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To the Editor:

In November 2013, the HCV NS3 protease inhibitor simeprevir was approved for treatment of chronic hepatitis C virus (HCV) genotype 1 infection, in combination with pegylated interferon and ribavirin (PR). However, the Q80K polymorphism (glutamine to lysine mutation) in the NS3 region of HCV genotype 1a, present in approximately 45% of North Americans with HCV genotype 1a infection, confers resistance to simeprevir in the replicon system (1) and resulted in lower rates of sustained virological response (SVR) in clinical trials (2,3). Accordingly, the United States simeprevir product monograph states that "Screening patients with HCV genotype 1a infection for the presence of virus with the NS3 Q80K polymorphism at baseline is strongly recommended. Alternative therapy should be considered for patients infected with HCV genotype 1a containing the Q80K polymorphism" (3). The Canadian product monograph states "When accessible, testing for Q80K polymorphism in patients with HCV genotype 1a could be considered" (2).

The presence of the Q80K polymorphism in HCV genotype 1a does not reduce the activity of the HCV NS3 protease inhibitors telaprevir or boceprevir in transient replication assays (1); however, clinical data have not been reported. We retrospectively examined the presence of the Q80K polymorphism at baseline and the effect of the Q80K polymorphism on SVR rates in treatment-naïve patients with HCV genotype 1a infection in phase 3 clinical trials of telaprevir with PR. The phase 3 clinical trials included in this analysis were ADVANCE, ILLUMINATE and OPTIMIZE. The design, efficacy and safety results of these trials have been reported elsewhere (4-6). This analysis included all genotype 1a patients who received telaprevir (given for 12 weeks) in combination with PR and PR alone, and evaluated rates of SVR (SVR24 from ADVANCE and ILLUMINATE and SVR12 from OPTIMIZE) in patients with and without the Q80K polymorphism at baseline.

Results for these treatment-naïve patients with HCV genotype 1a infection were as follows:

- 975 patients were treated with telaprevir plus PR, of whom 39% had the Q80K polymorphism at baseline. The SVR rate was 72% in patients with the Q80K polymorphism compared with 71% without the polymorphism.
- 200 patients were treated with PR alone, of whom 41% had the Q80K polymorphism at baseline. The SVR rates were also unchanged in patients receiving PR; 43% with Q80K versus 41% without.

These clinical data are consistent with the findings in the transient replication assay. The presence of the Q80K polymorphism did not adversely affect SVR rates with telaprevir plus PR.

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