Sofosbuvir/Velpatasvir for 12 Weeks in Patients Coinfected With HCV and HIV-1: The ASTRAL-5 Study

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Disclosures

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Advisory Boards: AbbVie, BMS, Gilead, Merck
Speaker Bureau: AbbVie, BMS, Gilead, Merck
**Background**

- **Sofosbuvir (SOF)**\(^1,2\)
  - Potent antiviral activity against HCV GT 1–6
  - Once-daily, oral, 400-mg tablet

- **Velpatasvir (VEL; GS-5816)**\(^3\)
  - Picomolar potency against GT 1–6
  - 2\(^{nd}\)-generation inhibitor with improved resistance profile

- **SOF/VEL FDC**\(^4,6\)
  - Once daily, oral, FDC (400/100 mg)
  - Treatment with SOF/VEL for 12 weeks in Phase 3 studies resulted in high SVR in patients with HCV GT 1–6

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FDC, fixed-dose combination.

Background and Aim

• Liver-related disease remains a major cause of morbidity and mortality in patients coinfected with HCV and HIV-1\(^1\)
  – Accelerated progression of liver disease
  – Higher rates of cirrhosis, end-stage liver disease, and hepatocellular cancer

• Direct-acting antiviral (DAA) therapy that is effective across all HCV genotypes with limited drug-drug interactions with antiretroviral therapy (ART) is needed

• This Phase 3 study aimed to evaluate safety and efficacy of SOF/VEL in patients coinfected with HCV and HIV-1

Study Design
ASTRAL-5 HIV/HCV Coinfection Study

- Open-label, single-arm, multicenter, Phase 3 study
- Broad inclusion criteria
  - HCV genotypes 1–6
  - Treatment naïve or experienced
  - 30% with compensated cirrhosis
  - On stable ART for ≥8 weeks, CD4 cell count ≥100 cells/mm³, and HIV RNA ≤50 copies/mL
- Inclusion of non-nucleoside reverse-transcriptase inhibitor (NNRTI), integrase inhibitor, and protease inhibitor (PI) regimens with TDF/FTC or ABC/3TC

3TC, lamivudine; ABC, abacavir; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.
Study Endpoints
ASTRAL-5 HIV/HCV Coinfection Study

• Primary endpoint: SVR12
  – HCV RNA <LLOQ at post-treatment Week 12
    • COBAS AmpliPrep/COBAS TaqMan HCV Quantitative Test, v2.0; LLOQ=15 IU/mL

• Safety
  – Adverse events and discontinuations
  – Maintenance of HIV-1 RNA <50 copies/mL
  – Laboratory abnormalities
  – Changes in renal function
# Demographics and Baseline Characteristics

## ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>54 (25–72)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>91 (86)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>48 (45)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>27 (19–43)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>19 (18)</td>
</tr>
<tr>
<td>Treatment experienced,* n (%)</td>
<td>31 (29)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>24 (23)</td>
</tr>
<tr>
<td>Mean HCV RNA, log_{10} IU/mL (range)</td>
<td>6.3 (5.0–7.4)</td>
</tr>
</tbody>
</table>

### HCV genotype

- 1a / 1b: 66 (62) / 12 (11)
- 2: 11 (10)
- 3: 12 (11)
- 4: 5 (5)

*Includes PEG + RBV failures and PI + PEG + RBV failures.*
### HIV Baseline Characteristics

#### ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Mean CD4 count, cells/µL (range)</th>
<th>598 (183–1513)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTI backbone</strong></td>
<td></td>
</tr>
<tr>
<td>TDF-based with boosted agent (RTV or COBI)</td>
<td>56 (53)</td>
</tr>
<tr>
<td>TDF-based without boosted agent</td>
<td>35 (33)</td>
</tr>
<tr>
<td>ABC/3TC-base</td>
<td>15 (14)</td>
</tr>
<tr>
<td><strong>ART use at baseline</strong></td>
<td></td>
</tr>
<tr>
<td>PI (DRV, LPV or ATV)</td>
<td>50 (47)</td>
</tr>
<tr>
<td>NNRTI (RPV)</td>
<td>13 (12)</td>
</tr>
<tr>
<td>Integrase inhibitor (RAL or EVG)</td>
<td>36 (34)</td>
</tr>
<tr>
<td>Other (&gt;1 of the above classes)</td>
<td>7 (7)</td>
</tr>
</tbody>
</table>

