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Therapeutic Options and Strategies for the Uveitis Patient

Jessica Ackert, MD

Drexel Eye Physicians, Philadelphia, PA, USA

Keywords

• Uveitis • Immunosuppression
• Fluocinolone Acetonide 0.59 mg intravitreal implant (Retisert) • Cataract
• Glaucoma • Neoplasm

Key points

- Uveitis is a potential cause of irreversible blindness, although effective therapeutic options are available.
- The Multicenter Uveitis Steroid Treatment (MUST) trial has confirmed that both the Fluocinolone Acetonide intravitreal implant (FAI) and systemic therapy with immunomodulation are associated with modest gains in vision, are effective at controlling inflammation, and are generally well tolerated.
- Systemic immunosuppression typically has few systemic side effects, but the literature is recently inconclusive regarding risk of a secondary malignancy.
- The FAI also is well tolerated and effective, although a high percentage of phakic patients develop a cataract, and most will develop elevated intraocular pressure.

INTRODUCTION

Kempen and colleagues [1,2] have reported the 2-year results of a cohort study comparing outcomes in patients with noninfectious intermediate, pan, and posterior uveitis treated with either systemic therapy or the Fluocinolone Acetonide 0.59 mg implant (FAI) (Retisert, Bausch & Lomb, Rochester, NY). Although the 2 groups had a comparable visual acuity outcome, and it is clear that implementation of best practice patterns is associated with a favorable

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E-mail address: jessica.x.ackert@gsk.com

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outcome, it is important to consider the patient and side-effect profile of both options when determining the optimal treatment course.

SIGNIFICANCE

Uveitis is a cause for visual impairment and is a potentially blinding condition. A strong need exists for evidence-based, best-practice patterns to optimize patient outcomes. Historically uveitis has been treated with a combination of systemic corticosteroids, regional corticosteroids, and systemic immunosuppression. Systemic corticosteroids are not acceptable for long-term use owing to well-described systemic side effects, although data exist that a dose of 5.0 mg to 7.5 mg may be acceptable in longer-term use [2,3]. Regional corticosteroids similarly have limitations, mainly due to a substantial side-effect rate of cataract and glaucoma and often uncertain therapeutic windows [4].

The FAI was approved by the Food and Drug Administration in 2005 for the treatment of noninfectious posterior uveitis [5] and has a duration of activity of approximately 30 months. There previously was a lack of rigorous clinical studies comparing outcomes between patients receiving primarily corticosteroids and those on systemic immunosuppression. The Multicenter Uveitis Steroid Treatment (MUST) trial was initiated in part to rigorously study the clinical outcomes of patients treated with either the FAI or systemic immunomodulation [2,6–8].

The MUST trial was designed as a comparative effectiveness trial to optimally inform physicians and patients regarding treatment choices. This study was funded by the National Eye Institute. A total of 479 eyes of 255 persons were prospectively enrolled in a randomized fashion in 1 of 23 centers [9] with the goal of understanding the effectiveness of the FAI compared with systemic immunosuppression for longer-term controls of uveitis. Change in visual acuity was the primary outcome; secondary outcomes included ophthalmologist-graded uveitis activity, patient-reported quality of life (QoL), and both local and systemic complications of uveitis or therapy.

The 2-year results were published previously [10] and reported both groups saw an improvement in visual acuity; neither treatment option was clinically superior to the other. Patients showed a modest improvement in visual acuity from baseline. Those patients randomized to the implant arm had a higher risk of cataract (80% with cataract, hazard ratio [HR] 3.3, $P<.0001$), required treatment for elevated intraocular pressure (IOP) (61%, HR 6.2, $P<.0001$), or had a glaucoma diagnosis (17%, HR 4.2, $P = .0008$).

Patients randomized to the systemic treatment arm had a trend toward a higher rate of requiring prescriptions of antibiotics for infection, although that did not meet statistical significance (0.60 vs 0.36/person-year, $P = .034$). Both groups had low rates of systemic complications. Additionally, there was a slight tendency toward better QoL scores in the implant group, although not a statistically significant difference.

In terms of uveitis control, most patients with active uveitis in both groups were controlled by 9 months, although patients in the implant arm had a higher

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