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Optimized HBsAg titer monitoring improves interferon therapy in patients with chronic hepatitis delta

To the Editor:

Hepatitis delta virus (HDV) is a defective virus requiring the simultaneous presence of hepatitis B virus (HBV) to fully express its pathogenicity; thus, HDV infection always occurs in the presence of HBV. Active HDV co- or superinfection with HDV is confirmed by the presence of detectable HDV RNA, and immunohistochemical staining for HDV antigen or IgM anti-HDV. Interferon alpha (conventional or pegylated) is the only drug effective on HDV replication [1–5]. However, the optimal duration of interferon (IFN) therapy is not well defined [6,7]. The efficacy of IFN therapy can be assessed during treatment (after 3–6 months) by measuring HDV RNA levels, but HDV RNA assays are not standardized and not widely available [7]. Treatment with pegylated interferon alfa-2a (PegIFN-α-2a) for 48 weeks, which is considered as the treatment of choice for HDV infection, with or without adefovir, resulted in sustained HDV RNA clearance in about one quarter of patients [8]. A sustained off-treatment virological response with HDV RNA-negative is accompanied by improved histology, while some patients lose the HBV surface antigen (HBsAg) [6,7].

The aim of our study was first to prospectively monitor HBsAg titers during interferon therapy for the treatment of chronic HDV and, second, to adapt the duration of the therapy based on the titer.

We analyzed HBsAg levels of four patients who received PegIFN-α-2a as a time-individualized therapy according to the evolution of HBsAg titer. All patients were male, HBe Ag-negative, and with an age of 43–46 years. Metavir score was F4 for one patient and F3 for the others. Pretherapeutic HBsAg levels were 7900, 4200, 3500, and 1320 IU/ml (Fig. 1).

We prospectively assessed the HBsAg titers using the Quantitative Architect Abbott Method (Abbott France, Rungis, France) every three months in these four patients who received PegIFN-α-2a at 180 µg per week. The treatment was stopped when HBsAg levels reached negative values (<0.5 IU/ml). During interferon treatment, HBsAg titers decreased in all patients and reached a negative value (<0.5 IU/ml) after seven months, two years, three years, and four years of therapy. This negative HBsAg value was stable (normal ALT and loss of HBsAg) in all patients 12 months after the end of therapy.

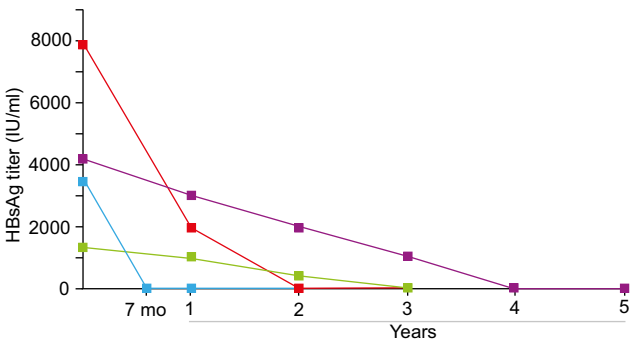

Fig. 1. HBs antigen monitoring during interferon treatment for chronic hepatitis delta in four patients.

Few data are reported on extended treatment for chronic HDV. Yurdaydin *et al.* treated patients during two years, without increased sustained response rates during one year of treatment [9]. In their study, the treatment duration was fixed and not based on HBsAg monitoring of patients. In our study, the decline of HBsAg titers varied among the patients. Loss of HBsAg occurred after seven to 48 months, and only close monitoring of HBsAg revealed the end of therapy. HBsAg titer decline constitutes a useful tool to predict HBsAg loss and the best duration of interferon treatment in chronic HDV. Even with a limited number of patients, this study demonstrates, for the first time, that adapting interferon treatment duration through HBsAg titer monitoring provides a loss of HBsAg and the cure of chronic HDV.

Conflict of interest

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

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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

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