NRTI, nucleoside-analog reverse-transcriptase inhibitor; NNRTI, non-nucleoside analog reverse-transcriptase inhibitor; 3TC, lamivudine; ABC, abacavir; ATV, atazanavir; COBI, cobicistat; DRV, darunavir; EVG, elvitegravir; LPV, lopinavir; RAL, raltegravir; RPV, rilpivirine; RTV, ritonavir.
Results: SVR12 by Genotype

ASTRAL-5 HIV/HCV Coinfection Study

Error bars represent 95% confidence intervals.
Results: SVR12 by Genotype

ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Total</th>
<th>1a</th>
<th>1b</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>101</td>
<td>63</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>106</td>
<td>66</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>5</td>
</tr>
</tbody>
</table>

SVR12 (%)

LTFU, lost to follow-up. Error bars represent 95% confidence intervals.
Results: SVR12 by Genotype

ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Genotype</th>
<th>SVR12 (%)</th>
<th>Total</th>
<th>1a</th>
<th>1b</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>101/106</td>
<td>95</td>
<td>63/66</td>
<td>11/12</td>
<td>11/11</td>
<td>11/12</td>
<td>5/5</td>
<td></td>
</tr>
</tbody>
</table>

LTFU, lost to follow-up. Error bars represent 95% confidence intervals.
Results: SVR 12 by Cirrhosis or Prior Treatment

ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Cirrhosis Status</th>
<th>Treatment History</th>
<th>SVR12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Naïve</td>
<td>71</td>
</tr>
<tr>
<td>Yes</td>
<td>Experienced</td>
<td>30</td>
</tr>
</tbody>
</table>

Total: 101/106

LTFU, lost to follow-up. Error bars represent 95% confidence intervals.
**Results: SVR12 by Baseline NS5A RAVs**

**ASTRAL-5 HIV/HCV Coinfection Study**

Total, N=103

- **98% SVR12**
  - 89/91

- **12% BL RAVs**
  - 12/103

- **88% No BL RAVs**
  - 91/103

All patients with NS5A Class RAVs achieved SVR:

- **15% cutoff**: 12/12 patients
- **1% cutoff**: 19/19 patients

NS5A class RAVs; 15% deep-sequencing cut-off.

3 patients without post-treatment samples were excluded from analysis.
Results: Overall Safety
ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Total N=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>75 (71)</td>
</tr>
<tr>
<td>Grade 3–4 AE</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>2 (2)</td>
</tr>
<tr>
<td>D/C due to AE</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 or 4 laboratory abnormality*</td>
<td>19 (18)</td>
</tr>
<tr>
<td>HIV virologic rebound</td>
<td>0</td>
</tr>
</tbody>
</table>

*8 out of 19 were elevated total bilirubin; all 8 were on atazanavir/ritonavir

- SAEs: Acute radial nerve palsy and left toe infection/sepsis/UTI, neither deemed related to study drug
- Most common laboratory abnormality was elevated bilirubin in patients receiving atazanavir/ritonavir
Results: Adverse Events in ≥5%

ASTRAL-5 HIV/HCV Coinfection Study

<table>
<thead>
<tr>
<th>Adverse event, n (%)</th>
<th>Total N=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>26 (25)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Nausea way</td>
<td>7 (7)</td>
</tr>
</tbody>
</table>

- The majority of AEs were mild in severity (Grade 1 and 2)
Results: Renal Function

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Median Creatinine Clearance (mL/min)

FU-4/12, follow-up Week 4/12; Creatinine Clearance calculated using the Cockroft-Gault method; errors bars represent Q1, Q3.

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Conclusions
ASTRAL-5 HIV/HCV Coinfection Study

• SOF/VEL treatment for 12 weeks resulted in 95% SVR12 rate in patients coinfected with HIV and HCV GT 1, 2, 3, and 4
  – 100% SVR12 in patients with cirrhosis
  – 97% SVR12 in patients who failed prior HCV therapy
• Presence of baseline NS5A RAVs did not impact SVR12
• Treatment with SOF/VEL for 12 weeks was safe and well tolerated with ART, including TDF-based with boosted regimens
• SOF/VEL for 12 weeks provides a simple, safe, and highly effective treatment for patients coinfected with HIV-1 and HCV
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