HCV: Highlights From EASL 2013

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San Antonio, TX
Boceprevir and Telaprevir
CONCISE Study: Design and Primary Endpoint Population

- Subjects who are RVR+ and complete 12 wks of TVR and 12 wks of Peg-IFN and RBV treatment will be randomized 2:1 to receive a total of 12 weeks TPR only or to receive a further 12 weeks of Peg-IFN and RBV only
  - Primary endpoint is SVR12; SVR24 and SVR at week 72 also assessed
  - BID Dosing (1125mg twice daily)
  - Subjects without RVR or not completing 12 weeks of TPR were not randomized and were assigned to 24 or 48 weeks total therapy

RND=randomized; T/TVR=Telaprevir; P/Peg-IFN=Peginterferon alfa; R/RBV=Ribavirin; HCV=hepatitis C; RVR=rapid viral response, week 4 HCV RNA < 25 IU/mL; SVR=Sustained Viral Response.

**CONCISE Study: Patient Baseline Data**

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>60%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>- White</td>
<td>88%</td>
</tr>
<tr>
<td>- Asian</td>
<td>8%</td>
</tr>
<tr>
<td>Mean Age</td>
<td>47.4 years</td>
</tr>
<tr>
<td>Genotype 1a</td>
<td>65.1%</td>
</tr>
<tr>
<td>Treatment Naïve</td>
<td>86%</td>
</tr>
<tr>
<td>Median Baseline HCV RNA</td>
<td>5,945,000 IU/mL</td>
</tr>
<tr>
<td>Median BMI</td>
<td>25.3 kg/m</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>0%</td>
</tr>
</tbody>
</table>

HCV=hepatitis C virus;
CONCISE Study: Efficacy

238 Subjects

158 Randomized

52 T12/PR24

100% SVR 4 (38/38)

97% SVR 12 (29/30)

106 T12/PR12

89% SVR 4 (93/104)

87% SVR 12 (74/85)

80 Not Randomized

19 T12/PR24I

Did not complete 12 weeks of drug but did achieve eRVR

61 T12/PR48

Did not complete 12 weeks of drug and/or did not achieve eRVR

Efficacy of Telaprevir Dosed Twice Daily versus Every 8 Hours by IL28B Genotype: Results from the Phase III OPTIMIZE Study

<table>
<thead>
<tr>
<th></th>
<th>CC and F0-F2</th>
<th>CC and F3-F4</th>
<th>Non-CC and F0-F2</th>
<th>Non-CC and F3-F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>q8h</td>
<td>89</td>
<td>93</td>
<td>75</td>
<td>48</td>
</tr>
<tr>
<td>bid</td>
<td>92</td>
<td>93</td>
<td>75</td>
<td>47</td>
</tr>
<tr>
<td>N</td>
<td>79</td>
<td>29</td>
<td>183</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>28</td>
<td>192</td>
<td>74</td>
</tr>
</tbody>
</table>

Buti M, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 798.
# CUPIC: Patient Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Telaprevir N=295</th>
<th>Boceprevir N=190</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh score A/B, n (%)*</td>
<td>280 (95) / 6 (2)</td>
<td>177 (93) / 1 (1)</td>
</tr>
<tr>
<td>MELD score, mean (range)</td>
<td>8.1 (6-22)</td>
<td>8.1 (6-28)</td>
</tr>
<tr>
<td>Prothrombin time ratio, mean % (range)</td>
<td>86 (27–100)</td>
<td>87 (23–100)</td>
</tr>
<tr>
<td>Serum albumin g/L, mean (range)</td>
<td>40.0 (20.7–53.2)</td>
<td>40.7 (27.0–50.3)</td>
</tr>
<tr>
<td>Total bilirubin μmol/L, mean (range)</td>
<td>15.5 (4.0–73.0)</td>
<td>15.2 (4.0–78.0)</td>
</tr>
<tr>
<td>Hb level g/dL, mean (range)</td>
<td>14.5 (9.0–19.7)</td>
<td>14.8 (10.8–18.4)</td>
</tr>
<tr>
<td>Neutrophils, mean (range) (10⁹/mm³)</td>
<td>3.3 (0.8-8.5)</td>
<td>3.2 (0.5-8.5)</td>
</tr>
<tr>
<td>Platelet count, mean (range) (10³/mm³)</td>
<td>151 (18–604)</td>
<td>144 (34–346)</td>
</tr>
<tr>
<td>Esophageal varices, n (%)</td>
<td>51/145 (35.2)</td>
<td>37/97 (38.1)</td>
</tr>
</tbody>
</table>

