Hepatitis C Screening, Prevention, and Treatment: Lo que aprendimos trabajando con comunidades Latinas

Center for Research to Advance Community Health (ReACH)  
University of Texas Health Science Center at San Antonio

Andrea Rochat, MFA – Project Manager, Writer at the ReACH Center  
Dolores Cortez, LVN – Brownsville Community Health Center  
Barbara J Turner, MD, MSED – ReACH Director, Professor of Medicine
Overview

- Hepatitis C Virus (HCV) Prevalence
- Effects of Hepatitis C
- Prevention, Screening, and Diagnosis
- Education, counseling, and care coordination
- Treatment
- Barriers and Solutions
Screening and Care Coordination

- **Settings**
  - Inpatient in safety net hospital in Bexar County (Dec 2012 – Sept 2014)
    - CDC funded
  - Outpatient/Primary care (2014 – Ongoing)
    - CMS funding through 1115 Medicaid Waiver:
      - Bexar County
        - 2 safety net clinics in Bexar County within University Health System
        - 3 UT-affiliated primary care clinics in Bexar County
      - Rio Grande Valley – 2 Federally Qualified Health Centers (FQHCs)
        - Brownsville Community Health Center
        - Nuestra Clinica del Valle
    - Cancer Prevention Research Inst. of TX (CPRIT) funding
      - Parkland Health and Hospital System
      - 18 clinics across 14 counties in South Texas
Screening and Care Coordination

**Methods**
- Electronic medical record (EMR) **flag** for eligibility
  - Birth year 1945-65
  - Never-tested for HCV
  - No prior diagnosis of HCV
- Posters and flyers for **education** and **opt out** consent
- Order for **HCV Antibody test** with confirmatory **HCV RNA Quantitative test**
- Personalized counseling, **case management**
- Follow-up **linkage to care** and treatment
  - Remote or onsite
HCV Prevalence
United States and Texas
HCV Statistics

- An estimated 3.7 to 5 million persons have HCV
- Nationally, HCV is the most common blood borne infection
- Cirrhosis develops in 10% - 20% of persons with chronic HCV after 20 to 30 years
- HCV deaths total more than the next 60 infectious diseases combined (including HIV)

Chou R. Screening for Hepatitis C Virus Infection: Systematic Evidence Review No. 24. AHRQ
In 2000, nearly 400,000 Texans (1.79%) were estimated to be chronically HCV+.
HCV is Nearly 4 Times as Prevalent as HIV and HBV

Prevalence of Chronic Viral Infections

- **HIV**:
  - Undiagnosed: ~800,000 to 1.4 Million
  - Diagnosed: 1.1 Million
  - 75% Unaware of Infection

- **HBV**:
  - Undiagnosed: 2.7 to 3.9 Million
  - Diagnosed: ~800,000 to 1.4 Million
  - 65% Unaware of Infection

- **HCV**:
  - Undiagnosed: 75% Unaware of Infection

HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus.

HIV and HCV – Quick Facts

• Of people with HIV in the United States:
  • ~25% are coinfected with HCV
  • ~10% are coinfected with HBV

• About 80% of people with HIV who inject drugs also have HCV

• HIV co-infection more than triples the risk for liver disease, liver failure, and liver-related death from HCV
Two of Three Americans Infected With HCV Were Born From 1945-1965

- Reflects high incidence in past
- 5x higher prevalence than other birth cohorts (3.4 vs. 0.5%)
- 81% of HCV infected adults and 73% of HCV mortality

**CDC RECOMMENDATION:** Screen all individuals born between 1945-1965

Smith. AASLD SF 2011.
Kramer. Hepatology 2011
Ly. An Int. Med 2011
Prevalence of HCV by Birth Year

