Combination Therapy With BMS-790052 and BMS-650032 Alone or With Pegylated Interferon and Ribavirin (pegIFN/RBV) Results in Undetectable HCV RNA Through 12 Weeks of Therapy in HCV Genotype 1 Null Responders

**Background:** BMS-790052 is a potent NS5A inhibitor with broad genotype coverage while BMS-650032 is a potent NS3 protease inhibitor with coverage of HCV genotypes (GT) 1a and 1b. Clinical studies combining these compounds alone and with pegylated interferon/ribavirin (pegIFN/RBV) are under way in HCV-infected subjects who are treatment intolerant.

**OBJECTIVES**

- To assess the decrease in HCV RNA levels from baseline to days 4, 7, and 14 (primary endpoints), and to evaluate the proportion of subjects with extended RVR (eRVR), defined as undetectable HCV RNA at both weeks 4 and 12.

- To describe drug-resistant variants associated with virologic failure.

**MATERIALS AND METHODS**

**Study Design**

- 21 patients were randomized in a sentinel cohort: 11 Group A, 10 Group B. Median age was 58 years, 65% were male, 59% were white.

**RESULTS**

**Virologic Response**

<table>
<thead>
<tr>
<th>Group</th>
<th>RVR by week 4 (%)</th>
<th>eRVR by weeks 4 and 12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>90</td>
<td>71</td>
</tr>
<tr>
<td>B</td>
<td>90</td>
<td>80</td>
</tr>
</tbody>
</table>

**DISCLOSURES**

- No other significant drug-drug or drug-food interactions.
- No other significant laboratory abnormalities.
- No deaths occurred during the study.
- No serious adverse events occurred.
- No significant laboratory abnormalities occurred.
- No clinically relevant changes in ECGs, vital signs.

**CONCLUSIONS**

- Combination therapy with BMS-790052 and BMS-650032 with or without pegIFN/RBV demonstrated similar RVR among null responders. Further studies are warranted to evaluate the potential benefit from combination therapy including 2 direct-acting antiviral agents with or without pegIFN/RBV.

**RESULTS (cont'd)**

- Viral breakthrough was observed in 2 patients (1 in group A, 1 in group B). The 2 GT 1b subjects in group A remained HCV RNA undetectable. The 6 subjects with viral breakthrough had pegIFN/RBV added to their regimen. HCV RNA levels fell to undetectable in 2 subjects and to <25 IU/mL in another 2 subjects, while the other 2 subjects had ≥2 log10 decline in HCV RNA.

**Other Safety Findings**

- AEs were mainly mild to moderate in severity.
- No severe AEs were observed.
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