Hepatitis C: Pre-treatment Evaluation

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Learning Objectives

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

– Identify HCV pre-treatment needs for patients with HIV/HCV co-infection
– Explain importance of staging liver fibrosis
– Review current HCV treatment options
– Identify drug-drug interactions in the treatment of HIV/HCV patients

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

Off-Label Disclosure
There will be no off-label/investigational uses discussed in this presentation.
Treatment of HIV/HCV Coinfection: Factors to Consider

- **HIV work-up if starting/switching ART:**
  - HIV-1 RNA level
  - HLA B-5701 status
  - CD4+ cell count
  - Resistance testing
- **All patients**
  - Creatinine Clearance
  - Non-ART, non-DAA comediations
  - Comorbidities

- **HCV workup if starting DAA:**
  - HCV genotype
  - HCV RNA
  - Staging of liver disease
  - Previous DAAs
  - HBV status

Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

• Past History:
  – Type 1 diabetes mellitus, insulin-dependent since age 7
  – HIV dx: 2012 (CD4=525 cells/mm³; HIV= 46 copies/mL)
  – Depression
  – Hepatitis C –recent screening due to elevated transaminases
• Medications:
  – Insulin
  – Elvitegravir/cobicistat/emtricitabine/tenofovir(TDF)
  – Sertraline

Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

• Social History:
  – Works full-time, excellent private insurance
  – Past use IV methamphetamines- last used 2016
  – Denies alcohol intake, occasional marijuana
  – Husband also HIV+, suppressed viral load, plans to get tested for hepatitis C
WHEN TO DO HCV SCREENING?  
ENTRY INTO HIV CARE AND....

Recommendation for HCV Testing for Persons With Ongoing Risk Factors

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual HCV testing is recommended for persons who inject drugs and for HIV-infected men who have unprotected sex with men.</td>
<td>IIa, C</td>
</tr>
<tr>
<td>Periodic testing should be offered to other persons with ongoing risk factors for HCV exposure.</td>
<td></td>
</tr>
</tbody>
</table>

Available at: www.hcvguidelines.org


Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)

ACTHIV 2019: A State-of-the-Science Conference for Frontline Health Professionals
Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

• Physical exam:
  – African American
  – Ht 5’ 11”, Weight 165 lbs
  – No hepatomegaly, stigmata of liver disease

• Laboratory data:
  – ALT 196; AST 205
  – Total bilirubin 0.8; Alb 4.0; INR 1.0
  – HCV RNA quant 5,134,675 copies/mL

• Laboratory data (cont)
  – WBC 4.5; Hgb 12.9
  – Platelets 325
  – Creat 0.86
  – Hemoglobin A1c- 11.3
  – HBsAg (-)
  – anti-HBc (-)
  – anti-HBs (+)
  – HAV IgG (+)
  – HLA B5701 negative
Question:
What would you do next?

A. Obtain AFP

B. Stage his liver fibrosis

C. Initiate sofosbuvir/ledipasvir, Genotype 1a

D. Post-pone treatment until Hgb A1c in normal range

How to Determine Liver Fibrosis Stage

Liver Biopsy

Serum Markers
HCV FibroSure
FIB-4 = age (years) x AST (U/L)
platelets (10^9/L) x \( \sqrt{ALT} \) (U/L)

APRI = \( \frac{AST \text{ (U/L)}}{\text{AST (upper limit normal)}} \times \frac{100}{\text{platelets (10}^9\text{/L)}} \)

Transient Elastography
Liver stiffness (kPa)
Liver fibrosis

Liver Stiffness Measurement (LSM) Ranges in Chronic Liver Disease

<table>
<thead>
<tr>
<th>METAVIR Score</th>
<th>Liver Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0 – F1</td>
<td>Mild</td>
</tr>
<tr>
<td>F2</td>
<td>Moderate</td>
</tr>
<tr>
<td>F3</td>
<td>Severe</td>
</tr>
<tr>
<td>F4</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

LSM 2.5 – 7.0 kPa → Mild or absent fibrosis is likely
LSM > 12.5 kPa → Cirrhosis is likely


Vibration Controlled Transient Elastography

**Strengths**
- Potential for assessing hepatic steatosis with CAP
- Validated technology
- Excellent at determining advanced fibrosis and cirrhosis
- Low sampling error

**Limitations**
- Cut-off uncertain
- Reduced accuracy in obese patients
- Limited availability

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Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

- Fibroscan results: Stiffness 8.1 kPa (F2), CAP score 253
- Ultrasound of liver: no masses, hepatic steatosis
- Change ART in anticipation of initiating HCV treatment
  - Current ART: Elvitegravir/cobicistat/emtricitabine/tenofovir (TDF)
  - Not recommended with DAAs
  - Switch antiretrovirals to...