NHANES, 2002
Patient Characteristics and Prevalence of HCV: National Data

<table>
<thead>
<tr>
<th></th>
<th>NHW</th>
<th>NHB</th>
<th>MA</th>
<th>&lt; HS</th>
<th>&gt; HS</th>
<th>&gt; 2 times</th>
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<tr>
<td>Race/Ethnicity</td>
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<td>3.3</td>
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<tr>
<td>Poverty threshold income</td>
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</tr>
</tbody>
</table>

NHW: Non-white Hispanic  
NHB: Non-Hispanic Black  
MA: Mexican American  
HS: High School  

Figure 1: 2013 HCV Population by Disease State and Payer

In 2013, Most of the People with Undiagnosed HCV Have No Insurance
Most People with HCV Have Mild/Moderate Disease

- Undiagnosed: 1,317,090
- Diagnosed w/ Mild/Moderate: 888,810
- Diagnosed w/ Cirrhosis: 401,810
- Diagnosed w/ Advanced Liver Disease: 34,790

Source: Authors’ analysis of NHANES, MarketScan 2010, Medicare 5% Sample, and Medicaid Contributor data. Does not include prison population.

Effects of Hepatitis C
Hepatitis C infection:

- There is NO vaccine for HCV infection
- Often few or no symptoms for years
- Acute infection: short term illness but in 60-85% can lead to:
- Chronic infection: long-term, potentially deadly disease of the liver and may lead to:
  - Fibrosis (scarring)
  - Cirrhosis (permanent scarring and liver failure)
  - Liver cancer (HCC)

http://www.webmd.com/hepatitis/ss/slideshow-hepatitis-overview
Time From HCV Infection Until Serious Complications

- Normal Liver
- Fibrosis
- Cirrhosis
- End Stage Liver Disease
- Stable Disease
- HCC

About 30 years

Cure reduces but does not eliminate the risk of liver failure and Hepatocellular Carcinoma (HCC)
Liver Failure

- Significant cause of morbidity and mortality – high demand for health care services

- About 50% of all U.S. liver transplantations result from liver damage from HCV infection at a cost of >$100,000

- Although most persons with HCV will not need a transplant, even a few are very expensive

Picture from: http://www.who.int/patientsafety/education/curriculum/course10_handout.pdf
Hepatocellular Carcinoma (HCC)

- Most common type of liver cancer
- Chronic HCV increases the risk
- Treated with surgery, medications or liver transplant
- Poor prognosis:
  - HCC related to HCV is the fastest rising cause of cancer related deaths in the US
  - **Best option**: primary prevention
How is HCV spread?

Source: CDC and Prevention
Previous CDC Guidelines for **Risk-based** Screening:

- **High Risk Clinical Conditions**
  - e.g. Transfusions or organ transplants before July 1992; clotting factor given before 1987, HCV+ transfusion; Children born to HCV-infected women; HIV infection

- **High Risk Behaviors**
  - e.g. Injection-drug; intranasal drug abuse; tattoo in unregulated setting

- **High Risk Settings**
  - e.g. Incarceration; Healthcare/public safety workers exposed to HCV+ blood; Born in a high risk country
Risk-Based Screening is **NOT** Enough

- **70-80%** of people with hep C don’t show any symptoms
- **Up to 75%** of people living with Hepatitis C do not know they are infected

Talk to your doctor about getting tested. It could save your life.
Remember the Baby Boomers?

- 5x higher prevalence than other birth cohorts (3.4 vs. 0.5%) 
- 81% of HCV infected adults and 73% of HCV mortality 
- New research points to incidence rising earlier than thought – due to lapses in the healthcare system

**CDC RECOMMENDATION:** Screen all individuals born between 1945-1965

NEW US Preventive Services Task Force (USPSTF) Guidelines - 2012

- One time screening of all baby boomers (born 1945 through 1965) for HCV infection (USPSTF Rating: Class I, Level B)
Hepatitis C
Testing baby boomers saves lives

3 Million
About 3 million adults in the US are infected with the hepatitis C virus, most are baby boomers.

3 in 4
Up to 3 in 4 people who are infected don’t know they have hepatitis C so they aren’t getting the necessary medical care.

