HCV Screening, Management, and Treatment Guidelines

Paulina Deming, PharmD, PhC
Associate Professor of Pharmacy-College of Pharmacy
Project ECHO
University of New Mexico Health Sciences Center

April 4, 2019
Agenda

1. Recognize and stage a patient’s level of liver disease using common laboratory tests and imaging
2. Describe new therapeutic options for the treatment of chronic HCV
3. Recognize and assess the clinical significance of common drug-drug interactions with oral-HCV therapies
4. Use national algorithms and guidelines to guide treatment strategies for patients with HCV infection
Conflict of Interest Disclosure Statement
Hepatitis

- Spread via blood-to-blood contact
  - usually asymptomatic
- Leading cause for liver transplantation in the US
- ~75-80% of acute infections become chronic
  - chronic infection- detection of virus 6 months post-exposure
- No vaccine available
- Prevalence is 1.6% of US population
Hepatitis C is a Global Health Problem

Estimated 170 million persons with HCV infection worldwide

Prevalence of infection
- > 10%
- 2.5%-10%
- 1%-2.5%
- 1%-
- NA

World Health Organization 2008 (http://www.who.int/ith/es/index.html)
Risk Factors for HCV Infection

• Persons born between 1945-1965
• Received blood transfusion or organ donation prior to 1992
• Current or former injection drug users
• Chronic hemodialysis patients
• Any known blood exposure to HCV-positive blood
• Persons with HIV
• Children born to HCV-infected mother
CDC Testing Algorithm for Chronic HCV

Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

- **Nonreactive**
  - No HCV antibody detected
  - STOP

- **Reactive**
  - HCV antibody detected
  - HCV RNA
    - Not Detected
      - No current HCV infection
      - Additional testing as appropriate
    - Detected
      - Current HCV infection
      - Link to care
Hepatitis C Genotypes

- 6 major genotypes (1-6), most with subtypes

- Genotype 1
  - GT 1b different than GT 1a

- GT 2 easier to treat than GT 3

- GT 3 associated with higher mortality, steatohepatitis

Natural history following initial infection with HCV

HCV Infection → Chronic Hepatitis → Cirrhosis → HCC ESLD

- Normal Liver
- Chronic Hepatitis: 75-85%
- Cirrhosis: 20-30%
- HCC: 2-7% per year

Time:
- 20-25 years
- 25-30 years
HCV is Not Just a Liver Disease

Common Symptoms of HCV in Absence of Cirrhosis

• Fatigue
• Impaired cognitive function (brain fog)
• Migratory arthralgia or myalgia
• Depression

Extrahepatic Manifestations of Chronic HCV

• Renal Disease
• Lymphomas
• Neuropathy
• Dermatologic Manifestations
• Diabetes
• Neurological Impairments
Overview: Routine Evaluation and Follow Up of Persons with Chronic HCV

• Baseline studies
• Screening for other causes of liver disease
• Vaccinations
• Staging of Liver Disease
• Special considerations for cirrhotic patients:
  – Monitoring for hepatocellular carcinoma
  – Evaluation for cirrhosis related complications
  – Referral for liver transplantation
• Assessment and management of alcohol and substance abuse
Overview: Part 2- HCV Therapy

- HCV Therapies
- Special populations
- Choosing a regimen
- Common side effects and laboratory abnormalities
- Drug-drug interactions
- Monitoring of patients on HCV therapy
- Monitoring of patients after HCV therapy
Baseline Studies in Persons with Chronic HCV

- Complete blood count with differential
- Comprehensive metabolic panel including serum creatinine
- Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, serum albumin
- International normalized ratio (INR)
- HCV genotype and subtype
- Quantitative HCV RNA
- HIV antibody
- Hepatitis A serology (IgG or total)
- Hepatitis B serology (HBsAg, anti-HBs, anti-HBc)
- Alpha-fetal protein (AFP)
- Abdominal ultrasound with measurement of spleen size
Baseline Studies in Persons for Evaluation of Liver

- Complete blood count with differential
  Identify changes consistent with cirrhosis; identify anemia especially if requiring ribavirin therapy

- Comprehensive metabolic panel including serum creatinine
  Evaluate renal function for choosing appropriate HCV therapy

- Alanine aminotransferase (ALT), aspartate aminotransferase (AST)
  Recognize level of inflammation and liver injury

- International normalized ratio (INR), total and direct bilirubin, serum albumin
  Assess hepatic synthetic function
Why is the CBC Important to Understand Liver Disease Severity?