* Missing data: 21

Fontaine H, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 60.
**CUPIC: Virological response (ITT) SVR12**

**TELAPREVIR**

 Patients with undetectable HCV RNA (Percentage)

<table>
<thead>
<tr>
<th>Week</th>
<th>49%</th>
<th>79%</th>
<th>81%</th>
<th>77%</th>
<th>68%</th>
<th>56%</th>
<th>40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>W4</td>
<td>146</td>
<td>234</td>
<td>239</td>
<td>227</td>
<td>200</td>
<td>165</td>
<td>118</td>
</tr>
<tr>
<td>W8</td>
<td>295</td>
<td>295</td>
<td>295</td>
<td>295</td>
<td>295</td>
<td>295</td>
<td></td>
</tr>
<tr>
<td>W12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W48</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W60</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**BOCEPREVIR**

 Patients with undetectable HCV RNA (Percentage)

<table>
<thead>
<tr>
<th>Week</th>
<th>16%</th>
<th>51%</th>
<th>62%</th>
<th>65%</th>
<th>67%</th>
<th>57%</th>
<th>41%</th>
</tr>
</thead>
<tbody>
<tr>
<td>W4</td>
<td>31</td>
<td>97</td>
<td>118</td>
<td>124</td>
<td>128</td>
<td>108</td>
<td>79</td>
</tr>
<tr>
<td>W8</td>
<td>190</td>
<td>190</td>
<td>190</td>
<td>190</td>
<td>190</td>
<td>190</td>
<td></td>
</tr>
<tr>
<td>W12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W48</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>W60</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Fontaine H, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 60
CUPIC: SVR 12 According to HCV Subtype

**TELAPREVIR**

- **Genotype 1a**: 34% (33/98)
- **Genotype 1b**: 46% (75/162)
- Undetermined genotype 1: 27% (9/33)

**BOCEPREVIR**

- **Genotype 1a**: 31% (24/77)
- **Genotype 1b**: 51% (49/96)
- Undetermined genotype 1: 37% (6/16)

**P = 0.004**

**P = 0.03**

Fontaine H, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 60
### CUPIC: Safety Findings

<table>
<thead>
<tr>
<th>Patients, n (% patients with at least one event)</th>
<th>Telaprevir n=295</th>
<th>Boceprevir n=190</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events (SAEs)</td>
<td>535 in 160 patients (54.2%)</td>
<td>321 in 97 patients (51.0%)</td>
</tr>
<tr>
<td>Premature discontinuation / Due to SAEs</td>
<td>139 (47.1%) / 63 (21.3%)</td>
<td>80 (42.1%) / 27 (14.2%)</td>
</tr>
<tr>
<td>Death</td>
<td>7 (2.4%)</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td>Infection (Grade 3/4)</td>
<td>27 (9.1%)</td>
<td>8 (4.2%)</td>
</tr>
<tr>
<td>Hepatic decompensation (Grade 3/4)</td>
<td>15 (5.1%)</td>
<td>9 (4.7%)</td>
</tr>
<tr>
<td>Anemia (Grade 3/4 : Hb &lt; 8 g/dL)</td>
<td>38 (12.9%)</td>
<td>19 (10%)</td>
</tr>
<tr>
<td>Rash (Grade 3/SCAR)</td>
<td>16 (5.4%) / 2 (0.6%)</td>
<td>2 (1.0%) / 0</td>
</tr>
<tr>
<td>EPO use / Blood transfusion</td>
<td>168 (57%) / 53 (18%)</td>
<td>119 (62.6%) / 26 (13.7%)</td>
</tr>
<tr>
<td>GCSF use</td>
<td>8 (2.7%)</td>
<td>13 (6.8%)</td>
</tr>
<tr>
<td>TPO use</td>
<td>6 (2%)</td>
<td>3 (1.6%)</td>
</tr>
</tbody>
</table>