1945–1965
Baby boomers, anyone born from 1945 through 1965, should get tested for hepatitis C.

Source: CDC Vital Signs, May 2013 | www.cdc.gov/vitalsigns
Diagnosing HCV

Lab Tests and Risk Measures
Screening Flow

Recommended Testing Sequence for Identifying Current HCV Infection

- **HCV Antibody**
  - **Nonreactive**
    - No HCV antibody detected
    - STOP*
  - **Reactive**
    - No current HCV infection
    - Additional testing as appropriate†
    - Current HCV infection
    - Link to care
  - **HCV RNA**
    - Not Detected
    - Additional testing as appropriate†
    - Detected

*For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

†To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.
HCV Genotype 1a: Most Common in U.S.

2/3 genotype 1a
1/3 genotype 1b
Baseline Labs for Evaluation of Chronic Infection

- Basic: CMP, CBC, and INR
- Genotype
  - Including subgenotype (1a vs. 1b)
- Screen for Hepatitis A and B
  - Consider vaccination if not immune
- HIV screen
Staging Liver Disease

Liver biopsy has been gold standard but noninvasive evaluation are increasingly used to reduce risk and cost.

- FIB-4 measure (algorithm of age, ALT, platelet, AST)
- Imaging (liver ultrasound or CT)
- FibroSure (Expensive—not widely available)
Patients With Cirrhosis
Serial Screening with Ultrasound

• Ultrasound is the recommended for HCC surveillance

• Advantages:
  • cheap, safe, readily available, supported by data

• Drawbacks:
  • operator dependent, limited sensitivity, difficult in obese patients
  • Masses detected by ultrasound require further characterization with other modalities (CT, MRI)

Sonogram shows a small hypoechoic mass

Questions for the audience:
What do you think are common misconceptions about patients with HCV?

How do these misconceptions impact a patient’s healthcare experience?
Patient Education and Lessons Learned by an LVN

~Dolores Cortez, LVN – Brownsville Community Health Center
Methods

• One-on-one case management and counseling
• Motivational interviewing
• Customized, bilingual mobile app, educational materials
Key Points for Patient Counseling

- Reduce the risk of transmission
  - Exposure to blood, rough sex, sharing needles

- Strategies to reduce damage to the liver
  - No alcohol, herbal meds, some prescription drugs (eg Tylenol)

- Destigmatize HCV, offer hope
  - Highly effective treatment options

- Gauge, improve compliance

- Offer support
  - Insurance coverage, access to costly drugs, close monitoring for complications
Factors That Can Worsen HCV-Related Liver Damage

• Alcohol consumption
• HIV
• Co-infection with hepatitis A or B
• Older age (>40 years) at infection
• Diet – high cholesterol
• Obesity related fatty liver disease?
HIV Shortens Time to Cirrhosis

http://hcv.guidelinecentral.com/toolbox/patient-resources/co-infection-timeline-hiv/
The Good News! Highly Effective Direct-Acting Drugs = Cure
Preparing for HCV Therapy

**HCV Evaluation and Staging**
- Treatment history (interferon therapy or DAA)
- Genotype (1, 2, 3..) and subgenotype (1a vs 1b)
- Imaging
- Viral load (copies/mL)
- Fibrosis score (i.e. Fib-4)
- Drug-drug interactions (DDIs)
Goal of Treatment

- Most regimens offer >90% cure
- Newer regimens are simpler, present fewer complications than prior approaches
Selecting HCV Regimens

- Interferon-free, all-oral regimens with cure rates >90%
- Most regimens 12 weeks with few side effects
- Choice of regimen and treatment duration
  - Genotype
  - Presence of cirrhosis
  - Prior HCV treatment experience (uncommon in most patients)
- Watch for drug-drug interactions
HCV Cure: Sustained Virologic Response (SVR)

