Telaprevir in Treatment Naïve GT-1 ADVANCE (Study 108)

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: Results by Fibrosis Stage

ADVANCE: SVR24 by Fibrosis Stage

<table>
<thead>
<tr>
<th></th>
<th>SVR 79%</th>
<th>SVR 81%</th>
<th>SVR 69%</th>
<th>SVR 75%</th>
<th>SVR 48%</th>
<th>SVR 58%</th>
<th>SVR 62%</th>
<th>SVR 33%</th>
<th>SVR 42%</th>
<th>SVR 62%</th>
<th>SVR 33%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No or Minimal Fibrosis</td>
<td>101/128</td>
<td>109/134</td>
<td>67/147</td>
<td>104/151</td>
<td>117/156</td>
<td>67/141</td>
<td>34/59</td>
<td>32/52</td>
<td>17/52</td>
<td>11/26</td>
<td>13/21</td>
</tr>
<tr>
<td>Portal Fibrosis</td>
<td>46</td>
<td></td>
<td>69</td>
<td>75</td>
<td></td>
<td></td>
<td>58</td>
<td>62</td>
<td></td>
<td>42</td>
<td></td>
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<tr>
<td>Bridging Fibrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33</td>
</tr>
</tbody>
</table>

SVR = Sustained Virologic Response; T = Telaprevir; PR = Peginterferon + Ribavirin

Telaprevir for Treatment-Naïve HCV Genotype 1 ADVANCE Study: Adverse Effects

ADVANCE: Percentage of Patients with Anemia

Hemoglobin (Hb) Nadir Through Week 12

T = Telaprevir; PR = Peginterferon + Ribavirin

Telaprevir for Treatment-Naïve HCV Genotype 1

ADVANCE Study: Adverse Effects

ADVANCE: Percentage of Patients with Rash

- **Rash**
  - T8/PR24 or 48: 35 patients (129/364)
  - T12/PR24 or 48: 37 patients (133/363)
  - PR48: 24 patients (88/361)

- **Severe (Grade 3) Rash**
  - T8/PR24 or 48: 4 patients (15/364)
  - T12/PR24 or 48: 6 patients (22/363)
  - PR48: 1 patient (4/361)

T = Telaprevir; PR = Peginterferon + Ribavirin

Telaprevir for Treatment-Naïve HCV Genotype 1
SVR Rates by IL28B rs12979860 Genotype

ADVANCE: SVR24 by rs12979860 Genotype

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>T/T</th>
<th>C/T</th>
<th>C/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR48</td>
<td>23%</td>
<td>25%</td>
<td>35%</td>
</tr>
<tr>
<td>T12/PR24 or 48</td>
<td>73%</td>
<td>71%</td>
<td>90%</td>
</tr>
</tbody>
</table>

PR48 = Peginteron/Ribavirin x 48 weeks
PR/T12 = Peginteron/Ribavirin + Telaprevir x 12 weeks

Source: Telaprevir (Incivek) Prescribing Information. Vertex Pharmaceuticals.
Conclusions: “Telaprevir with peginterferon–ribavirin, as compared with peginterferon–ribavirin alone, was associated with significantly improved rates of sustained virologic response in patients with HCV genotype 1 infection who had not received previous treatment, with only 24 weeks of therapy administered in the majority of patients.”

Telaprevir for Treatment-Naïve HCV Genotype 1

**ADVANCE: Study Design**

**ADVANCE: Study Features**

- N = 1,088 enrolled
- Randomized, double-blind, placebo-controlled, Phase 3 trial
- Genotype 1 HCV and treatment naïve
- 77% with HCV RNA ≥ 800,000 IU/ml
- Randomized to one of 3 arms
- RVR = HCV RNA undetectable at week 4
- eRVR = HCV RNA undetectable at weeks 4 & 12
- Erythroid stimulating agents not allowed
- Telaprevir-treated patients without eRVR received PR up to week 48

**Drug Dosing**

- Telaprevir = 750 mg every 8 hours
- Peginterferon alfa-2a = 180 μg weekly
- Ribavirin = 1000 mg/day for wt < 75 kg; 1200 mg/day for wt ≥ 75 kg