• Thrombocytopenia (<150 thousand)
  – Due to portal hypertension caused by cirrhosis
  – Portal hypertension causes:
    ▪ Platelets to become “stuck” in spleen
    ▪ More platelets damaged/destroyed

• Neutropenia
  – Cirrhosis can cause bone marrow suppression
Abnormalities in Hepatic Panel

- Elevations in AST or ALT useful for measuring liver cell injury
  - What is normal AST or ALT? 40 IU/mL
  - Studies suggest this is too high and normal should be lower and different for men vs. women
  - **Healthy ALT** is <30 IU/mL for men and <19 IU/mL for women
- Elevations in conjugated bilirubin suggest liver disease
- Loss of liver’s ability to synthesize (lack of synthetic function) can be seen with:
  - Low serum albumin
  - Prolonged prothrombin time (elevated INR)
  - Important to look at trends in labs over time
Baseline Studies in Persons with Chronic HCV

- HCV genotype and subtype
- Quantitative HCV RNA

- HIV antibody
- Hepatitis A serology (IgG or total)
- Hepatitis B serology (HBsAg, anti-HBs, anti-HBc)

- Alpha-fetal protein (AFP)
- Abdominal ultrasound with measurement of spleen size

Determine appropriate HCV therapy and treatment duration; demonstrate chronic HCV

Share similar routes of transmission; determine need for HAV and/or HBV vaccination; determine risk for HBV reactivation

Evaluate for cirrhosis; screen for hepatocellular carcinoma
Other Viral Hepatitis

- **Hepatitis A**
  - Check HAV antibody (total or IgG)

- **Hepatitis B**
  - Check hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs; total or IgG), and hepatitis B core antibody (anti-HBc)
  - Labs needed irrespective of vaccination
# Hepatitis B Serologies

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg Anti-HBc Anti-HBs</td>
<td>Negative Negative Negative</td>
<td>Susceptible to HBV</td>
</tr>
<tr>
<td>HBsAg Anti-HBc Anti-HBs</td>
<td>Negative Positive or Negative</td>
<td>Previous exposure to HBV. These patients are not immune or “protected” and frequently have subclinical infection and are at risk for reactivation with immunosuppression. There is no role to vaccinate (or boost) these patients.</td>
</tr>
<tr>
<td>HBsAg Anti-HBc Anti-HBs</td>
<td>Negative Positive</td>
<td>Immune to HBV due to HBV vaccine</td>
</tr>
<tr>
<td>HBsAg Anti-HBc IgM anti-HBc Anti-HBs</td>
<td>Positive Positive Positive Positive Negative</td>
<td>Acute HBV infection</td>
</tr>
<tr>
<td>HBsAg Anti-HBc IgM anti-HBc Anti-HBs</td>
<td>Positive Positive Negative</td>
<td>Chronic HBV infection</td>
</tr>
</tbody>
</table>
HBV Reactivation Risk in HCV

• FDA warning issued 2016 following 24 reported cases of HBV reactivation in patients treated with HCV DAAs
  – 2 deaths
  – 1 liver transplant

• Mechanism of reactivation unclear
  – HCV DAAs do not have immunosuppressive effects

• Current recommendations are to “evaluate patients for potential coinfection of HCV and HBV”
Project ECHO HBV Monitoring for Patients on HCV Treatment

Check HBsAg, anti-HBc and anti-HBs

(+) anti-HBc

(-) HBsAg

Liver Panel* every 4 weeks

ALT ≥2x baseline OR ≥2xULN

(-) HBsAg

(+)

HBVDNA quant

AND

Start TDF or ETV

HBsAg‡

HBVDNA quant

AND

Consult viral hepatitis specialist regarding the management of HBV treatment after completing HCV DAA treatment

No additional HBV monitoring required

HBV Vaccination if anti-HBs negative

* Liver panel every 4 weeks while on HCV treatment and at 12 weeks post-treatment.

