Telaprevir Activity in Treatment-Naive Patients Infected Hepatitis C Virus Genotype 4: A Randomized Trial

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Background. This partially blinded, randomized, phase 2a C210 study evaluated the antiviral activity of telaprevir-based regimens in treatment-naive patients with chronic hepatitis C virus (HCV) genotype 4 infection.

Methods. Twenty-four patients received telaprevir 750 mg every 8 hours for 15 days (T; n = 8), telaprevir in combination with pegylated interferon alfa-2a and ribavirin (Peg-IFN/RBV) for 15 days (TPR; n = 8), or Peg-IFN/RBV plus placebo for 15 days (PR; n = 8), followed by Peg-IFN/RBV for 46 or 48 weeks. The primary objective was to assess the effect of telaprevir on HCV RNA levels.

Results. HCV RNA levels decreased slightly with T and PR; TPR produced substantial, rapid declines. On day 15, median reductions in the HCV RNA load from baseline were −0.77, −4.32, and −1.58 log10 IU/mL for T, TPR, and PR, respectively, and 0 patients in the T group, 1 in the TPR group, and 0 in the PR group had undetectable HCV RNA. Five of 8 patients who received telaprevir monotherapy had viral breakthrough within 15 days of treatment. Adverse event incidence was similar across treatments and comparable with the incidences from previous clinical trials. One patient (in T group) had a serious adverse event (considered unrelated to telaprevir) that led to treatment discontinuation.

Conclusions. Telaprevir with Peg-IFN/RBV had greater activity than Peg-IFN/RBV treatment or telaprevir monotherapy against HCV genotype 4. Telaprevir was generally safe and well tolerated. Further investigation of telaprevir combination therapy in patients with HCV genotype 4 infection is warranted.

Clinical Trials Registration. NCT00580801.

Keywords. viral kinetics; HCV RNA; SVR; Study C210.

Around 170 million people worldwide are estimated to have chronic hepatitis C virus (HCV) infection [1]. HCV is genetically heterogeneous, with 6 major genotypes (1–6) and nucleotides sequences that differ by 30%–35% [2–5]. HCV genotype 4 (G4) is common in the Middle East and Egypt [6–8], and has become increasingly prevalent in Southern European countries including Italy, France, Greece, and Spain due to changes in population structure, immigration, and transmission routes [9–14]. G4 HCV is highly genetically heterogeneous, with more subtypes than genotypes 1–3 (G1–3). The 18 G4 subtypes identified to date have different patterns of prevalence in different geographic regions [3,15].

Current standard therapy for G4 HCV–infected patients is a 48-week course of pegylated interferon (Peg-IFN) and ribavirin (RBV) [16]. The treatment goal is a sustained virologic response (SVR), defined as an undetectable HCV RNA load 6 months after treatment cessation. The SVR rate for G4 HCV–infected patients after Peg-IFN/RBV treatment is approximately 60% [17], which is typically higher than that in patients with G1 HCV infection treated with 48 weeks of Peg-IFN/RBV. Furthermore, Roulot et al reported higher SVR rates...
after Peg-IFN/RBV treatment for G4a-infected patients, compared with patients infected with other G4 subtypes [18].

Telaprevir, a potent HCV NS3•4A protease inhibitor, was investigated as monotherapy and in combination with Peg-IFN/RBV in patients infected with G1, G2, and G3 HCV [19–26]. When administered with Peg-IFN/RBV, telaprevir is approved for the treatment of treatment-naive and treatment-experienced adult patients with chronic G1 HCV infection and compensated liver disease [27, 28]. This was based on data from 3 phase 3 trials (ADVANCE [23], ILLUMINATE [19], and REALIZE [22]), in which therapy with telaprevir plus Peg-IFN/RBV produced significantly higher SVR rates than Peg-IFN/RBV alone in G1 HCV–infected treatment-naive patients (79% vs 46%; ADVANCE) [27, 28] and treatment-experienced patients (65% vs 16%; REALIZE) [27, 28]. Telaprevir can also be administered with a reduced overall duration for appropriate treatment-naive and relapers after prior Peg-IFN/RBV therapy [27, 28]. A small phase 2a study, C209, found that while telaprevir plus Peg-IFN/RBV had greater activity against G2 HCV than Peg-IFN/RBV alone, activity against G3 HCV was low [20].

