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Usefulness of Lead-In phase in determining risk/benefit of telaprevir treatment in patients with HCV cirrhosis

To the Editor:

We read with interest the paper published by Dr. Foster and co-authors [1]. As clearly stated in the manuscript, irrespective of the previous definition of response, the overall SVR rates at week 4, after Lead-In phase (LI), were 33% in those with <1 log decline and 82% in the subset with >1 log decline, respectively. Multiple logistic regression analysis confirmed that LI is a strong independent predictor of SVR (OR 5.1, 95% CI 2.6–10.1). This finding enhances the concept that the degree of interferon sensitivity plays a major role in modulating the efficacy of first generation protease inhibitors. Despite this result, the data provided by this study did not fully assess the potential usefulness of LI phase in the context of triple therapy with telaprevir (TVR), because they lack to further detail the effect of LI according to the fibrosis stage. Along this line, it also should be taken into account that patients with advanced fibrosis/cirrhosis represent, in real life, the majority of those to deal with for re-treatment, and missing or unreliable data on virologic on-therapy response during previous treatment is common.

In previous subanalyses carried out in the Realize study [2,3], the overall SVR rates in null and partial responders with cirrhosis (Metavir F4) were 14% and 34% (pooled TVR arms), respectively. More recently, the same group of investigators also reported that the proportion of patients with cirrhosis increased from relapsers to null responders, whatever the response after 4 weeks of therapy [5]. Considering this result, a further decrease of response rate across the prior failure categories, according to the presence of a more severe liver damage, should be suspected. Regrettably, in these reports, SVR rates according to fibrosis stages and LI were not illustrated. In the same way, of main interest, the present paper missed to provide the rate of SVR in F4 patients who had less than 1 log decline after LI (overall and according to their prior definition of response). This information, by contrast, was recently stated for boceprevir (BOC, SPRINT 2 and RESPOND 2 combined) [4].

To date, while waiting for more effective molecules that will eliminate the need of IFN, a detailed analysis of week 4 response by severity of liver damage represents a no longer deferrable unmet clinical need. Using this information, both Scientific Community and Clinicians worldwide could better determine the utility of LI in assessing the risk/benefit of treatment in cirrhotic patients with either BOC or TVR triple combination therapy [6,7].

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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