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: Treatment Regimens

<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>8</th>
<th>12</th>
<th>24</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 364</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T8</td>
<td>PR 24 or 48</td>
<td>Telaprevir + PEG + RBV</td>
<td>PEG + RBV</td>
<td>eRVR: PEG + RBV</td>
<td>No eRVR: PEG + RBV</td>
</tr>
<tr>
<td>N = 363</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T12</td>
<td>PR 24 or 48</td>
<td>Telaprevir + PEG + RBV</td>
<td>eRVR: PEG + RBV</td>
<td>No eRVR: PEG + RBV</td>
<td></td>
</tr>
<tr>
<td>N = 361</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR48</td>
<td>PEG + RBV</td>
<td>Placebo + PEG + RBV</td>
<td>PEG + RBV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: Results

ADVANCE: SVR24 by Regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Patients with SVR (%)</th>
<th>Count/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T8/PR24 or 48</td>
<td>69</td>
<td>250/364</td>
</tr>
<tr>
<td>T12/PR24 or 48</td>
<td>75</td>
<td>271/363</td>
</tr>
<tr>
<td>PR 48</td>
<td>44</td>
<td>158/361</td>
</tr>
</tbody>
</table>

SVR = Sustained Virologic Response; T = Telaprevir; PR = Peginterferon + Ribavirin

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: RVR and eRVR Rates

ADVANCE: Patients with RVR and eRVR

<table>
<thead>
<tr>
<th></th>
<th>RVR (week 4)</th>
<th>eRVR (week 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T8/PR24 or 48</td>
<td>66/364</td>
<td>57/364</td>
</tr>
<tr>
<td>T12/PR24 or 48</td>
<td>68/363</td>
<td>58/363</td>
</tr>
<tr>
<td>PR48</td>
<td>34/361</td>
<td>8/361</td>
</tr>
</tbody>
</table>

T = Telaprevir; PR = Peginterferon + Ribavirin; RVR = rapid virologic response; eRVR = extended rapid virologic response

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: Results According to eRVR

ADVANCE: SVR24 by eRVR Status

- **With eRVR**
  - T8/PR24 or 48: 83/207 (40.0%)
  - T12/PR24 or 48: 89/212 (42.0%)
  - PR48: 28/29 (96.6%)

- **Without eRVR**
  - T8/PR24 or 48: 79/157 (50.3%)
  - T12/PR24 or 48: 82/151 (54.4%)
  - PR48: 130/342 (38.0%)

T = Telaprevir; PR = Peginterferon + Ribavirin; SVR = Sustained Virologic Response
eRVR = extended rapid virologic response (undetectable HCV RNA at weeks 4 and 12)

Telaprevir for Treatment-Naïve HCV Genotype 1 ADVANCE Study: Results According to eRVR

ADVANCE: SVR24 by eRVR Status

SVR = Sustained Virologic Response; T = Telaprevir; PR = Peginterferon + Ribavirin; eRVR = extended rapid virologic response (undetectable HCV RNA at weeks 4 and 12)

Telaprevir for Treatment-Naïve HCV Genotype 1
ADVANCE Study: Results According to Race

ADVANCE: SVR24 by Race

<table>
<thead>
<tr>
<th>Race</th>
<th>T8/PR 24 or 48</th>
<th>T12/PR24 or 48</th>
<th>PR48</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>70</td>
<td>75</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>221/315</td>
<td>244/325</td>
<td>147/318</td>
</tr>
<tr>
<td>Black</td>
<td>58</td>
<td>62</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>23/40</td>
<td>16/26</td>
<td>7/28</td>
</tr>
<tr>
<td>Hispanic</td>
<td>66</td>
<td>74</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>29/44</td>
<td>26/35</td>
<td>15/38</td>
</tr>
</tbody>
</table>

SVR = Sustained Virologic Response; T = Telaprevir; PR = Peginterferon + Ribavirin

Telaprevir for Treatment-Naïve HCV Genotype 1 ADVANCE Study: Results by Baseline HCV RNA

ADVANCE: SVR24 by Baseline HCV RNA Level

- **T8/PR 24 or 48**
  - < 800,000 IU/ml: 67/85
  - ≥800,000 IU/ml: 184/279

- **T12/PR 24 or 48**
  - < 800,000 IU/ml: 64/82
  - ≥800,000 IU/ml: 207/281

- **PR 48**
  - < 800,000 IU/ml: 57/82
  - ≥800,000 IU/ml: 101/279

Patients with SVR (%)

Baseline HCV RNA Level: < 800,000 IU/ml vs. ≥800,000 IU/ml

SVR = Sustained Virologic Response; T = Telaprevir; PR = Peginterferon + Ribavirin