Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Ira M. Jacobson, Eric Lawitz, Edward J. Gane, et al. Sofosbuvir, Velpatasvir, and Voxilaprevir for 8 weeks for Chronic HCV
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Table S1. Reasons for screen failure: POLARIS-2

<table>
<thead>
<tr>
<th>Screened Subjects</th>
<th>1116</th>
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<tbody>
<tr>
<td>Screen Failure Subjects</td>
<td>173/1116 (15.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screen Failure Subjects Who Did Not Meet Eligibility Criteria</th>
<th>161/173 (93.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusion Criterion 3: Screening laboratory values not within acceptable ranges</td>
<td>50/161 (31.1%)</td>
</tr>
<tr>
<td>Exclusion Criterion 7: Clinically-relevant alcohol or drug abuse within 12 months of screening</td>
<td>39/161 (24.2%)</td>
</tr>
<tr>
<td>Inclusion Criterion 8: Liver imaging within 6 months of Day 1</td>
<td>17/161 (10.6%)</td>
</tr>
<tr>
<td>Inclusion Criterion 4: HCV RNA $\geq 10^4$ IU/mL at Screening</td>
<td>15/161 (9.3%)</td>
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<tr>
<td>Inclusion Criterion 6: Meeting HCV treatment status specified in protocol</td>
<td>14/161 (8.7%)</td>
</tr>
<tr>
<td>Exclusion Criterion 8: Use of any prohibited concomitant medications</td>
<td>13/161 (8.1%)</td>
</tr>
<tr>
<td>Inclusion Criterion 13: Subject must be able to comply with the dosing instructions</td>
<td>12/161 (7.5%)</td>
</tr>
<tr>
<td>Exclusion Criterion 1: History of clinically-significant illness or any other major medical disorder</td>
<td>12/161 (7.5%)</td>
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<tr>
<td>Exclusion Criterion 4: HCV Genotype 3 and the presence of cirrhosis</td>
<td>9/161 (5.6%)</td>
</tr>
<tr>
<td>Inclusion Criterion 7: Cirrhosis determination</td>
<td>8/161 (5.0%)</td>
</tr>
<tr>
<td>Inclusion Criterion 9: Negative pregnancy tests for females of childbearing potential</td>
<td>7/161 (4.3%)</td>
</tr>
<tr>
<td>Inclusion Criterion 12: Subject must be of generally good health</td>
<td>7/161 (4.3%)</td>
</tr>
<tr>
<td>Inclusion Criterion 5: Chronic HCV infection</td>
<td>6/161 (3.7%)</td>
</tr>
<tr>
<td>Inclusion Criterion 1: Willing and able to provide written informed consent</td>
<td>4/161 (2.5%)</td>
</tr>
<tr>
<td>Exclusion Criterion 2: Screening ECG with clinically significant abnormalities</td>
<td>4/161 (2.5%)</td>
</tr>
<tr>
<td>Exclusion Criterion 3: BMI $\geq 18$ kg/m²</td>
<td>3/161 (1.9%)</td>
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<tr>
<td>Inclusion Criterion 11: Agree to discontinue nursing</td>
<td>2/161 (1.2%)</td>
</tr>
<tr>
<td>Exclusion Criterion 6: Infection with HBV or HIV</td>
<td>2/161 (1.2%)</td>
</tr>
<tr>
<td>Exclusion Criterion 9: Known hypersensitivity to the study drug, the metabolites, or formulation excipient</td>
<td>2/161 (1.2%)</td>
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<tr>
<td>Inclusion Criterion 10: Agree to use protocol specified method(s) of contraception</td>
<td>1/161 (0.6%)</td>
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<tr>
<td>Exclusion Criterion 5: Chronic liver disease of a non-HCV etiology</td>
<td>1/161 (0.6%)</td>
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| Screen Failure Subjects Who Met Eligibility Criteria | 12/173 (6.9%) |

<table>
<thead>
<tr>
<th>Reasons for Nonenrollment of Subjects Who Met Eligibility Criteria</th>
<th>7/12 (58.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrew Consent</td>
<td>3/12 (25.0%)</td>
</tr>
<tr>
<td>Lost to Follow-Up</td>
<td>1/12 (8.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>1/12 (8.3%)</td>
</tr>
<tr>
<td>Outside of Visit Window</td>
<td>1/12 (8.3%)</td>
</tr>
</tbody>
</table>
Table S2. Reasons for screen failure: POLARIS-3