Limited in vitro data suggest that telaprevir has activity against G4 HCV; the 50% inhibitory concentration (IC50) of telaprevir was approximately 6-fold for G4 HCV versus G1 HCV [29]. We report a phase 2a clinical trial that investigated telaprevir given alone or with Peg-IFN alfa-2a and RBV for 2 weeks in treatment-naive patients with chronic G4 HCV infection.

**PATIENTS AND METHODS**

**Patients**

This exploratory phase 2a trial, which involved 24 patients with chronic G4 HCV infection, was conducted from January 2008 to January 2010 at a single site in France. HCV-infected treatment-naive patients aged 18–65 years and in good health (except for chronic G4 HCV infection) were eligible if they had a plasma HCV RNA load of >10,000 IU/mL, an absolute neutrophil count of ≥1500 neutrophils/mm3, and a platelet count of ≥100,000 platelets/mm3. Key exclusion criteria were contraindications to interferon (Peg-IFN in particular) or RBV treatment; history or evidence of cirrhosis, end-stage liver disease, or decompensated liver disease (as shown by screening laboratory results); human immunodeficiency virus or hepatitis B virus co-infection; history of alcohol or illicit drug use; and pregnancy/current breast-feeding.

The trial protocol was reviewed and approved by independent ethics committees, and the study was conducted in accordance with the Declaration of Helsinki and good clinical practice guidelines. All patients provided written, informed consent before initiation. The trial was registered with ClinicalTrials.gov (NCT00580801).

**Study Design**

Patients were randomly assigned in a ratio of 1:1:1 to receive telaprevir 750 mg every 8 hours for 2 weeks (T group; n = 8); telaprevir 750 mg every 8 hours, Peg-IFN alfa-2a 180 μg once weekly, and RBV 1000–1200 mg/day (weight based) for 2 weeks (TPR group; n = 8); or placebo every 8 hours, Peg-IFN alfa-2a 180 μg once weekly, and RBV 1000–1200 mg/day (weight based) for 2 weeks (PR group; n = 8). Telaprevir was administered every 8 hours for 14 days, plus a morning dose on day 15. This 2-week investigational treatment phase was followed by a standard treatment phase comprising 46 or 48 weeks of Peg-IFN/RBV and a follow-up period of 24–48 weeks.

The investigational treatment phase was partially blinded: group T was open label, but both the patient and investigator were blinded in groups TPR and PR. Randomization was conducted using a central system.

Patients could be withdrawn from the trial because of a serious adverse event or if they did not comply with the protocol requirements or cooperate with the investigator. Patients had to discontinue or modify treatment in case of pregnancy (in the patient or their partner), grade 3 rash, or use of prohibited medications. Dose modification of telaprevir was not permitted.

**Efficacy Assessments and End Points**

Plasma HCV RNA load was quantified using the COBAS TaqMan HCV test (version 2.0; lower limit of quantification, 25 IU/mL). Values below the lower limit of quantification were reported as <25 IU/mL detectable if a signal was detected or as <25 IU/mL undetectable if no HCV target was detected. The plasma HCV RNA load was measured at screening, baseline (day 1, the first day of the investigational treatment phase); on days 2, 3, 4, 8, 12, and 15 (the last day of the investigational treatment phase and the first day of the standard treatment phase); and during weeks 4, 12, 24, 36, and 48 after starting Peg-IFN/RBV treatment.

If HCV RNA was undetectable at the end of treatment, follow-up visits were planned at weeks 4, 8, 12, and 24. If HCV RNA was confirmed to be detectable at the end of treatment, follow-up visits were planned at weeks 4 and 24. If viral relapse occurred, an additional visit was scheduled 24 weeks after relapse was detected.

The primary objective of the study was to assess the effect of telaprevir on early viral kinetics during the 2-week investigational treatment period. Secondary objectives included the investigation of safety and tolerability, the emergence of viral variants, and pharmacokinetics. The proportion of patients with SVR, viral breakthrough, or viral relapse was also assessed. SVR was defined as an undetectable HCV RNA load at the end of treatment and no confirmed detection of HCV RNA between the end of treatment and 24 weeks after the last dose of study medication. Viral breakthrough was defined as a
confirmed increase of $>1 \log_{10}$ in the HCV RNA load from the nadir level or as a confirmed HCV RNA load of $>100$ IU/mL in patients who had achieved an HCV RNA load of $<25$ IU/mL. Viral relapse was defined as confirmed detection of HCV RNA during the follow-up period in patients with an undetectable HCV RNA load at the end of treatment.

