Correspondence

Telaprevir Activity in Treatment-Naive Patients Infected With Hepatitis C Virus Genotype 4

To the Editor—Benhamou et al demonstrated that the tolerability and pharmacokinetics of telaprevir in patients infected with hepatitis C virus (HCV) genotype 4 were similar to those found in HCV genotype 1 patients [1]. In their study, patients infected with HCV genotype 4 were randomly assigned to receive (1) telaprevir monotherapy for 15 days; (2) telaprevir, pegylated interferon alfa-2a, and ribavirin (TPR) for 15 days; or (3) placebo, pegylated interferon alfa-2a, and ribavirin (PR) for 15 days. After the initial 15-day treatment period, study drugs in each group were replaced with standard PR treatment, which was administered for an additional 46–48 weeks.

Findings from the study by Benhamou et al supported the investigation of TPR for 12 weeks, followed by PR for an additional 12 weeks, in HCV genotype 4–infected patients. With institutional review board approval, we performed a chart review of HCV genotype 4–infected patients who received TPR at Mount Sinai Hospital, New York, between April 2011 and October 2012. The aim was to determine the rate of sustained virologic response at week 24 of follow-up (SVR24), which was defined as undetectable HCV RNA 24 weeks after the end of treatment. Patients who were chronically infected with HCV genotype 4 and received at least 1 dose of telaprevir were included.

The demographic characteristics of our patients are described in Table 1. Patients received the TPR regimen approved for treatment of HCV genotype 1 infection (ie, TPR for 12 weeks then PR for an additional 12 weeks [response-guided therapy] or 36 weeks), with the following exceptions [2]. Patient 1 began TPR treatment, and after 2 weeks it was discovered that he was given 200 mg ribavirin twice daily instead of 600 mg twice daily. Telaprevir therapy was mistakenly discontinued after 8 weeks, and PR treatment was discontinued because of virologic breakthrough (ie, HCV RNA was detected after the HCV RNA level had fallen below the limit of detection during treatment) that occurred after 41 weeks of treatment.

Table 1. Demographic Characteristics, Baseline Characteristics, and Treatment Outcomes Among Patients Infected With Hepatitis C Virus (HCV) Genotype 4

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Race</th>
<th>Previous HCV Treatment</th>
<th>HIV Infection</th>
<th>Cirrhosis</th>
<th>Baseline HCV RNA Load, Log IU/mL</th>
<th>Treatment Duration, wk</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>M</td>
<td>White</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>5.38</td>
<td>41</td>
<td>Virologic breakthrough</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>M</td>
<td>White</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>5.00</td>
<td>24</td>
<td>SVR24</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>M</td>
<td>Unknown</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>6.33</td>
<td>40</td>
<td>SVR24</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>M</td>
<td>White</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>6.27</td>
<td>48</td>
<td>SVR24</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>M</td>
<td>White</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>4.04</td>
<td>48</td>
<td>SVR5</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>M</td>
<td>White</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5.47</td>
<td>41</td>
<td>Relapse</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>White</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>4.78</td>
<td>2</td>
<td>Treatment failure</td>
</tr>
</tbody>
</table>

Abbreviations: HIV, human immunodeficiency virus; SVR5, sustained virologic response at week 5 of follow-up; SVR24, sustained virologic response at week 24 of follow-up.
not limited to influenza-like symptoms, rash, fatigue/weakness/shortness of breath, anemia, low neutrophil count, low platelet count, low white blood cell count, anorectal conditions, nausea/vomiting/diarrhea, abdominal/stomach pain, pruritus, and constipation. Two patients experienced liver decompensation (hepatic encephalopathy in patient 5 and hepatic encephalopathy, ascites, thrombocytopenia requiring platelet transfusion, and neutropenia in patient 7). One patient required epoetin alfa therapy, and 2 required epoetin alfa therapy and a blood transfusion. Less common adverse events included but were not limited to difficulty controlling diabetes until telaprevir therapy was discontinued, conjunctivitis, hypothyroidism, vision changes, and depression and moodiness. Overall, 4 patients had visits to the emergency department. Reasons for emergency care included but were not limited to hepatic encephalopathy (International Classification of Diseases, Ninth Revision–Clinical Modification code 572.2), urinary tract infection (599.0), anemia (285.9), abdominal pain (789.0), headache (784.0), back pain (724), and severe interferon reaction (995.29). Patient 1 developed hepatocellular carcinoma within a year after treatment ended, and patient 7 had a history of hepatocellular carcinoma.

We observed a SVR24 in 50% of patients. All of the patients who did not obtain a SVR24 were cirrhotic and did not follow the TPR treatment protocol approved for HCV genotype 1 infection. At the time of writing, for 1 patient, 24 weeks had not passed since the end of treatment. The SVR24 rate obtained in our study reflects the same SVR24 rate that Benhamou et al found in patients treated with TPR for 15 days and then PR for 46 weeks. It is important to note that our patients differed from those in the study by Benhamou et al, as we included a patient coinfected with human immunodeficiency virus, patients with cirrhosis, and patients who were older (median age, 56 years [range, 43–68 years] vs 41 years [range, 28–52 years]).

Our results reinforce the findings by Benhamou et al and support additional research of TPR therapy in patients with HCV genotype 4 infection [1].

Notes

Disclaimer. The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

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Potential conflicts of interest. K. B. is a consultant for companies that include Gilead Sciences and Janssen Pharmaceuticals. A. D. B. is a consultant for companies that include Gilead Sciences and Janssen Pharmaceuticals. D. T. D. is as a paid lecturer and consultant for and a member of scientific advisory boards of companies that either develop or assess medicines used for the treatment of viral hepatitis. These companies include Gilead Sciences, Boehringer Ingelheim, Novartis, Vertex Pharmaceuticals, Achillion, Tibotec, Idenix, Merck, Kadmon, Bayer Healthcare, Genentech and Hoffman-La Roch, and Bristol-Myers Squibb. T. D. S. is a paid lecturer for, consultant for, and participant on the data safety monitoring boards of companies that include Bristol-Myers Squibb/Sanoﬁ-Aventis, Novartis, Pfizer, and Salix Pharmaceuticals. All other authors report no potential conflicts.

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References


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