Cases: Treatment of and Monitoring for Hepatitis C in Patients with Cirrhosis

Andrew Aronsohn, MD
Associate Professor of Medicine
University of Chicago
Chicago, Illinois

Learning Objectives

After attending this presentation, learners will be able to:

• Describe disease severity and mortality risk in patients with cirrhosis
• Describe the current guidance in HCV treatment in patients with cirrhosis

Case 1:

• RT is a 48 yo female with HCV diagnosed 20 years ago
  • IDU, significant alcohol for 15 years, none now
  • Fatigue, loss of energy on disability
  • PH upper GI bleed 1 year ago
• She saw a commercial where people born between 1945 and 1965 with HCV are riding horses and talking about being cured of HCV
• She is interested in treatment
Case 1: Labs

- ALT 54; AST 68; bilirubin 2.7; albumin 3.2;
- INR 1.4; AFP 22.4; creatinine 0.8
- WBC 3,000; Hgb 14; platelets 82,000
- HCV RNA 607,509 IU/mL
- HCV genotype 1a

Case 1: ARS Question 1

Which of the statements are NOT true?
1. She likely has cirrhosis
2. She needs an upper endoscopy
3. She needs HCC screening
4. She should not be treated with an NS5a inhibitor
5. She should be screened for HBV and HIV

The Natural History of Cirrhosis in HCV

Decompensation:
- Variceal hemorrhage
- Ascites
- Encephalopathy
- Jaundice
Cirrhosis Prevalence 35% - 80%

30% - 40%

50% - 70%
Survive

30% - 50%
Die

70%
Rebleed

Risk of Bleeding from Esophageal Varices

Don’t Cry Liver, It Will be OK...

Ascites

• Fluid within the peritoneal cavity
• Occurs in 50-60% of patients with cirrhosis over 10-15 years
  • 1 yr survival 50%
• Mixture of liver and intestinal lymph
Hepatic Encephalopathy

- Results from a combination of:
  - Portosystemic shunting and failure to metabolize neurotoxic substances
  - Ammonia remains the most important neurotoxic substance but poorly correlates with stage
- Treatment to reduce production of NH3 from the colon via
  - nonabsorbable disaccharides
    - lactulose: 3-4 BM per day
  - nonabsorbable antibiotics
    - rifaximin 550 mg bid, neomycin rarely used
  - Protein restriction promotes protein degradation and, if maintained for long periods, worsens nutritional status and decreases muscle mass
  - No longer recommended

Things to remember about HE

Case 1: ARS Question 2

- A right upper quadrant ultrasound is ordered for RT. Which showed:
Case 1: ARS Question 2

A mass is noted in a cirrhotic appearing liver. The next step should be:
1. Ultrasound guided liver biopsy
2. Triple phase CT scan
3. PET Scan
4. Repeat ultrasound in 3 months to confirm stability

Hepatocellular Carcinoma

- Late complication of end-stage liver disease
- Exceptions: HBV seen in non cirrhotics
- Diagnosis by CT scan, MRI
- Histology is not essential
- Alpha-fetoprotein level may be elevated
  - 20-40% with HCC have normal AFP
  - 20-30% without HCC have abnormal AFP
- The higher the AFP, the more likely the diagnosis of HCC

Triple phase CT scan

Hypervascular lesion that washes out on portal venous phase
Health Maintenance for Cirrhosis

1. EGD to screen for varices
2. Ultrasound +/- AFP q 6 months
   • May want to alternate with CT or MR
3. MELD score q 3-6 months
   • INR, Creatinine, Bili
4. Screen for decompensation
   • Bleeding, volume, encephalopathy

Big Questions in HCV and Cirrhosis

• What are the treatment options for patients with cirrhosis?
• Who should be treated by non hepatologists?
• When is a patient too sick to be treated?

Case 2

DW is 55 year old with Genotype 1b HCV who is naïve to treatment. Staging via fibroscan reveals cirrhosis. She has no evidence of decompensation. EGD is normal. CTP score is A. MELD score is 8.
Case 2: ARS Question 3

Which of the following is true?
1. This patient should be referred to a transplant center prior to treatment
2. If she is cured, she can discontinue HCC screening
3. Ribavirin will be necessary for most regimens in cirrhosis
4. Glecaprevir / pibrentasvir x 12 weeks would be a safe and effective regimen to treat her

Compensated Cirrhosis

• Treatment options are essentially the same
• May be some differences in duration of therapy
• Protease inhibitors OK
  • But only for use in Childs A
• In most cases can be treated outside of transplant setting

One Stop Shopping...
Benefits of Treatment

![Graph showing rates per 100 person-years for Any Event, All-Cause Mortality, HCC, and Liver Failure with and without SVR.]

