Pegylated interferon/telbivudine sequential therapy in Hepatitis Be antigen negative severe chronic hepatitis B patient

Sir,

We report the effect of sequential Pegylated-Interferon-alpha-2a (Peg-IFN-alpha-2a)/telbivudine treatment in a patient affected by a severe Hepatitis B e Antigen (HBeAg) negative chronic Hepatitis B Virus (HBV) infection treated at our facility. We discuss the rationale of this innovative therapeutic strategy for the prolonged/long life treatment of severe chronic hepatitis B (CHB).

A 63-year-old man with a 22 years history of CHB presented at our center for HBV infection evaluation. He was affected by a clinically documented severe CHB infection, confirmed also by Fibroscan® (fibroscan stiffness Kp 13). The patient was HBeAg negative, HBV deoxyribonucleotide (DNA) positive (basal HBV DNA levels 2,700,000 IU/mL by real time polymerase chain reaction (rt-pcr)), serum alanine aminotransferase (ALT) levels 140 IU/L (upper normal limit, UNL 41 IU/L), functional class on admission Child-Pugh score was A5 without portal hypertension, negative for anti-Hepatitis delta virus (HDV) and anti-Hepatitis C virus (HCV) antibodies.

At the basal screening, several possible causes of liver diseases including, autoimmune, thesaurismosic and metabolic origin-were excluded.

On February 23rd 2007, patient began antiviral therapy with Peg-IFN-alpha-2a (180 μg weekly subcutaneously) with a satisfactory virologic suppression at week 4 (HBV DNA 159,000 IU/mL; ALT 339 IU/L) and week 12 (HBV DNA levels <30 IU/mL, ALT 65 IU/L). At follow-up, 48 weeks after beginning of Peg-IFN-alpha-2a, blood tests documented a complete suppression of HBV DNA levels (<12 IU/mL) and a normalization in ALT plasma values (38 IU/L). Antiviral treatment ended on February 6th 2008.

At week 4 and 8 following treatment suspension, we recorded an increase in HBV DNA plasma levels (28,200 IU/mL) with normal ALT values [Figure 1].

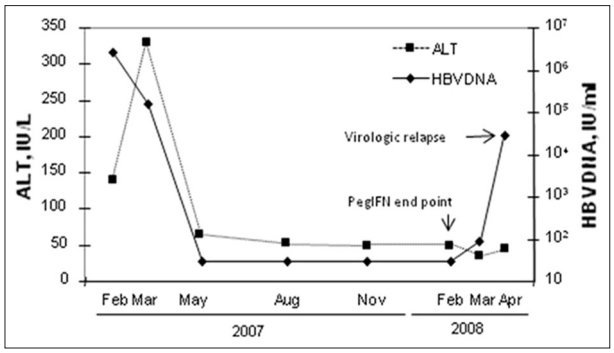

Figure 1: Alanine aminotransferase values and Hepatitis B Virus DNA plasma levels during Peg-IFN-alpha-2a (180 μg/week) treatment

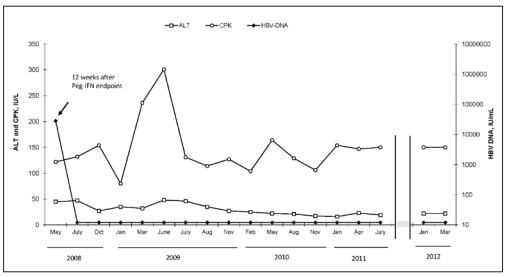

Figure 2: Alanine aminotransferase, creatine phosphokinase and Hepatitis B Virus DNA plasma levels during telbivudine oral therapy (600 mg/day)

After 12-week drug-free period, on May 6th 2008 we decided to start antiviral therapy for HBV reactivation using telbivudine 600 mg/day in oral therapy. A rapid virologic and biochemical response was observed after 4 weeks; specifically, HBV DNA was undetectable (<12 UI/mL) and ALT values were normal. No increase in plasma creatine phosphokinase (CPK) levels was observed [Figure 2].

At the 52nd week of telbivudine therapy, we recorded an increase in CPK levels. Anamnesis suggested CPK peak was related to an intense physical activity. After 3 days of muscular rest, CPK levels spontaneously returned to normal values as documented by a following medical checkup.

Currently, on March 2012 after 167 weeks from the beginning of telbivudine, blood tests show normal ALT and CPK plasma values, and HBV DNA remains undetectable (<12 UI/mL). Moreover, no adverse drug reactions associated with telbivudine treatment have been observed [Figure 2].

In conclusion, we report the effect of Peg-IFN-alpha-2a/telbivudine sequential treatment in severe chronic HBV infection. To our knowledge, this is the first report on the efficacy of a sequential therapy including the administration of telbivudine as NA.

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