Providing Inflammatory Control in a Patient With Birdshot Chorioretinopathy

**Case Report: Birdshot Chorioretinopathy**

**BACKGROUND:** A 54-year-old man presented with complaints of episodic blurry vision lasting up to 5 minutes. The blurry episodes oscillated in severity and had been occurring for a few months. The most recent episode had lasted for 10 minutes. He also experienced photophobia in both eyes, with greater frequency in the left eye. The patient’s prior medical history included prostate cancer, acute lymphocytic leukemia, hypertension, chronic anxiety, and fibromyalgia, which were all medically managed as appropriate. He had no other prior history of ocular disease.

**Indication**

RETISERT® (fluocinolone acetonide intravitreal implant) 0.59 mg is a corticosteroid indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

**Important Safety Information**

- Surgical placement of RETISERT® (fluocinolone acetonide intravitreal implant) 0.59 mg is contraindicated in active viral, bacterial, mycobacterial or fungal infections of the eye.

Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® on pages 5-7.

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March 2019 | Insert to Retina Today

**Uveitis and Sarcoidosis**

Levels were all within normal limits, and the fluorescent treponemal antibody absorption test was negative, minimizing the possibility of infectious etiology. Furthermore, red-free fundus photography showed bright spots among the retinal vasculature, consistent with the yellow lesions observed in the fundus photos (Figure 1C, D). FA revealed window defects corresponding to atrophic areas in the nasal retina of both eyes and optic nerve head leakage in the left eye (Figure 2). His complete blood count, comprehensive metabolic panel, chest x-ray, and angiotensin converting enzyme levels were all within normal limits, and the fluorescent treponemal antibody absorption test was negative, minimizing the possibility of infectious uveitis and sarcoidosis.1,2 Additionally, his blood test results revealed that he was positive for HLA-A29. Based on these clinical evaluations, the patient was diagnosed with BCR.

**TREATMENT**

Like many BCR patients, the patient was given a steroid-sparring IMT to control inflammation and preserve visual function.3 OCT imaging after 1 year of IMT revealed a prominent epiretinal membrane (ERM) in the right eye and a small ERM in the left eye, consistent with late structural complications observed in BCR (Figure 3).4 Both eyes also exhibited inner retinal irregularities (Figure 3). Fundus photography taken around the time of ERM surgery (Figure 4). Despite these improvements, the patient had continued to experience visual symptoms, and his VA was 20/50 in the right eye and 20/40 in the left eye. Although the patient’s inflammation was well-controlled, he was unable to tolerate the IMT due to side effects. It is generally accepted that some systemic IMT agents conventionally used to treat uveitis have the potential to cause side effects.5

**WHY RETISERT?**

As a corticosteroid implant indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye, RETISERT is a viable alternative for patients with BCR who are unable to tolerate systemic corticosteroids or IMTs.6 The patient was counselled on the risks and benefits of RETISERT, including cataract development and IOP elevation, and elected to receive bilateral RETISERT implants.

**FOLLOW-UP**

The patient was advised again that nearly all phakic RETISERT-implanted eyes are expected to develop cataracts and require surgery.7 The patient was also counseled about the possibility of IOP elevation, which may require management. In clinical trials, 37% of RETISERT-implanted eyes required surgical intervention to manage elevated IOP, and approximately 77% of RETISERT-implanted eyes required topical IOP-lowering medications.8 The patient developed bilateral cataracts that required surgical removal. He also experienced IOP elevation that was initially managed through maximal tolerated medical therapy but ultimately required microincisional glaucoma surgery to control IOP levels.

The patient’s RETISERT implants were exchanged at 44 months and 71 months postimplantation in the right and left eyes, respectively. His most recent follow-up occurred approximately 30 months following the second RETISERT implant in the left eye. The patient did not experience any flares while on RETISERT treatment and was not taking any systemic medication. His VA had improved to 20/25 in the right eye and 20/20 in the left eye, and he did not require surgery to correct his ERM. Additionally, both eyes exhibited stable visual fields and electroretinography tests. The patient was able to tolerate RETISERT treatment. Based on discussions with his physician, the patient plans to continue RETISERT therapy and receive a third RETISERT implant in each eye through an exchange surgery.

**REIMPLANTATION**

• 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, before it is reabsorbed.9

• Following depletion of fluocinolone acetonide as evidenced by recurrence of uveitis, RETISERT may be replaced.

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**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 intracocular 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 intracocular inflammation, retinal detachment, vitreous hemorrhage, vitreous loss, and wound dehiscence. Please see additional Important Safety Information throughout and full Prescribing Information for RETISERT® on pages 5-7.
Retisert®
(Fluocinolone acetonide intravitreal implant)
0.59 mg
STERILE

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RETISERT safely and effectively. See full prescribing information for RETISERT.

