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Adalimumab as treatment for venous thrombosis in Behçet's syndrome: comment on the article by Emmi et al

To the Editor:

We read with interest the article by Emmi et al (1) regarding the effect of adalimumab (ADA)–based treatment versus disease-modifying antirheumatic drug (DMARD) therapy for venous thrombosis in Behçet's syndrome (BS). Their findings add important data to help answer the difficult questions on the treatment of BS. However, there are some concerns.

The age at BS onset is usually in the third or fourth decade, and there is a male predominance in severe BS (2). However, after several years, disease burnout may occur, and if there is major organ/system involvement, it usually occurs within the first 5 years (3). In the article by Emmi and colleagues, the patient age at disease onset and disease duration were not described in detail. The mean ± SD age at treatment initiation was 42.8 ± 11.2 years for ADA-based regimens and 53.8 ± 32.1 years for DMARD therapy. The timing of venous thrombosis occurrence also should have been reported to better define the course of disease in the patients. Nineteen men and 16 women were treated with DMARDs alone, and 18 men and 17 women were treated with ADA-based regimens. There were no differences in clinical characteristics between the sexes, and the mean age of the 2 groups at ADA or DMARD initiation was quite high. Comparing the effectiveness of ADA and DMARDS in groups that are not homogenous in terms of disease manifestations may not reflect the real picture in a disease with an expanded clinical spectrum like BS.

In the intervention group that received ADA-based regimens, 8 of the 35 patients were also treated with DMARDs. We question whether the authors excluded these patients in their data analysis. If not, this could have confounded the assessment of the effectiveness of ADA.

Additionally, venous thrombosis can vary from superficial thrombosis to very severe superior/inferior vena cava thrombosis. Postthrombotic syndrome is a major problem in patients with BS (4). Emmi and colleagues' report includes no quantification of the severity of thrombosis. We believe this is an important consideration in treatment choices. Further, we do not understand why postthrombotic syndrome was not taken into account in the evaluation of vascular outcomes.

We thank Dr. Emmi et al for this important and useful study and look forward to clarification of some of these questions.

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2. Seyahi E. Behçet's disease: how to diagnose and treat vascular involvement. Best Pract Res Clin Rheumatol 2016;30:279–95.
3. Kural-Seyahi E, Fresko I, Seyahi N, Ozyazgan Y, Mat C, Hamuryudan V, et al. The long-term mortality and morbidity of Behçet syndrome: a 2-decade outcome survey of 387 patients followed at a dedicated center. Medicine (Baltimore) 2003;82:60–76.
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Reply

To the Editor:

We thank Dr. Farisogullari and colleagues for their comments on our article reporting on how an ADA-based regimen is more effective and rapid than DMARD therapy in inducing resolution of venous thrombosis in patients with BS, allowing significant reduction of steroid exposure. Farisogullari et al suggested that our results may have been influenced by the heterogeneity between the ADA group and the DMARD group, specifically considering age (mean ± SD age at treatment initiation was 42.8 ± 11.2 years in the ADA group and 53.8 ± 32.1 years in the DMARD group). However, we are confident this difference had a minor impact on our results. In fact, the 2 groups were similar in terms of disease duration from the time of BS diagnosis to the time the considered venous events occurred and the subsequent start of ADA or DMARD treatment (mean ± SD 82.3 ± 17.3 months in the ADA group versus 89.6 ± 15.6 months in the DMARD group; $P = 0.753$). Thus, the results were obtained from groups that were homogeneous with similar disease duration.