Identifying the Optimal Patient Type for RETISERT Treatment

RETISERT READY™
RETISERT® PATIENT CASE STUDY SERIES

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This supplement captures content from a roundtable discussion held in July 2018 at the American Society of Retina Specialists (ASRS) meeting in Vancouver, British Columbia, Canada.

Participants

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Participants of the roundtable are paid consultants of Bausch + Lomb.

The burden of noninfectious posterior uveitis

Noninfectious posterior uveitis imposes a burden in adults of all ages.[1] This potentially blinding condition requires vigilant treatment.[1] Noninfectious posterior uveitis can be present in patients with either systemic or strictly ocular conditions, and thus may respond differently to immunosuppressive medications.[2] Patients with noninfectious posterior uveitis, especially those with persistent disease, are at a greater risk for ocular complications if their ocular inflammation is not adequately controlled.[3]

Sunir Garg, MD: In my practice, most referral patients have noninfectious posterior uveitis. It is important to remember that unlike the more typical acute anterior uveitis, which can be resolved in 6 weeks, noninfectious posterior uveitis patients have chronic disease that is active for years, if not decades.[3,4]

Thomas Albini, MD: It has been shown that noninfectious posterior uveitic eyes have higher rates of vision-threatening complications, such as cataracts, retinal detachment, and glaucoma.[3] There is a greater risk of blindness if patients are poorly controlled.[3]

Christopher Riemann, MD: Noninfectious posterior uveitis is a chronic disease and needs a chronic, sustained level of steroid to control inflammation.

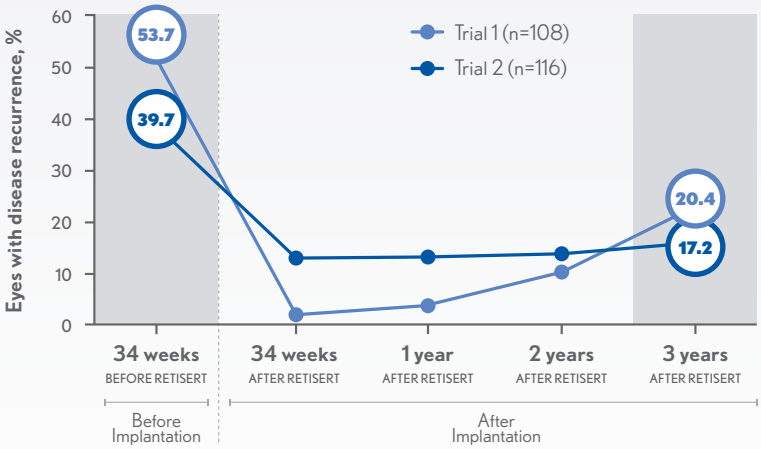
Sunir Garg, MD: We have to spend the time to educate our patients and help them understand the disease. It is important to reset the conversation and expectations, which takes time. By the time they get to us, our patients have usually seen an optometrist, a general ophthalmologist, and another retina specialist. It sometimes takes several visits to get patients to understand that we, as uveitis specialists, are going to do things differently.

Long-term control is possible with RETISERT

RETISERT 0.59 mg is a sterile implant designed to release fluocinolone acetonide locally to the posterior segment of the eye to deliver corticosteroid therapy for approximately 2.5 years where it is needed.[5]

For patients with chronic noninfectious posterior uveitis, RETISERT delivers long-term control of inflammation.[5]

Uveitis recurrence rates decreased by more than 50% with RETISERT[1]



P < .01 compared to preimplant rate at all time points

Study Design: Patients with chronic* noninfectious uveitis affecting the posterior segment of one or both eyes were randomized to receive a 0.59 mg RETISERT implant in two independent, randomized, double-masked, multicentered, controlled clinical trials. In both trials, recurrence of uveitis for all postimplantation time points was compared to the 34-week preimplantation time point.[5]

Recurrence was defined as any one of the following: 1) increase in the number of cells in the anterior chamber of ≥ 2 steps compared to baseline; 2) increase in vitreous haze of ≥ 2 steps compared with baseline; or 3) deterioration of vision of at least + 0.30 logMAR from baseline, not attributable to conditions other than noninfectious posterior uveitis.[7]

*Chronic is defined as having 1 year or greater history of disease.

Figure 1. Uveitis recurrence rates in two randomized, double-masked, multicenter clinical trials of patients with chronic* noninfectious uveitis affecting the posterior segment.

Thomas Albini, MD: The primary outcome from the pivotal trial data was uveitis recurrence rate, which showed a significant reduction after RETISERT implantation.[5] Uveitis recurrence rates decreased by more than 50% at 34 weeks, demonstrating the efficacy of RETISERT treatment (Figure 1).[5]

Christopher Riemann, MD: The reduction in uveitis recurrence with RETISERT treatment was also maintained for up to 3 years.

