Real-World HIV and Liver Disease Cases

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Faculty and Planning Committee Disclosures
Please consult your program book or Conference App.

This case discussion may contain discussion of off-label uses.

Learning Objectives
Upon completion of this presentation, learners should be better able to:

• Discuss some real-world HCV treatment issues related to choice of direct-acting antiviral (DAA) therapy in HIV-HCV coinfected patients
• Identify relevant drug interactions with DAAs and antiretroviral therapy
• Recognize the potential for adverse events in selected patients undergoing DAA therapy
• Discuss treatment of hepatitis C in patients with ongoing substance use disorders
HCV Life Cycle and DAA Targets

Recommended combinations of oral DAA as applied to different HCV genotypes

- **Combination Therapies**
- **Preferred Regimens**
  - Elbasvir (EBR) + Grazoprevir (GZR) (GT1,4)*
  - Ledipasvir (LDV) + Sofosbuvir (SOF) (FDC, GT1,4,5,6)
  - Pibrentasvir (PIB) + Glecaprevir (GLE) (GT1, 2, 3, 4, 5, 6)
  - Velpatasvir (VEL) + Sofosbuvir (SOF) (GT1, 2, 3, 4, 5, 6)
  - Velpatasvir (VEL) + Sofosbuvir (SOF) + Voxilaprevir (GT1, 2, 3, 4, 5, 6)

Hcvguidelines.gov accessed 3/14/2019
Choosing an HCV regimen: Based on virus and patient characteristics

- HCV RNA level (< or > 6 million IU/mL) (Only applies to non-HIV infected)
- HCV genotype; if genotype 1, subtype 1a or 1b
- eGFR (CMP)
- Cirrhosis: Yes or No
- If cirrhosis, CTP score (albumin, bilirubin, INR), MELD and liver imaging
- HBsAb, HBsAg, HBCAb total, HAV total
- Concurrent medications
  - ART, PPIs, anti-seizure medications, amiodarone
- Prior HCV treatment: Yes or No

Mr. B

- 67 year old African-American man with HIV, well controlled on HAART; hypertension, diabetes and prior injection drug use.
- On initial review of medical record:
  - CD4: 628, HIV RNA: < 20 copies/mL
  - HCV antibody: reactive
  - HCV RNA 5,654,567 IU/ml
  - HCV genotype 1A
  - No previous HCV treatment history

Medications:
- Darunavir, 800mg daily
- Norvir, 100mg daily
- TDF/FTC, 1 tablet daily
- Metoprol XL, 50 mg daily
- Lisinopril, 20mg daily
- Metformin, 500mg BID
- Rosuvastatin, 10 mg daily
- Omeprazole, 20mg daily
67 year old with well controlled HIV, HCV genotype 1a, HCV RNA 5.6 million IU/ml

What HCV treatment regimen would you recommend?

a. Elbasvir/grazoprevir for 12 weeks
b. Ledipasvir/sofosbuvir for 8 weeks
c. Glecaprevir/Pibrentasvir for 12 weeks
d. I need more information to recommend a regimen

Choosing an HCV regimen: Based on virus and patient characteristics

- HCV RNA level (< or > 6 million IU/mL)
- HCV genotype; if genotype 1, subtype 1a or 1b
- eGFR (CMP)
- Cirrhosis: Yes or No
  - If cirrhosis, CTP score (albumin, bilirubin, INR) and liver imaging
- Concurrent medications
  - PPIs, anti-seizure medications, amiodarone, ART
- Prior HCV treatment: Yes or No
Genotype 1a: Recommended regimens for patients without cirrhosis and no prior HCV treatment

<table>
<thead>
<tr>
<th>Recommended and alternative regimens listed by evidence level and alphabetically for:</th>
<th>Treatment-Naive 1a Patients Without Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECOMMENDED</td>
<td>DURATION</td>
</tr>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs for elbasvir</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is &lt;6 million IU/mL</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

a Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.
### Genotype 1a: Regimens for patients with cirrhosis

** Recommended and alternative regimens listed by evidence level and alphabetically for: Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis**

**RECOMMENDED**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs for elbasvir</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

**ALTERNATIVE**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs for elbasvir</td>
<td>16 weeks</td>
<td>IIa, B</td>
</tr>
</tbody>
</table>

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**STAGING TO ASSESS FOR PRESENCE OR ABSENCE OF CIRRHOSIS**

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* For decompensated cirrhosis, please refer to the appropriate section.

* Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer entecavir resistance.

