RESPONSE TO SOFOSBUVIR/LEDIPASVIR FOR 8 OR 12 WEEKS IN HCV-MONOINFECTED AND HIV/HCV-COINFECTED PATIENTS IN CLINICAL PRACTICE

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• An 8-week sofosbuvir/ledipasvir (SOF/LDV) regimen has been proven to be non-inferior to a 12-week course of this combination among HCV-genotype 1 monoinfected patients, naïve for treatment, without cirrhosis and with baseline HCV RNA levels below 6 million IU/mL.

• HIV/HCV-coinfected patients, treated with DAA, reach slightly lower rates of SVR than HCV-monoinfected subjects in real life.

• There are limited comparative data on the efficacy of an 8-week SOF/LDV regimen among HIV/HCV-coinfected individuals in real life.
Objectives

• To compare the efficacy of an 8-week SOF/LDV regimen versus a 12-week course of this combination among HIV/HCV-coinfected patients in clinical practice.

• To compare the rate of SVR achieved with an 8-week SOF/LDV regimen in HCV-monoinfected and HIV/HCV-coinfected patients in a real-life setting.
Methods (I)

- **Design:** Multicenter prospective study
- **Setting:** 25 Infectious Diseases Units (Spain).
- **Patients:** Subjects from HEPAVIR and GEHEP cohorts* treated from October 2011 to September 2017, meeting the following criteria:
  - Infected with genotype 1
  - Began treatment with SOF/LDV
  - Naïve for treatment
  - Baseline liver stiffness <12.5 kPa
  - Baseline plasma HCV viral load <6x10^6 IU/mL
  - Had reached the scheduled time-point for SVR assessment

*(GEHEP-MONO Cohort, ClinicalTrials.gov ID: NCT02333292 and HEPAVIR-DAA Cohort, ClinicalTrials.gov ID: NCT02057003)*
Methods (II)

**Study assessments:**
- Relapse: re-emergence of plasma HCV viremia after undetectable HCV RNA at the end of therapy, provided that:
  - If phylogenetic analysis available: high degree of homology between baseline and re-emergent strains
  - If not: HCV-RNA detectable at week 4 post-treatment without genotype switching

**Data analysis:**
- Primary outcome: SVR; primary analysis: ITT
- Comparison of SVR and relapse rates between HIV/HCV-coinfected patients treated 8 and 12 weeks
- Comparison of SVR and relapse rates between HCV-monoinfected and HIV/HCV-coinfected patients treated 8 and 12 weeks
Results (I)

Patient Disposition

HCV-Genotype 1 patients treated with SOF/LDV
N=2173

SOF/LDV for 8-week
N=263
Reasons for not inclusion: 54
- Previously treated: 10
- Cirrhosis: 8
- Baseline viral load >6.10^6: 11
- Treatment still ongoing: 25

N=209
- HCV-monoinfected N=107
- HIV/HCV-coinfected N=102

SOF/LDV for 12-week
N=1910
Reasons for not inclusion: 1526
- Previously treated: 608
- Cirrhosis: 598
- Baseline viral load >6.10^6: 368

N=384
- HCV-monoinfected N=164
- HIV/HCV-coinfected N=220
## Results (II)