Controversy: HCV Treatment and HCC

- Hypothesis: immune dysregulation
- Highly effective DAA therapy eradicates HCV but may dismantle the immune “brake” on HCC

Survival Free of HCC Recurrence

![Graph showing survival probability over time for patients treated and untreated.]

Fig. 2. Recurrence of HCC according to DAA treatment in the HEPATOMAS cohort. Pseudo-survival curves were plotted for dose-dependent DAA treatment.
Case 3

WR is a 62 year old with HCV genotype 2 who is a nonresponder to interferon based therapy. She has no encephalopathy and mild ascites which is controlled with low dose lasix and aldactone. Bilirubin = 2.7, Albumin 2.2, INR = 2.

Case 3: ARS Question 4

What is this patient’s Childs Classification?

1. A
2. B
3. C
4. D

Childs-Turcotte-Pugh Review
Case 3 Continued: ARS Question 5

Would you...
1. Treat this patient
2. Refer the patient to a transplant center
3. Arrange for palliative care / hospice services

Childs B and C

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with HCV infection who have decompensated cirrhosis—moderate or severe hepatic impairment, ie, Child-Turcotte-Pugh (CTP) class B or class C—should be referred to a medical practitioner with expertise in that condition, ideally in a liver transplant center.</td>
<td>I, C</td>
</tr>
</tbody>
</table>
Avoiding Protease Inhibitors in Decompensated Cirrhosis

Regimens not recommended for patients with decompensated cirrhosis (moderate or severe hepatic impairment; Child-Turcotte-Pugh Class B or C):

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Rating</th>
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</thead>
<tbody>
<tr>
<td>Peginterferon-based regimens</td>
<td>II, B</td>
</tr>
<tr>
<td>Simtrevir-based regimens</td>
<td>III, B</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir-based regimens</td>
<td>III, C</td>
</tr>
<tr>
<td>Glecaprevir/paritaprevir</td>
<td>III, C</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir/ombitasvir</td>
<td>III, C</td>
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SOLAR-1/2: Overall Safety Summary in CPT B and C Cirrhosis

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>CTP B + C (n=215)</th>
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<tbody>
<tr>
<td>Any AE</td>
<td>208 (97)</td>
</tr>
<tr>
<td>Grade 3-4 AE</td>
<td>51 (24)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>61 (28)</td>
</tr>
<tr>
<td>Serious treatment-related AE</td>
<td>5 (2)</td>
</tr>
<tr>
<td>AE leading to D/C of LDV/SOF</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Death</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>11</td>
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- Treatment-related SAEs were mostly related to RBV treatment.
- Deaths and AEs that led to D/C of LDV/SOF were not attributed to study treatment.
Sofosbuvir / Velpatasvir in Decompensated Cirrhosis

- Open-label, randomized (1:1:1) US study (NCT02201901)
- HCV GT 1-6 treatment-naïve or -experienced patients with Child-Pugh-Turcotte (CPT) B cirrhosis
- Key eligibility criteria: creatinine clearance (CL_{cr}) >50 mL/min, platelets >30,000/mm^3, no hepatocellular carcinoma or liver transplant

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Overall SVR12

<table>
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<tr>
<th>Treatment</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
</tr>
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<tbody>
<tr>
<td>SOF/VEL</td>
<td>75/90</td>
<td>77/90</td>
<td></td>
</tr>
<tr>
<td>SOF/VEL + RBV</td>
<td>82/87</td>
<td>86</td>
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P-value < 0.001 for comparison of SVR12 rates in SOF/VEL vs. SOF/VEL + RBV

Error bars represent 95% confidence intervals.

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Treatment in Decompensated Cirrhosis

Recommendations listed by evidence level and stratified for:

Patients With Decompensated Cirrhosis Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Eligible

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Memphis, Tennessee, October 12, 2018
Decrease in Wait list additions for HCV

What to Tell Patients

Take Home: HCV and Cirrhosis

• In most cases Low MELD (<15) and Childs A are OK to treat in non transplant setting
• In cirrhosis (compensated and decompensated) outcomes improve, on all metrics, after SVR
• All patients with cirrhosis require HCC monitoring, variceal screening– even after SVR
Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!