**Virology Assessments**

Population sequencing analysis (limit of detection, approximately 1000 HCV RNA IU/mL) was performed on all baseline samples, at the time of viral breakthrough or relapse (when relevant), and at the end of telaprevir treatment. The presence of known telaprevir-resistant variants (V36A/M, T54A/S, R155I/ K/M/T, or A156S/T/V) [30] was investigated.

The Trugene 5′ noncoding method (Visible Genetics, Toronto, Canada) was used to determine HCV genotype and subtype.

**Safety and Pharmacokinetic Assessments**

The incidence and severity of adverse events was recorded at every visit up to and including follow-up week 4. Causality was assessed by the investigator. From the week 4 follow-up visit onward, only at least possibly related serious adverse events and at least possibly related grade 3 adverse events were reported. Adverse events requiring specific management included rash (any type) and anemia; clinical laboratory tests including hematologic analysis, clinical chemistry, urinalysis, cardiovascular assessments, and physical examinations, were also conducted regularly throughout the trial.

Plasma samples were collected for pharmacokinetic assessments on days 1, 2, 4, 8, 12, and 15. Steady-state pharmacokinetics of telaprevir were assessed on day 15.

**Statistical Analyses**

All analyses were conducted on the intent-to-treat population, comprising all randomized patients who received $\geq 1$ dose of telaprevir or placebo. Statistical analyses, except pharmacokinetic analyses, were performed by SGS Life Science Services, Meche len, Belgium, using SAS, version 9.1. The primary analysis was performed when all randomly assigned patients had completed the 2-week course of investigational treatment or had discontinued treatment before completion. Once all randomized patients had completed treatment and follow-up or discontinued the trial, a final analysis was performed. Statistical significance was not assessed, because of the small sample size and exploratory nature of the study.

Sample size calculations assumed an SD of 1.34 (based on data from a previous trial of G1 HCV–infected patients) for the change in HCV RNA load from baseline to week 2. This method provided a 1-sided precision of 0.93 log$_{10}$ for the 95% confidence of the difference versus baseline if 8 patients were included per group.

Pharmacokinetic and statistical pharmacokinetic analyses were conducted by Kinesis Pharma, Breda, the Netherlands, using WinNonlin Professional (version 4.1; Pharsight Corporation, Mountain View, CA). Statistical pharmacokinetic analyses compared the T group (reference) with the TPR group (test) on days 1 and 15. The primary pharmacokinetic parameters were the area under the plasma concentration-time curve over the dosing interval (AUC$_{0-15}$), minimum and maximum plasma concentrations (C$_{min}$ and C$_{max}$, respectively), and time to C$_{max}$ (t$_{max}$).

**RESULTS**

**Patient Disposition and Baseline Characteristics**

Of the 29 patients screened, 24 were randomly assigned to a study group and treated (8 patients per treatment group; Figure 1). All patients completed the 15-day investigational phase, except 1 in the T group, who permanently discontinued telaprevir because of a serious adverse event (cholelithiasis, which was not considered related to treatment). All other patients then received standard treatment with Peg-IFN/RBV for $\geq 23$ weeks. All patients were compliant with the assigned treatment during the investigational phase; the patient who prematurely discontinued was compliant before this time. One patient (in the PR group) prematurely discontinued treatment during the standard treatment phase because of noncompliance. Seven patients (29%) deviated from the predefined intake time (ie, after a meal) on at least 1 occasion.

Baseline characteristics were generally comparable across treatment groups, except for some variation between groups with respect to sex and race (Table 1). No enrolled patients had cirrhosis, and 54% had an HCV RNA load of $\geq 800\,000$ IU/mL. G4a HCV was the most prevalent subtype, with detection in 50% of patients.