### HIV/HCV Drug–Drug Interactions

<table>
<thead>
<tr>
<th>ARV(s)</th>
<th>GLE/PIB</th>
<th>GZR/EBR</th>
<th>SOF/LDV</th>
<th>SOF/VEL</th>
<th>SOF/VEL/VOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV + (RTV or COBI)</td>
<td>X</td>
<td>X</td>
<td>✓*</td>
<td>✓*</td>
<td>X</td>
</tr>
<tr>
<td>DRV + (RTV or COBI)</td>
<td>X</td>
<td>X</td>
<td>✓*</td>
<td>✓*</td>
<td>✓*†△</td>
</tr>
<tr>
<td>LPV + RTV</td>
<td>X</td>
<td>X</td>
<td>✓*</td>
<td>✓*</td>
<td>X</td>
</tr>
<tr>
<td>EFV</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RPV</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>BIC</td>
<td>–§</td>
<td>–§</td>
<td>✓†</td>
<td>✓†</td>
<td>✓†</td>
</tr>
<tr>
<td>DTG</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>RAL</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EVG/COBI/FTC/TDF</td>
<td>✓*†</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
<td>✓*†</td>
</tr>
<tr>
<td>EVG/COBI/FTC/TAF</td>
<td>✓†</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓†</td>
</tr>
<tr>
<td>3TC/ABC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>TAF or TDF</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
<td>✓*</td>
<td>✓*</td>
</tr>
</tbody>
</table>

*Monitor for tenofovir toxicity if used with TDF. □Guidelines recommend monitoring liver enzymes owing to lack of clinical safety data

Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

- Discussed care with PCP/HIV provider
- Changed ART to dolutegravir/lamivudine/abacavir
- 4 weeks later: Wait to assess tolerance and HIV suppression
  - No complaints on new regimen
  - Tolerating without adverse effects
  - HIV RNA suppressed

Factors to Consider in Selection of a DAA Regimen

- HCV genotype: determines selection of DAA …and insurance!
- Cirrhosis: duration of treatment
- Prior treatment experience (Interferon, Ribavirin, DAAs): Resistance testing
- Drug-drug interactions: statins, PPI, ART(boosted/TDF)
- Renal impairment: glecaprevir/pibrentasvir and elbasvir/grazoprevir can be used safely
Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

- Switch ART to dolutegravir/lamivudine/abacavir
- Initiated sofosbuvir/ledipasvir, on insurer’s formulary
- Treat for 8 weeks or 12 weeks?
  - HCV RNA 5.1 million IU/mL
  - African American
  - HIV +
  - Fibrosis stage F2

Regimens Not Recommended for Patients With HIV/HCV Coinfection

<table>
<thead>
<tr>
<th>NOT RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ledipasvir/sofosbuvir for 8 weeks</td>
<td>IIb, C</td>
</tr>
<tr>
<td>is not recommended, regardless of baseline HCV RNA level.</td>
<td></td>
</tr>
</tbody>
</table>
AASLD/IDSA Recommendations for First-line HCV Treatment in HCV/HIV Coinfection

<table>
<thead>
<tr>
<th>Regimen by HCV GT</th>
<th>Duration, Wks</th>
<th>No Cirrhosis</th>
<th>Compensated Cirrhosis*</th>
<th>eGFR &lt; 30 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 4</td>
<td>8</td>
<td>GLE/PIB</td>
<td>–</td>
<td>GLE/PIB†</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>GZR/EBR,*</td>
<td>GLE/PIB, GZR/EBR,*</td>
<td>GZR/EBR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF/LDV,† SOF/VEL</td>
<td>SOF/LDV, SOF/VEL</td>
<td></td>
</tr>
<tr>
<td>2, 3</td>
<td>8</td>
<td>GLE/PIB</td>
<td>–</td>
<td>GLE/PIB†</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>SOF/VEL</td>
<td>GLE/PIB, SOF/VEL§</td>
<td>–</td>
</tr>
<tr>
<td>5, 6</td>
<td>8</td>
<td>GLE/PIB</td>
<td>–</td>
<td>GLE/PIB†</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>SOF/LDV, SOF/VEL</td>
<td>GLE/PIB, SOF/LDV, SOF/VEL</td>
<td></td>
</tr>
</tbody>
</table>

*If GT1a with BL NS5A RASs for EBR, 12 wks not recommended; can increase duration to 16 wks with RBV (alternative). †Some data to support 8 wks in GT1, but 8 wks not recommended in HCV/HIV coinfection. ‡If decompensated cirrhosis, do not use HCV protease inhibitors. ††If BL Y93H RAS present in GT3, add RBV or consider SOF/VEL/VOX. †‡If also cirrhotic, increase duration to 12 wks.

