Ledipasvir/Sofosbuvir ± Ribavirin in HCV and HIV/HCV Prior SOF-based Virologic Failures (RESCUE and ACTG A5348 Studies)

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Introduction

**Ledipasvir (LDV)**
- DAAs that inhibit NS5B (RNA-dependent RNA polymerase) of HCV
- PEG-IFN heavily used in the past
- LDV/SOF ± RBV regimen for treatment of HCV infection was approved in 2015

**Sofosbuvir (SOF)**
- First-generation NS5B inhibitor
- Direct-acting antiviral
- PEG-IFN has been associated with serious adverse events

**Methods (cont’d)**
- 109* 0
- 11** 0
- 1a M 0 6.2 (3.0-7.2)
- 12

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
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<tbody>
<tr>
<td>LDV patients treated in clinical trials</td>
<td>9,361</td>
</tr>
<tr>
<td>GT 1 patients treated in clinical trials</td>
<td>5,027</td>
</tr>
<tr>
<td>GT 4 patients treated in clinical trials</td>
<td>850</td>
</tr>
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<table>
<thead>
<tr>
<th>NS5A RASs</th>
<th>LDV GT 1a</th>
</tr>
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<tbody>
<tr>
<td>Frequency</td>
<td>86%</td>
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</table>

**Background**

- Phase 2 clinical trials showed that GT 1: Subjects who failed prior Sofosbuvir-based therapy (n=163) with LDV+SOF and/or RBV (12 weeks) demonstrated 91% SVR12, with a median of 2.78 million integrated copies/mL (IC/mL)
- GT 4: 8/8 GS patients (8 patients treated with SMV+SOF and 4 patients treated with SMV+Peg+RBV) achieved SVR12

**Objectives**

- Primary objectives:
  - To evaluate the efficacy and safety of LDV/SOF±RBV in subjects with chronic HCV infection who have failed prior Sofosbuvir-based therapy

**Results**

- **GT 1a**:
  - A total of 63 subjects were treated with LDV/SOF±RBV
  - SVR12 was achieved in 61/63 (97%) subjects

**Table 5. Safety Summary**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients, n (%)</th>
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<tr>
<td>Grade 1 lab abnormalities</td>
<td>51 (82%)</td>
</tr>
<tr>
<td>Grade 2 lab abnormalities</td>
<td>10 (17%)</td>
</tr>
<tr>
<td>Grade 3 lab abnormalities</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Grade 4 lab abnormalities</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (2%)</td>
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</tbody>
</table>

Conclusions

- In the NSO-experienced NS5A-inhibitor naive population, high SVR12 rates were achieved with LDV/SOF/RBV for 12 or 24 weeks, including patients with HIV/HCV co-infection
- Highest SVR rates were observed with 12 weeks LDV/SOF/RBV in non-cirrhotics and 24 weeks LDV/SOF/RBV in cirrhotics, suggesting RBV may not be needed when duration is extended in cirrhatics
- Baseline RASs did not impact treatment outcome, as the majority of treatment failures in RESCUE occurred in the absence of pretreatment NS5A resistance (71%). All virologic failures developed emergent NS5A RASs, but none developed NS5B RASs.
- LDV/SOF/RBV for 12 or 24 weeks was safe and well tolerated. RESCUE and A5348 studies support the current recommendations of the AASLD/IDSA guidance.

References


Acknowledgements