INDICATIONS AND USAGE
• RETISERT is a corticosteroid indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. (1)

DOSEAGE AND ADMINISTRATION
• RETISERT is surgically implanted into the posterior segment of the affected eye through a pars plana incision. (2.1)
• RETISERT is designed to release fluocinolone acetonide at a nominal initial rate of 0.6 mcg/day, decreasing over the first month to a steady state between 0.3-0.4 mcg/day and then stabilizing at a level of 0.2-0.3 mcg/day over approximately 20 months. (2.1)
• Aseptic technique should be maintained at all times prior to and during the surgical implantation procedure. (2.2)

FULL PRESCRIBING INFORMATION
• 0.59 mg fluocinolone acetonide intravitreal implant. (3)

FULL PRESCRIBING INFORMATION: CONTENTS*
• INDICATIONS AND USAGE
• DOSAGE AND ADMINISTRATION
• CONTRAINDICATIONS
• ADVERSE REACTIONS
• DOSAGE FORMS AND STRENGTHS
• CONTRAINDICATIONS

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ADVERSE REACTIONS
• Clinical Trials Experience - Non-Ocular Events
• Cataract Formation
• Increase in Intraocular Pressure
• Separation of Implant Components
• Endophthalmitis and Surgical Complications
• Conjunctival Induced Adverse Reactions

DOSAGE FORMS AND STRENGTHS
• 0.59 mg fluocinolone acetonide intravitreal implant. (3)

CONTRAINDICATIONS
• Surgical placement of RETISERT is contraindicated in active viral, bacterial, mycobacterial and fungal infections of ocular structures. (4.1)
• CabotAir Formation: Fluctus pupils are expected to develop cataracts and require cataract surgery. (5.1)
• Endophthalmitis: Late onset endophthalmitis has been observed. (5.2)
• Increase in intraocular pressure: Use of corticosteroids may result in elevated IOP and/or glaucoma. (5.3)
• IOP lowering medications were required in > 75% of patients; filtering surgeries were required in > 35% of patients. (5.3)
• Separation of implant components: Physicians should periodically monitor the integrity of the implant by visual inspection. (5.4)
• ADVERSE REACTIONS
• Ocular adverse events included conjunctival complications, and eye pain > 30%.
• The most common ocular event reported was increased visual acuity. (6.1)

Retisert® (fluocinolone acetonide intravitreal implant) 0.59 mg

Important Safety Information (cont’d)
• 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 two 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.
• 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. (33.3)

Please see additional Important Safety Information and full Prescribing Information for RETISERT® on pages 5-7.

References
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience – Ocular Events
The available safety data includes exposure to RETISERT in patients with chronic non-infectious uveitis affecting the posterior segment of one or both eyes. Patients were randomized to dosage regimens of 0.59 mg or 2.1 mg based on the standard of care at the investigator's discretion. The most frequently reported ocular adverse events were cataract, increased intraocular pressure, and conjunctival hyperemia. In a subset of patients who received the intravitreal implant, and had blood samples collected, retention of systemic fluocinolone acetonide protein in plasma was observed.

6.2 Clinical Trials Experience – Non-Ocular Events
The most frequently reported non-ocular adverse event was headache (33%). Other non-ocular adverse events occurring in approximately 5 - 9% of patients in decreasing order of incidence were ocular/conjunctival hyperemia, reduced visual acuity, glaucoma, conjunctival hemorrhage, blurred vision, abnormal sensation in the eye, eye irritation, maculopathy, vitreous floaters, hypotony, pruritus, ptosis, increased tearing, and dry eye symptoms, conjunctival hyperemia, and decreased vision. These non-ocular adverse events occurred at a rate of 5% or greater.

6.3 Nursing Mothers
There are no adequate and well-controlled studies in pregnant women. RETISERT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

11 DESCRIPTION
Fluocinolone acetonide intravitreal implant 0.59 mg is a sterile implant designed to release fluocinolone acetonide locally to the posterior segment of the eye in a 3-year period. The implant is composed of a silicone elastomer reinforced with a polyester mesh. Physicians should periodically examine the eye, examine the retina, and monitor the visual field for any persistent corneal ulceration where steroid treatment has been used.

12 CLINICAL PHARMACOLOGY
Fluocinolone acetonide is a white crystalline powder, insoluble in water, and soluble in methanol. It has a melting point of 265-266ºC. Fluocinolone acetonide is a corticosteroid with anti-inflammatory activity. It is a potent and long-acting topical corticosteroid for the treatment of patients with a history of herpes simplex requires great caution.

12.1 Mechanism of Action
Corticosteroids inhibit the inflammatory response to a variety of inciting agents and promote anti-inflammatory effects. Topically applied anti-inflammatory drugs have been shown to induce inhibitory effects on the production of inflammatory mediators such as cytokines and prostaglandins. The anti-inflammatory effect of corticosteroids is mediated by suppression of the synthesis of these inflammatory mediators. These effects are believed to be mediated by the inhibition of cyclooxygenase and lipoxygenase pathways, which result in the production of less pro-inflammatory mediators. The corticosteroids are believed to act in the posterior segment of the eye to reduce inflammation and pain.

12.2 Pharmacokinetics
Fluocinolone acetonide is a corticosteroid. It is a potent and long-acting topical corticosteroid for the treatment of patients with a history of herpes simplex requires great caution.

13 NONCLINICAL TOXICOLOGY
No acute, subacute, or subchronic toxicity studies have been performed on fluocinolone acetonide.

14 CLINICAL STUDIES
In one controlled, double-blind, multicenter clinical trial, 234 patients with chronic (a one year or greater history) non-infectious uveitis affecting the posterior segment of one or both eyes were randomized to receive a 0.3-0.4 mcg/day over approximately 30 months. The drug is applicable for the surgical treatment of patients with a history of a viral, bacterial, or fungal infection in any part of the globe where there is interference of vision.

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