SCAR: severe cutaneous adverse reaction

Fontaine H, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 60
CUPIC Multivariate Analysis: Baseline factors related to anemia <8g/dL or blood transfusion*

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Female</td>
<td>2.19</td>
<td>1.11-4.33</td>
<td>0.023</td>
</tr>
<tr>
<td>No lead-in phase</td>
<td>2.25</td>
<td>1.15-4.39</td>
<td>0.018</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>3.04</td>
<td>1.54-6.02</td>
<td>0.0014</td>
</tr>
<tr>
<td>Hemoglobin level</td>
<td>5.30</td>
<td>2.49-11.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>• ≤12 g/dL for female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ≤13 g/dL for male</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*n=71 (14.3%)

CUPIC: Risk of Occurrence of Death or Severe Complications

<table>
<thead>
<tr>
<th>Factors</th>
<th>Platelet count &gt;100,000/mm³</th>
<th>Platelet count ≤100,000/mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin ≥35 g/L</td>
<td>3.4% (10/298)</td>
<td>4.3% (3/69)</td>
</tr>
<tr>
<td>Albumin &lt;35 g/L</td>
<td>7.1% (2/28)</td>
<td>44.1% (15/34)</td>
</tr>
</tbody>
</table>

Emerging Interferon Based Therapies
The NEUTRINO Study: Design

- SOF 400 mg QD + Peg-IFN-alfa-2a 180 µg/week + RBV 1000–1200 mg/day for 12 weeks
- Treatment-naïve, genotype 1, 4, 5, and 6 HCV-infected patients
  - 20% cirrhosis

Lawitz E, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1411.
The NEUTRINO Study Results: Demographics

<table>
<thead>
<tr>
<th></th>
<th>SOF + Peg-IFN + RBV N=327</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>52 (19–70)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>209 (64)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>54 (17)</td>
</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>46 (14)</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>29 (18–56)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>95 (29)</td>
</tr>
<tr>
<td>GT 1, n (%)</td>
<td>292 (89)</td>
</tr>
<tr>
<td>GT 4/5/6, n (%)</td>
<td>35 (11)</td>
</tr>
<tr>
<td>Mean baseline HCV RNA, log_{10} IU/mL (range)</td>
<td>6.4 (2.1–7.6)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>54 (17)</td>
</tr>
</tbody>
</table>
NEUTRINO: SVR12 by Genotype

Error bars represent 95% confidence intervals.

Lawitz E, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1411.
Patients enrolled from Europe and Japan

Criteria for response guided therapy
- Early Treatment Success (ETS): HCV RNA <25 IU/mL at Week 4 and undetectable at Week 8
- Patients with ETS in active treatment arms were eligible to stop all treatment at Week 24

Primary endpoint: SVR 12 weeks

Ferenci P, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1416.
STARTVerso1: SVR12 (ITT)

(Δ = 26.7; 95% CI, 17.1–36.3; p <0.0001)

(Δ = 28.6; 95% CI, 19.0–38.2; p <0.0001)

SVR12 rates adjusted for race and genotype
ITT, intention-to-treat

Ferenci P, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1416.
- RGT in simeprevir arm: if HCV RNA < 25 IU/mL at week 4 and undetectable at Week 12, complete treatment at Week 24

- Stopping rules: if HCV RNA > 1000 IU/mL Week 4, stop SMV/placebo; if HCV RNA < 2 \log_{10} IU/mL reduction at Week 12, or confirmed > 25 IU/mL at Week 24 or 36, stop all treatment

PR, peginterferon a-2a 180µg/wk + ribavirin 1000-1200mg/day; QD, once daily.
Jacobson I, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1425.
**QUEST-1 and QUEST-2 (Phase III): Simeprevir (PI) + Peg-IFN + RBV in Treatment-naive GT1**

