Re: Dick et al.: Guidance on noncorticosteroid systemic immunomodulatory therapy in noninfectious uveitis: Fundamentals Of Care for UveitiS (FOCUS) Initiative

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**TO THE EDITOR:** We read with interest the article by Dick et al. The aim of the Fundamentals Of Care for UveitiS (FOCUS) initiative was to support an optimal management of noninfectious uveitis, with the ultimate aim of improving patients’ outcomes. This program, supported by AbbVie, Inc (North Chicago, IL), included for the first time an academically rigorous process, with a large number of worldwide uveitis specialists. Although part of the thought-leading ophthalmologists and rheumatologists selected to act as national faculties in France, we have concerns about 2 of the statements from the guidelines.

First, although it was not part of the original analysis nor discussed when developing the final statements at the meeting in late 2016, Dick et al asserted that adalimumab and infliximab are, according to recent international recommendations, the preferred biologic agents for the treatment and prevention of uveitis as an extra manifestation of spondyloarthritis. Several observational studies and one meta-analysis have shown that the soluble tumor necrosis factor (TNF) receptor fusion protein etanercept is less effective in preventing anterior uveitis, compared with the TNF monoclonal antibodies infliximab and adalimumab. However, this difference was not considered sufficient enough by the American and European rheumatology organizations to recommend a treatment with these drugs over treatment with etanercept in patients with a single uveitis episode. The TNF monoclonal antibodies are recommended over etanercept for patients with frequently recurrent iritis or, in our opinion, should be preferred in patients with a previous history of severe uveitis related to HLA-B27. In our experience, which is supported by the literature, salazopyrin and methotrexate are effective in preventing uveitis flares and could be considered first in patients with disabling and recurrent uveitis, if there is no rheumatologic indication for biologics.

Adalimumab is indicated for the treatment of nonanterior noninfectious uveitis in adult patients (grade A recommendation) who have had an inadequate response to corticosteroids, in whom corticosteroid treatment is inappropriate, or when a corticosteroid sparing is necessary. Such recommendations, based on the results of the VISUAL studies, should be discussed for several reasons. First, the prednisone tapering schedule within 16 and 20 months, respectively, used in these 2 studies, is questionable; in many countries, prednisone is usually maintained for several months before withdrawal, as recommended by previous guidelines and experts. Moreover, the definition of an inadequate response (active uveitis despite the use of prednisone at 10–60 mg for ≥2 weeks) used in the VISUAL I study differs from the definition of resistance to steroids previously proposed (failure of prednisone at 1 mg/kg body weight per day used for 2 or 4 weeks). Furthermore, in the VISUAL I study, adalimumab was not more effective than the placebo in the subgroup of patients who were not using immunosuppressive agents. Finally, although contradictory data have been reported in the settings of rheumatoid arthritis and Crohn’s disease, previous studies have suggested an overall and cancer-related increase in mortality among patients with ocular inflammation treated with TNF inhibitors. Such reports still need to be evaluated over longer follow-up times.

Important, the VISUAL I and II studies were not designed to address the superiority of adalimumab over immunosuppressive agents. In our opinion, adalimumab, which has shown a rapid steroid-sparing effect in noninfectious uveitis, should be preferred in severe uveitis that requires a rapid treatment or in patients with severe side effects. Infliximab and/or adalimumab are recommended early in the management of vision-threatening uveitis in patients with Behçet disease.

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**References**


