Sofosbuvir/Velpatasvir/Voxilaprevir for 12 Weeks as a Salvage Regimen in NS5A Inhibitor-Experienced Patients with Genotype 1–6 Infection: The Phase 3 POLARIS-1 Study


Abstract 194

POLARIS-1: 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-1: Study Design

- Double-blind, randomized, placebo-controlled trial in NS5A-experienced GT 1–6 patients conducted at 109 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with GT 1 at screening randomized equally to SOF/VEL/VOX or matching placebo (all other GTs assigned to SOF/VEL/VOX)
  - Stratified by presence of cirrhosis

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

POLARIS-1: Demographics

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL/VOX 12 weeks n=263</th>
<th>Placebo 12 weeks n=152</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>58 (27–84)</td>
<td>59 (29–80)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>200 (76)</td>
<td>121 (80)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>211 (80)</td>
<td>124 (82)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>29 (18–67)</td>
<td>29 (18–61)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>121 (46)</td>
<td>51 (34)</td>
</tr>
<tr>
<td>Genotype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a / 1b / Other</td>
<td>101 (38) / 45 (17) / 4 (2)</td>
<td>117 (77) / 31 (20) / 2 (1)</td>
</tr>
<tr>
<td>2</td>
<td>5 (2)</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>78 (30)</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>22 (8)</td>
<td>—</td>
</tr>
<tr>
<td>5 / 6 / Unknown</td>
<td>1 (&lt;1) / 6 (2) / 1 (&lt;1)</td>
<td>0 / 2 (1) / 0</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>47 (18)</td>
<td>27 (18)</td>
</tr>
<tr>
<td>Mean HCV RNA, log_{10} IU/mL (range)</td>
<td>6.3 (1.6–7.7)</td>
<td>6.3 (3.7–7.6)</td>
</tr>
</tbody>
</table>

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.
POLARIS-1: Results: Prior NS5A Treatment

3 patients received both LDV and DCV. DCV, daclatasvir; LDV, ledipasivir; OMB, ombitasvir.
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POLARIS-1: Results: SVR12

- No patients who received placebo achieved SVR
- p < 0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX

* Exposure was consistent with non-adherence.
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POLARIS-1: Results (SVR12) by Cirrhosis Status

SOF/VEL/VOX 12 Weeks (n=263)

No Cirrhosis

- 99%
- 140/142
- 1 withdraw consent
- 1 LTFU

Cirrhosis

- 93%
- 113/121
- 6 relapses
- 1 on-treatment failure
- 1 withdraw consent

POLARIS-1: Results (SVR12) by Subtype/Genotype

SOF/VEL/VOX 12 Weeks (n=263)

GT 1: 97/150
GT 1a: 96/101
GT 1b: 100/45
GT 2: 100/5
GT 3: 95/74
GT 4: 91/22
GT 5: 100/1
GT 6: 100/6

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POLARIS-1: Results (SVR12)  

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SOF/VEL/VOX 12 Weeks (n=263)

<table>
<thead>
<tr>
<th></th>
<th>No RASs</th>
<th>Any RASs</th>
<th>NS3 Only</th>
<th>NS5A Only</th>
<th>NS3 + NS5A</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12, %</td>
<td>146</td>
<td>208</td>
<td>9</td>
<td>120</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>208</td>
<td>9</td>
<td>127</td>
<td>72</td>
</tr>
</tbody>
</table>

Two patients had S282T at baseline, both achieved SVR12

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A Randomized, Controlled, Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir or Sofosbuvir/Velpatasvir for 12 Weeks in Direct-Acting Antiviral-Experienced Patients with Genotype 1–6 HCV Infection: The POLARIS-4 Study


Abstract 109
**POLARIS-4: Study Design**

- Open-label, randomized, active-comparator trial in DAA-experienced GT 1–6 patients without prior NS5A inhibitor experience conducted at 102 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with HCV GT 1, 2, and 3 at screening were randomized equally to SOF/VEL/VOX or SOF/VEL (all other GTs assigned to SOF/VEL/VOX)
- Stratified by GT and presence of cirrhosis

**POLARIS-4: Demographics**

- Randomized controlled trial of persons who failed non-NS5A containing DAA regimens (SOF 73% or SOF+RBV/IFN)
- SOF/VEL/VOX for 12 weeks (n=182) versus SOF/VEL for 12 weeks (n=151)

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL/VOX 12 Weeks n=182</th>
<th>SOF/VEL 12 Weeks n=151</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>57 (25-85)</td>
<td>57 (24-80)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>143 (79)</td>
<td>114 (75)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>160 (88)</td>
<td>131 (87)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>29 (18-45)</td>
<td>29 (18-53)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>84 (46)</td>
<td>69 (46)</td>
</tr>
<tr>
<td>Genotype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a / 1b</td>
<td>54 (30) / 24 (13)</td>
<td>44 (29) / 22 (14)</td>
</tr>
<tr>
<td>2</td>
<td>31 (71)</td>
<td>33 (22)</td>
</tr>
<tr>
<td>3</td>
<td>54 (30)</td>
<td>52 (34)</td>
</tr>
<tr>
<td>4</td>
<td>19 (10)</td>
<td>-</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>33 (18)</td>
<td>29 (19)</td>
</tr>
<tr>
<td>Mean HCV RNA, log₁₀ IU/mL (range)</td>
<td>6.3 (5.0 – 7.5)</td>
<td>6.3 (3.6 - 7.3)</td>
</tr>
</tbody>
</table>

POLARIS-4: Prior HCV Treatment

- Other NS5B included mericitabine (n=7); other NS5B+NS3 included deleobuvir+faldaprevir (n=14), mericitabine+danoprevir (n=4), and SOF+telaprevir (n=6); one patient without prior DAA exposure is excluded; SMV, simeprevir; SOF, sofosbuvir

POLARIS-4: Results SVR12

- p <0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX
- p=0.092 for SOF/VEL

Error bars represent 95% confidence intervals.
POLARIS-4: Results SVR12 by Cirrhosis Status

No Cirrhosis
n=180

Cirrhosis
n=153

SVR12, %
0 20 40 60 80 100
SOF/VEL/VOX SOF/VEL

98/96 94

96/98 77/82

81/84 59/69

Error bars represent 95% confidence intervals.

POLARIS-4: Results SVR12 by Genotype

SVR12, %
0 20 40 60 80 100
GT 1a GT 1b GT 2 GT 3 GT 4

12 weeks (n=182)
12 weeks (n=151)

53 39 23 31 51 19
54 44 24 31 54 19

98 96 95 100 94 100
89 95 97 85 89 95

Error bars represent 95% confidence intervals.
 Twenty-two patients had NS5B RASs – all achieved SVR12
 No treatment-emergent RASs were observed in the patient who relapsed following SOF/VEL/VOX
 In the SOF/VEL group, 10 of the 15 patients with virologic failure developed Y93H or Y93C


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


Abstract LB-12
**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: Demographics**

- 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 (16–54)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>90 (18)</td>
<td>84 (19)</td>
</tr>
</tbody>
</table>

Genotype, n (%)*:

- 1a / 1b / Other: 169 (34) / 63 (13) / 1 (<1)
- 2: 63 (13)
- 3: 92 (18)
- 4: 63 (13)
- 5 / 6 / Unknown: 18 (4) / 30 (6) / 2 (<1)

IFN experienced, n (%): 118 (24) / 100 (31)

IL28B CC, n (%): 166 (33) / 136 (31)

Mean HCV RNA, log₁₀ IU/mL (range): 6.1 (2.7–7.8) / 6.2 (4.0–7.6)

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