Management of HCV and HIV Coinfection

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Disclosures

None
Disclaimer

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Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities
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. an approximately 5% of persons with chronic HCV have HIV coinfection.
• 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.

Sources: PMID 23440167; 11732009; 24723077; 11462196; 21459211; 25522874;
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
  - HCV genotype in patients with cirrhosis
  - HBV serologic testing

• Medication and drug-drug interaction review
# HCV Treatment Outcomes in Patients with HIV

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

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 HIV-HCV Coinfected Patients
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

### Week 0-24

- **GT 1-6 Non-Cirrhotic**
  - n = 137
  - GLE-PIB
  - SVR12

- **GT 1-6 Cirrhotic**
  - n = 16
  - GLE-PIB
  - SVR12

Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
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 HIV-HCV Coinfected Patients
EXPEDITION-2: Results

EXPEDITION-2: Overall SVR by Treatment Regimen


*Excludes one patient with missing data who achieved SVR24
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 HIV-HCV Coinfected Patients
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 HIV-HCV Coinfected Patients
ASTRAL-5: Study Design

HIV-HCV Coinfected
Treatment-naïve or Treatment-experienced
GT 1, 2, 3, 4, or 6

n = 106

Sofosbuvir-Velpatasvir

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

Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
ASTRAL-5: Results

**SVR12 Results by Genotype**

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Overall</th>
<th>1a</th>
<th>1b</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with SVR12 (%)</td>
<td>101/106</td>
<td>63/66</td>
<td>11/12</td>
<td>11/11</td>
<td>11/12</td>
<td>5/5</td>
</tr>
</tbody>
</table>

- **Overall**: 95%
- **1a**: 95%
- **1b**: 92%
- **2**: 100%
- **3**: 92%
- **4**: 100%

Legend:
- 2 Relapses
- 1 LTFU
- 1 LTFU
- 1 Withdrew Consent

Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
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 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


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**No Genotype**

- **Cirrhosis Status by Fib-4**
  - All pills provided at Entry

**Sofosbuvir-Velpatasvir (SOF-VEL)**

0  4  8  12  16  20  22  24

**SVR**

Week

# Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection

**ACTG A5360 (MINMON): Study Population**

<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>
</tr>
<tr>
<td>Identity across transgender spectrum, n (%)</td>
<td>22 (6)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
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<tr>
<td>White</td>
<td>166 (42)</td>
</tr>
<tr>
<td>Black</td>
<td>72 (18)</td>
</tr>
<tr>
<td>Asian</td>
<td>113 (28)</td>
</tr>
<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>
</tr>
</tbody>
</table>

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
  1. Glecaprevir/pibrentasvir for 8 weeks
  2. Sofosbuvir/velpatasvir for 12 weeks

- Treatment-naïve with compensated cirrhosis (GT 1,2,4-6)
  1. Glecaprevir/pibrentasvir for 8 weeks
     - Although 12-week duration is better studied, real world data suggest 8wk duration ok. 12wk duration listed as “alternative” in OI guidelines
  2. Sofosbuvir/velpatasvir for 12 weeks

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

*Sofosbuvir/velpatasvir requires pre-treatment NS5A RAS testing in pt’s w/ GT3 + cirrhosis
  - if no resistance 12wks of sof/vel ok; if resistance, must add ribavirin

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<tr>
<td><strong>Protease Inhibitors</strong></td>
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<tr>
<td>Boosted Atazanavir</td>
<td>A</td>
<td>A</td>
<td>Yellow</td>
<td>ND</td>
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<tr>
<td>Boosted Darunavir</td>
<td>A</td>
<td>A</td>
<td>Yellow</td>
<td>ND</td>
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<tr>
<td>Boosted Lopinavir</td>
<td>ND, A</td>
<td>A</td>
<td>Yellow</td>
<td>ND</td>
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<tr>
<td><strong>NNRTIs</strong></td>
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<tr>
<td>Doravirine</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Efavirenz</td>
<td>ND</td>
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<td>Rilpivirine</td>
<td>ND</td>
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<tr>
<td>Eltrevirine</td>
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<td>ND</td>
<td>ND</td>
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<td><strong>Integrase Inhibitors</strong></td>
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<tr>
<td>Bictegravir</td>
<td>ND</td>
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<tr>
<td>Cabotegravir</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Cobicistat-boosted elvitegravir</td>
<td>Yellow</td>
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<tr>
<td>Dolutegravir</td>
<td>ND</td>
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<td>Raltegravir</td>
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<td><strong>Entry Inhibitors</strong></td>
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<tr>
<td>Fostemsavir</td>
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<td>Maraviroc</td>
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<td><strong>NRTIs</strong></td>
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<tr>
<td>Abacavir</td>
<td>ND</td>
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<tr>
<td>Emtricitabine</td>
<td>ND</td>
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<tr>
<td>Lamivudine</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Tenofovir disoproxil fumarate</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Tenofovir alafenamide</td>
<td>D</td>
<td>D</td>
<td>ND</td>
<td>ND</td>
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</tbody>
</table>
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.

Source: AASLD/IDSAHCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C
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 PWH.

• 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.

• G/P and sof/vel ”play well” with most first line ART but have several drug-drug interactions with PIs and NNRTIs.
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