- Check HCV RNA after 12 and 24 weeks post treatment
  - Typically negative at 12 weeks post treatment, though some patients take up to 24 weeks to clear infection
  - An undetectable level at 12 weeks post treatment is generally maintained through week 24
Question for the audience:

What do you think are the most pressing barriers facing patients diagnosed with chronic HCV?
Cost of Drugs for Treatment

<table>
<thead>
<tr>
<th>Treatment Duration</th>
<th>Cost in USA</th>
<th>Cost per Pill</th>
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</thead>
<tbody>
<tr>
<td>8-week treatment</td>
<td>$63,000</td>
<td>$1,125</td>
</tr>
<tr>
<td>12-week treatment</td>
<td>$94,500</td>
<td>$1,125</td>
</tr>
<tr>
<td>24-week treatment</td>
<td>$189,000</td>
<td>$1,125</td>
</tr>
</tbody>
</table>
Barriers— a growing list!

Patient
- Competing priorities
- Substance use
- Low perceived health risks
- Fear (for person, for family)
- Stigma
- Education / Health Literacy

Provider
- Access
  - To insurance
  - To specialists
- Costs/Financial Toxicity
  - Testing
  - Treatment
  - Transportation

System
- Insurance coverage/lack thereof Medicaid eligibility
Solutions – a growing list!

**Patient**
- Competing priorities
- Substance use
- Low perceived health risks
- Stigma

**Provider**
- Lengthy application process for compassionate drug programs
- Fear (for person, for family)
- Education / Health Literacy
- Costs/Financial Toxicity
  - Testing
  - Treatment
  - Transportation
- Access
  - To insurance
  - To specialists

**System**
- Insurance coverage/lack thereof Medicaid eligibility

**Patient Provider System**
- Individualized case management
- HCV mobile app
- Motivational interviewing/change language
- Address peripheral barriers in patients’ lives

**Education of community**
- Increase visibility, increase dialogue, decrease stigma
- National advocacy
- Partnership with social services

**System**
- Activate primary care as treatment setting (remote medical mentoring)
- Compassionate drug programs with leniency re: SSN#
- Patient Advocacy Foundation (to support copays)
- National advocacy (incentivize screening, expand Medicaid)
- Drug costs are lowering
Final thoughts

- Screen all baby boomers for HCV infection
- Diagnose chronic HCV infection and counsel patients with chronic infection
- Evaluate disease stage
- Partner with hepatologists to bring treatment patients with chronic HCV
Question for the audience:

What are the next steps to confront a less visible disease in less visible populations? What can we be working on/toward?
Thank You!
More on HCV/HIV (if needed)
More on HCV and HIV

• Of people with HIV in the United States
  • About 25% are coinfected with HCV
  • About 10% are coinfected with HBV

• About 80% of people with HIV who inject drugs also have HCV

• HIV co-infection more than triples the risk for liver disease, liver failure, and liver-related death from HCV

• In the United States, HCV is twice as prevalent among blacks as among whites

• HCV deaths are more than the next 60 infectious diseases combined
  • 30,000 deaths per year

CDC, 2015
Preparing for HCV Therapy

HCV Evaluation and Staging
- Treatment history (interferon therapy or DAA)
- Genotype (1, 2, 3..) and subgenotype (1a vs 1b)
- Imaging
- Viral load (copies/mL)
- Fibrosis score (i.e. Fib-4)
- Drug-drug interactions (DDIs)
Treatment depends on the type of hepatitis C virus infection.
Staging Still Matters
*Cirrhosis or No Cirrhosis, That Is the Question*

- The presence of cirrhosis may affect:
  - Treatment decisions\(^a\)
    - Timing of initiation of treatment
    - Choice of treatment regimen
    - Decision to use ribavirin
    - Duration of treatment
  - Clinical management decisions
  - Post-treatment follow-up and screening for liver cancer\(^b\)