* This is a 3-foalalc formulation. Please refer to the prescribing information.
Detection of cirrhosis is important

- Risk of hepatic decompensation in patients with cirrhosis
- Increased risk of liver cancer with cirrhosis even after HCV cure
  - Imaging to assess for hepatocellular cancer
  - Ongoing hepatocellular cancer screening every 6 months (life long)
- Cirrhosis may impact HCV treatment regimen and duration
- Esophagogastroduodenoscopy (EGD) required to screen for varices

Rationale for NS5A RAS testing in persons with genotype 1a prior to Elbasvir/Grazoprevir

<table>
<thead>
<tr>
<th></th>
<th>GT1a</th>
<th>GT1b</th>
</tr>
</thead>
<tbody>
<tr>
<td>No NS5A RAVs</td>
<td>99%</td>
<td>100%</td>
</tr>
<tr>
<td>NS5A RAVs ≤ 5-fold</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>NS5A RAVs &gt; 5-fold</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>shift to EBR</td>
<td>94%</td>
<td>16%</td>
</tr>
<tr>
<td>shift to EBR</td>
<td>2%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Rationale for avoiding 8 weeks of Ledipasvir/Sofosbuvir in persons with HIV coinfection

Wyles D et al. NEJM 2015

ALLY-2 trial: Randomized controlled trial of sofosbuvir and daclatasvir

Rationale for 8 weeks of Glecaprevir/Pibrentasvir in non-cirrhotic persons with HIV coinfection

- 8 weeks: 137 patients with HIV and no cirrhosis
- 12 weeks: 16 patients with HIV and cirrhosis

Mr. B

- 67 year old man with hypertension, diabetes
- Acquired HIV/HCV through IDU
- Coronary artery disease
- No previous evaluation or treatment for HCV
- ROS: + Fatigue

Social history
- Drinks 2-3 beers daily
- No injection drug use in over 10 years
- PE: + for cardiac murmur

Labs
- CD4 628, HIV RNA < 20 copies
- HCV RNA: 5,654,567 IU/ml
- HCV Genotype 1a
- ALT 48; AST 90; plt 125k; INR 1.2; Total bilirubin 1.2; Albumin 3.3, Hb 13.6; Cr 1.8 eGFR 49ml/min/1.73mm²

Evaluation of liver disease with serum markers

APRI

AST to Platelet Ratio Index (APRI) Calculator

This is an AST to Platelet Ratio Index (APRI) calculator tool. Enter the required values to calculate the Score will appear in the oval on the far right (highlighted in yellow). Most experts recommend using the AST upper limit of normal when calculating an APRI value.

FIB-4

Fibrosis-4 (FIB-4) Calculator

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

APRI ≥ 1.0
76% sensitive, 72% specific for cirrhosis

FIB 4 >3.25
97% specificity for cirrhosis

http://www.hepatitisc.uw.edu/page/clinical-calculators/ctp
Transient Elastography

Mr B’s Fibroscan score: 12.6KPa
Affected by weight, access of probe (2 cm), steatosis
Evaluation of liver disease: Cirrhosis

- Compensated
- Asymptomatic
- Decompensated-Symptomatic
  - ascites,
  - encephalopathy

Child-Turcotte-Pugh score ≥7
Reports of fatality with use of NS3 protease inhibitors in patients with decompensated cirrhosis
- Grazoprevir (GZR) + Elbasvir (EBR)
- Glecaprevir/Pibrentasvir
- Sofosbuvir/velpatasvir/voxilaprevir

Calculate the CTP for all cirrhotics

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>&lt;4</td>
</tr>
<tr>
<td>Seconds prolonged</td>
<td>&lt;1.7</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td></td>
</tr>
</tbody>
</table>

*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)

- Class A = 5 to 6 points (least severe liver disease)
- Class B = 7 to 9 points (moderately severe liver disease)
- Class C = 10 to 15 points (most severe liver disease)

Mr. B

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No encephalopathy</td>
<td>1</td>
</tr>
<tr>
<td>No Ascites</td>
<td>1</td>
</tr>
<tr>
<td>Bilirubin: 1.2 mg/dl</td>
<td>1</td>
</tr>
<tr>
<td>Albumin: 3.3 g/dl</td>
<td>2</td>
</tr>
<tr>
<td>INR: 1.2</td>
<td>1</td>
</tr>
<tr>
<td>Total Score</td>
<td>6</td>
</tr>
<tr>
<td>CTP Class</td>
<td>A</td>
</tr>
</tbody>
</table>

