Dr. Wendling, et al reply

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*The Journal of Rheumatology* is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
To the Editor:

We read with interest the comment by Nagashima and Minota about our editorial. 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). 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, and tocilizumab may be able to reactivate viral infection, such as Epstein-Barr virus.

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. 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. These considerations emphasize the need for systematic screening for HBV status in rheumatic diseases before starting biologic therapy with anti-TNF agents, rituximab, and abatacept; this is also the case for tocilizumab.

International guidelines 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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REFERENCES