| Screened Subjects | 315 |
| Screen Failure Subjects | 95/315 (30.2%) |
| Screen Failure Subjects Who Did Not Meet Eligibility Criteria | 94/95 (98.9%) |
| Inclusion Criterion 8: Cirrhosis determination | 29/94 (30.9%) |
| Exclusion Criterion 3: Screening laboratory values not within acceptable ranges | 29/94 (30.9%) |
| Exclusion Criterion 6: Clinically-relevant alcohol or drug abuse within 12 months of screening | 15/94 (16.0%) |
| Exclusion Criterion 1: History of clinically-significant illness or any other major medical disorder | 14/94 (14.9%) |
| Inclusion Criterion 9: Liver imaging within 6 months of Day 1 | 10/94 (10.6%) |
| Inclusion Criterion 4: HCV RNA > 10^4 IU/ml at Screening | 6/94 (6.4%) |
| Inclusion Criterion 5: HCV genotype 3 | 5/94 (5.3%) |
| Inclusion Criterion 7: Treatment-naïve, or IFN treatment-experienced, DAA-naïve | 4/94 (4.3%) |
| Inclusion Criterion 13: Subject must be of generally good health | 3/94 (3.2%) |
| Exclusion Criterion 7: Use of any prohibited concomitant medications | 3/94 (3.2%) |
| Inclusion Criterion 10: Negative pregnancy tests for females of childbearing potential | 2/94 (2.1%) |
| Exclusion Criterion 2: Screening ECG with clinically significant abnormalities | 2/94 (2.1%) |
| Inclusion Criterion 1: Willing and able to provide written informed consent | 1/94 (1.1%) |
| Inclusion Criterion 14: Subject must be able to comply with the dosing instructions | 1/94 (1.1%) |

Screen Failure Subjects Who Met Eligibility Criteria | 1/95 (1.1%) |

Reasons for Nonenrollment of Subjects Who Met Eligibility Criterion

Withdrawn Consent | 1/1 (100.0%)
Figure S1. Patient disposition: POLARIS-2

1116 screened

173 were not randomized/enrolled

943 randomized/enrolled

502 randomized/enrolled to receive sofosbuvir-velpatasvir-voxilaprevir for 8 weeks

501 began treatment

1 discontinued treatment due to pregnancy

500 completed treatment

501 assessed for efficacy

441 randomized to receive sofosbuvir-velpatasvir for 12 weeks

440 began treatment

3 discontinued treatment
2 due to adverse event
1 lost to follow-up

437 completed treatment

440 assessed for efficacy

501 began treatment
Figure S2. Patient disposition: POLARIS-3

315 screened

95 were not randomized/enrolled

220 randomized/enrolled

110 randomized/enrolled to receive sofosbuvir-velpatasvir-voxilaprevir for 8 weeks

110 began treatment

110 completed treatment

110 assessed for efficacy

110 randomized to receive sofosbuvir-velpatasvir for 12 weeks

109 began treatment

2 discontinued treatment
1 due to adverse event
1 due to lack of efficacy

107 completed treatment

109 assessed for efficacy

110 were randomized/enrolled to receive sofosbuvir-velpatasvir-voxilaprevir for 8 weeks

109 began treatment

107 completed treatment

109 assessed for efficacy

110 were randomized to receive sofosbuvir-velpatasvir for 12 weeks

109 began treatment

2 discontinued treatment
1 due to adverse event
1 due to lack of efficacy

107 completed treatment

109 assessed for efficacy

95 were not randomized/enrolled
Table S3. Characteristics of patients who relapsed in POLARIS-2

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>BMI (kg/m²)</th>
<th>Geno-type</th>
<th>Cirrhosis</th>
<th>IL28B</th>
<th>HCV RNA</th>
<th>Treatment history</th>
<th>NS3 RASs*</th>
<th>NS5A RASs*</th>
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<tr>
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<td>BL Relapse</td>
<td></td>
</tr>
<tr>
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<td>Q80K</td>
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<td>Q80K</td>
<td>Q80K</td>
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<td>Q80K</td>
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</tbody>
</table>

A/W=Asian White; PI=Pacific Islander; Peg/Rbv=peginterferon + ribavirin; BL=baseline; BMI=body mass index.
*Using a 15% reporting threshold.
# Table S4. Characteristics of patients who relapsed in POLARIS-3

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>BMI</th>
<th>Genotype</th>
<th>Cirrhosis</th>
<th>IL28B</th>
<th>HCV RNA</th>
<th>Treatment history</th>
<th>NS3 RASs*</th>
<th>NS5A RASs*</th>
</tr>
</thead>
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<td>BL</td>
<td>Relapse</td>
</tr>
<tr>
<td>Sofosbuvir-velpatasvir-voxilaprevir for 8 weeks</td>
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<td>CT</td>
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<td>Peg/Rbv</td>
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<td>6.3</td>
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Peg/Rbv=peginterferon + ribavirin; BL=baseline; BMI=body mass index.

