Ledipasvir-Sofosbuvir +/- Ribavirin in HCV Genotype 1

ION-2

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1
ION-2 Study: Features

- **Design**: Open-label, randomized, phase 3, using fixed-dose combination of ledipasvir-sofosbuvir with or without ribavirin for 12 or 24 weeks in treatment-experienced patients with GT1 HCV

- **Setting**: 64 sites in United States

- **Entry Criteria**
  - Chronic HCV Genotype 1 (n = 440) 18 years or older
  - Treatment experienced
  - Did not achieve SVR with prior dual therapy (peginterferon + ribavirin), or triple therapy (NS3/4A protease inhibitor plus peginterferon + ribavirin)
  - Patients with cirrhosis accepted (up to 20% of patients)

- **Primary End Point**: SVR12

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Study Design

**Summary:**

- **Study Design:**
  - GT-1 Experienced
  - **n = 109** for LDV-SOF
  - **n = 111** for LDV-SOF + RBV
  - **n = 109** for LDV-SOF
  - **n = 111** for LDV-SOF + RBV

**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

**Abbreviations:**

LDV=ledipasvir; SOF=sofosbuvir; RBV=ribavirin

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>12-Week Treatment</th>
<th>24-Week Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDV-SOF (n = 109)</td>
<td>LDV-SOF + RBV (n = 111)</td>
</tr>
<tr>
<td>Mean age, y (range)</td>
<td>56 (24–67)</td>
<td>57 (27–75)</td>
</tr>
<tr>
<td>BMI, kg/m² mean (range)</td>
<td>29 (19–47)</td>
<td>28 (19–45)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>74 (68)</td>
<td>71 (64)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, n (%)</td>
<td>84 (77)</td>
<td>94 (85)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>24 (22)</td>
<td>16 (14)</td>
</tr>
<tr>
<td>HCV Genotype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a, n (%)</td>
<td>86 (79)</td>
<td>88 (79)</td>
</tr>
<tr>
<td>1b, n (%)</td>
<td>23 (21)</td>
<td>23 (21)</td>
</tr>
<tr>
<td>IL28B non CC, n (%)</td>
<td>99 (91)</td>
<td>100 (90)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>22 (20)</td>
<td>22 (20)</td>
</tr>
<tr>
<td>Prior nonresponse</td>
<td>49 (45)</td>
<td>46 (41)</td>
</tr>
<tr>
<td>HCV RNA, log₁₀ IU/ml (mean)</td>
<td>6.5</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Results

ION-2: SVR 12* by Treatment Duration and Regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>12-Week Patients</th>
<th>24-Week Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDV-SOF</td>
<td>102/109 (95% CI, 87-97)</td>
<td>108/109 (95% CI, 87-97)</td>
</tr>
<tr>
<td>LDV-SOF + RBV</td>
<td>107/111 (95% CI, 91-99)</td>
<td>110/111 (95% CI, 95-100)</td>
</tr>
</tbody>
</table>

* Primary end point by intention-to-treat analysis

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

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1
ION-2 Study: Results

ION-2: SVR12 by Treatment Regimen and Liver Disease

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Results for Ledipasvir-Sofosbuvir

ION-2: SVR12 by Treatment Regimen and Liver Disease

![Bar chart showing SVR12 rates for Ledipasvir-Sofosbuvir with and without cirrhosis.](chart.png)

- **Ledipasvir-Sofosbuvir x 12 weeks**
  - Without Cirrhosis: 83/87 (95% CI, 89-99)
  - With Cirrhosis: 19/22 (95% CI, 65-97)

- **Ledipasvir-Sofosbuvir x 24 weeks**
  - Without Cirrhosis: 86/87 (95% CI, 94-100)
  - With Cirrhosis: 22/22 (95% CI, 85-100)

Note: subgroup results do not include patients who withdrew consent or were lost to follow-up

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1
ION-2 Study: Results

ION-2: SVR12 by Prior Treatment Regimen

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Resistance Data

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

- **NS5A resistant variants**
  - Baseline resistance in 62 (14%) of 439 patients tested
  - SVR12 in 55 (89%) of 62 patients with NS5A resistance
  - All 11 patients with viral relapse had detectable NS5A resistant variants at relapse

- **NS3/4A resistant variants**
  - Baseline resistance in 163 (71%) of 228 patients tested
  - SVR12 in 159 (98%) of 163 patients with resistance

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Conclusions

**Conclusions:** “Treatment with a once-daily, single-tablet regimen of ledipasvir and sofosbuvir resulted in high rates of sustained virologic response among patients with HCV genotype 1 infection who had not had a sustained virologic response to prior interferon-based treatment.”

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