- 85-91% qualified for shortened therapy

<table>
<thead>
<tr>
<th></th>
<th>Patients Achieving SVR12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QUEST-1</td>
</tr>
<tr>
<td>Simeprevir + PR (RGT 12+12)</td>
<td>80</td>
</tr>
<tr>
<td>Placebo + PR</td>
<td>50/65</td>
</tr>
</tbody>
</table>

n/N = 211/264 and 208/257

Jacobson I, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1425.
Interferon-Free Regimens
Protease Inhibitor Based DAA Regimens
AVIATOR Study: ABT-450/r, ABT-267, ABT-333 +/- RBV in Non-Cirrhotic, Naïve and Null Responders N = 571

<table>
<thead>
<tr>
<th>Regimen/duration</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 ABT333 RBV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT333 RBV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 RBV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 ABT333</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 ABT333 RBV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Null response</th>
<th>Regimen/duration</th>
<th>SVR12 (%)</th>
<th>SVR24* (%)</th>
<th>VBT/Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABT450 ABT267 RBV</td>
<td>89</td>
<td>89</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 ABT333 RBV</td>
<td>93</td>
<td>93</td>
<td>3/0</td>
<td></td>
</tr>
<tr>
<td>ABT450 ABT267 ABT333 RBV</td>
<td>98</td>
<td>95</td>
<td>1/0</td>
<td></td>
</tr>
</tbody>
</table>

* 8 patients with SVR12 have not returned for >24 weeks and are counted as virologic failures for SVR24; 3 patients relapsed between SVR12 and SVR24.

Kowdley K, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 3.
IFN- and RBV-free: Daclatasvir (DCV) Asunaprevir (ASV), and BMS-791325

- Treatment-naïve, non-cirrhotic adults with 1a (74%) or 1b infection
  - n=66 treated for 12 or 24 weeks of therapy
- SVR>90%; well-tolerated
- Two patients with virologic failure – breakthrough (n=1); relapse (n=2)
  - Resistant variants to 3 DAAs detected

Phase 2 study randomized treatment-naïve, HCV GT1, non-cirrhotic patients (N=32)
One patient was missing SVR2, SVR12, and SVR36; this patient achieved SVR24
One patient was missing SVR24 and SVR36; this patient achieved SVR4 and SVR12

Everson GT, et al. 48th EASL; Amsterdam, The Netherlands; April 24-28, 2013; Abstract 1423.
Nucleotide Based Oral DAA Regimens
<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SOF + RBV, n=256</strong></td>
<td></td>
<td></td>
<td>SVR12</td>
<td></td>
</tr>
<tr>
<td><strong>Peg-IFN + RBV (SOC), n=243</strong></td>
<td></td>
<td></td>
<td></td>
<td>SVR12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>SOF + RBV n=256</th>
<th>Peg-IFN + RBV n=243</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>48 (20‒72)</td>
<td>48 (19‒77)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>171 (67)</td>
<td>156 (64)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>223 (87)</td>
<td>212 (87)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>108 (43)</td>
<td>106 (44)</td>
</tr>
<tr>
<td>GT3, n (%)</td>
<td>183 (72)</td>
<td>176 (72)</td>
</tr>
<tr>
<td>Mean HCV RNA, ( \log_{10} ) IU/mL (range)</td>
<td>6.0 (3.2–8.3)</td>
<td>6.0 (3.2–7.6)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>50 (20)</td>
<td>50 (21)</td>
</tr>
</tbody>
</table>

*RBV dose 1000-1200 mg/day for SOF + RBV and 800 mg/day for Peg-IFN + RBV
Gane E, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 5.
FISSION: SVR12 by Genotype and Cirrhosis

Error bars represent 95% confidence intervals.