Compensated Cirrhosis

http://www.hepatitisc.uw.edu/page/clinical-calculators/ctp
Patients with advanced kidney disease

<table>
<thead>
<tr>
<th>CrCl &gt; 30ml/min</th>
<th>CrCl &lt;30ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No dosage adjustments required for any DAAs</td>
<td>• Sofosbuvir not recommended: metabolite GS-331007 (half-life 27 hours) – unknown effects</td>
</tr>
</tbody>
</table>

Recommended regimens listed by evidence level and alphabetically for: Patients With CKD Stage\(^a\) 4 or 5 (eGFR <30 mL/min or End-Stage Renal Disease)

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>GENOTYPE</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>1a, 1b, 4</td>
<td>12 weeks</td>
<td>I, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>8 to 16 weeks(^b)</td>
<td>I, B(^c)</td>
</tr>
</tbody>
</table>

hcvguidelines.gov accessed 3/14/2019

67 year old with HIV, genotype 1a HCV with compensated cirrhosis, eGFR 49 on DRV/RTV, TDF/FTC

Which of the following would you do next?

A. Send him for liver transplant evaluation
B. Consider switching his antiretroviral regimen in anticipation of HCV treatment.
C. Start elbasvir-grazoprevir one tablet daily for 12 weeks
D. Start glecaprevir-pibrentasvir 3 tablets daily for 8 weeks
E. Start ledipasvir-sofosbuvir one tablet daily for 12 weeks
ARV Interaction Score Card

- Treatment regimens for HIV/HCV infected patient identical to those recommended for HIV monoinfected patients
- Special attention to drug interactions with HIV antiretrovirals

LDV/SOF with TDF

- LDV/SOF + TDF increases tenofovir plasma concentrations
  - Greatest effect in presence of HIV ritonavir-boosted PI’s, which independently increase tenofovir levels
  - Avoid combination of LDV and TDF
    - CrCl < 60 mL/min
    - RTV-boosted PIs + TDF
    - Consider switching TDF to TAF
Other major drug interactions of oral DAAs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Elbasvir/Grazoprevir</th>
<th>Glecaprevir/Pibrentasvir</th>
<th>Sofosbuvir/Velpatsvir</th>
<th>Sofosbuvir/Ledipasvir</th>
<th>Daclatasvir + Sofosbuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Max: 20 mg/d</td>
<td>↑ statin; Avoid</td>
<td>Monitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Monitor</td>
<td>↑ statin; Avoid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Monitor</td>
<td>↑ statin; Avoid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Max: 10 mg/d</td>
<td>Max: 10 mg</td>
<td>Max: 10 mg/d</td>
<td>↑ statin; Avoid</td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Monitor</td>
<td>Reduce dose by 50%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mr B continued

- Insurance has ledipasvir/sofosbuvir on formulary
- Antiretroviral regimen was switched to DTG and TAF/FTC
- Confirmed undetectable HIV RNA, 1 month after ARV switch prior to HCV treatment initiation
- Took ledipasvir/sofosbuvir for 12 weeks
- HCV RNA <15 IU/ml at end of treatment
- HCV RNA 3,013,478 IU/ml 4 weeks after end of treatment, HCV genotype 1a
- Denied substance use or other HCV exposure
In addition to adherence counselling, which of the following would you do next?

A. Retreat with glecaprevir-pibrentasvir 3 tablets daily for 12 weeks
B. Retreat with ledipasvir-sofosbuvir one tablet daily for 12 weeks
C. Retreat with sofosbuvir-velpatasvir for 16 weeks
D. Retreat with sofosbuvir-velpatasvir-voxilaprevir for 12 weeks

Treatment options for NS5A experienced patients

NS5A Inhibitor DAA-Experienced Genotype 1 Patients

Recommended and alternative regimens for:
NS5A Inhibitor DAA-Experienced, Genotype 1 Patients With or Without Compensated Cirrhosis*

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ALTERNATIVE</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)* except NS3/4 protease inhibitor inclusive DAA combination regimens</td>
<td>16 weeks</td>
<td>IIIa, B</td>
</tr>
</tbody>
</table>

*For decompensated cirrhosis, please refer to the appropriate section.
This is a 6-tablet coformulation. Please refer to the prescribing information.

hcvguidelines.gov accessed 3/14/2019
SOF/VEL/VOX in DAA-Experienced Patients

- 263 DAA-experienced patients treated with SOF/VEL/VOX for 12 wks
- 46% with cirrhosis
- 205/248 (83%) with NS3 or NS5A RAS
  - RASs assessed by deep sequencing (15% assay cutoff)
- High SVR rates regardless of presence of RAS

Mr B got cured!


