


Hepatitis C Virus RNA Levels During Interferon-Free Combination Direct-Acting Antiviral Treatment in Registrational Trials

TO THE EDITOR—We read with interest the unexpected findings by Sidharthan et al that indicate that detected or quantifiable hepatitis C virus (HCV) RNA at the end of direct-acting antiviral (DAA) treatment does not preclude sustained virologic response (SVR12) [1]. Using the Abbott HCV real-time assay (lower limit of quantitation [LLOQ], 12 IU/mL), the authors reported that among patients treated with sofosbuvir + ledipasvir ± GS-9669 or GS-9451 for 6 or 12 weeks, HCV RNA was detected (>LLOQ or ≥LLOQ) or quantifiable in 29/59 (49%) and 6/59 (10%) patients, respectively, and all but 1 patient achieved an SVR12.

To compare the results by Sidharthan et al with those obtained in other DAA trials, we reanalyzed HCV RNA data from 12 registrational trials of interferon-free, combination DAA treatments [2–4] to assess the frequency of HCV RNA detection at the end of treatment among patients who achieved SVR12. In these trials, the Roche COBAS TaqMan HCV v1.0 assay (LLOQ = 43 IU/mL) also appeared higher than expected. For example, among patients treated with sofosbuvir + ledipasvir, 12/19 (63%) and 2/19 (11%) had detected or quantifiable HCV RNA at week 4, respectively. In contrast, among patients treated with sofosbuvir + ledipasvir ± ribavirin in the ION-1, -2, and -3 trials, 268/1504 (18%) and 5/1504 (0.3%) patients had detected or quantifiable (≥25 IU/mL, Roche v2.0) HCV RNA at week 4, respectively (Table 1).

Similarly low HCV RNA levels at week 4 were observed in other combination DAA trials. By week 8, HCV RNA was detected in <1% of patients overall. We encourage further analyses of HCV RNA levels using multiple sensitive assays in other short-course DAA combination studies, as these studies will help refine HCV kinetic models and guide future trial design.

Notes

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Potential conflicts of interest. All authors: No potential conflicts of interest.

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Reply to Harrington et al

TO THE EDITOR—Harrington et al raise 3 important points in a detailed analysis of pooled data from 12 registrational trials of interferon-free, direct-acting antiviral (DAA) therapies [1]. First, the authors point out that hepatitis C virus (HCV) RNA was detected at the end of treatment in only 0.3% (12/3671) of patients who achieved sustained virological response 12 (SVR12) in the larger trials compared to 29% (28/96) in our studies [2]. As suggested by