‡ HBsAg can be drawn at the same as HBVDNA for convenience or can ask for HBsAg with reflex HBVDNA.
Vaccinations

- HAV
- HBV
- Pneumococcal vaccine for all patients with chronic liver disease, including on-going alcoholism
- Annual flu
Disease States Potentiating Fibrosis

- NASH
- NAFLD
- Alcohol
- Viral Hepatitis
- HIV
- Autoimmune

Practice guidelines: http://www.aasld.org/practiceguidelines/Pages/default.aspx
Natural history following initial infection with HCV

- **Time**: 20-25 years, 25-30 years
- **HCV Infection**: 75-85%
- **Chronic Hepatitis**: 20-30%
- **Cirrhosis**: 2-7% per year
- **HCC ESLD**
Findings Suggestive of Advanced Fibrosis/ Cirrhosis

- Presence or history of ascites or esophageal varices
- Low platelet count (<150,000 mm\(^3\))
- APRI > 1.0
- FIB-4 > 3.25
- Fibrosure > 0.72
- Imaging with evidence of cirrhosis (nodular contour of liver or evidence of portal hypertension)
- Liver biopsy with F3 or F4 fibrosis
- Transient elastography consistent with advanced fibrosis/cirrhosis
Use an upper limit of normal of 40

Interpretation:
In a meta-analysis of 40 studies, investigators concluded that an APRI cutoff of 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. Similarly, an APRI cutoff of 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

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

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 ( Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Sources


https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4
# Child-Pugh Classification of Cirrhosis for Drug Dosing

<table>
<thead>
<tr>
<th></th>
<th>1 Point</th>
<th>2 Points</th>
<th>3 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Mild-Moderate</td>
<td>Severe/Refractory</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
<td>2 - 3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
<td>2.8 - 3.5</td>
<td>&lt; 2.8</td>
</tr>
<tr>
<td>INR (PT Prolongation sec over control)</td>
<td>&lt;1.7 (0-4)</td>
<td>1.7-2.3</td>
<td>&gt;2.3 (&gt;6)</td>
</tr>
</tbody>
</table>
Child-Pugh Interpretation of Hepatic Function in a Patient with Cirrhosis

<table>
<thead>
<tr>
<th>C-P Score (Class)</th>
<th>Liver Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6 (A)</td>
<td>Mild Dysfunction</td>
</tr>
</tbody>
</table>
| 7-9 (B)          | Moderate Dysfunction  
|                  | Moderate dose reduction (~25%) for drugs that are mostly hepatically metabolized |
| > 9 (C)          | Severe Dysfunction  
|                  | Significant dose reduction (~50%) for drugs that are mostly hepatically metabolized |

Note: Child Pugh Score is calculated only for patients with cirrhosis
Liver biopsy is not reliable gold standard

- Sampling error leads to misinterpretation in 10-15% of cases
- Can miss the diagnosis of cirrhosis
- Invasive procedure with complications
- Expensive
- Poor patient acceptance
- Interpretation has significant inter observer variability

Hepatocellular Carcinoma

- Incidence of HCC is estimated at 2-8% per year in patients with chronic HCV and advanced fibrosis/cirrhosis
- All patients with cirrhosis should be screened for HCC and continue with HCC surveillance every 6 months (indefinitely)
  - Abdominal ultrasound plus AFP
  - Biomarkers
  - MRI or CT for suspicious lesions or concerns for HCC
Natural History of Chronic Liver Disease

Chronic liver disease → Compensated cirrhosis → Decompensated cirrhosis → Death

Development of complications:
- Variceal hemorrhage
- Ascites
- Encephalopathy
- Jaundice
Evaluating Patients with Cirrhosis: Related Complications

- Physical exam for edema, muscle wasting, encephalopathy, and/or ascites
- Endoscopy for presence of esophageal varices and need for esophageal banding/prophylaxis

- Additional info at AASLD guidelines: [https://www.aasld.org/publications/practice-guidelines-0](https://www.aasld.org/publications/practice-guidelines-0)
Patients with Cirrhosis
Decompensation Shortens Survival

![Graph showing survival rates for patients with cirrhosis and decompensated cirrhosis.]

- **All patients with cirrhosis**: Median survival ~9 years.
- ** Decompensated cirrhosis**: Median survival ~1.6 years.

Indications for Referral to Hepatologist and for Liver Transplantation

• Periodic assessment of cirrhotic patients using a validated prognostic tool such as MELD score (Model for End-Stage Liver Disease) can predict mortality and is used as indicator for liver transplantation

• Patients with a score of 15 or higher should be considered for evaluation of liver transplant
MELD Calculator and Interpretation

Model For End-Stage Liver Disease (MELD) for ages 12 and older

The Model for End Stage Liver Disease (MELD) predicts survival for patients with advanced liver disease.

