Sofosbuvir and Ledipasvir Combination with and without Ribavirin in Patients with Hepatitis C Virus Infection; Preliminary Report of an Experience from Iran

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Selecting an Appropriate Treatment Regimen

- Genotype
- Cirrhosis
- Contraindications
- Special populations
- Treatment Naïve or Experienced
- Cost

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Treatment of Cirrhotic Patients

Available Approaches

- Increasing Treatment Duration
- Adding RBV to the Regimen

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Treatment Regimen

- Sofosbuvir (SOF)/ Pegylated Interferon (PEG)/Ribavirin (RBV)
- Sofosbuvir (SOF)/ Ribavirin (RBV)
- Sofosbuvir (SOF)/ Simeprevir (SIM)
- Ledipasvir (LDV)/ Sofosbuvir ±RBV
- Daclatasvir (DAC)/ Sofosbuvir ±RBV
- Ombitasvir (OMV) / Paritaprevir (PTV)/ Ritonavir (R)/ Dasabuvir (DSV)
- Ombitasvir (OMV) / Paritaprevir (PTV)/ Ritonavir (R)/ Ribavirin (RBV)
- Grazoprevir/Elbasvir

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**Background**

- **Interferon free regimens** for treatment of hepatitis C infection can lead to a treatment strategy with:
  - shorter duration
  - effective response
  - fewer adverse events

One of these new treatment approaches is using the combination of **Ledipasvir/Sofosbuvir with and without Ribavirin** which is specially used for genotype-1 HCV infected patients.
Background

Ledipasvir

+ Sofosbuvir

= Harvoni

Once-daily, oral, 90-mg tablet

Once-daily, oral, 400-mg tablet

Once-daily, oral fixed-dose (400/90 mg)

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Administered orally twice daily,

1000 mg daily (patients with a body weight of <75 kg)

1200 mg daily (patients with a body weight ≥75 kg)
✓ Hear we want to share our experience regarding treatment of treatment-naïve and previously treated patients with and without cirrhosis
✓ **Study Type**: Prospective Cohort

✓ **Broad Eligibility Criteria**
  - No upper limit for age and BMI
  - No patients had HIV infection
  - Normal Creatinine

✓ **Endpoint**
  - SVR 12
    - HCV RNA <Lower limit of detection (10 IU/ml) at post-treatment Week 12
  - Safety
Treatment Groups

Group A
N = 17
Harvoni for 12 Weeks

Group B
N = 8
Harvoni for 24 Weeks

Group C
N = 43
Harvoni + RBV for 12 Weeks

Group D
N = 11
Harvoni + RBV for 24 weeks

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## Characteristics of Treatment Groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A (n=17)</th>
<th>Group B (n=8)</th>
<th>Group C (n=43)</th>
<th>Group D (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>46.06 (11.91)</td>
<td>57.86 (8.21)</td>
<td>51.47 (11.06)</td>
<td>51.70 (6.36)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>13 (76.5)</td>
<td>8 (100)</td>
<td>31 (72.1)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (SD)</td>
<td>26.72 (5.05)</td>
<td>26.33 (2.18)</td>
<td>26.96 (6.08)</td>
<td>26.86 (3.58)</td>
</tr>
<tr>
<td>Baseline HCV RNA (log₁₀ IU/mL), Median (IQR)</td>
<td>5.79 (5.07-6.91)</td>
<td>6.83 (5.51-7.33)</td>
<td>6.14 (5.44-6.90)</td>
<td>5.85 (5.06-6.23)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>3 compensated (17.64)</td>
<td>7 compensated and 1 decompensated (100)</td>
<td>32 compensated and 2 decompensated (79.1)</td>
<td>7 compensated and 4 decompensated (100)</td>
</tr>
<tr>
<td>Esophageal Varices, n (%)</td>
<td>0</td>
<td>4 (50)</td>
<td>6 (14.3)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td>Genotype, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>14 (82.4)</td>
<td>7 (12.5)</td>
<td>30 (69.8)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>1b</td>
<td>2 (11.8)</td>
<td>1 (25)</td>
<td>4 (9.3)</td>
<td>2 (18.2)</td>
</tr>
<tr>
<td>3a</td>
<td>0</td>
<td>0</td>
<td>4 (9.3)</td>
<td>2 (18.2)</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>3 (7)</td>
<td>0</td>
</tr>
<tr>
<td>Previous Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naive</td>
<td>8 (47.1)</td>
<td>2 (25)</td>
<td>19 (44.2)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td>Resistant</td>
<td>5 (29.4)</td>
<td>4 (50)</td>
<td>16 (37.2)</td>
<td>5 (45.5)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>4 (23.5)</td>
<td>2 (25)</td>
<td>5 (11.6)</td>
<td>2 (18.2)</td>
</tr>
</tbody>
</table>
Because some of our patients are being treated yet, we have different total number of patients in each of the following steps.

