Ledipasvir-Sofosbuvir for 8 or 12 weeks in HCV GT1

ION-3

# ION-3 Trial

- **Design**: Open-label, randomized, phase 3, comparing ledipasvir-sofosbuvir with or without ribavirin for 8 weeks and ledipasvir-sofosbuvir for 12 weeks in treatment-naïve, non-cirrhotic patients with GT1 HCV
- **Setting**: 58 sites in United States
- **Entry Criteria**
  - Chronic HCV Genotype 1 (n=647)
  - 18 years or older
  - No prior HCV treatment
  - Patients with cirrhosis were excluded
  - HCV RNA ≥ 10,000 IU/ml
  - No limits on BMI
- **Primary End-Point**: SVR12

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Study Design

**GT-1 Naïve Non-cirrhotic**

- **n = 215**
  - LDV-SOF
  - SVR12

- **n = 216**
  - LDV-SOF + RBV
  - SVR12

**GT-1 Naive**

- **n = 216**
  - LDV-SOF
  - SVR12

**Abbreviations**: LDV = ledipasvir; SOF = sofosbuvir; RBV = ribavirin

**Drug Dosing**

- Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily
- Ribavirin (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

### Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>8 Weeks</th>
<th>12 Week-Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDV-SOF n=215</td>
<td>LDV-SOF + RBV n=216</td>
</tr>
<tr>
<td>Mean age, y (range)</td>
<td>53 (22–75)</td>
<td>51 (21–71)</td>
</tr>
<tr>
<td>BMI, kg/m² mean (range)</td>
<td>28 (18–43)</td>
<td>28 (18–56)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>130 (60)</td>
<td>117 (54)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
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<tr>
<td>White, n (%)</td>
<td>164 (76)</td>
<td>176 (81)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>45 (21)</td>
<td>36 (17)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>6 (3)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>HCV Genotype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a, n (%)</td>
<td>171 (80)</td>
<td>172 (68)</td>
</tr>
<tr>
<td>1b, n (%)</td>
<td>43 (20)</td>
<td>44 (20)</td>
</tr>
<tr>
<td>IL28B non CC, n (%)</td>
<td>159 (74)</td>
<td>156 (72)</td>
</tr>
<tr>
<td>F3 fibrosis, n (%)</td>
<td>29 (13)</td>
<td>28 (13)</td>
</tr>
<tr>
<td>HCV RNA, log_{10} IU/ml, mean</td>
<td>6.5</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1

ION-3 Study: Results

ION-3: SVR 12* by Treatment Duration and Regimen

![Bar chart showing SVR 12 results by treatment duration and regimen.

- LDV-SOF: 202/215 patients with SVR 12 (8.9%)
- LDV-SOF +RBV: 201/216 patients with SVR 12 (9.3%)
- LDV-SOF: 206/216 patients with SVR 12 (9.5%)

Abbreviations: LDV-SOF = ledipasvir-sofosbuvir; RBV = ribavirin

*Primary end-point by intention-to-treat analysis

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Results

<table>
<thead>
<tr>
<th>Response to Ledipasvir-Sofosbuvir Based on 8 or 12 Weeks of Therapy</th>
<th>8 Weeks</th>
<th>12 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Responders at End of Treatment</td>
<td>100% (215/215)</td>
<td>100% (216/216)</td>
</tr>
<tr>
<td>SVR</td>
<td>94% (202/215)</td>
<td>96% (206/216)</td>
</tr>
<tr>
<td>Relapse</td>
<td>5% (11/215)</td>
<td>1% (3/216)</td>
</tr>
</tbody>
</table>

Relapse According to Baseline HCV RNA

| HCV RNA ≤6 million IU/mL          | 2% (2/123)       | 2% (2/131)       |
| HCV RNA ≥6 million IU/mL          | 10% (9/92)       | 1% (1/85)        |

Source: Harvoni Prescribing Information. Gilead Sciences
Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1
ION-3 Study: Resistance Data

• **NS5B S282T variant** *(reduces susceptibility to sofosbuvir)*
  - Not observed in any patients at baseline or after treatment by deep sequencing

• **NS5A resistant variants**
  - Baseline resistance in 116 (18%) of 647 patients
  - SVR12 in 104 (90%) of 116 patients with NS5A resistance
  - Of the 23 patients who had viral relapse, 15 (65%) had NS5A-resistant variants at time of relapse

Conclusions: “Ledipasvir-sofosbuvir for 8 weeks was associated with a high rate of sustained virologic response among previously untreated patients with HCV genotype 1 infection without cirrhosis. No additional benefit was associated with the inclusion of ribavirin in the regimen or with extension of the duration of treatment to 12 weeks.”
This slide deck is from the University of Washington’s *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online
www.hepatitisc.uw.edu

Hepatitis Web Study
http://depts.washington.edu/hepstudy/

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