Efficacy of Ledipasvir/Sofosbuvir (LDV/SOF) for 8 weeks in real life setting for Patients with HCV/ HIV1 co-infection

Jurgen RockStroh

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Ledipasvir/Sofosbuvir: A Single Tablet Regimen (STR)

- **Ledipasvir (LDV)**
  - Picomolar potency against multiple HCV genotypes
  - Effective against NS5B RAS S282T
  - Once-daily, oral, 90 mg

- **Sofosbuvir (SOF)**
  - Potent antiviral activity against HCV GT 1–6
  - Effective against NS5A RASs
  - High barrier to resistance
  - Once-daily, oral, 400-mg tablet

- **Ledipasvir/Sofosbuvir STR**
  - Once-daily, oral fixed-dose (90/400 mg) combination tablet, RBV-free
  - Limited DDIs, no food effect
Background

- With the introduction of Direct Acting Antivirals (DAAs), the EASL and AASLD/ IDSA/IAS-USA Guidance state “HIV/HCV coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications”.

- LDV/SOF was approved by the FDA and EMA for HIV/HCV coinfection with dosage recommendations the same as in HCV monoinfection.

- Real world cohorts (RWC) have demonstrated excellent efficacy of LDV/SOF for 8 weeks in HCV monoinfected patients.

- The aim of this analysis was to describe the effectiveness of LDV/SOF for 8 weeks in HCV genotype 1 patients with HIV/HCV coinfection in RWC and clinical trials using a pooled analysis.
Objectives & Methods

- **Objectives**
  - Descriptive analysis to evaluate the effectiveness of LDV/SOF 8 week treatment regimens in HIV/HCV coinfection patients in the real world.
  - Describe SVR12 rates in real-world and clinical trial cohorts.
  - Describe SVR12 rates in HIV/HCV coinfection versus monoinfection.

- **Methods**
  - Two prospective clinical trials and four real-world cohorts were reviewed and pooled.
  - Cohorts with fewer than 15 patients were excluded.
## Studies Included

<table>
<thead>
<tr>
<th>Study/Cohort Name</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russian/Estonia Cohort</td>
<td>59</td>
</tr>
<tr>
<td>Ruane Medical and Liver Health Institute</td>
<td>20</td>
</tr>
<tr>
<td>DHC-R</td>
<td>76</td>
</tr>
<tr>
<td>Madrid-CoRe</td>
<td>93</td>
</tr>
<tr>
<td>Department of Veterans Affairs</td>
<td>31</td>
</tr>
<tr>
<td>Saint Michaels Medical Center</td>
<td>15</td>
</tr>
</tbody>
</table>

- **Gilead Sponsored or Investigator Sponsored Trials** (n=79)
  - Isakov et al.
  - Ain et al.*
  - Deutsches Hepatitis C-Register

- **Real World Cohorts** (n=215)
  - Madrid Coinfection Registry
  - Backus et al.
  - Slim et al.

* Supported by Gilead Sciences
### Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Russian/Estonia Cohort N=59</th>
<th>Ruane Medical N=20</th>
<th>DHC-R N=76</th>
<th>Madrid-CoRe N=93</th>
<th>VA N=31</th>
<th>Saint Michaels N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (range)</td>
<td>34 (23-58)</td>
<td>52 (35-66)</td>
<td>43 (24-67)</td>
<td>49 (45-53)</td>
<td>61 (49-73)</td>
<td>61 (41-77)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>34 (58)</td>
<td>18 (90)</td>
<td>67 (88)</td>
<td>70 (75)</td>
<td>31 (100)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>59 (100)</td>
<td>11 (55)</td>
<td>73 (96)</td>
<td>93 (100)</td>
<td>9 (29)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Non-White</td>
<td>0</td>
<td>9 (45)</td>
<td>3 (4)</td>
<td>0</td>
<td>22 (71)</td>
<td>14 (93)</td>
</tr>
<tr>
<td>Tx Experienced, n (%)</td>
<td>0</td>
<td>0</td>
<td>58 (76)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>0</td>
<td>0</td>
<td>3 (4)</td>
<td>0</td>
<td>7 (23)</td>
<td>0</td>
</tr>
<tr>
<td>Mean HCV RNA log_{10} IU/mL</td>
<td>6.1</td>
<td>6.0</td>
<td>5.6*</td>
<td>5.9</td>
<td>6.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Median CD4 count (range)</td>
<td>531 (417-1006)</td>
<td>514 (106-1038)</td>
<td>400 (200-400)**</td>
<td>N/A</td>
<td>553 (186-1131)</td>
<td>578 (226-1318)</td>
</tr>
<tr>
<td>On HIV ARVs, n (%)</td>
<td>49 (83)</td>
<td>19 (95)</td>
<td>69 (91)</td>
<td>89 (95)</td>
<td>30 (97)</td>
<td>14 (93)</td>
</tr>
<tr>
<td>TDF-containing regimen, n (%)</td>
<td>21 (36)</td>
<td>15 (75)</td>
<td>49 (64)</td>
<td>N/A</td>
<td>22 (71)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>GT 1a, n (%)</td>
<td>15 (25)</td>
<td>17 (85)</td>
<td>64 (84)</td>
<td>67 (72)</td>
<td>21 (68)</td>
<td>9 (60)</td>
</tr>
</tbody>
</table>

