Primary Care Approach to Diagnosis and Management of Chronic Hepatitis C

Brian Viviano, D.O.
Objectives

- Epidemiology of chronic hepatitis C
- CDC guidelines on screening or hepatitis C
- Diagnosing hepatitis C
- New treatments and application in certain patient populations
Hepatitis C - epidemiology

- CDC recommends that an average 17,000 new cases of chronic hepatitis C are diagnosed yearly in the United States
  - Most common bloodborne infection
- Prevalence- 5.2 million people in the United States are chronically infected with hepatitis C
  - 2% of the population
  - 75% of those people were born between 1945 and 1965
Incidence by year

![Graph showing incidence by year](image-url)
Hepatitis C - epidemiology (cont.)

- 40-85% of patient’s infected with HCV are unaware

- In the United States, approximately 70% of chronic HCV infections are caused by hepatitis C genotype 1, 15 to 20% by genotype 2, 10 to 12% genotype 3, 1% genotype 4, and less than 1% genotype 5 or 6.
Hepatitis C- risk factors

- IVDA (intranasal cocaine as well)
- Blood transfusion prior to 1992
- Solid organ transplantation
- Hemophilia- receipt of factor concentrates prior to 1987
- MSWM
- Tattoos
- Unknown
Hepatitis C - Special circumstances

- **Perinatal** - 5% will transmit HCV to child
  - Risk factor → elevated viral load at birth
    - Increased risk in co-infected patients
  - No increased risk with breastfeeding

- **Sexual exposure** - controversial
  - Most accurate study - 0.07% per year (1/190,000)
  - Higher in MSWM
Hepatitis C - Disease burden

- Infected patients all-cause mortality >2 times that of HCV-negative patients
- 20% of HCV infected patient will develop cirrhosis after 20 years of infection if left untreated
- Number 1 reason for liver transplantation
  - THIS WILL BE CHANGING SOON
- Number one cause of hepatocellular carcinoma (50%)
Forecasted annual deaths - HCV
CDC screening guidelines- HCV

- Adults born from 1945-1965
- IVDA
- Clotting factor prior to 1987
- Long-term hemodialysis
- Persistently elevated transaminases
- HIV
- Transfusions prior to 1992
- Exposure in healthcare professional
HCV- diagnosis

- Initial screening test is Hepatitis C IgG
- A reactive antibody should be followed by HCV RNA testing
  - If positive, diagnosis is confirmed
  - If negative -> past HCV infection vs false positive

- Once diagnosis is established, genotype should be tested along with metavir score
Metavir score

- Knowledge of fibrosis stage guides treatment
  - FOR THE INSURANCE COMPANY
- Can be assessed indirectly through H/P, labs, or other non-invasive tests
  - FibroSure
  - FibroScan
- Liver biopsy
Differential Diagnosis

- NASH - US + exclude other causes
- Hepatitis B - serology (core and surface)
- Hemochromatosis - iron studies, genetic test
- Autoimmune hepatitis - ASMA, ANA
- Primary biliary cirrhosis - AMA
- DILI - careful history + exclude other causes
- Wilson’s disease - Ceruloplasmin, eye exam
Hepatitis C- Treatment

- Many advances over last 20 years
- First available treatment was interferon
- Then pegylated interferon + ribavirin
  - SVR obtained in 10-40% of cases
  - Treatment for 52 weeks and terrible side effects
- Then protease inhibitors boceprevir and telepravir
  - Again bad side effects an lots of monitoring
  - Increased SVR rates to 60-75
Hepatitis C - Specific treatments

- Many new medicines over last several years
- Most are specific for particular genotypes
- Goal is pan-genotypic, low side effects, one pill once daily with little laboratory monitoring
  - In addition, use in cirrhotic (compensated and decompensated), transplant, co-infected, renal failure and few drug interactions
Harvoni (ledipasvir/sofosbuvir)

- Genotype 1a or 1b - NO RESISTANCE TESTING
  - 12 weeks of 1 pill daily with minimal side effects
  - Treatment naïve, experienced, cirrhosis
    - If decompensated, add ribavirin (same with transplant patients)
- No drug or lab monitoring during treatment
- Drug interactions
  - Requires acidic environment - Stop PPI therapy and H2RA therapy or alter timing
  - Amiodarone - contraindicated due to risk of bradycardia
<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment Regimen</th>
<th>and Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naive without cirrhosis or with compensated cirrhosis (Child-Pugh A)</td>
<td>HARVONI</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment-experienced* without cirrhosis</td>
<td>HARVONI</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment-experienced* with compensated cirrhosis (Child-Pugh A)</td>
<td>HARVONI</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Treatment-naive and treatment-experienced* with decompensated cirrhosis (Child-Pugh B or C)</td>
<td>HARVONI + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1 or 4</td>
<td>HARVONI + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment-naive and treatment-experienced** liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)</td>
<td>HARVONI</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 4, 5 or 6</td>
<td>HARVONI</td>
<td>12 weeks</td>
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</tbody>
</table>
Sofosbuvir/velpatasvir- Epclusa

- Fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection
- No drug or lab monitoring
- Drug interactions- Same as Harvoni due to sofosbuvir component
### Table 1: Recommended Treatment Regimen in Patients with Genotype 1, 2, 3, 4, 5, or 6 HCV