<table>
<thead>
<tr>
<th>RAS present</th>
<th>No RAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>199</td>
<td>42</td>
</tr>
<tr>
<td>205</td>
<td>43</td>
</tr>
</tbody>
</table>

Mr. C

- 23 year old white male with HIV infection well controlled on DTG + TAF/FTC
- Transitioned from oxycodone to heroin in teens
- 3 previous inpatient rehab stays for substance use treatment
- Multiple previous referrals to outpatient substance use treatment
- Recent discharge from substance use rehab
- HCV antibody negative 6 months ago

ACTHIV 2019: A State-of-the-Science Conference for Frontline Health Professionals
What is your next step related to HCV testing?

- A. Nothing additional. He got tested 6 months prior
- B. Test for HCV antibody and reassure him that he does not have HCV if that test comes back negative
- C. Test for HCV antibody and HCV RNA

Mr C

- 23 year old who injects drugs
- HIV RNA undetectable on DTG + TAF/FTC
- HCV antibody negative 6 months prior
- Recent discharge from inpatient rehab 3 months prior

- HCV RNA 6,060,000 IU/mL
- HCV genotype 3
- PLT 200K
- INR 1.0; Albumin 3.5 g/dL; AST 52 U/L (normal 8-37) and ALT 40 U/L (normal 8-35).
- Cr 0.8
- Fibroscan 5.0 KPA
23 year old with well controlled HIV, HCV genotype 3 infection, no cirrhosis

What HCV treatment regimen would you recommend?

a. Elbasvir/grazoprevir for 12 weeks
b. Ledipasvir/sofosbuvir for 8 weeks
c. Ledipasvir sofosbuvir for 12 weeks
d. Glecaprevir/Pibrentasvir for 8 weeks
e. Sofosbuvir/Velpatasvir for 8 weeks

Recommended regimens for genotype 3 patients without cirrhosis

<table>
<thead>
<tr>
<th>Treatment-Naive Genotype 3 Patients Without Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECOMMENDED</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)²</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
</tr>
</tbody>
</table>

² This is a 3-tablet coformulation. Please refer to the prescribing information.
Glecaprevir/Pibrentasvir for 8 weeks in persons with GT3 and no cirrhosis (Endurance 3 RCT)

<table>
<thead>
<tr>
<th>Outcomes, n (%)</th>
<th>2:1 randomization</th>
<th>Non-randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GLE-PIB 12 x 12 weeks n=233</td>
<td>SOF + DCV x 12 weeks n=115</td>
</tr>
<tr>
<td>SVR12</td>
<td>222 (95)</td>
<td>111 (97)</td>
</tr>
<tr>
<td>Virologic failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breakthrough</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Relapse</td>
<td>3 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Failure due to other reasons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>1 (&lt;1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Withdrawal of consent</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Non-compliance</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Lost to follow-up / missing SVR12</td>
<td>4 (2)</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Foster G et al. EASL 2017

SOF/VEL in GT3: SVR12 by Cirrhosis and Treatment History (ASTRAL-3)

Only 84% (21/25) with Y93H achieved SVR12
C-EDGE CO-STAR: Efficacy of GZR + EBR in PWID receiving opioid agonist therapy (OAT)

- Phase 3, double-blind RCT in pts on OAT for >3 months
  - 20% with cirrhosis
  - 7% HIV coinfected
  - 79% had positive drug toxicology during follow up

![Graph showing SVR12 (Full Analysis Set, FAS)]

Mr. C

- 23 year old Caucasian male
- Diagnosed with HCV in inpatient rehab heroin and alcohol
- Presented for HCV care 3 months later
- HCV genotype 3, no cirrhosis
- Referred to outpatient addiction care
- Started on sofosbuvir/velpatasvir 1 tablet daily for 12 weeks

Week 4 follow up

- Fresh track marks
- Toxicology: +ve for heroin
- Discussed need for addiction care and referred
- HCV RNA undetectable at week 8, 12 and end of treatment
- HCV RNA 5 months after EOT 60,325 IU/ml
- HCV genotype 1a
Which of the following would you do at that visit?

