Abstract
Background: Changes in HCV RNA at week 4 are predictive of SVR. We hypothesized that the magnitude of reduction of HCV RNA by treatment week (TW) 4 was highly associated with the likelihood of SVR. Patients with a decline of HCV RNA by TW 4 <1 log10 had a greater than 95% probability of attaining SVR.

Methods: Chronic HCV patients infected with genotype 1, age 18 to 70 years, weight 40 to 125 kg, were randomized (1:1:1) and treated for 48 weeks with PEG-IFN α-2a 180 μg/wk + RBV, PEG-IFN α-2b 1.5 μg/kg/wk + RBV, or placebo. PEG-IFN or RBV alone was ineffective. HCV RNA levels were measured at baseline and at TW 2, 4, 12, 24, and follow-up weeks 48, 52, and 72. The change in HCV RNA for each patient was categorized according to log10 change from baseline to TW 4: <1 log10, <2 log10, <3 log10, <4 log10; and undetectable (HCV RNA <27 IU/mL).

Results: Patients (n = 957) had similar characteristics across groups: male, 66%; Caucasian, 71%; Black, 6%; Hispanic, 19%; Asian, 1%. Weight, 83.4 kg; HCV RNA >600,000 IU/mL, 82%; F3/4, 11%. The number (%) of patients in each category and the observed SVR are shown in Table 2 (see figure). The magnitude of changes in HCV RNA at TW 4 was highly associated with the likelihood of attaining SVR (P < 0.001).

Conclusions: Changes in HCV RNA at TW 4 are predictive of SVR. The magnitude of reduction in HCV RNA from baseline to TW 4 was significantly associated with the likelihood of attaining SVR (P < 0.001).

Table 3, Percentage of Patients in Each Treatment Group Categorized According to the Magnitude of Reduction in HCV RNA Baseline to Baseline at Week 4

<table>
<thead>
<tr>
<th>Category</th>
<th>PEG-IFN α-2a 180 μg/wk + RBV</th>
<th>PEG-IFN α-2b 1.5 μg/kg/wk + RBV</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 log10</td>
<td>27 (23%)</td>
<td>23 (24%)</td>
<td>15 (25%)</td>
</tr>
<tr>
<td>1-&lt;2 log10</td>
<td>48 (43%)</td>
<td>44 (46%)</td>
<td>31 (50%)</td>
</tr>
<tr>
<td>2-&lt;3 log10</td>
<td>40 (37%)</td>
<td>40 (41%)</td>
<td>23 (38%)</td>
</tr>
<tr>
<td>3-&lt;4 log10</td>
<td>6 (6%)</td>
<td>5 (5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Undetectable</td>
<td>14 (14%)</td>
<td>10 (10%)</td>
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Table 3, Predictability of Change in HCV RNA Baseline to Baseline at Week 4 for SVR

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Results

Patient Characteristics

- Patients (n = 3070) had similar characteristics across the 3 treatment groups (Table 2).

- Variables that were significant on univariate analysis and had a p-value <0.10 on multivariate analysis were included into the multivariate models.

- Multivariate models included treatment, baseline HCV RNA log10, weight, age, and race.

- For the HCV RNA models, a log2 transformation was used to allow normality of the residuals.

- For the weight models, a square root transformation was used to allow normality of the residuals.

- For the age models, a square root transformation was used to allow normality of the residuals.

- For the race models, ethnicity (Caucasian vs. non-Caucasian) was used.

- The models were adjusted for race.

- For the HCV RNA models, baseline HCV RNA log10 was included as a categorical variable.

- For the weight models, weight was included as a categorical variable.

- For the age models, age was included as a categorical variable.

- For the race models, ethnicity was included as a categorical variable.

- The models were adjusted for age.

- For the HCV RNA models, baseline HCV RNA log10 was included as a continuous variable.

- For the weight models, weight was included as a continuous variable.

- For the age models, age was included as a continuous variable.

- For the race models, ethnicity was included as a continuous variable.

- The models were adjusted for race.

- For the HCV RNA models, baseline HCV RNA log10 was included as a continuous variable.

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