*Using a 15% reporting threshold.
Table S5. SVR12 rates in POLARIS-2 and POLARIS-3 by baseline resistance

<table>
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<th></th>
<th>POLARIS-2</th>
<th>POLARIS-3</th>
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<tbody>
<tr>
<td></td>
<td>8 Wk of Sofosbuvir, Velpatasvir and Voxilaprevir (N=497)</td>
<td>12 Wk of Sofosbuvir, Velpatasvir and Voxilaprevir (N=435)</td>
</tr>
<tr>
<td>No NS3 or NS5A RASs</td>
<td>223/228 (98)</td>
<td>206/208 (99)</td>
</tr>
<tr>
<td>Any NS3 or NS5A RASs</td>
<td>234/250 (94)</td>
<td>217/218 (&gt;99)</td>
</tr>
<tr>
<td>NS3 Only</td>
<td>100/110 (91)</td>
<td>97/97 (100)</td>
</tr>
<tr>
<td>NS5A Only</td>
<td>114/120 (95)</td>
<td>90/91 (99)</td>
</tr>
<tr>
<td>NS3 and NS5A</td>
<td>20/20 (100)</td>
<td>30/30 (100)</td>
</tr>
<tr>
<td>RASs Not Determined for Both NS3 and NS5A</td>
<td>19/19 (100)</td>
<td>9/9 (100)</td>
</tr>
</tbody>
</table>

*Using a 15% reporting threshold.
Patients who did not have observed virologic failure (ie, those who were lost to follow-up or withdrew consent) are excluded from this analysis.
Table S6. Serious adverse events in POLARIS-2

<table>
<thead>
<tr>
<th>Number of Subjects Experiencing Any Treatment-Emergent Serious Adverse Event</th>
<th>SOF/VEL/Vox 0 Weeks (N=551)</th>
<th>SOF/VEL 12 Weeks (N=445)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects Experiencing Any Treatment-Emergent Serious Adverse Event</td>
<td>15 (3.0%)</td>
<td>7 (1.6%)</td>
</tr>
<tr>
<td>Event by Preferred Term</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pylonephritis</td>
<td>1 (0.2%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Alcohol withdrawal syndrome</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Back pain</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Biliary colic</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Chest pain</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Clostridium difficile colitis</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Flank pain</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Multiple fractures</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Musculoskeletal chest pain</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Mynitis</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Perineal abscess</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral artery occlusion</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Road traffic accident</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Small intestinal obstruction</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Squamous cell carcinoma of lung</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Suicide attempt</td>
<td>0</td>
<td>1 (0.2%)</td>
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Table S7. Serious adverse events in POLARIS-3

<table>
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<tr>
<th>Term</th>
<th>SOF/VEL/VOX (N=110)</th>
<th>SOF/VEL (N=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiencing Any Treatment-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergent Serious Adverse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event</td>
<td>2 (1.8%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>Number of Subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiencing Any Treatment-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergent Serious Adverse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event by Preferred Term</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costochondritis</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Hypertensive crisis</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Pelvic fracture</td>
<td>0</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Pseudarthrosis</td>
<td>0</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Transient ischaemic attack</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Upper gastrointestinal</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>0</td>
<td>1 (0.9%)</td>
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Table S8. Grade 3 and 4 adverse events in POLARIS-2

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<th>Event</th>
<th>SU/F/VGL/VEX</th>
<th>SU/F/VGL</th>
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<tbody>
<tr>
<td>Number of Subjects Experiencing Any Grade 3 or Above Treatment-Emergent Adverse Event</td>
<td>11 (2.2%)</td>
<td>6 (1.4%)</td>
</tr>
<tr>
<td>Highest Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>11 (2.2%)</td>
<td>5 (1.1%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Number of Subjects Experiencing Any Grade 3 or Above Treatment-Emergent Adverse Event by Preferred Term And Highest Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Back pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Clostridium difficile colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Multiple fractures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Nystagmus</td>
<td></td>
<td></td>
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<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Peripheral artery occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Road traffic accident</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Squamous cell carcinoma of lung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Suicide attempt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>0</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Thromboembol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4 (Life-Threatening)</td>
<td>1 (0.2%)</td>
<td>0</td>
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Table S9. Grade 3 and 4 adverse events in POLARIS-3