\(^a\) AASLD website.\(^1\)
Liver Biopsy

No Longer the Gold Standard for Staging Liver Disease

- Most done in hospital settings
- Requires preparation
- Invasive
- Requires technical skill
- Time consuming
- Uncomfortable to patient
- Potential complications and harm
- Yields small amount of tissue
- Expensive

Alternatives for staging

i. Liver biopsy
ii. Ultrasound
iii. Fib-4/APRI
iv. Fibroscan/elastography
v. Fibrotest/fibrasure/hepatsure
Traditional Noninvasive Methods of Fibrosis Assessment

- Clinical examination is specific, but not sensitive
  - The patient with physical signs of cirrhosis probably has cirrhosis
  - The absence of physical signs does not exclude the presence of cirrhosis

- Ultrasound
  - The patient with splenomegaly and an enlarged portal vein probably has cirrhosis
  - The absence of splenomegaly and an enlarged portal vein does not exclude the presence of cirrhosis
Vibration-Controlled Transient Elastography

Vibrations of mild amplitude and low frequency are transmitted by the transducer, inducing an elastic shear wave that propagates within the liver. Pulse echo ultrasonic acquisitions are performed to follow the shear wave and measure its speed, which is directly related to the tissue stiffness. The harder the tissue, the faster the shear propagates.

Challenges With VCTE™

• Not available to all clinicians
• Unreliable in some conditions
  – Obesity
  – NAFLD with BMI >30 kg/m²
  – Acute hepatitis with ALT flares
  – Extrahepatic cholestatis, hepatic congestion, hepatic amyloidosis
  – Food intake with 60 minutes of test
• Use for monitoring patient who achieves SVR is unclear

Platelet Count

Thrombocytopenia

- Portal Hypertension/Hypersplenism
- Anti-Platelet Antibodies
- Viral Suppression
- Cirrhosis
- Hepatocellular Carcinoma Chemotherapy
- Decreased Thrombopoietin Levels/Activity

Laboratory Evaluation of Chronic HCV

- HCV genotype
- CBC with platelets
- Hepatic function panel
  - including total bilirubin, AST, ALT, Alk phos
- INR
- Albumin
- Creatinine
- HIV
  - 1% of HCV pts will be HIV + whereas 40% of HIV pts will be HCV positive
Case

• Lab tests obtained for this patient
  • AST 53, ALT 42, AP 136
  • ALB 3.1, T BILI 1.2,
  • WBC 3.4, HGB 13.5, PLT 105,000
  • INR 2.0
  • HIV negative

• Ultrasound notes irregular liver border, mild splenomegaly and no masses
  • Impression: cirrhosis
FIB-4 Calculation

• To estimate the amount of scarring in the liver.

\[
FIB-4 = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10^9/L)} \times \sqrt{\text{ALT (U/L)}}}
\]

= 4.21

• Interpretation:
  • Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis. In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Direct Acting Antivirals

### HCV Therapy

<table>
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<th>Time Period</th>
<th>Therapy Duration</th>
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<td>48 weeks</td>
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<td>2011-2013</td>
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<td>2014</td>
<td>12 weeks</td>
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<td>2015</td>
<td>8-24 weeks</td>
<td>2016</td>
</tr>
<tr>
<td>2016</td>
<td>12-16 weeks</td>
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## Table 1. Current Recommended Treatments and Future Regimens for Treatment-Naïve and -Experienced HCV Patients

