Response-Guided Therapy for Boceprevir Combination Treatment: Results from HCV SPRINT-1

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Abstract

Background: HCV SPRINT-1 investigated a 4-week lead-in of PegPort (P:1.5 g/kg/week) plus Ribavirin (R:800-1400 mg/day) prior to the addition of Boceprevir (B:800 mg TID) for 24 or 48 weeks. Analysis of this data may lead to RGT paradigms.

Methods: Viral response was assessed by Roche TaqMan (LLD=15 IU/mL) at multiple time points including treatment weeks 4, 8, 12, 24, and 24 weeks post-treatment (sustained virologic response: SVR).

Results: Patients were all G1 (75% with 1a>1b) with 69% cirrhotics, and 31% high viral load. Virology (LLD=15 IU/mL) at multiple time points including treatment weeks 4, 8, 12, 24, and 24 weeks post-treatment (sustained virologic response: SVR).

Aims

To evaluate early viral responses to (time to first undetectable HCV RNA) predictors of duration of therapy (28 or 48 weeks with boceprevir combination therapy)

Methods

1. Open-label randomized trial enrolled previously untreated adults with genotype 1 HCV

2. Viral response was assessed with Roche COBAS TaqMan (LLD=15 IU/mL).

3. Virology assessed at multiple time points including:
   - Treatment weeks 0, 4, 8, 12, 24, and 48 weeks of boceprevir combination therapy
   - 24 weeks post-treatment
   - Subtypes assessed by Trengen assay

Conclusions

The majority of patients achieved undetectable HCV RNA after 4 weeks of triple therapy with boceprevir (SVR97% vs 21% ; p<0.004) but only 13% were sustained responders. Eighteen percent of patients first achieved viral negativity between week 4 and 12 of boceprevir triple therapy (TPR97%; p<0.005 vs 28-week lead-in arm). These late responders benefited from 48 weeks of therapy (79% vs 28 weeks 24% of therapy). All patients achieving SVR were viral negative by week 12 of triple therapy (TPR97%), but those after the 4-week lead-in period (>1.5 log drop) may also be less precise, a population only needing short triple therapy.

Baseline characteristics cannot predict which patients will benefit from longer therapy, in-treatment virologic responses appear likely to do so (response-guided therapy).

Conclusions

• Boceprevir significantly improves SVR

• Although baseline characteristics cannot predict which patients will benefit from longer therapy, in-treatment virologic responses appear likely to do so (response-guided therapy)

• Data from the larger phase 3 trial, HCV SPRINT-2, will more precisely define response-guided RGT for boceprevir triple therapy

Table 1. Baseline Characteristics were Similar Between Treatment Arms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Treatment Arm</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Age, yrs</td>
<td>P/R 48</td>
<td>0.002*</td>
</tr>
<tr>
<td>Mean weight, kg</td>
<td>P/R 48</td>
<td>0.004*</td>
</tr>
<tr>
<td>Mean viral load, log10 (IU/mL)</td>
<td>P/R 48</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Cirrhosis, %  (n/N )</td>
<td>P/R 48 24</td>
<td>0.40 *</td>
</tr>
<tr>
<td>Gender, %  (n/N )</td>
<td>P/R 48 24</td>
<td>0.17 *</td>
</tr>
</tbody>
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Figure 1. SPRINT-1 Study Design

Figure 2. SVR by Treatment Arm

Figure 3. Predictibility of SVR Based on Response During 4-Week P/R Lead-in

Summary

The majority of patients achieved undetectable HCV RNA after 4 weeks of triple therapy with boceprevir (SVR97% vs 21% ; p<0.004) but only 13% were sustained responders. Eighteen percent of patients first achieved viral negativity between week 4 and 12 of boceprevir triple therapy (TPR97%; p<0.005 vs 28-week lead-in arm). These late responders benefited from 48 weeks of therapy (79% vs 28 weeks 24% of therapy). All patients achieving SVR were viral negative by week 12 of triple therapy (TPR97%), but those after the 4-week lead-in period (>1.5 log drop) may also be less precise, a population only needing short triple therapy.

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HCV SPRINT-1 Investigators


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