<table>
<thead>
<tr>
<th>Event</th>
<th>SOP/VEL/FOX 9 Weeks (N=110)</th>
<th>SOP/VEL 12 Weeks (N=109)</th>
</tr>
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<tbody>
<tr>
<td>Number of Subjects Experiencing Any Grade 3 or Above Treatment-Emergent Adverse Event</td>
<td>3 (2.7%)</td>
<td>4 (3.7%)</td>
</tr>
<tr>
<td>Highest Grade</td>
<td>3 (2.7%)</td>
<td>4 (3.7%)</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Subjects Experiencing Any Grade 3 or Above Treatment-Emergent Adverse Event by Preferred Term And Highest Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive crisis</td>
<td>1 (0.9%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.9%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Costochondritis</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Depression</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.9%)</td>
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</tr>
<tr>
<td>Duodenal ulcer</td>
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</tr>
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<td>Grade 3 (Severe)</td>
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</tr>
<tr>
<td>Headache</td>
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<td>1 (0.9%)</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>0</td>
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</tr>
<tr>
<td>Pain in extremity</td>
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<td>1 (0.9%)</td>
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<td>1 (0.9%)</td>
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<tr>
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</tr>
<tr>
<td>Grade 3 (Severe)</td>
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<td>1 (0.9%)</td>
</tr>
<tr>
<td>Transient ischaemic attack</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>1 (0.9%)</td>
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<tr>
<td>Upper gastrointestinal haemorrhage</td>
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<td>0</td>
</tr>
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<td>Grade 3 (Severe)</td>
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<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (0.9%)</td>
<td>0</td>
</tr>
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<td>Grade 3 (Severe)</td>
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Table S10. Grade 3 and 4 laboratory abnormalities in POLARIS-2

<table>
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<tr>
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<th>SOF/VEL/VOX (N=501)</th>
<th>SOF/VEL (N=449)</th>
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<tr>
<td><strong>Maximum Postdose Toxicity Grade</strong></td>
<td>501</td>
<td>439</td>
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<tr>
<td>Grade 3</td>
<td>21 ( 4.2%)</td>
<td>12 ( 2.7%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>3 ( 0.6%)</td>
<td>4 ( 0.9%)</td>
</tr>
<tr>
<td><strong>Hematology</strong></td>
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</tr>
<tr>
<td>Hemoglobin</td>
<td>501</td>
<td>439</td>
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<td>Grade 3</td>
<td>2 ( 0.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>501</td>
<td>439</td>
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<tr>
<td>Grade 3</td>
<td>1 ( 0.2%)</td>
<td>2 ( 0.5%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>1 ( 0.2%)</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>501</td>
<td>439</td>
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<tr>
<td>Grade 3</td>
<td>2 ( 0.4%)</td>
<td>2 ( 0.5%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Platelets</td>
<td>501</td>
<td>439</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3 ( 0.6%)</td>
<td>2 ( 0.5%)</td>
</tr>
<tr>
<td>Grade 4</td>
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<td><strong>Hematology (cont)</strong></td>
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<tr>
<td>WBC</td>
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<td>439</td>
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<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
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<tr>
<td>APTT</td>
<td>476</td>
<td>426</td>
</tr>
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<td>Grade 4</td>
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</tr>
<tr>
<td>INR</td>
<td>476</td>
<td>426</td>
</tr>
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<td>Grade 3</td>
<td>1 ( 0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
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<td>0</td>
</tr>
<tr>
<td><strong>Chemistry</strong></td>
<td></td>
<td></td>
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<td>ALT</td>
<td>501</td>
<td>439</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>1 ( 0.2%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AST</td>
<td>501</td>
<td>439</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1 ( 0.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
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</tr>
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</table>
Table S10. Grade 3 and 4 laboratory abnormalities in POLARIS-2 (continued)

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<th>Test</th>
<th>Grade 3</th>
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</tr>
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<tbody>
<tr>
<td>Albumin</td>
<td>501</td>
<td>439</td>
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<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
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<td>Lipase</td>
<td>501</td>
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<td>1 (0.2%)</td>
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<tr>
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## Table S11. Grade 3 and 4 laboratory abnormalities in POLARIS-3

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<td></td>
<td>8 Weeks</td>
<td>12 Weeks</td>
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<td></td>
<td>(N=110)</td>
<td>(N=109)</td>
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### Maximum Postdose Toxicity Grade

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>12 (10.9%)</td>
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### Hematology

<table>
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<tr>
<td></td>
<td>8 Weeks</td>
<td>12 Weeks</td>
</tr>
<tr>
<td></td>
<td>(N=110)</td>
<td>(N=109)</td>
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#### Hemoglobin

<table>
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<tbody>
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#### Lymphocytes

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#### Neutrophils

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#### Platelets

<table>
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#### WBC

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### Coagulation

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#### APTT

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#### INR

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### Chemistry

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#### ALT

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#### AST

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### Table S10. Grade 3 and 4 laboratory abnormalities in POLARIS-3 (continued)

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