Drug-Drug Interactions Between HCV Antivirals and Other Drugs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>G/P</th>
<th>GZR/EZR</th>
<th>SOF/LED</th>
<th>SOF/VEL</th>
<th>SOF/VEL/VOX</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>Monitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Monitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Monitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Max: 10 mg/d</td>
<td>↑ statin; Avoid</td>
<td>Max: 10 mg/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Decrease pravastatin dose by 50%</td>
<td>Monitor</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>Can be taken together; Max: omeprazole 20 mg/d or equivalent</td>
<td>Take DAA w/ food 4 hrs before PPI; Max: omeprazole 20 mg/d or equivalent</td>
<td>Avoid coadministration when possible. If necessary: Take DAA w/ food 4 hrs before PPI; Max: omeprazole 20 mg/d or equivalent</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Case 1: 33 yo Male with HIV and Chronic HCV Genotype 1a

<table>
<thead>
<tr>
<th>Week of Treatment</th>
<th>Lab. Results (HCV RNA Quant copies/mL)</th>
<th>ALT</th>
<th>AST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0 - Baseline</td>
<td>&gt;5 million copies/mL</td>
<td>ALT 96</td>
<td>AST 205</td>
</tr>
<tr>
<td>Week 4</td>
<td>464 copies/mL</td>
<td>ALT 37</td>
<td>AST 29</td>
</tr>
<tr>
<td>Week 8</td>
<td>Not detected</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Week 12</td>
<td>Not detected</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Week 16</td>
<td>Not detected</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Follow up care: Refer to endocrinologist, repeat ultrasound of liver in 6 months

Risk Factors Associated with Faster Fibrosis Progression in Chronic HCV

- Disease State Factors
  - Fibrosis stage
  - Inflammation grade
  - Persistently elevated ALT
- Host/Viral Factors
  - Male gender
  - Age
  - Obesity
  - Diabetes
  - Metabolic syndrome
  - HIV, HBV co-infection
  - Immune system compromise
  - Steatosis
  - Iron overload
  - Genotype 3

**Risk of HBV Reactivation in with DAA’s**

- November 2013 – July 2016: 24 cases of HBV Reactivation
  - Reactivation typically 4–8 weeks after HCV treatment initiation
  - 2 deaths, 1 liver transplant
  - Baseline HBV characteristics:
    - 7 HBsAg+ and HBV DNA
    - 4 HBsAg+ undetectable HBV DNA
    - 3 HBsAg and HBV DNA negative; presumed isolated core +
    - 10 HBV testing not reported/available


---

### Hepatitis B and HCV

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>HB core AB</th>
<th>Meaning</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Prior vaccination with immunity</td>
<td>No HBV infection</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Prior HBV infection with immunity</td>
<td>Monitor during DAAs</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Active HBV infection</td>
<td>Consider HBV Rx concurrent with DAAs</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Isolated HBV core antibody, prior infection, no immunity</td>
<td>Consider HBV DNA prior to DAAs for “occult” HBV, monitor during DAAs</td>
</tr>
</tbody>
</table>

Hcvguidelines.org Version May 24, 2018

ACTHIV 2019: A State-of-the-Science Conference for Frontline Health Professionals
Risk of HBV reactivation during HCV treatment: Suggestions for HBV Management/Monitoring

- sAg+ and detectable HBV DNA
  - HBV treatment initiated 4-6 weeks prior to HCV therapy

- sAg+, undetectable HBV DNA
  - Close monitoring (ALT/AST q2weeks; HBV DNA monthly)
  - Duration?

- Isolated core +, HBV DNA negative
  - Close monitoring
  - Double dose vaccine?


Harm Reduction

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Take-Home Points…

• Liver fibrosis stage important pre-HCV therapy  
  -Any method acceptable → just be sure to stage
• Consider drug-drug interactions with DAAs
• DAAs efficacious, well tolerated in HIV/HCV  
  -genotype, cirrhosis, renal disease influence choice
• Important to educate regarding reinfection