Thomas Albini, MD: Over the course of the study, ≥ 3 lines were gained in approximately 20% of the RETISERT-implanted eyes versus a much smaller percentage in the fellow eyes (Figure 2).[6,7]

Visual acuity improved by 3 lines in RETISERT treated eyes

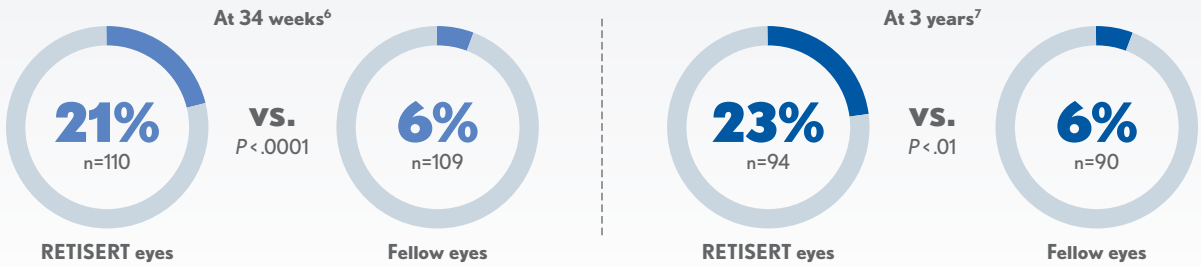


Figure 2. Percentage of patients with ≥ 3 lines improvement at 34 weeks[6] and 3 years[7] postimplantation.
Data is derived from a 3-year, prospective, dose-randomized, dose-masked trial in patients with unilateral or bilateral posterior uveitis.

Sunil Srivastava, MD: In clinical trials, greater improvement of vision was exhibited by patients with vascular leakage at baseline. The decrease in the area of macular hyperfluorescence and the proportion of eyes with reduced hyperfluorescence were significantly greater in the RETISERT-implanted eyes versus fellow eyes—25.2% versus 5.3% ($P < .001$), respectively.[6] In my experience, this has been consistent for my RETISERT-treated patients.

Sunir Garg, MD: Widefield fluorescein angiography (FA) is useful not only to establish the extent of the disease, but also to see if inflammation is reduced and quiescence is maintained.[8] Sometimes, FA reveals substantial leakage everywhere. In my experience, I tend to see low leakage in eyes that have RETISERT implantation.

Thomas Albini, MD: One major trend I have observed in the community is that patients are not consistently receiving FAs. For example, FA may be used initially to make the diagnosis, but it may not be used consistently to monitor if the patient's leakage due to inflammation is being controlled. We can miss clinically important vascular leakage without doing FA, and without repeating them, so I think they are very important.

Sunil Srivastava, MD: After 3 years following RETISERT implantation, I am following up my patients every 3 months and examining them with FA. In my clinic, our average time until reimplantation is about 4 to 4.5 years, with satisfactory vision outcomes.

Which patients may be RETISERT READY?

Thomas Albini, MD: In my experience, treatment with RETISERT has demonstrated efficacy across many different etiologies of noninfectious uveitis involving the posterior segment. In particular, RETISERT should be considered in patients with severe inflammation who require long-term control of inflammation.

Sunil Srivastava, MD: I've used RETISERT successfully in various types of noninfectious posterior uveitis patients, including those suffering from multiple sclerosis, Vogt-Koyanagi-Harada disease, sarcoidosis, and birdshot retinochoroidopathy. RETISERT can work in aggressive etiologies such as white dot syndromes and serpiginous choroiditis. Pars planitis is also very responsive to intravitreal corticosteroid therapy.

Sunir Garg, MD: In my opinion, RETISERT can be a great first-line therapy for patients with noninfectious posterior uveitis who primarily have ocular involvement. Systemic therapy makes a lot of sense for patients who have a systemic condition, like Behçet disease or ankylosing spondylitis, where multiple organ systems are involved.

Sunil Srivastava, MD: RETISERT is also a good option for noninfectious posterior uveitis patients who cannot tolerate systemic therapy or have inflammation that is not adequately controlled with systemic therapy.

Thomas Albini, MD: In my practice, I have seen patients who were on multiple agents, including oral prednisone and serial intravitreal injections, and could not tolerate systemic therapy. RETISERT should be considered in these patients who require a high level of ocular immunosuppression.

Sunil Srivastava, MD: RETISERT is an appropriate therapy to use when you need inflammatory control, especially in aggressive disease.