**Efficacy**

Median HCV RNA values were comparable across treatment groups at baseline: 5.83 log$_{10}$ IU/mL in the T group, 6.16 log$_{10}$ IU/mL in the TPR group, and 5.88 log$_{10}$ IU/mL in the PR group. During the 15-day investigational phase, decreases in median HCV RNA loads were observed in all treatment groups, with a marked, rapid decline in patients receiving telaprevir plus Peg-IFN/RBV. The median changes in HCV RNA loads from baseline to day 2 were $-0.93$ log$_{10}$ IU/mL (range, $-1.5$ to 0.1 log$_{10}$ IU/mL), $-1.28$ log$_{10}$ IU/mL (range, $-2.7$ to $-0.6$ log$_{10}$ IU/mL), and $-0.26$ log$_{10}$ IU/mL (range, $-1.6$ to 0.0 log$_{10}$ IU/mL) for the T, TPR, and PR groups, respectively. On day 4, the median changes from baseline were $-1.16$ log$_{10}$ IU/mL (range, $-2.2$ to $-0.3$ log$_{10}$ IU/mL), $-2.57$ log$_{10}$ IU/mL (range, $-3.3$ to $-0.9$ log$_{10}$ IU/mL), and $-0.78$ log$_{10}$ IU/mL (range, $-2.5$ to 0.1 log$_{10}$ IU/mL) for the T, TPR, and PR groups, respectively. On day 15, the median changes from baseline were $-0.77$ log$_{10}$ IU/mL (range, $-2.9$ to 0.3 log$_{10}$ IU/mL), $-4.32$ log$_{10}$ IU/mL (range, $-5.2$
to $0.0 \log_{10}$ IU/mL, and $-1.58 \log_{10}$ IU/mL (range, $-4.0$ to $-0.8 \log_{10}$ IU/mL) for the T, TPR, and PR groups, respectively. In the T group, an initial decrease in HCV RNA load was followed by a slight increase between days 8 and 15, because of viral breakthroughs in 5 patients. HCV RNA levels then decreased in this treatment group after the introduction of Peg-IFN/RBV on day 15. Figure 2 shows individual patients’ HCV RNA profiles. On day 15, 1 patient in the TPR group and no patients in the T or PR groups had undetectable HCV RNA.

Virologic responses were similar between groups after the standard treatment phase. At the end of treatment, 7 patients (87.5%), 6 (75.0%), and 6 (75.0%) in the T, TPR, and PR groups, respectively, had undetectable HCV RNA. Five patients (62.5%), 4 (50.0%), and 5 (62.5%) in the T, TPR, and PR groups, respectively, achieved a SVR. Two patients (50%), 3 (75%), and 3 (75%) with genotype 4a HCV in the T, TPR, and PR groups, respectively, had achieved a SVR at 24 weeks. Among patients with undetectable HCV RNA at the end of
treatment, 1 (14.3%), 2 (33.3%), and 1 (16.7%) in the T, TPR, and PR groups, respectively, had a viral relapse.

Virology
No known telaprevir-resistant variants were identified in 23 patients with available baseline blood samples. During the 2-week investigational treatment phase, no patients in the TPR or PR groups had viral breakthrough. However, 5 patients (62.5%) in the T group had viral breakthrough. Of these, 4 patients had available viral sequencing data at the time of breakthrough; a T54A/T mutation emerged in virus from 2 patients, while no known amino acid substitutions associated with reduced telaprevir susceptibility were detected in virus from the 2 others. Three of these 4 patients achieved a SVR after the Peg-IFN/RBV standard treatment phase. In addition, 2 patients in the TPR group had viral breakthrough during the standard treatment phase. No known amino acid substitutions associated with reduced telaprevir susceptibility were detected in virus from these patients, and both had detectable HCV RNA at the end of treatment.

Safety and Tolerability
The most frequently reported adverse events during the overall treatment period were influenza-like illness and asthenia (Table 2). The incidence of adverse events was similar across groups, apart from a higher incidence of influenza-like illness in the TPR group versus the other groups.

Serious adverse events were reported in 1 patient in the T group (cholelithiasis during the investigational phase; not considered related to treatment) and 2 in the PR group (delirium and cholelithiasis). The patient in the T group permanently discontinued the trial. No other discontinuations occurred during the investigational phase. A further 2 and 1 patients in the T and PR groups, respectively, permanently discontinued Peg-IFN/RBV during the standard treatment phase because of adverse events. No deaths occurred during the trial.

