**INTRODUCTION**

Sofosbuvir (SOF)/Velpatasvir (VEL)
- SOF: nucleoside polymerase inhibitor with activity against HCV genotype (GTs) 1–6
- GS-117667: predominant circulating metabolite
- VEL: 2nd generation NS5A inhibitor with picomolar potency against HCV GT 1–6
- Favorable resistance profile

Voxilaprevir (VOX)
- HCV NS3/4A PI with potent antiviral activity against HCV GT 1–6
- Demonstrated high efficacy in Phase 3 clinical trials in DAAs-naive and DAA-experienced patients

SOF/VEL/VOX
- Once-daily, oral, fixed-dose combination (400/100/100 mg)
- Demonstrated high efficacy in Phase 3 clinical trials vs DAAs-naive and DAA-experienced patients

POLARIS studies for HCV patients who failed with DAA-containing regimens

Few data from real-world cohorts exist

**AIM**

The objective of this cohort was to Report the efficacy and safety of SOF/VEL/VOX ± RBV in DAA failure patients with cirrhosis included in the French compassionate use program

**ACKNOWLEDGEMENTS**

This work has been realized with the support of Gilead Sciences

**CONTACT INFORMATION**

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**METHOD**

Key patient eligibility criteria

Inclusion criteria
- Adult ≥18 years
- HCV chronic infection with positive HCV RNA
- Compensated cirrhosis
- Failure with an all oral DAA-based regimen containing 1st generation NSSA inhibitor

Exclusion criteria
- Child B or C cirrhosis
- Active cancer diagnosis
- Contraindication for SOF/VEL/VOX

Assessments
- Primary endpoint was SVR12 rate
  - Proportion of patients with HCV RNA < LLOQ 12 weeks post-treatment who received ≥1 dose of SOF/VEL/VOX ± RBV (ITT population)
- Additional assessments:
  - On-treatment virologic failure and post-treatment virologic relapse
  - Resistance-associated substitutions (RAS) at baseline and at time of failure by next generation sequencing (≥ 15% detection threshold)
  - Serious adverse events

Flow-chart of the French compassionate use program

- Patients included in the program: n = 52
- Patients without collection of data: n = 6
- Patients with available data: n = 46
- Patients who did not start treatment: n = 2
- Patients with available data who started treatment: n = 44 (ITT population)

**RESULTS**

Baseline characteristics of the patients (n = 46)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>56.7</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>52 (100)</td>
</tr>
<tr>
<td>Race (n, %)</td>
<td></td>
</tr>
<tr>
<td>White (n, %)</td>
<td>32 (70)</td>
</tr>
<tr>
<td>Black/other (n, %)</td>
<td>20 (43)</td>
</tr>
<tr>
<td>HCV genotype (n, %)</td>
<td></td>
</tr>
<tr>
<td>1 (n, %)</td>
<td>18 (40)</td>
</tr>
<tr>
<td>2 (n, %)</td>
<td>6 (13)</td>
</tr>
<tr>
<td>3 (n, %)</td>
<td>12 (26)</td>
</tr>
<tr>
<td>4 (n, %)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Previous DAA-based regimen</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir-based regimen</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir alone (n, %)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Sofosbuvir + Daclatasvir (n, %)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Paritaprevir (n, %)</td>
<td></td>
</tr>
<tr>
<td>Paritaprevir + einesavir (n, %)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Paritaprevir + dasabuvir (n, %)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Velpatasvir-based regimen</td>
<td></td>
</tr>
<tr>
<td>Velpatasvir alone (n, %)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Velpatasvir + sofosbuvir (n, %)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Velpatasvir + grazoprevir (n, %)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>
| Viologenic responses (n = 44*, ITT population)
  - 100 (22/22 patients), 96 (21/22 patients), 95 (20/22 patients)
  - Safety profile
    - Patients with virologic success (n, %): 46 (100)
    - Serious adverse events (n, %): 4 (9)
    - Successful virologic success (n, %): 42 (91)
    - Virologic success (n, %): 46 (100)

 Among the 46 patients who were treated two relapse were observed

**CONCLUSIONS**

- This strategy is safe in patients with compensated cirrhosis
- In this real-world cohort, the combination SOF/VEL/VOX ± RBV for 12 weeks is effective in patients with cirrhosis who failed with DAA combination containing 1st generation NSSA inhibitor with or without protease inhibitor

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