Gane E, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 5.
**FUSION: Non responder G2/3 Study**

<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>12</th>
<th>16</th>
<th>24</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SOF + RBV, n=103</strong></td>
<td></td>
<td></td>
<td></td>
<td>SVR12</td>
<td></td>
</tr>
<tr>
<td><strong>SOF + RBV, n=98</strong></td>
<td></td>
<td></td>
<td>SVR12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>SOF + RBV 12 week n=103</th>
<th>SOF + RBV 16 week n=98</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>54 (30–69)</td>
<td>54 (24–70)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>73 (71)</td>
<td>67 (68)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>31 (30)</td>
<td>30 (31)</td>
</tr>
<tr>
<td>GT 3, n (%)</td>
<td>64 (62)</td>
<td>63 (64)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>36 (35)</td>
<td>32 (33)</td>
</tr>
<tr>
<td>Prior relapse, n (%)</td>
<td>78 (76)</td>
<td>73 (75)</td>
</tr>
</tbody>
</table>

* SOF dose 400 mg once daily; RBV dose 1000-1200 mg/day
FUSION: SVR12 by HCV Genotype/Cirrhosis

SOF + RBV 12 weeks

SOF + RBV 16 weeks

Error bars represent 95% confidence intervals.

## POSITRON: IFN Intolerant Study

<table>
<thead>
<tr>
<th>Week</th>
<th>SOF + RBV (n=207)</th>
<th>Placebo (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>SVR12</strong></td>
<td><strong>SVR12</strong></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Week 0

- **SOF + RBV**, n=207
- **Placebo**, n=71

### Mean age, y (range)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Age (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>52 (21–75)</td>
</tr>
<tr>
<td>Placebo</td>
<td>52 (28–67)</td>
</tr>
</tbody>
</table>

### Male, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Male (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>117 (57)</td>
</tr>
<tr>
<td>Placebo</td>
<td>34 (48)</td>
</tr>
</tbody>
</table>

### IL28B CC, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>IL28B CC (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>97 (47)</td>
</tr>
<tr>
<td>Placebo</td>
<td>29 (41)</td>
</tr>
</tbody>
</table>

### GT 2, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>GT 2 (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>109 (53)</td>
</tr>
<tr>
<td>Placebo</td>
<td>34 (48)</td>
</tr>
</tbody>
</table>

### Cirrhosis, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cirrhosis (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>31 (15)</td>
</tr>
<tr>
<td>Placebo</td>
<td>13 (18)</td>
</tr>
</tbody>
</table>

### Interferon unwilling, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Interferon unwilling (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>102 (49)</td>
</tr>
<tr>
<td>Placebo</td>
<td>30 (42)</td>
</tr>
</tbody>
</table>

### Interferon ineligible, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Interferon ineligible (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>88 (43)</td>
</tr>
<tr>
<td>Placebo</td>
<td>33 (47)</td>
</tr>
</tbody>
</table>

### Interferon intolerant, n (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Interferon intolerant (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>17 (8)</td>
</tr>
<tr>
<td>Placebo</td>
<td>8 (11)</td>
</tr>
</tbody>
</table>

*Patients randomized to placebo were offered open-label SOF+RBV following study completion.

POSITRON: SVR12 by Cirrhosis Status

SVR with Daclatasvir Plus Sofosbuvir ± RBV in CHC GT1 Patients who Previously Failed Telaprevir (TVR) or Boceprevir (BOC)

- 41 adult HCV GT1-infected patients who had virologic non-response, relapse, or breakthrough during prior treatment with TVR or BOC + pegIFN/RBV were treated with:
  - Daclatasvir (DCV): 60 mg QD NS5A replication complex inhibitor
  - Sofosbuvir (SOF): 400 mg QD NS5B nucleotide inhibitor
- with or without RBV for 24 weeks of therapy

Key Demographics:
- 83% (34/41) GT1a
- Mean baseline HCV RNA 6.3 log_{10} IU/mL
- 98% (40/41) IL-28B “non-CC”

Key Safety Findings:
- No patients discontinued due to adverse events (AEs)
- Most common AEs (≥30% total) were fatigue and headache
- No Grade 3/4 hematologic or hepatic laboratory abnormalities

Sulkowski M, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1417.
Virologic response

1 patient missing at post-treatment (PT) Week 12: HCV RNA was undetectable at PT Week 4 and at PT Week 24

21/41 patients have reached PT Week 24; all have achieved SVR<sub>24</sub>

Sulkowski M, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abstract 1417.