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<tr>
<td>Patients without cirrhosis and patients with compensated cirrhosis (Child-Pugh A)</td>
<td>EPCLUSA 12 weeks</td>
</tr>
<tr>
<td>Patients with decompensated cirrhosis (Child-Pugh B or C)</td>
<td>EPCLUSA + ribavirin 8 12 weeks</td>
</tr>
</tbody>
</table>

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*When administered with EPCLUSA, the recommended dosage of ribavirin is based on weight (administered with food): 1000 mg per day for patients less than 75 kg and 1200 mg for those weighing at least 75 kg, divided and administered twice daily. The starting dosage and on-treatment dosage of ribavirin can be decreased based on hemoglobin and creatinine clearance. For ribavirin dosage modifications, refer to the ribavirin prescribing information.*
Elbasvir/grazoprevir-Zepatier

- Combo nucleoside and protease inhibitor
- Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended
- If present, treat for 16 weeks with ribavirin
- No renal impairment dose adjustments
- Perform hepatic laboratory testing prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, perform additional hepatic laboratory testing at treatment week 12. For ALT elevations on ZEPATIER, follow recommendations in full prescribing information.
Elbasvir/grazoprevir-Zepatier

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<tr>
<td>Genotype 1a:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-naive or PegIFN/RBV-</td>
<td>ZEPATIER</td>
<td>12 weeks</td>
</tr>
<tr>
<td>experienced* without baseline NS5A</td>
<td></td>
<td></td>
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<tr>
<td>polymorphisms*</td>
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<td>Genotype 1b:</td>
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<tr>
<td>Treatment-naive or PegIFN/RBV-</td>
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<td>12 weeks</td>
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<tr>
<td>experienced*</td>
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<td>Genotype 1a or 1b: PegIFN/RBV/PI-</td>
<td>ZEPATIER +</td>
<td>12 weeks</td>
</tr>
<tr>
<td>experienced*</td>
<td>ribavirin</td>
<td></td>
</tr>
<tr>
<td>Genotype 4:</td>
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<td></td>
</tr>
<tr>
<td>Treatment-naive</td>
<td>ZEPATIER</td>
<td>12 weeks</td>
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<tr>
<td>Genotype 4:</td>
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<td></td>
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<tr>
<td>PegIFN/RBV-experienced*</td>
<td>ZEPATIER +</td>
<td>16 weeks</td>
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<tr>
<td>ribavirin</td>
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*Peginterferon alfa + ribavirin.
†Polymorphisms at amino acid positions 28, 30, 31, or 93.
‡Peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor.
Paritaprevir/ritonavir/ombitasvir
dasabuvir + ribavirin (Veikira)

- 12 week regimen for Genotype 1
- Not to be used in Child B or worse cirrhotics due to risk of decompensation
- Increased risk of drug interactions
- Many side effects with ribavirin
Veikira Pak

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<th>Duration</th>
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<tr>
<td>Genotype 1a, without cirrhosis</td>
<td>VIEKIRA PAK + ribavirin</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a, with cirrhosis</td>
<td>VIEKIRA PAK + ribavirin</td>
<td>24 weeks**</td>
</tr>
<tr>
<td>Genotype 1b, without cirrhosis</td>
<td>VIEKIRA PAK</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1b, with cirrhosis</td>
<td>VIEKIRA PAK + ribavirin</td>
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*Note: Follow the genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection.

**VIEKIRA PAK administered with ribavirin for 12 weeks may be considered for some patients based on prior treatment history [See Clinical Studies (14.3)].

- HCV/HIV-1 co-infection: For patients with HCV/HIV-1 co-infection, follow the dosage recommendations in the table above. (2.1)
- Liver Transplant Recipients: In liver transplant recipients with normal hepatic function and mild fibrosis (Metavir fibrosis score ≤2), the recommended duration of VIEKIRA PAK with ribavirin is 24 weeks. (2.2)
Simeprevir / sofosbuvir

- Indicated for Genotype 1 and 4
- Screening for the presence of virus with the NS3 Q80K polymorphism is strongly recommended and alternative therapy should be considered if Q80K is detected.
- 12 weeks in non-cirrhotic patients
- 24 weeks in compensated cirrhotic patients
Daclatasvir + sofosbuvir

- Indicated for genotype 1 and genotype 3
- Treat for 12 weeks
  - If cirrhosis present- add ribavirin

- Dose modifications based on drug interactions make this a confusing regimen
What can you as a primary care physician take from this info?

- Knowing initial blood work and diagnostic testing to guide treatment plan
- Once genotype and fibrosis status are established choosing a treatment regimen you are comfortable with
My recommendations...

- Decide which patient’s you are willing to treat comfortably
  - What genotypes?
  - Cirrhosis
  - Co-infected?
- Pick a treatment plan that works for you and only treat that type of patient
- Consult your look gastroenterologist or ID for remainder
Cirrhosis

- There are certain things that need monitored in cirrhosis
  - HCC status- US +/- AFP q 6 months
  - Esophageal variceal screening- EGD q 1-2 years
    - Banding +/- non-selective Beta blocker
  - Fluid management- ascites
  - Encephalopathy- psychometric evaluation
Thank you...