Management of HCV and HIV Coinfection

Maria Corcoran, MD, MPH
Associate Editor, Hepatitis C Online and Hepatitis B Online
Assistant Professor
Division of Allergy and Infectious Diseases
University of Washington

Last Updated: July 30, 2023
Disclosures

None
Epidemiology

- Coinfection with hepatitis C virus (HCV) and HIV is common, owing to shared risk factors.
  - All persons with HIV should be screened for HCV.

- Among persons living with HIV in the U.S., an estimated 15 to 30% have HCV coinfection.

- In the U.S., approximately 5% of persons with chronic HCV have HIV coinfection.

Prevalence and Incidence of HCV Infection in MSM: Systematic Review and Meta-Analysis

- Systematic review and meta-analysis evaluating HCV prevalence and incidence in MSM.

- Pooled HCV prevalence in MSM was 3.4%
  - 1.5% in HIV-negative MSM
  - 6.3% in HIV-positive MSM

- In HIV-negative MSM, pooled HCV incidence was:
  - 0.12/1000 PY in individuals not on PrEP
  - 14.80/1000 PY in individuals on PrEP

HCV and HIV: Natural History

- Coinfection with HIV accelerates the progression of hepatic fibrosis in patients with HCV, and patients with HIV are less likely to spontaneously clear HCV.

- Cirrhosis has been observed to occur 12 to 16 years earlier in persons with HCV + HIV vs. HCV alone.

- Up to 80-90% of liver-related deaths in persons living with HIV are attributable to HCV infection.

Pre-Treatment Assessment

- Assess fibrosis
  - Non-invasive tests (e.g., FIB-4)
  - Transient elastography (e.g., FibroScan)
  - Liver biopsy is the gold standard but not routinely recommended

- Laboratory evaluation
  - CBC, CMP
  - HCV RNA
  - HBV serologic testing
  - +/- HCV genotype in patients with cirrhosis

- Medication and drug-drug interaction review

Source: Opportunistic Infections Guidelines. Hepatitis C. January 18, 2023
### HCV Treatment Outcomes in Patients with HIV

<table>
<thead>
<tr>
<th>Regimen (12 weeks)</th>
<th>Genotype 1</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HCV-HIV Coinfection</td>
<td>HCV Monoinfection</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>SVR</td>
<td>Study</td>
<td>SVR</td>
</tr>
<tr>
<td>Elbasvir-Grazoprevir</td>
<td>C-EDGE Coinfection</td>
<td>95%</td>
<td>C-EDGE TN</td>
<td>95%</td>
</tr>
<tr>
<td>Glecaprevir-Pibrentasvir</td>
<td>EXPEDITION-2</td>
<td>98%</td>
<td>ENDURANCE-1</td>
<td>99%</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir</td>
<td>ION-4</td>
<td>96%</td>
<td>ION-1</td>
<td>99%</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir</td>
<td>ASTRAL-5</td>
<td>95%</td>
<td>ASTRAL-1</td>
<td>98%</td>
</tr>
</tbody>
</table>

Source: Hepatitis C Online (www.hepatitisc.uw.edu)
Glecaprevir-Pibrentasvir

- First pangenotypic NS3/4A protease inhibitor-NS5A inhibitor combination to be approved
- Not an option for patients with decompensated cirrhosis due to the presence of a protease inhibitor.
- SVR-12 rates ≥95% for treatment naïve individuals with and without compensated cirrhosis
Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection
EXPEDITION-2: Study Features

- **Design:** Open-label, phase 3 trial to evaluate the safety and efficacy of the fixed-dose combination of glecaprevir-pibrentasvir for 8 or 12 weeks in persons with HIV-HCV coinfection, without or with compensated cirrhosis

- **Setting:** Australia, Europe, Russian Federation, UK, US

- **Key Eligibility Criteria**
  - Adults with chronic HCV GT 1, 2, 3, 4, 5, or 6
  - HCV RNA ≥1,000 IU/mL at screening
  - Naïve or treated with peginterferon +/- ribavirin (PR) or PR +/- sofosbuvir
  - Compensated cirrhosis allowed
  - On ART or ART-naïve with CD4 ≥500 cells/mm³ or CD4 percentage ≥29%

- **Primary End Point:** SVR12

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

**EXPEDITION-2: Study Design**

**Abbreviations**: GLE-PIB = Glecaprevir-pibrentasvir

**Drug Dosing**: Glecaprevir-pibrentasvir (100/40 mg) fixed-dose combination; three pills (300/120 mg) once daily

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection
EXPEDITION-2: Results

One GT3 patient with cirrhosis and 85% compliance had on-treatment virologic failure.