Important Safety Information (cont'd)

- Based on clinical trials with RETISERT®, during the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery.
- As with any surgical procedure, there is risk involved. Potential complications accompanying intraocular surgery to place RETISERT® into the vitreous cavity may include, but are not limited to, the following: cataract formation, choroidal detachment, endophthalmitis, hypotony, increased intraocular pressure, exacerbation of intraocular inflammation, retinal detachment, vitreous hemorrhage, vitreous loss, and wound dehiscence.
- Following implantation of RETISERT®, nearly all patients will experience an immediate and temporary decrease in visual acuity in the implanted eye which lasts for approximately one to four weeks post-operatively.
- Use of corticosteroids may result in elevated IOP and/or glaucoma. Based on clinical trials with RETISERT®, within 3 years post-implantation, approximately 77% of patients will require IOP lowering medications to control intraocular pressure and 37% of patients will require filtering procedures to control intraocular pressure.
- Patients should be advised to have ophthalmologic follow-up examinations of both eyes at appropriate intervals following implantation of RETISERT®. Physicians should periodically monitor the integrity of the implant by visual inspection.

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® here.

Managing patient expectations with RETISERT treatment

Christopher Riemann, MD: I tell my patients that they are very likely to get a cataract, and it is a risk that needs to be weighed for good uveitis control. I let them know that there are plenty of specialists with the skill set to remove cataracts.

Thomas Albini, MD: Cataract surgery in a uveitis patient who is not well controlled can result in poor outcomes. Thus, it is important to control inflammation prior to cataract surgery.[9]

Sunil Srivastava, MD: I tell my patients that there are trade-offs. In a worst-case scenario, treatment with RETISERT may result in essentially three surgeries in each eye, and in my experience, RETISERT surgery only takes about 20 to 25 minutes. The alternative is 3 years of systemic therapy. However, I warn my patients about the possibility of glaucoma with RETISERT treatment. Approximately 30% to 40% of my patients undergo some sort of antiglaucoma procedure, and 70% to 80% of them are going to be on some form of topical antiglaucoma drops within a year.

Christopher Riemann, MD: Validation of the patient's frustration is the first and most important step. I emphasize that we are on the same side, and then I go through the options. I give them a sense that I'm really listening to their concerns—the things they worry about. I customize a solution that is going to control their inflammation. I also acknowledge any other biological, psychological, and social concerns.

Sunil Srivastava, MD: I think being direct is what a lot of patients want. I tell them, "You're going to see me a lot, and you're going to have questions each time." I always tell them we're going to build a relationship over time. "Each time you see me, it's going to get a little easier and a little better. We'll get through this."

Adverse events that may need to be managed with RETISERT patients

- During the 3-year postimplantation period, 37% of RETISERT-implanted eyes required surgical intervention to manage elevated IOP across three trials.[5]
- Topical IOP-lowering medications were administered to approximately 77% of RETISERT-implanted eyes over 3 years.[5]
- Nearly all phakic RETISERT-implanted eyes are expected to develop cataracts and require surgery.[5]

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Important Safety Information (cont'd)

- Ocular administration of corticosteroids has been associated with delayed wound healing and perforation of the globe where there is thinning of the sclera.
- The most frequently reported ocular adverse events in clinical trials with RETISERT® occurring in 50-90% of patients included: cataract, increased intraocular pressure, procedural complications and eye pain. The most common non-ocular event reported was headache (33%).

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® here.

References: 1. Thorne JE, Suhler E, Skup M, et al. Prevalence of noninfectious uveitis in the United States: a claims-based analysis. *JAMA Ophthalmol.* 2016;134(11):1237-1245. **2.** Yeh S, Shantha JG. The burden of noninfectious uveitis of the posterior segment: a review. *Retina Today.* 2016;11(5):47-51. **3.** Dick AD, Tundia N, Sorg R, et al. Risk of ocular complications in patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis. *Ophthalmology.* 2016;123(3):655-662. **4.** Alexander KL, Dul MW, Lalle PA, et al. *Optometric Clinical Practice Guideline: Care of the Patient With Anterior Uveitis*. St Louis, MO: American Optometric Association; revised March 1999. Reviewed 2004. **5.** RETISERT [prescribing information]. **6.** Jaffe GJ, Martin D, Callanan D, et al. Fluocinolone Acetonide Uveitis Study Group. Fluocinolone acetonide implant (Retisert) for noninfectious posterior uveitis: thirty-four-week results of a multicenter randomized clinical study. *Ophthalmology.* 2006;113(6):1020-1027. **7.** Callanan DG, Jaffe GJ, Martin DF, et al. Treatment of posterior uveitis with a fluocinolone acetonide implant: three-year clinical trial results. *Arch Ophthalmol.* 2008;126(9):1191-1201. **8.** Herbort CP. Fluorescein and indocyanine green angiography for uveitis. *Middle East Afr J Ophthalmol.* 2009;16(4):168-187. **9.** Foster SC. Cataract surgery and uveitis. https://www.aao.org/current-insight/cataract-surgery-uveitis. Published 2006. Accessed August 28, 2018.

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Retisert®
(fluocinolone acetonide intravitreal implant) 0.59 mg