The United Network for Organ Sharing (UNOS) made a policy change regarding a revision in the MELD scoring system on January 11, 2016 that is related to transplant listing. The new MELD scores are calculated first by determining the traditional MELD score as an initial score (MELD₀); if the initial MELD₀ scores is 12 or greater, the score is adjusted by incorporating the serum sodium value.

MELD

Serum Bilirubin (mg/dL):

INR (International Normalized Ratio):

Serum Creatinine (mg/dL):

Did the patient have dialysis at least twice in the past week, or received 24 hours of CVVHD within the prior week?

No   Yes

Serum Sodium (mmol/L):

MELD₀ score less than 12 do not require Serum Sodium correction.

MELD Score:  

MELD Score:

Interpretation:

3-Month Mortality Based on MELD Scores

The estimated 3-month mortality is based on the MELD score highlighted in yellow above.

<table>
<thead>
<tr>
<th>MELD Score</th>
<th>Mortality Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>71.3% mortality</td>
</tr>
<tr>
<td>30-39</td>
<td>52.6% mortality</td>
</tr>
<tr>
<td>20-29</td>
<td>19.6% mortality</td>
</tr>
<tr>
<td>10-19</td>
<td>6.0% mortality</td>
</tr>
<tr>
<td>9 or less</td>
<td>1.9% mortality</td>
</tr>
</tbody>
</table>

https://www.hepatitisc.uw.edu/page/clinical-calculators/meld
Alcohol and On-going Substance Abuse

• No indications to withhold HCV therapy based on active alcohol or substance use

• Tobacco- can increase risk of HCC
• Marijuana- daily use associated with increased fibrosis
• Alcohol- hepatotoxic
Patient should be counseled on maintaining a healthy diet and normal BMI (<25 kg/m²)
• Mental health assessment
  – Patients with HCV have higher rates of depression
  – Underlying depression can affect medication adherence
When Will There Be Good News?

- Coffee and tea may be liver protective
- Statins may be hepatoprotective and may decrease the risk of HCC

Summary: Pre-Treatment Laboratories (within 60 days of start of treatment)

• CBC with differential
• Chem 7
• Liver enzymes: ALT, AST, alkaline phosphatase
• Liver function tests: albumin, total and direct bilirubin, INR
• Vitamin D 25-OH
• Urine or serum pregnancy test for women of childbearing capacity (ribavirin only)
• Alpha fetoprotein (if cirrhosis)
• HIVRNA and CD4 count (if HIV infected)

• The following labs should be current within the past 12 months*:
  – HCV-RNA Quant
• Patients must have documentation of the following labs:
  – HCV GT and subtype
  – HBsAg, anti-HBs, anti-HBc (irrespective of vaccine history)
  – HAV Ab (unless documentation of vaccination)
  – HIV Ab

*For non-cirrhotic, treatment naïve patients with genotype 1, an HCV-RNA within 6 months of starting therapy must be available for consideration of an 8 week course of treatment.
Pre-Treatment Resistance Testing

• VERY LIMITED

• Prior to using sofosbuvir/velpatasvir in patients with HCV GT3 who have cirrhosis and/or are treatment experienced
  – RAS testing for HCV GT3- looking for Y93 mutation

• All patients with HCV GT1a when considering use of elbasvir/grazoprevir require pre-treatment resistance testing for NS5A resistance associated substitutions (RASs)
Changes in HCV Therapy
Goals of HCV Therapy

- Cure
  - Defined as sustained virologic response (SVR)
- Improvements in liver function
  - Improvements in fibrosis, reversal of cirrhosis?
  - Prevent decompensation
- Improvements in extrahepatic manifestations of HCV
- Prevent deaths due to liver disease complications
- Prevent liver cancer
- Reduce rates of liver cancer recurrence
Differences in Therapy

• Interferon Based
  – Injectable
  – Long duration of treatment
  – High side effect profile
  – Multiple laboratory abnormalities
  – Low cure rates

• Direct Acting Antivirals
  – Oral
  – Short durations
  – Minimal side effects
  – Minimal laboratory abnormalities
  – High cure rates
Treatment Terminology