<table>
<thead>
<tr>
<th>Response</th>
<th>Group A (n=17)</th>
<th>Group B (n=8)</th>
<th>Group C (n=43)</th>
<th>Group D (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At week 4 after starting therapy,</td>
<td>16/16 (100)</td>
<td>8/8 (100)</td>
<td>39/39 (100)</td>
<td>10/10 (100)</td>
</tr>
<tr>
<td>End of treatment</td>
<td>14/14 (100)</td>
<td>8/8 (100)</td>
<td>30/30 (100)</td>
<td>10/0 (100)</td>
</tr>
<tr>
<td>SVR 4</td>
<td>9/9 (100)</td>
<td>3/3 (100)</td>
<td>19/19 (100)</td>
<td>7/7 (100)</td>
</tr>
<tr>
<td>SVR 12</td>
<td>9/9 (100)</td>
<td>3/3 (100)</td>
<td>19/19 (100)</td>
<td>7/7 (100)</td>
</tr>
<tr>
<td>Relapse</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Loss to Follow-up</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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### Characteristics of Treatment Groups for Special Patients and Response to Treatment

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<thead>
<tr>
<th>Characteristics</th>
<th>Group A (n=17)</th>
<th>Group B (n=8)</th>
<th>Group C (n=43)</th>
<th>Group D (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia, n</td>
<td>1 (5.9) (4 weeks after starting therapy)</td>
<td>1 (12.5) (EOT)</td>
<td>1 (2.3) (Starting)</td>
<td>0</td>
</tr>
<tr>
<td>Thalassemia, n</td>
<td>0</td>
<td>0</td>
<td>1 (2.3) (SVR12)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma, n</td>
<td>0</td>
<td>0</td>
<td>1 (2.3) (EOT)</td>
<td>1 (9.1) (SVR12)</td>
</tr>
<tr>
<td>History of Kidney Transplantation, n</td>
<td>1 (5.9) (EOT)</td>
<td>0</td>
<td>1 (2.3) (SVR12)</td>
<td>0</td>
</tr>
<tr>
<td>History of Liver Transplantation, n</td>
<td>0</td>
<td>0</td>
<td>1 (2.3) (EOT)</td>
<td>1 (9.1) (EOT)</td>
</tr>
</tbody>
</table>

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Group A (n=13), No adverse event was seen

Group B (n=8), Two patients were complaining from myalgia and weakness and two from fatigue.

Group C (n=32), One patients with Ecema, Three patients with weakness, Two patients with myalgia, One patients with severe Thrombocytopenia

Group D (n=11), No adverse event was seen in this group, we observed one death (unknown reason) for a patients after 5 months of therapy, He had achieved undetectable HCV-RNA at week four of therapy
Combination of Ledipasvir and Sofosbuvir With and Without Ribavirin for Treatment of Genotype one Hepatitis C Virus Infected Patients: A Meta-Analysis

Mohammad Saeid Rezaee-Zavareh, Khashayar Hesamizadeh, Heidar Sharafi, Mohammad Gholami-Fesharaki, Bita Behnava, Seyed Moayed Alavian
Our Meta-Analysis for Harvoni

Overall SVR for Each Types of Treatment Regimens

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>LDP/SOF for 12 Weeks</th>
<th>LDP/SOF for 24 Weeks</th>
<th>LDP/SOF + RBV for 12 Weeks</th>
<th>LDP/SOF + RBV for 24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall SVR</td>
<td>95%</td>
<td>97%</td>
<td>96%</td>
<td>98%</td>
</tr>
</tbody>
</table>

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History of previous treatment has no significant effect on the SVR in Harvoni regimens

Alavian. Consensus on HCV Treatment, July, 22, 2016, Harvoni in Iran
Cirrhosis has only significant effect on the SVR in regimen SOF/LDP for 12 weeks.
While increasing efficacy has moderate declines in all HCV-related indicators, an aggressive treatment strategy would eliminate HCV in Iran, bringing the viremic prevalence to approximately 0.02% by 2030.

Increase treatment by 5000 individuals every year starting in 2016 until reaching a maximum treatment of 20 500 in 2018. By treating over 20 000 individuals annually for 5 years, the treatment could then decrease to below current levels by 2030.

Due to the large numbers of individuals being treated, there would need to be an increase in diagnosis rate to keep pace with the treatment rate. Utilizing a birth cohort with the young infected population could make diagnosis, treatment and thus elimination, a real possibility in Iran.
I would like to thank patients and their families for cooperation with this project and also the investigators and personnel of MELD center which participated in this project.
Thanks for your attention