Neither rash nor anemia occurred with telaprevir-based therapy during the investigational treatment phase. During the overall treatment period, rash events occurred in 2 patients

Table 1. Baseline Demographic and Patient Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>T (n = 8)</th>
<th>TPR (n = 8)</th>
<th>PR (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>5 (62.5)</td>
<td>6 (75.0)</td>
<td>4 (50.0)</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>2 (25.0)</td>
<td>2 (25.0)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>White</td>
<td>6 (75.0)</td>
<td>6 (75.0)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>Age, y, median (range)</td>
<td>43 (36–61)</td>
<td>41 (28–52)</td>
<td>46 (30–56)</td>
</tr>
<tr>
<td>HCV RNA load, log10 IU/mL, median, (range)</td>
<td>5.8 (5–7)</td>
<td>6.2 (5–7)</td>
<td>5.9 (5–7)</td>
</tr>
<tr>
<td>Baseline HCV RNA load ≥800 000 IU/mL</td>
<td>4 (50.0)</td>
<td>5 (62.5)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HCV subtype^a^</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td>4 (50.0)</td>
<td>4 (50.0)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>4c</td>
<td>3 (37.5)</td>
<td>3 (37.5)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>4f</td>
<td>1 (12.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4g</td>
<td>0</td>
<td>0</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>4 (unknown subtype)</td>
<td>0</td>
<td>1 (12.5)</td>
<td>2 (12.5)^b</td>
</tr>
</tbody>
</table>

Data are no. (%) of patients, unless otherwise indicated.

Abbreviations: HCV, hepatitis C virus; PR, pegylated interferon alfa-2a/ribavirin plus placebo; T, telaprevir alone; TPR, telaprevir with pegylated interferon alfa-2a/ribavirin.

^a Performed by the Trugene 5′ noncoding method at screening.

^b Trugene method–based HCV genotyping data were missing for 2 patients. Genotype 4 was determined by a local laboratory.

Figure 2. Changes in the hepatitis C virus (HCV) RNA load over the investigational treatment phase for each patient, by G4 HCV subtype and treatment group. Trugene method–based HCV genotyping data were missing for 2 patients. Abbreviations: BAS, baseline; LLOQ, lower limit of quantification; PR, Peg-IFN/RBV plus placebo; T, telaprevir alone; TPR, telaprevir with Peg-IFN/RBV.

Figure 2. Changes in the hepatitis C virus (HCV) RNA load over the investigational treatment phase for each patient, by G4 HCV subtype and treatment group. Trugene method–based HCV genotyping data were missing for 2 patients. Abbreviations: BAS, baseline; LLOQ, lower limit of quantification; PR, Peg-IFN/RBV plus placebo; T, telaprevir alone; TPR, telaprevir with Peg-IFN/RBV.
of patients in any treatment group) were hypernatremia, increases in uric acid level, and decreases in white blood cell count, neutrophil count, and platelet count. During the overall treatment period, the most frequent treatment-emergent graded toxicities (observed in ≥25% of patients in any treatment group) were hypophosphatemia, increases in aspartate aminotransferase level, and decreases in hemoglobin level and lymphocyte counts. Changes from baseline in vital signs and electrocardiogram parameters were generally small, and none were considered clinically relevant.

**Pharmacokinetic Analyses**

Telaprevir C\(_{\text{max}}\) and AUC\(_{\text{8h}}\) on day 1 were comparable between the T and TPR groups. On the basis of least square mean ratios on day 15, telaprevir C\(_{\text{min}}\), C\(_{\text{max}}\), and AUC\(_{\text{8h}}\) values were 24%, 32%, and 33% higher, respectively, in the TPR group versus the T group (Table 3).

**DISCUSSION**

This was the first clinical trial to evaluate the antiviral activity of telaprevir in G4 HCV–infected patients. G4 HCV–infected patients are an important subgroup, given the high prevalence of this subtype in Africa and the Middle East [31, 32], the increasing prevalence in several European countries [9–13], and the suboptimal SVR rates achieved with the current standard therapy (Peg-IFN/RBV for 48 weeks) [16, 17].