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Preferred and Alternative</th>
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<tbody>
<tr>
<td>1a</td>
<td>SOF/LDV 12 wk^a</td>
</tr>
<tr>
<td></td>
<td>PAR/r+OMB+DAS+RBV 12 wk^b</td>
</tr>
<tr>
<td></td>
<td>PAR/r+OMB+DAS 12 wk^c</td>
</tr>
<tr>
<td>1b</td>
<td>SOF+DCV±RBV 12-24 wk^g,h</td>
</tr>
<tr>
<td></td>
<td>GRA+ELB±RBV for 12 wk^h</td>
</tr>
<tr>
<td>2</td>
<td>SOF+RBV 12 wk or 16 wk (if cirrhosis)</td>
</tr>
<tr>
<td>3</td>
<td>SOF+RBV 24 wk</td>
</tr>
<tr>
<td></td>
<td>SOF/LDV+RBV 12 wk^h</td>
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<td>4</td>
<td>SOF+DCV±RBV 12-24 wk^g,h</td>
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<tr>
<td></td>
<td>SOF+PegIFN+RBV 12 wk</td>
</tr>
<tr>
<td></td>
<td>SOF+SMV±RBV 12 wk^f,h</td>
</tr>
<tr>
<td>5</td>
<td>SOF+PegIFN+RBV 12 wk^h</td>
</tr>
<tr>
<td>6</td>
<td>SOF/LDV 12 wk^h</td>
</tr>
</tbody>
</table>

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DAS, dasabuvir; DCV, daclatasvir; ELB, elbasvir; GRA, grazoprevir; LDV, ledipasvir; OMB, ombitasavir; PAR, paritaprevir; PegIFN, pegylated interferon; R, ritonavir; RBV, ribavirin; SMV, simeprevir; SOF, sofosbuvir
Recommended regimens per guidelines

• HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed). Rating: Class I, Level B

• Daily daclatasvir plus sofosbuvir (400 mg), with or without RBV (refer to Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed sections for duration) is a Recommended regimen when antiretroviral regimen changes cannot be made to accommodate alternative HCV direct-acting antivirals. Rating: Class I, Level B

• Do not use course shorter than 12 weeks
Ledipasvir + Sofobuvir (Harvoni)

- Neither drug inhibits any cytochrome P450 enzyme
- Daily fixed-dose combination can be used with most antiretrovirals.
- Because ledipasvir increases tenofovir levels, when given as tenofovir disoproxil fumarate (TDF) should be avoided in those with CrCl below 60 mL/min.
- Also do not use with ritonavir-boosted regimens
- In a study of HCV treatment-naïve and -experienced HIV/HCV-coinfected patients were enrolled in the study and received ledipasvir/sofosbuvir once daily for 12 weeks,
  - 20% of patients had cirrhosis, 34% were black, and 55% had not responded to prior HCV treatment
  - 96% SVR
Changes in ARV therapy with HCV drugs

• Mild inhibitor of CYP3A4 substrate
• In combination with other antivirals:
  • Dose adjustment with ritonavir-boosted atazanavir (a decrease to 30 mg daily) and efavirenz or etravirine (an increase to 90 mg daily).
  Rating: Class IIa, Level B

• Daily fixed-dose combination of elbasvir/grazoprevir:
  • Avoid interactions so can use: abacavir, emtricitabine, enfuvirtide, lamivudine, raltegravir, dolutegravir, rilpivirine, and tenofovir.
  Rating: Class IIa, Level B
Paritaprevir/ritonavir/ombitasvir plus dasabuvir

- Use with drugs that do not have significant interactions: atazanavir, dolutegravir, emtricitabine, enfuvirtide, lamivudine, raltegravir, and tenofovir. Again ritonavir may need to be reduced or stopped.
- Ribavirin should NOT be used with didanosine, stavudine, or zidovudine (especially serious with DDI).
- RBV has the potential for dangerous drug interactions with didanosine resulting in mitochondrial toxicity with hepatomegaly and steatosis, pancreatitis, and lactic acidosis.
- Results in >90% response -
New HCV agents 2016

• Elbasvir/grazoprevir
  • Genotypes 1 and 4
  • Treatment naïve and experienced
  • Cirrhotic and non-cirrhotic
  • 12-16 weeks, >90% SVR
  • Use in CKD including hemodialysis and no PPI interactions
  • *Without ribavirin* seems to be effective and well tolerated for patients coinfected with HIV with or without cirrhosis

• Velpatasvir
  • Pangenotypic!