Dr. Wendling, *et al* reply

To the Editor:

We read with interest the comment by Nagashima and Minota about our editorial[1]. We had mentioned the very interesting paper of our Japanese colleagues, reporting the first case of HBsAg-positive RA patient treated more than 5 years with an anti-interleukin 6 receptor monoclonal antibody (tocilizumab)[2]. Indeed, antiviral therapy (entecavir) was added after 7 years of tocilizumab therapy. It is noteworthy, even if the patient was retrospectively diagnosed as HBsAg-positive with high viral load before starting tocilizumab, that there was no evidence of exacerbation of hepatitis during these years of tocilizumab treatment, even without antiviral therapy for more than 5 years. This is of interest because interleukin 6 reduces HBV replication[3], and tocilizumab may be able to reactivate viral infection, such as Epstein-Barr virus[4].

This isolated and exceptional case is, of course, not a proof of safety of tocilizumab in every HBsAg-positive carrier, and we fully agree with the concluding comments of Nagashima and Minota, concordant with our previous statements about biologic agent use in this situation[5]. The longterm effects of antiviral therapy are unknown, and mutations and acquired resistance may occur, as shown in some cases with anti-tumor necrosis factor (anti-TNF) treatment in HBsAg-positive patients[6]. These considerations emphasize the need for systematic screening for HBV status in rheumatic diseases before starting biologic therapy with anti-TNF agents[7], rituximab[8], and abatacept[9]; this is also the case for tocilizumab.

International guidelines[10] suggest that in HBsAg-positive patients, when immunosuppressive therapy is indicated, a preemptive treatment with lamivudine, entacavir, or tenofovir is required to prevent viral reactivation. This preemptive therapy should be given 7 days prior and maintained as long as the immunosuppressive treatment is present, and for 6 months after cessation. Tight control of transaminases and viral load is mandatory during treatment, and at least 3 months after discontinuation of the immunosuppressive agent.

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