We manage approximately 1,400 patients monthly, about half of whom are at risk for flares of inflammation, tissue damage, and vision loss associated with chronic noninfectious uveitis. Local, continuous, long-term control of inflammation helps minimize uveitis flares and mitigates noncompliance and poor toleration of systemic therapy.

When a patient presents with steroid-dependent recurrent or chronic uveitis, our first-line approach focuses on quieting the inflammation, typically achieved with corticosteroid administration. To achieve uveitis quiescence in the long run, however, we prefer a corticosteroid-sparing regimen that may involve oral NSAIDs, antimetabolites, calcineurin inhibitors, various biologics, and even alkylating agents. The decision of which therapeutic agent to use depends on various factors such as the location of uveitis, severity of intraocular inflammation, risk of permanent visual loss, underlying systemic disease, and patient compliance and tolerance of therapy.

Of course, not every patient is a candidate for steroid-sparing immunomodulatory treatment. A woman who wants to become pregnant may wish to avoid systemic medication and choose local inflammatory control with a steroid via a periocular or intraocular route. A patient with consistent unilateral uveitis without an underlying autoimmune disorder may also prefer a local approach. This is especially relevant during the COVID-19 pandemic, as some patients have shown concern about the use of immunomodulatory therapy in general. For elderly patients, those with comorbidities, or those with a history of poor tolerance or adherence to medications, avoidance of systemic immunosuppression via use of local corticosteroid therapy may be the most viable and safe option.

A REVIEW OF THERAPIES

Local therapies include injectable and implantable corticosteroids. The two triamcinolone acetonide injectable suspensions used to treat uveitis are Kenalog (Bristol-Myers Squibb) and Triesence (Alcon). Steroid implants approved by the US FDA to treat uveitis include the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan),

Two fluocinolone acetonide formulations—a newly approved one and a familiar one—offer options for long-term inflammation control.

BY STEPHEN D. ANESI, MD, FACS; AND PETER Y. CHANG, MD

CONTROLLING FLARES IN CHRONIC NONINFECTIONOUS UVEITIS
the fluocinolone acetonide intravitreal implant 0.59 mg (Retisert, Bausch + Lomb), and the fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq, EyePoint Pharmaceuticals).

In 2019, several European regulatory bodies approved or recommended for approval the fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, Alimera Sciences) as a treatment for posterior uveitis; the drug is not approved for this indication in the United States.

**FLUOCINOLONE ACETONIDE OPTIONS**

In our practice, triamcinolone and dexamethasone are used for acute flares and short-term control of uveitis. When immunomodulatory therapy fails or is not tolerated by a patient, fluocinolone acetonide intravitreal implants are an option.

**SURGICAL IMPLANT**

The fluocinolone acetonide intravitreal implant 0.59 mg is implanted surgically in the operating suite. It has been in use for 15 years, and has a rich data set supporting its efficacy.

FDA approval of the drug was based on a pair of double-masked multicenter trials. Researchers found that in patients receiving the fluocinolone acetonide intravitreal implant 0.59 mg, there was a statistically significant decrease in recurrence of uveitis in the 34-week period after implantation compared with the 34-week period before implantation. At 7 years’ follow-up, patients who were treated with the implant performed as well as those undergoing systemic therapy during the first 5 years.

The implant is not without risks. Cataract progression is certain, and cataract extraction is often performed after or even during implantation. The risk of steroid-induced glaucoma is considerable: 30% to 40% of patients eventually required incisional glaucoma surgery. There is also the risk of dislodgement of the steroid-eluting pellet, or the entire strut itself, which has been seen with earlier versions of this implant; however, the newer implants do not yet seem to have a known problem with this.

**IN-OFFICE IMPLANT**

The fluocinolone acetonide intravitreal implant 0.18 mg is designed to deliver a sustained release of therapeutic agent for up to 36 months in patients with chronic noninfectious uveitis affecting the posterior segment. The drug may be a suitable adjunctive therapy for patients with severe uveitis associated with systemic disease that has improved with immunosuppressive therapy and need additional inflammatory control for the eye.

The implant is supplied in a sterile single-dose preloaded applicator that is injected via the pars plana under local anesthetic in the office. Based on our experience, along with others involved in the initial clinical trials studying this implant for use in uveitis, we believe that the fluocinolone acetonide intravitreal implant 0.18 mg may effectively control inflammation for at least 30 to 36 months.

**CASE STUDY**

A 29-year-old woman presented with bilateral chronic pars planitis with significant macular edema and retinal vasculitis in the right eye. Baseline fluorescein angiography showed macular leakage and diffuse abnormal punctate hyperfluorescence (A). The patient intended to become pregnant, so she did not want to start systemic immunomodulatory therapy. Treatment with the fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq, EyePoint Pharmaceuticals) was initiated. Two months after the administration, resolution was observed on fluorescein angiography, and the patient reported significant improvement in visual acuity and reduction in floaters (B).

**WE BELIEVE THAT THE FLUOCINOLONE ACETONIDE INTRAVITREAL IMPLANT 0.18 MG MAY EFFECTIVELY CONTROL INFLAMMATION FOR AT LEAST 30 TO 36 MONTHS.**

(Continued on page 35)
The FDA approved the fluocinolone acetonide intravitreal implant 0.18 mg based on clinical data from two randomized, sham injection-controlled, double-masked, phase 3 clinical trials with patient follow-up for 3 years. After 6 and 12 months, both clinical trials achieved the primary efficacy endpoint of preventing recurrent uveitis flares compared with sham injection.

At year 1 in both studies, eyes treated with the implant demonstrated significantly lower rates of inflammatory flares (28% and 33%) compared with those in the control group (86% and 60%). Cataract rates in phakic eyes were higher in the implanted group (56%) compared with the sham group (23%). IOP elevation and rates of pressure-lowering surgery were similar at 1 year.

Three-year data from one of the phase 3 studies showed that fewer patients in the treatment arm demonstrated uveitis recurrence compared with those in the control arm (56% vs 93%).

For an illustration of the efficacy of this fluocinolone acetonide option, see Case Study.

**PIPELINE**

Future treatment options for chronic noninfectious posterior uveitis look promising. Among the noteworthy formulations in the pipelines are a preservative-free triamcinolone acetonide formulation delivered via suprachoroidal injection (Xipere, Clearside Biomedical) and a platform that uses plasmid encoding for the production of anti–TNF-alpha to treat noninfectious uveitis (EYS606, Eyevensys).


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