A Randomized Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks Compared to Sofosbuvir/Velpatasvir for 12 Weeks in DAA-Naïve Genotype 1–6 HCV Infected Patients: The POLARIS-2 Study


Abstract LB-12

POLARIS-2: Pangenotypic Single Tablet Regimen with Inhibitors of HCV NS5B (Nucleotide) + NS5A + NS3

Sofosbuvir (SOF)/Velpatasvir (VEL)
  
  • SOF: Nucleoside polymerase inhibitor with activity against HCV GT 1-6
  • VEL: Potent pangenotypic NS5A inhibitor

Voxilaprevir (VOX)
  
  • HCV NS3/4A PI with potent antiviral activity against GT 1-6, including most RASs

SOF/VEL/VOX
  
  • Once daily, oral, fixed-dose combination (400/100/100 mg) for GT 1-6
Polaris-2: Study Design

- Open-label, randomized, active-comparator trial at 117 sites (USA, Canada, France, Germany, UK, Australia, and New Zealand)
- Genotypes 1–6 with and without compensated cirrhosis
  - GT 3 patients with cirrhosis were enrolled in a separate study (Polaris-3)
  - 1:1 randomization for GT 1–4 (other GTs assigned to SOF/VEL/VOX)
  - Stratified by GT, cirrhosis, and prior treatment experience (naïve or IFN experienced)

Polaris-2: Randomized Controlled Trial of SOF/VEL/VOX for 8 Weeks versus SOF/VEL for 12 Weeks

- Open-label
- Treatment-naïve and experienced (interferon/ribavirin only)
- HCV genotype 1, 2, 3, 4, 5, 6

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL/VOX 8 Weeks n=501</th>
<th>SOF/VEL 12 Weeks n=440</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>53 (18–78)</td>
<td>52 (19–82)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>255 (51)</td>
<td>237 (54)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>391 (78)</td>
<td>365 (83)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>27 (17–57)</td>
<td>27 (18–54)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>90 (18)</td>
<td>84 (19)</td>
</tr>
<tr>
<td>Genotype, n (%)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a / 1b / Other</td>
<td>169 (34) / 63 (13) / 1 (&lt;1)</td>
<td>172 (39) / 59 (13) / 1 (&lt;1)</td>
</tr>
<tr>
<td>2</td>
<td>63 (13)</td>
<td>53 (12)</td>
</tr>
<tr>
<td>3</td>
<td>92 (18)</td>
<td>89 (20)</td>
</tr>
<tr>
<td>4</td>
<td>63 (13)</td>
<td>57 (13)</td>
</tr>
<tr>
<td>5 / 6 / Unknown</td>
<td>18 (4) / 30 (6) / 2 (&lt;1)</td>
<td>0 / 9 (2) / 0</td>
</tr>
<tr>
<td>IFN experienced, n (%)</td>
<td>118 (24)</td>
<td>100 (31)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>166 (33)</td>
<td>136 (31)</td>
</tr>
<tr>
<td>Mean HCV RNA, log₁₀ IU/mL (range)</td>
<td>6.1 (2.7–7.6)</td>
<td>6.2 (4.0–7.6)</td>
</tr>
</tbody>
</table>

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

Jacobson I, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-12.
POLARIS-2: Results (SVR12)

Jacobson I, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-12.

POLARIS-2:
Results - SVR12 by Genotype (GT 1)

AEDC, Discontinuation due to AE. Error bars represent 95% confidence intervals.
0 of 2 patients (0%) with GT 1b Other achieved SVR12 (1 each in the SOF/VEL/VOX and SOF/VEL group).

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.
POLARIS-2:
Results - SVR12 by Genotype (GT 2–6)

AEDC, Discontinuation due to AE. Error bars represent 95% confidence intervals.

SOF/VEL/VOX 8 weeks, n=501
SOF/VEL 12 weeks, n=440

GT 2
GT 3
GT 4
GT 5
GT 6
Unknown

SVR12, %

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

POLARIS-2:
Results - SVR12 by Cirrhosis Status

No Cirrhosis
n=767

Cirrhosis
n=174

Error bars represent 95% confidence intervals.

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.
All 64 patients with baseline NS5B nucleoside inhibitor RASs achieved SVR12.
POLARIS-3: Study Design

- Open-label, randomized, active-comparator trial conducted at 84 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with GT 3, all of whom had cirrhosis
- 1:1 randomization
  - Stratified by prior treatment experience (IFN experienced or naïve)

Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

POLARIS-3: Randomized Controlled Trial of SOF/VEL/VOX for 8 Weeks Versus SOF/VEL for 12 Weeks in Patients with HCV Genotype 3 and Cirrhosis

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL/VOX 8 Weeks n=110</th>
<th>SOF/VEL 12 Weeks n=109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age, y (range)</td>
<td>54 (25–75)</td>
<td>55 (31–69)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>74 (67)</td>
<td>83 (76)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>100 (91)</td>
<td>97 (89)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>28 (20–50)</td>
<td>27 (18–46)</td>
</tr>
<tr>
<td>Mean Platelets, x10³/µL (range)</td>
<td>14 (37–351)</td>
<td>150 (51–292)</td>
</tr>
<tr>
<td>IFN Experienced, n (%)</td>
<td>35 (32)</td>
<td>32 (29)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>41 (37)</td>
<td>52 (48)</td>
</tr>
<tr>
<td>Mean HCV RNA, log₁₀ IU/mL (range)</td>
<td>6.0 (1.6–7.6)</td>
<td>6.3 (4.1–7.5)</td>
</tr>
</tbody>
</table>

Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.
POLARIS-3: Results (SVR12)

- There were 6 patients with Y93H in the SOF/VEL/VOX group and 4 in the SOF/VEL group; all achieved SVR12.
- No treatment emergent RASs in the SOF/VEL/VOX group.
  In the SOF/VEL group, both virologic failures had Y93H.

Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

POLARIS-3: Results - SVR12 by Prior Treatment

Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.
• There were 6 patients with Y93H in the SOF/VEL/VOX group and 4 in the SOF/VEL group; all achieved SVR12
• No treatment emergent RASs in the SOF/VEL/VOX group; in the SOF/VEL group, both virologic failures had Y93H

3 patients in the SOF/VEL/VOX group and 6 patients in the SOF/VEL group were excluded due to incomplete RAS data. RASs were analyzed using a 15% cut-off; error bars represent 95% confidence intervals.

Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.