**Abbreviations:** ITT = Intent-to-treat; mITT = modified intent-to-treat

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

EXPEDITION-2: Results

EXPEDITION-2: Overall SVR by Treatment Regimen

Sofosbuvir-Velpatasvir

- Pangenotypic NS5A-NS5B inhibitor, given as a single pill combination.
- Safe for use in patients with decompensated cirrhosis.
- SVR-12 rates ≥95% for treatment naïve individuals with and without compensated cirrhosis
Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection
ASTRAL-5: Study Features

- **Design**: Single-arm, open-label, multicenter, phase 3 trial of sofosbuvir-velpatasvir in HIV-HCV coinfected treatment-naïve and treatment-experienced patients with genotypes 1-6 HCV

- **Setting**: Multiple sites in US

- **Entry Criteria**
  - Chronic HCV GT 1-6
  - Age ≥18 years
  - HIV coinfection
  - CD4 count ≥100 cells/mm³ and HIV RNA ≤50 copies/mL
  - On stable ART for ≥8 weeks
  - Prior treatment failure allowed (but no prior NS5A or NS5B)
  - Patients with compensated cirrhosis allowed

- **Primary End Point**: SVR12

Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection
ASTRAL-5: Study Design

Drug Dosing: Sofosbuvir-velpatasvir (400/100 mg): fixed-dose combination; one pill once daily

Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection
ASTRAL-5: Results

SVR12 Results by Genotype

Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection
ASTRAL-5: Results

SVR12 Results by Treatment Experience and Cirrhosis Status

Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection
ACTG A5360 (MINMON): Study Overview

**Design**: Phase 4 open-label single-arm trial to examine the safety and efficacy of a minimal monitoring approach to HCV care delivery using 12 weeks of sofosbuvir-velpatasvir in treatment-naïve patients

**Setting**: Multiple sites in Brazil, South Africa, Thailand, Uganda & United States

**Entry criteria**:  
- Chronic HCV infection as determined by HCV RNA >1000 IU/mL  
- Treatment-naïve  
- Age 18 years or older  
- HIV coinfection permitted  
- Compensated cirrhosis permitted (FIB-4 ≥3.25, capped at ≤20% participants)  
- Absence of coinfection with HBV

**Primary End-point**: SVR ≥22 weeks post-treatment initiation

Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON):

- No pre-treatment genotyping
- Cirrhosis determination based on Fib-4
- All treatment medication provided at entry
- No scheduled on treatment visits/labs
- Remote contact at weeks 4 and 22

No Genotype

Cirrhosis Status by Fib-4

All pills provided at Entry

### Baseline Characteristic

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Sofosbuvir-Velpatasvir (n = 399)</th>
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<tbody>
<tr>
<td>Age, median (range)</td>
<td>47 (20-82)</td>
</tr>
<tr>
<td>Female sex at birth, n (%)</td>
<td>139 (35)</td>
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<tr>
<td>Identity across transgender spectrum, n (%)</td>
<td>22 (6)</td>
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<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>166 (42)</td>
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<tr>
<td>Black</td>
<td>72 (18)</td>
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<tr>
<td>Asian</td>
<td>113 (28)</td>
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<tr>
<td>HCV RNA log_{10} IU/mL, median (IQR)</td>
<td>6.1 (5.6 – 6.6)</td>
</tr>
<tr>
<td>Current injection drug use, n (%)</td>
<td>12 (3)</td>
</tr>
<tr>
<td>Current alcohol use, n (%)</td>
<td>161 (40%)</td>
</tr>
<tr>
<td>Cirrhosis (by FIB-4 ≥3.25), n (%)</td>
<td>34 (9)</td>
</tr>
<tr>
<td>HIV coinfection, n (%)</td>
<td>166 (42)</td>
</tr>
<tr>
<td>Suppressed on antiretroviral therapy, n (% of HIV/HCV)</td>
<td>164 (99)</td>
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IQR, interquartile range; FIB-4, Fibrosis-4 index

Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection
ACTG A5360 (MINMON): Results, Overall and by HIV Status

Recommendations for HCV Treatment in PLWH

- **Treatment-naïve without cirrhosis**
  - Glecaprevir/pibrentasvir for 8 weeks
  - Sofosbuvir/velpatasvir for 12 weeks

- **Treatment-naïve with compensated cirrhosis (GT 1,2,4-6)**
  - Glecaprevir/pibrentasvir for 8-12 weeks^\n  - Sofosbuvir/velpatasvir for 12 weeks

- **Treatment-naïve with compensated cirrhosis (GT 3)***
  - Glecaprevir/pibrentasvir for 8 weeks (12 week course is an alternative)

^Although 12-week duration is better studied, real world data suggest 8wk duration is ok. 12wk duration listed as “alternative” in OI guidelines

*Sofosbuvir/velpatasvir requires pre-treatment NS5A RAS testing in patients w/ GT3 + cirrhosis
  - If no resistance 12wks of sofosbuvir/velpatasvir is ok; if resistance, must add ribavirin
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<tr>
<td><strong>Protease Inhibitors</strong></td>
</tr>
<tr>
<td>Boosted Atazanavir</td>
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<td>Boosted Darunavir</td>
</tr>
<tr>
<td>Boosted Lopinavir</td>
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<td><strong>NNRTIs</strong></td>
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<tr>
<td>Doravirine</td>
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<tr>
<td>Efavirenz</td>
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<td>Rilpivirine</td>
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<tr>
<td>Elvitegravir</td>
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<td><strong>Integrase Inhibitors</strong></td>
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<tr>
<td>Bictegravir</td>
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<tr>
<td>Cabotegravir</td>
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<tr>
<td>Cobicistat-boosted elvitegravir</td>
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<td>Dolutegravir</td>
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<td>Raltegravir</td>
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<td><strong>Entry Inhibitors</strong></td>
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<td>Fostemsavir</td>
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<td>Ibalizumab-uiyk</td>
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<td>Maraviroc</td>
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<td><strong>NRTIs</strong></td>
</tr>
<tr>
<td>Emtricitabine</td>
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<tr>
<td>Lamivudine</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate</td>
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<td>Tenofovir alafenamide</td>
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Laboratory Monitoring

- Most patients will not require any on-treatment laboratory monitoring.
- Patients taking diabetes medications should monitor for hypoglycemia.
- Patients on warfarin should have INR monitoring to evaluate for subtherapeutic anticoagulation.
- In patients with compensated cirrhosis, providers may order liver function testing to monitor for liver injury during treatment.
- All patients should undergo repeat HCV RNA and liver function testing 12 weeks post-treatment to assess for HCV cure and transaminase normalization.
Conclusions

• HIV and HCV coinfection is common, owing to shared risk factors.

• Coinfection with HIV accelerates the progression of hepatic fibrosis in patients with HCV, and HCV is the leading cause of liver-related deaths in PLWH.

• Glecaprevir/pibrentasvir and sofosbuvir/velpatasvir are the preferred regimens to treat HCV in patients w/ and w/o HIV due to their efficacy and pangenotypic activity.

• Many patients with HIV can be treated for HCV using a minimal monitoring approach, and most will need on-treatment monitoring.

• Preferred HCV treatment regimens have limited interactions with most first line ART, but important drug-drug interactions with PIs and NNRTIs exist.
The production of this National HIV Curriculum Mini-Lecture was supported by Grant U1OHA32104 from the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS). Its contents are solely the responsibility of University of Washington IDEA Program and do not necessarily represent the official views of HRSA or HHS.