- **Treatment naïve (TN):** no prior HCV therapy
- **Treatment experienced (TE):** prior HCV therapy- important to clarify which prior treatment
  - Interferon
  - Direct acting antivirals only
- **Sustained virologic response (SVR):** cure, defined as undetectable HCV RNA at least 12 weeks after end of treatment (EOT)
  - Durable
- **Relapse:** a detectable HCV RNA after treatment is completed
The Evolution of Highly Effective Treatment

<table>
<thead>
<tr>
<th>Year</th>
<th>Treatment</th>
<th>SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>IFN 6 mos</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>IFN 12 mos</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>IFN/RBV 6 mos</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>IFN/RBV 12 mos</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>PegIFN 12 mos</td>
<td>55</td>
</tr>
<tr>
<td>2001</td>
<td>PegIFN/ RBV/ BOC or TPV 6-12 mos</td>
<td>70+</td>
</tr>
<tr>
<td>2011</td>
<td>PegIFN/ RBV/ SMV 24-48 wks</td>
<td>80+</td>
</tr>
<tr>
<td>2013</td>
<td>PegIFN/ RBV/ SOF 12-24 wks</td>
<td>89+</td>
</tr>
<tr>
<td>2014</td>
<td>LDV/ SOF &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td></td>
<td>DCV+ SOF &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2016</td>
<td>PrOD &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2017</td>
<td>SOF/ VEL/ VOX &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td></td>
<td>SOF/ PIB &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2018</td>
<td>SOF/ VEL/ VOX &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2019</td>
<td>SOF/ PIB &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2020</td>
<td>SOF/ VEL/ VOX &gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2021</td>
<td>GLE/ PIB &gt;90</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

Legend:
- IFN: Interferon
- RBV: Ribavirin
- PegIFN: Pegylated Interferon
- BOC and TPV: Boceprevir and Telaprevir
- SMV: Smvubavir
- SOF: Sofosbuvir
- LDV: Ledipasvir
- DCV: Dasabuvir
- EBR: Elbasvir
- GZR: Grazoprevir
- PrOD: Paritaprevir/Ritonavir/Elbasvir/Granulimide
- DCV+: Dasabuvir Plus
- SOF+: Sofosbuvir Plus
- GLE: Glecaprevir
- PIB: Pibrentasvir
- VEL: Velpatasvir
- VOX: Voxymavir
- wks: Weeks

Note: SVR represents the percentage of patients who achieve sustained virologic response.
## HCV Direct Acting Antivirals (DAAs)

<table>
<thead>
<tr>
<th>Target</th>
<th>NS3/4A: Protease Inhibitors (previr)</th>
<th>NS5A: Replication Complex Inhibitors (asvir)</th>
<th>NS5B: Polymerase Inhibitors (buvir)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulled from market</td>
<td>Boceprevir</td>
<td>Ledipasvir</td>
<td>Nucleotide: Sofosbuvir</td>
</tr>
<tr>
<td></td>
<td>Telaprevir</td>
<td>Ombitasvir</td>
<td>Non-nucleoside:</td>
</tr>
<tr>
<td></td>
<td>Simeprevir</td>
<td>Daclatasvir</td>
<td>Dasabuvir</td>
</tr>
<tr>
<td></td>
<td>Paritaprevir</td>
<td>Elbasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grazoprevir</td>
<td>Velpatavir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glecaprevir</td>
<td>Pibrentasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Voxilaprevir</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pulled from market
<table>
<thead>
<tr>
<th>HCV Direct Acting Antivirals (DAAs) Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>Zepatier®</td>
</tr>
<tr>
<td><strong>Glecaprevir/Pibrentasvir</strong></td>
<td><strong>Mavyret®</strong></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>Harvoni®</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/Ombitasvir</td>
<td>Technivie®</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/Ombitasvir with Dasabuvir</td>
<td>Viekira Pak®</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>Epclusa®</td>
</tr>
<tr>
<td><strong>Sofosbuvir/ Velpatasvir/Voxilaprevir</strong></td>
<td><strong>Vosevi®</strong></td>
</tr>
</tbody>
</table>

**Other Therapies**

| Ribavirin                                       | Ribasphere®, RibaPak®, Copegus®, Rebetol® |

**Single Agent Therapies**

| Daclatasvir                                     | Daklinza® |
| Sofosbuvir                                      | Sovaldi®  |
What Predicts Treatment Success or Failure?

• Patients who are treatment naïve and non-cirrhotic have very high SVR rates

• Underlying cirrhosis can decrease SVR

• Medication adherence