Management of HCV and HIV Coinfection

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Disclosures

None
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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>HCV-HIV Coinfection</th>
<th>HCV Monoinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study</td>
<td>SVR</td>
<td>Study</td>
</tr>
<tr>
<td>Elbasvir-Grazoprevir</td>
<td>C-EDGE Coinfection</td>
<td>95%</td>
<td>C-EDGE TN</td>
</tr>
<tr>
<td>Glecaprevir-Pibrentasvir</td>
<td>EXPEDITION-2</td>
<td>98%</td>
<td>ENDURANCE-1</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir</td>
<td>ION-4</td>
<td>96%</td>
<td>ION-1</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir</td>
<td>ASTRAL-5</td>
<td>95%</td>
<td>ASTRAL-1</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

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

- Pangentypic 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

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

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

SVR12 Results by Treatment Experience and Cirrhosis Status

<table>
<thead>
<tr>
<th>Treatment Experience</th>
<th>Cirrhosis Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>101/106</td>
</tr>
<tr>
<td>Naïve</td>
<td>71/75</td>
</tr>
<tr>
<td>Experienced</td>
<td>30/31</td>
</tr>
<tr>
<td>No cirrhosis</td>
<td>82/87</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>19/19</td>
</tr>
</tbody>
</table>

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

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

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

### Baseline Characteristic

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Sofosbuvir-Velpatasvir (n = 399)</th>
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</thead>
<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>
</tr>
<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


Patients with SVR (%)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>HCV monoinfection</th>
<th>HIV/HCV coinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV monoinfection</td>
<td>379/399 (95% CI, 92-97)</td>
<td>222/233 (95% CI, 92-97)</td>
<td>157/166 (95% CI, 90-97)</td>
</tr>
</tbody>
</table>
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/piprentasvir 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

<table>
<thead>
<tr>
<th>Protease Inhibitors</th>
<th>Ledipasvir/ Sofosbuvir (LDV/SOF)</th>
<th>Sofosbuvir/ Velpatasvir (SOF/VEL)</th>
<th>Elbasvir/ Grazoprevir (ELB/GRZ)</th>
<th>Glecaprevir/ Pibrentasvir (GLE/PIB)</th>
<th>Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boosted Atazanavir</td>
<td>A</td>
<td>A</td>
<td>ND, A</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Boosted Darunavir</td>
<td>A</td>
<td>A</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Boosted Lopinavir</td>
<td>ND, A</td>
<td>A</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

| NNRTIs              |                                 |                                  |                                 |                                   |                                               |
|                     | Doravirine                      | ND                               | ND                              | ND                                | ND                                            |
|                     | Efavirenz                       | NA                               | ND                              | ND                                | ND                                            |
|                     | Rilpivirine                     | ND                               | ND                              | ND                                | ND                                            |
|                     | Etravirine                      | ND                               | ND                              | ND                                | ND                                            |

| Integrase Inhibitors|                                 |                                  |                                 |                                   |                                               |
|                    | Bictegravir                     | ND                               | ND                              | ND                                | ND                                            |
|                    | Cabotegravir                    | ND                               | ND                              | ND                                | ND                                            |
|                    | Cocicistat-boosted elvitegravir | C                               | C                               | ND                                | ND                                            |
|                    | Dolutegravir                    | ND                               | ND                              | ND                                | ND                                            |
|                    | Raltegravir                     | ND                               | ND                              | ND                                | ND                                            |

| Entry Inhibitors    |                                 |                                  |                                 |                                   |                                               |
|                    | Fostemsavir                     | ND                               | ND                              | ND                                | ND                                            |
|                    | Ibalizumab-ISTRY                | ND                               | ND                              | ND                                | ND                                            |
|                    | Maraviroc                       | ND                               | ND                              | ND                                | ND                                            |

| NRTIs               |                                 |                                  |                                 |                                   |                                               |
|                    | Abacavir                        | ND                               | ND                              | ND                                | ND                                            |
|                    | Emtricitabine                   | ND                               | ND                              | ND                                | ND                                            |
|                    | Lamivudine                      | ND                               | ND                              | ND                                | ND                                            |
|                    | Tenofovir disoproxil fumarate   | B, C                             | B, C                            | ND                                | ND                                            |
|                    | Tenofovir alafenamide           | D                               | D                               | ND                                | D                                             |
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.
Acknowledgment

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