. The patients were treated for eight weeks with a combination of one of the above medications as a once-a-day dose.

The cure rates were 98% for genotype 1a (45 of 46 pts); 98% genotype 1b (46 of 47 pts). There were no treatment-related RAVs associated in the people who relapsed.

The cure rates across all three arms in genotype 2 patients was 60-71%. However, in the group that received grazoprevir/MK-3682 (450 mg)/MK-8408 regime achieved a 94% (15 of 16 patients) cure rate.

The cure rates in genotype 3 patients were 91% (78 of 86 pts) that was comparable across all arms (86 – 95%).

The Bottom Line: The 8-week therapy of grazoprevir/MK-3682 (450 mg)/MK-8408 produced high cure rates in genotypes 1, 2, and 3 treatment-naïve patients with mild disease.

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**COMMENTS:**

Regulus Therapeutic Inc.

The study included 79 treatment-naïve genotype 1 and 4 patients. RG-101 is a GalNAc-conjugated anti-miR targeting miR-122, a host factor for HCV infection. It is an injectable medication given at Day 1 and Day 29 plus 4 weeks of a once-a-day direct-acting antiviral medication –Harvoni (27 patients), Olysio (27 patients), Daklinza (25 patients). Sixty-four of the patients were evaluated through week 8 of follow-up, 41 reached 12 weeks post treatment.

The cure rate was 97% (40 of 41 pts).
This will be the last issue of the Mid-Month HCV Advocate Newsletter. We have decided to dedicate our time and resources to the Monthly HCV Advocate, the HCV Advocate News and Pipeline Blog and our social media accounts.

IMPORTANT ANNOUNCEMENT!

WE HAVE REVIEWED AND UPDATED THE FOLLOWING FACT SHEETS

A Guide to HIV/HCV Coinfection

Easy C: A Guide to Hepatitis C

The HCV Advocate offers information about various forms of intervention in order to serve our community. By providing information about any form of medication, treatment, therapy or diet we are neither promoting nor recommending use, but simply offering information in the belief that the best decision is an educated one.

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