* Data available for 75 patients; ** Data available for 60 patients
Clinical Trial Cohort:
Russia and Estonia Phase 3b Study

Phase 3b, nonrandomized, open label, multicenter, prospective study evaluated 8 weeks LDV/SOF in TN, NC HIV/HCV GT1 in Russia and Estonia*

- Two patients experienced virologic relapse:
- Overall treatment was well tolerated with no D/C due to AEs and no SAEs

* Study enrolled 7 patients with HCV RNA > 6 million IU/mL
Clinical Trial Cohort: Ruane Medical and Liver Health Institute

Phase 2, single-center, open-label pilot study with LDV/SOF for 8 Weeks in TN, non-cirrhotic, HIV/HCV coinfected patients with HCV VL <6 million IU/mL

- In both patients with virologic failure, no NS5A RASs or NS5B S282T were observed at baseline or at time of failure

**SVR12 (ITT)**

- 90%
- 18/20
Real-world Cohort: German Hepatitis C-Registry (DHC-R)

The German Hepatitis C registry, a national multicenter cohort, HIV/HCV-coinfected adults

LDV/SOF for 8 weeks achieves comparable SVR rates to 12 week treatment, including HIV co-infected patients.
Prospective registry of HIV/HCV-coinfected adults undergoing DAA therapy for HCV in the region of Madrid

No significant differences were found in effectiveness and safety with LDV/SOF for 8 or 12 weeks for GT 1 in treatment-naïve, noncirrhotic coinfect ed patients.
Real-world Cohort: Veteran’s Health Administration

Observational cohort analysis of HIV-infected veterans receiving HCV DAAs from the VA.

- LDV/SOF for 8 weeks achieves comparable SVR rates to 12 week treatment in HIV/HCV co-infected patients.

73% (22/30) of patients were Black; all achieved SVR.
Real-world Cohort: Saint Michaels

Retrospective review of HIV/HCV-coinfected adults undergoing DAA therapy for HCV in the region of Newark, NJ.

- 8 weeks of LDV/SOF was highly efficacious in predominantly Black (n=13), coinfection patient population.
SVR12 in HIV/HCV GT 1 Coinfected Patients Treated with LDV/SOF for 8 weeks: Clinical Trials Compared to Real-World Cohorts

Clinical Trials (ITT) | Real World Cohorts (PP)
--- | ---
Russian/Estonia Cohort | 97% | 90% | 57/59 | 18/20
Ain, et al. | 96% | 93% | 73/76 | 85/91
DHC-R | 100% | 100% | 30/30 | 14/14
Saint Michael's Medical Center | 100% |
Overall SVR12 in HCV GT 1 Clinical Trials and RWC Treated with LDV/SOF for 8 Weeks

- Similar response rates observed in HIV/HCV coinfected patients compared to HCV monoinfected patients

* TN, non-cirrhotic patients with HCV RNA<6 million IU/mL
Conclusions

- This descriptive analysis demonstrates that SVR rates from RWC are comparable to clinical trials.
- High SVR results in this presentation of a collection of studies support the use of LDV/SOF for 8 weeks in HIV/HCV GT 1 coinfected patients.
- The results support the EASL guidelines which recommends the same treatment regimens for HIV/HCV coinfected and HCV monoinfected persons (A1 GRADE).
- Early LDV/SOF initiation in coinfected patients before the onset of advanced fibrosis leads to high SVR12 and may reduce morbidity and mortality.
References


Disclosures

- **Peter Buggisch**: Janssen, Abbvie, BMS: Advisory Committees or Review Panels; Falk, MSD, Gilead, Merz Pharma: Speaking and Teaching.

- **Ana Moreno**: No conflict of interest.

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- **Juan Berenguer**: No conflict of interest.

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