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UVEITIS RESOURCE CENTER
An ongoing series offering different perspectives on diagnosing and managing uveitis.

REDUCING INFLAMMATION AND HALTING DISEASE PROGRESSION

A closer look at the use of anti-TNFα agents in the treatment of various forms of uveitis.

BY LUCIA SOBRIN, MD, MPH

Uveitis is the general term used to describe a group of inflammatory eye diseases that can significantly affect visual acuity. Treatments for these diseases typically aim to eliminate inflammation, avoid further tissue damage, restore lost visual acuity, and alleviate pain. Choices of treatment often depend on the location of the uveitis and can include corticosteroid eye drops and injections; immunosuppressive agents; steroidal antiinflammatory drops, pills, injections, and implants. In the past decade or so, biologic agents, such as anti–tumor necrosis factor alpha (anti-TNFα) drugs, have also found a place in treating uveitis.

Retina specialists who treat uveitis have a growing number of treatment options from which to choose and must recognize the importance of selecting regimens that are most efficient while minimizing patient burden. In an effort to help make the treatment decision process less daunting, Thomas Albini, MD, moderator of the Uveitis Resource Center, interviewed several clinicians to gain insights into their approaches to managing patients with uveitis. This print series complements videos of the interviews, found on the Uveitis Resource Center (bit.ly/RT_URC).

In this issue, Lucia Sobrin, MD, MPH, of Massachusetts Eye and Ear, talks with Dr. Albini about how anti-TNFα agents have changed the management of uveitis over the years. Dr. Sobrin's comments appear below as a short article.

The treatment of uveitis has changed in the past 10 years, namely with the emergence of biologics and more specifically with that of anti–tumor necrosis factor alpha (anti-TNFα) agents. However, not all anti-TNFα agents are equally efficacious for uveitis patients, so, for retina specialists, it is important to be well informed in order to make the best choice from all of the various available agents. This article briefly reviews the current options in the anti-TNFα drug category with a look at how they have been used in other disease states as well as in uveitis.

APPLICATIONS FOR ANTI-TNFα DRUGS

Infliximab (Remicade, Janssen Biotech) and adalimumab (Humira, AbbVie) are my go-to first-line agents as far as anti-TNFα agents, and my choice between the two is based on patient preference for administration and other related considerations. We have the most clinical evidence for the use of these two drugs, and, although no head-to-head trial has been conducted to compare them, from what we can tell in the literature they appear to be similar in efficacy.[1]

Etanercept (Enbrel, Amgen) is another anti-TNFα agent that is widely available and used often in rheumatology, but studies have shown that it is not as effective in the treatment of uveitis.[2] In fact, in some patients, it has been identified as the cause of uveitis, so we do not usually consider etanercept as an option for treating uveitis.[3,4]

Golimumab (Simponi, Janssen Biotech) and certolizumab pegol (Cimzia, UCB) are newer to the market. Both drugs have rheumatology and gastroenterology indications, and a few case reports show that they can be effective as rescue therapy for patients who do not respond well to infliximab or adalimumab.[5-9]

In general, anti-TNFα agents are reserved for patients who have a poor response to treatment with an antimetabolite. In such a situation, I may try a different drug in the class first, but I also consider switching the patient directly to an anti-TNFα drug—especially if he or she has a disease that I know responds well to this drug class (eg, Behçet disease or juvenile idiopathic arthritis [JIA] uveitis). Besides Behçet disease and JIA uveitis, anti-TNFα agents are also used successfully in patients with spondyloarthropathy (HLA–B27-associated uveitis).[10,11]

Some studies show that anti-TNFα agents work better when used with an antimetabolite such as methotrexate (various vendors),[12] while other studies show that the efficacy of anti-TNFα agents is the same when used as monotherapy.[13] I usually treat concomitantly with an antimetabolite and anti-TNFα agent when the patient has derived some benefit from the antimetabolite. Combination therapy has the advantage of potentially preventing antibody creation to the anti-TNFα agent in addition to the additional immunosuppressant power. If a patient has not shown response to the antimetabolite or has had significant side effects from it, I stop it when I start the anti-TNFα agent.

Anti-TNFα drugs are also my next go-to agent—over alternatives such as cyclosporine or an alkylating agent—for patients with Vogt-Koyanagi-Harada syndrome or sarcoid. I am not impressed with how cyclosporine works on its own, and alkylating agents come with a risk of malignancy and can affect fertility, so I will choose an anti-TNFα agent over either of these. Furthermore, I have no problem using anti-TNFα drugs in pediatric patients, as they tolerate them well.

THOUGHTS ON SAFETY

The big clinical trials in rheumatology and gastroenterology taught us quite a bit about the safety of anti-TNFα agents when used to treat adults.[14-16] They are generally safe, but we know that we need to watch out for a few things, mainly infection. The issue of malignancy is still a point of debate, even in the medical literature.[16] One review of the evidence on anti-TNFα agents for treatment of ocular inflammatory disorders concluded that TNF inhibitors may accelerate the diagnosis of cancer in the first 6 to 12 months of treatment but probably do not increase long-term cancer risk to a degree that outweighs the expected benefits of therapy.[17] The jury is still out on that one. That said, all of the potential safety concerns, even those that are not definite, are discussed with the patient.

Methotrexate has been used for 60 or 70 years, and we have many decades of good safety data that reassure us about the long-term safety of this agent in children. At present, we cannot say the same for anti-TNFα agents. However, thus far, we are not aware of any major safety issues that come up in children that are different from those discussed for adults.

CONCLUSION

The use of anti-TNFα agents for the treatment of selected cases of noninfectious uveitis has become increasingly common over the past 2 decades. There are substantial data in the literature supporting this therapy, although its use for treatment of uveitis remains off-label. Clinical trials evaluating anti-TNFα agents in uveitis have recently been completed or are ongoing, and we expect these will increase our ability to use these agents in the most efficacious and safe manner. It is important to understand and thoroughly discuss with the patient the potential side effects associated with these agents. ■

WATCH THE VIDEO

Dr. Sobrin discusses the use of anti-TNFα drugs in the management of uveitis.

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