This small phase 2a trial indicated that telaprevir plus Peg-IFN/RBV has antiviral activity against G4 HCV in treatment-naive patients. During the 2-week investigational treatment phase, the antiviral activity of telaprevir combined with Peg-IFN/RBV (the TPR group) was greater than that seen with telaprevir monotherapy (the T group) and Peg-IFN/RBV alone (the PR group). This apparent synergistic effect between telaprevir, Peg-IFN, and RBV is in agreement with findings observed in patients with G1 HCV infection [21, 24–26].

The use of telaprevir monotherapy for a 2-week period allowed determination of the intrinsic antiviral activity of the
drug. The reduction in median HCV RNA load from baseline to day 15 with telaprevir monotherapy in G4 HCV–infected patients was lower than that observed previously in G1- and G2-infected patients but slightly higher than that observed in patients with G3 HCV infection [20, 21]. Notably, an early decrease in median HCV RNA load after the initiation of telaprevir monotherapy was followed by a subsequent increase between days 8 and 15 due to viral breakthroughs, which were not observed in the TPR group. This finding underscores the importance of combining telaprevir with PR, suggesting that telaprevir monotherapy is not a viable treatment option in this patient population and that direct-acting antiviral monotherapy should only be investigated with caution.

Although this was a small study, the safety profile of telaprevir in HCV G4 infection was generally comparable to that in G1, G2, or G3 HCV–infected patients who received telaprevir for a similar duration [19–23, 33], and no new adverse events were reported. Neither rash nor anemia were observed during the 2-week telaprevir treatment phase. Most adverse events were grade 1 or 2 in severity, and no deaths occurred during the study.

In our study, G4 HCV–infected patients in the TPR group had higher telaprevir plasma concentrations at day 15 than patients in the T group. A similar trend was previously seen in G1 HCV–infected patients [21]. Our pharmacokinetic findings were generally consistent with those from a previous trial of telaprevir monotherapy involving patients with G1 HCV infection [21]; therefore, differences in efficacy between G1 and G4 HCV are not considered related to differences in exposure. The treatment regimen for G1 patients comprises a 12-week course of telaprevir therapy in combination with Peg-IFN/RBV, which is then followed up with either a 12- or 36-week course of Peg-IFN/RBV, dependent on the patient’s response. Because the pharmacokinetics and tolerability of telaprevir in this study were found to be comparable to those observed in G1 HCV–infected patients, further investigation of the potential of a 12-week TPR regimen for G4 HCV–infected patients is of interest.

The study was limited primarily by its small sample size and exploratory nature, and for these reasons the potential statistical significance of our findings was not assessed. In addition, interleukin 28B (IL28B) genotypes were not determined because the relationship between single-nucleotide polymorphisms near the IL28B gene and responses to Peg-IFN/RBV treatment [34, 35] had not been discovered at the time of study onset. Given this limitation and that IL28B genotype can affect viral kinetics in patients with G4 HCV infection during the first week of treatment [36], differences in efficacy between treatment arms in our study could relate to imbalances in the frequency of IL28B genotypes. However, in treatment-experienced, G1 HCV–infected patients receiving telaprevir, the IL28B genotype did not appear to influence SVR rates [37]. Differences in G4 subtype could also have influenced our results. However, subanalyses to investigate this were not appropriate because of the small sample size.

In conclusion, this phase 2a trial showed that telaprevir in combination with Peg-IFN/RBV had antiviral activity against HCV in treatment-naive patients with G4 HCV infection but that telaprevir monotherapy had limited antiviral activity in this patient population. Treatment with telaprevir was generally safe and well tolerated. Telaprevir is not currently approved for the treatment of G4 HCV–infected patients, and further investigation of telaprevir combination therapy in G4 HCV–infected patients may be warranted.

Notes

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Potential conflicts of interest. J. M. has served as a consultant for Roche, Merck, and Gilead. V. R. has received funding from Gilead Sciences, Janssen, Astellas Pharma, and Roche and has served as a consultant for Astellas, Axcan, Genentech, Gilead, Roche, and Sanofi. P. L. has received funding from Schering Plough and served as a consultant for Janssen, Gilead, and MSD. K. D., S. D., A. G., D. L., G. P., and M. B. are employees of Janssen Pharmaceuticals. Y. B. certifies no potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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