A. Tell the patient he has lost his chance for HCV cure and continue HIV management
B. Prescribe sofosbuvir/ledipasvir one tablet daily for 12 weeks
C. Prescribe glecaprevir-pibrentasvir 3 tablets daily for 8 weeks
D. Link patient to opioid agonist treatment, syringe service program, naloxone with follow up for HCV treatment decision

Probability of positive urine toxicology

<table>
<thead>
<tr>
<th></th>
<th>Clinic-based</th>
<th>Referral to OTP</th>
</tr>
</thead>
<tbody>
<tr>
<td>heroin</td>
<td><img src="heroin.png" alt="Graph" /></td>
<td><img src="heroin.png" alt="Graph" /></td>
</tr>
<tr>
<td>cocaine</td>
<td><img src="cocaine.png" alt="Graph" /></td>
<td><img src="cocaine.png" alt="Graph" /></td>
</tr>
</tbody>
</table>
24 year old person who injects drugs with HCV genotype 1 reinfection, no cirrhosis

- Prescribed buprenorphine/naloxone
- Addiction counseling with Case Manager
- Came in for weekly visits
- Weekly urine toxicology and buprenorphine
- Urine consistently positive for Buprenorphine/norbuprenorphine
- Prescribed glecaprevir/pibrentasvir 3 tablets daily for 8 weeks
- Approval denied by insurance due to low stage of liver disease
- Applying for access to free glecaprevir/pibrentasvir through manufacturer patient assistance program

Ms Q

- 64 year-old female with HIV CD4 count 350 cells/mm³ and HIV RNA <20 copies/mL.
- ARVs: abacavir, dolutegravir and rilpivirine
- History of TDF nephrotoxicity, M184V, and unable to tolerate PIs.
- HCV genotype 1b, HCV RNA 5 million IU/ml
- FibroScan score 8.8 consistent with F2 fibrosis
- AST 61, ALT 52, INR 1.0, Albumin 4.0, Cr 1.4
- HBsAg negative, anti-HBc positive, IgM anti-HBc negative, anti-HBs negative
Potential causes of isolated anti-HBc

- Resolved hepatitis B infection with loss of anti-HBs
  - Anamnestic anti-HBs response after HBV vaccination
- Occult chronic HBV infection with loss of detectable HBsAg
  - HBV DNA+
- Acute HBV Infection
  - Anti-HBc IgM positive, HBV DNA +
- False positive result

64 year old with HCV genotype 1b, no cirrhosis, isolated hepatitis B core ab

What HCV treatment regimen would you recommend?

a. Ledipasvir/sofosbuvir for 8 weeks
b. Ledipasvir/sofosbuvir for 12 weeks
c. Glecaprevir/Pibrentasvir for 12 weeks
d. Sofosbuvir/Velpatasvir for 8 weeks
Genotype 1b: No cirrhosis and no prior HCV treatment

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>DURATION</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>8 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is &lt;6 million IU/mL</td>
<td>8 weeks</td>
<td>I, B</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
</tbody>
</table>

MsQ

Her insurance has sofosbuvir/ledipasvir as the preferred agent

She returns 4 weeks into therapy with complaint of fatigue, irritability and malaise.

Week 4 Labs:

Total bilirubin is 3.2, ALT has risen to 365 (from 55) and AST 250 (from 40).
64 year old on ARVs in week 4 of LDV/SOF with malaise and new LFT elevations

Which of the following would you do next?

A. Discontinue ledipasvir/sofosbuvir
B. Check HBV DNA
C. Discontinue ARV
D. Send HCV RNA and decide what next based on result

HBV Reactivation on DAA Therapy

• Unexpected ALT and AST elevations 4-8 weeks (mean 53 days) from DAA initiation
  – 2 deaths and 1 liver transplantation reported
  – Case report of 29 cases of HBV reactivation, 13 (45%) were chronic HBV carriers (+HBsAg)
• Meta-analysis of 17 studies; 1621 (242 chronic; 1379 resolved) HBV pts
  • Higher prevalence in HBsAg + → 24%
  • Very low prevalence with resolved HBV (anti-HBc+) → 1.4%
• FDA added black box warning on risk of HBV reactivation to all oral DAAs

Conclusions

– There are multiple effective, safe options for HCV treatment and cure
– Genotype, cirrhosis status, and treatment experience may affect HCV treatment choice
– Substance use is not a contraindication to HCV treatment
– When in doubt look it up –hcvguidelines.org
Treatment of HCV

"First we're going to run some tests to see how your insurance reacts."

Thank you!

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