Ledipasvir-Sofosbuvir +/- 3rd DAA in HCV Genotype 1
NIAID SYNERGY: Genotype 1

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1 
NIAID SYNERGY GT-1 Trial: Features

### NIAID SYNERGY Trial

- **Design**: Open-label, phase 2a, using fixed dose ledipasvir-sofosbuvir alone or in combination with either GS-9669 (non-nucleoside NS5B inhibitor) or GS-9451 (NS3/4A protease inhibitor) in treatment-naïve GT 1
- **Setting**: single site, United States
- **Entry Criteria**
  - 18 years of age or older
  - Chronic HCV Genotype 1
  - Treatment naive
  - HCV RNA ≥2,000 IU/mL
  - Patients in 6 week group excluded if cirrhotic
- **Primary End-Point**: SVR12

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1
NIAID SYNERGY GT-1 Trial: Features

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Naïve</th>
<th>All stages fibrosis</th>
<th>n = 20</th>
<th>LDV-SOF</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Naïve</td>
<td>Cirrhosis excluded</td>
<td>n = 20</td>
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</tr>
</tbody>
</table>

**Abbreviations:** LDV-SOF = ledipasvir-sofosbuvir

**Drug Dosing**
Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily
GS-9669: 500 mg once daily
GS-9451: 80 mg once daily

### Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1

**NIAID SYNERGY GT-1 Trial: Participants**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>LDV-SOF x 12 weeks (n=20)</th>
<th>LDV-SOF + GS-9669 x 6 weeks (n=20)</th>
<th>LDV-SOF + GS-9451 x 6 weeks (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>57</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>Male, %</td>
<td>70</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Black, %</td>
<td>80</td>
<td>95</td>
<td>90</td>
</tr>
<tr>
<td>White, %</td>
<td>20</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>HCV genotype, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1A</td>
<td>55</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>1B</td>
<td>45</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>HCV RNA &gt;800,000 IU/ml, %</td>
<td>75</td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>IL28B CT/TT, %</td>
<td>75</td>
<td>90</td>
<td>75</td>
</tr>
<tr>
<td>Advanced fibrosis, %</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Knodell score 3</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Knodell score 4</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1
NIAID SYNERGY GT-1 Trial: Viral Kinetics

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1
NIAID SYNERGY GT-1 Trial: Results

NIH SYNERGY: SVR 12 by Treatment Regimen

Patients (%) with HCV RNA < 25 IU/ml

- Ledipasvir-sofosbuvir: 20/20
- Ledipasvir-sofosbuvir + GS-9669: 19/20*
- Ledipasvir-sofosbuvir + GS-9451: 19/20^

*1 patient relapsed 2 weeks after completion of treatment
^1 patient lost to follow-up after reaching SVR at 4 weeks

**Interpretation:** “In this small proof-of-concept study, two different three-drug regimens that were given for 6 weeks resulted in high cure rates for HCV infection with excellent tolerability. Addition of a third potent direct-acting antiviral drug can reduce the duration of treatment required to achieve sustained viral response in patients with chronic HCV genotype 1 infection without cirrhosis.”

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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