Baseline characteristics N=593

<table>
<thead>
<tr>
<th>Population</th>
<th>HIV negative</th>
<th>HIV positive</th>
<th>p</th>
<th>HIV negative</th>
<th>HIV positive</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>SOF/LDV 8-wks (N=107)</td>
<td>SOF/LDV 12-wks (N=164)</td>
<td>p</td>
<td>SOF/LDV 8-wks (N=102)</td>
<td>SOF/LDV 12-wks (N=220)</td>
<td>p</td>
</tr>
<tr>
<td>Age*, years</td>
<td>51 (45-63)</td>
<td>53.0 (46-61)</td>
<td>0.197</td>
<td>49 (45-53)</td>
<td>49 (46-53)</td>
<td>0.204</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>67 (62.6%)</td>
<td>105 (64.0%)</td>
<td>0.814</td>
<td>74 (72.5%)</td>
<td>178 (80.9%)</td>
<td>0.365</td>
</tr>
<tr>
<td>PWID, n (%)</td>
<td>45 (42.1%)</td>
<td>32 (19.5%)</td>
<td>&lt;0.001</td>
<td>79 (77.5%)</td>
<td>147 (66.8%)</td>
<td>0.091</td>
</tr>
<tr>
<td>Genotype n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>40 (37.4%)</td>
<td>75 (45.7%)</td>
<td>0.001</td>
<td>50 (49.0%)</td>
<td>156 (70.9%)</td>
<td>0.052</td>
</tr>
<tr>
<td>1b</td>
<td>45 (42.1%)</td>
<td>57 (34.8%)</td>
<td></td>
<td>25 (24.5%)</td>
<td>32 (14.5%)</td>
<td></td>
</tr>
<tr>
<td>1 other</td>
<td>22 (20.6%)</td>
<td>32 (19.5%)</td>
<td></td>
<td>27 (26.5%)</td>
<td>32 (14.5%)</td>
<td></td>
</tr>
<tr>
<td>HCV RNA*, log_{10} UI/ml</td>
<td>6.04 (5.44-6.41)</td>
<td>6.08 (5.69-6.44)</td>
<td>0.200</td>
<td>5.89 (5.47-6.35)</td>
<td>6.28 (5.87-6.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Liver stiffness*, KPa</td>
<td>7.9 (6.0-8.9)</td>
<td>8.5 (7.5-10.7)</td>
<td>0.003</td>
<td>8.1 (6.1-9.5)</td>
<td>8.5 (7.2-10.3)</td>
<td>0.043</td>
</tr>
</tbody>
</table>

*Median (Q1-Q3)
Results (III)

SVR12 and relapse rates according to the length of SOF/LDV therapy

SVR12 and relapse rates

- **HIV negative**
  - SVR12:
    - 8-weeks: 96.3%
    - 12-weeks: 98.2%
    - p=0.440
  - Relapse:
    - 8-weeks: 0.9%
    - 12-weeks: 1.2%
    - p=1.000

- **HIV positive**
  - SVR12:
    - 8-weeks: 92.2%
    - 12-weeks: 97.3%
    - p=0.044
  - Relapse:
    - 8-weeks: 4.9%
    - 12-weeks: 0.5%
    - p=0.013

3/5 relapses proven by phylogenetic analysis of sequences: No RASs
Results (IV)

Treatment outcomes in patients treated 8 weeks with SOF/LDV according to HIV status

- **SVR12**
  - HIV negative: 96.3% (103/107)
  - HIV positive: 92.2% (94/102)
  - p = 0.243

- **Relapse**
  - HIV negative: 0.9% (1/107)
  - HIV positive: 4.9% (5/102)
  - p = 0.112

- **Viral Breakthrough**
  - 0.0% (0/102)

- **Dropouts**
  - HIV negative: 2.8% (3/107)
  - HIV positive: 2.9% (3/102)
  - p = 1.000

- **Adverse Events**
  - 0.0% (0/102)
  - 0.0% (0/102)
Results (III)

Treatment outcomes in patients treated 12 weeks with SOF/LDV according to HIV status

- **SVR12**: 98.2% (HIV negative) vs. 97.3% (HIV positive) (p=0.738)
- **Relapse**: 1.2% (HIV negative) vs. 0.5% (HIV positive) (p=0.578)
- **Viral Breakthrough**: 0.0% (HIV negative) vs. 0.5% (HIV positive) (p=1.000)
- **Dropouts**: 0.0% (HIV negative) vs. 1.4% (HIV positive) (p=0.264)
- **Adverse Events**: 1.2% (HIV negative) vs. 0.9% (HIV positive) (p=1.000)
Conclusions

• SVR12 rate with 8-week SOF/LDV is lower than with a 12-week course among HIV/HCV-coinfected patients, which is mainly driven by a higher proportion of relapses with short therapy.

• Accordingly, SVR12 rates with SOF/LDV 8 weeks is numerically lower and the proportion of relapses higher in HIV/HCV-coinfected patients than in HCV-monoinfected subjects.

• Depending on economic issues, SOF/LDV 8-week, with salvage therapy for relapses, could be a more cost-effective strategy than other options in specific resource-limited areas.
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