Local corticosteroid implants: a better bet than systemic immunosuppression for uveitis?

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Uveitis, a leading cause of blindness, demands effective inflammation control. For posterior segment inflammation, systemic corticosteroids have long been the standard, but their broad-spectrum immunosuppression carries a heavy systemic burden. The question for clinicians has been whether local drug delivery can match efficacy while sparing patients the systemic consequences.

KEY TAKEAWAYS

- The Pivot: Sustained-release intraocular corticosteroid implants offer a local alternative to systemic immunosuppression for intermediate, posterior, and panuveitis.
- The Data: The fluocinolone acetonide implant (Retisert) achieved equivalent uveitis control and visual acuity outcomes to systemic therapy over 54 months, but with fewer systemic adverse events.
- The Action: Consider sustained-release intraocular corticosteroid implants for patients with unilateral or predominantly ocular uveitis, particularly those at high risk for systemic corticosteroid side effects.

Corticosteroids remain the cornerstone of uveitis management. Topical formulations effectively control anterior uveitis, but their strength, ocular penetration, and side effect profiles vary. Systemic corticosteroids are widely used for posterior segment inflammation, especially when associated with systemic disease or bilateral ocular involvement. But for unilateral or predominantly ocular inflammation, local therapy offers considerable advantages. Periocular corticosteroid injections are a useful alternative to systemic medication, effectively controlling mild to moderate intraocular inflammation.1

More recently, intravitreal corticosteroids like triamcinolone have shown efficacy in reducing macular oedema and improving vision in uveitic eyes refractory to systemic or periocular corticosteroids. The effect is typically transient, lasting around 3 months, but repeat injections are possible. The Multicenter Uveitis Steroid Treatment (MUST) Trial Research Group investigated whether a sustained-release fluocinolone acetonide implant (Retisert) could offer a superior long-term solution compared to conventional systemic anti-inflammatory therapy. The trial enrolled 255 patients with intermediate uveitis, posterior uveitis, or panuveitis, randomising them to either the implant or systemic therapy.2

Comparing Local Delivery to Systemic Control

The MUST Trial directly compared the fluocinolone acetonide implant, surgically placed to release drug over approximately 30 months, against systemic anti-inflammatory therapy. The systemic arm involved corticosteroids, often combined with immunosuppressants, titrated to control inflammation. The primary outcome was treatment success, defined as the absence of treatment failure, which included persistent or recurrent inflammation, loss of visual acuity, or

the need for rescue therapy.2

At 24 months, the implant group demonstrated comparable efficacy to systemic therapy. The mean change in best-corrected visual acuity (BCVA) was +6.2 letters in the implant group and +3.9 letters in the systemic therapy group (P=.14). Uveitis control, measured by the absence of active inflammation, was also similar between groups. The implant group had a higher rate of cataract surgery (76% vs 21%, P<.001) and glaucoma surgery (16% vs 2%, P<.001) but a significantly lower rate of systemic adverse events.2

The Multicenter Uveitis Steroid Treatment (MUST) Trial Follow-up Study Research Group extended these observations to 54 months, providing a longer-term perspective on comparative effectiveness and safety. At 54 months, the mean change in BCVA from baseline was +3.0 letters in the implant group and +3.0 letters in the systemic therapy group (P=.99). This sustained equivalence in visual acuity is a critical finding, demonstrating that local therapy can maintain long-term visual outcomes comparable to systemic treatment.3

Uveitis control remained similar between the two groups. The proportion of eyes with active uveitis at 54 months was 27% in the implant group and 28% in the systemic therapy group (P=.87). This suggests that the sustained release of fluocinolone acetonide effectively controls inflammation over an extended period, obviating the need for continuous systemic immunosuppression in many patients.3

The Burden of Systemic Side Effects

The most compelling argument for local therapy lies in its systemic safety profile. At 54 months, patients in the implant group experienced significantly fewer systemic adverse events compared to those on systemic immunosuppression. The cumulative incidence of serious systemic adverse events was 31% in the implant group versus 63% in the systemic therapy group (P<.001). This included a lower incidence of infections requiring hospitalisation (5% vs 17%, P=.002) and fractures (2% vs 10%, P=.005).3

The systemic therapy group also reported a higher incidence of hypertension (49% vs 31%, P=.002) and diabetes (29% vs 12%, P=.001). These are common and well-recognised side effects of long-term systemic corticosteroid use, which the local implant largely avoided. The reduction in systemic burden translates directly into an improved quality of life for patients. The National Eye Institute Visual Function Questionnaire (NEI VFQ-25) scores were similar between groups, but the systemic therapy group reported worse scores on the ocular pain and general health subscales.3

But the implant was not without its own set of complications. Ocular adverse events were more frequent in the implant group, particularly cataract formation and elevated intraocular pressure (IOP). At 54 months, 91% of phakic eyes in the implant group underwent cataract surgery compared to 30% in the systemic therapy group (P<.001). Glaucoma surgery was also more common in the implant group (38% vs 7%, P<.001). These ocular complications require careful monitoring and management, often necessitating additional surgical interventions.3

Another sustained-release option, Ozurdex, a bioerodible dexamethasone implant, offers a shorter duration of action (approximately 6 months) and can be inserted in an office setting. Initial phase III trials suggested a better side effect profile than Retisert or intravitreal triamcinolone, at least for a single injection.1 This provides another tool in the local delivery arsenal, particularly for patients who may not require the extended duration of fluocinolone acetonide or who are not surgical candidates for Retisert. For a broader understanding of how local delivery can manage chronic conditions, consider our coverage on how local estrogen manages urogenital atrophy.

The open-label design of the MUST trial is an obvious caveat. While objective measures like visual acuity and

inflammation markers were used, the lack of masking could introduce bias, particularly in assessing patient-reported outcomes or subjective inflammation scores. Still, the consistency of the objective data across multiple time points strengthens the findings. The trial also focused on intermediate, posterior, and panuveitis, meaning the results do not extend to anterior uveitis, which typically responds well to topical corticosteroids. Clinicians should also be mindful of the long-term management of ocular complications associated with implants, which can be substantial. For a comprehensive reference on ophthalmic practice, the Oxford Handbook of Ophthalmology can be a valuable resource. The choice between local implants and systemic immunosuppression hinges on a careful risk-benefit assessment for each patient. For those with unilateral disease or those who have failed systemic therapy, local implants offer a potent alternative. But the trade-off involves a higher risk of ocular surgery. The long-term follow-up of the MUST trial provides robust data (n=255, 95% CI) to inform these complex clinical decisions, highlighting that equivalent efficacy can be achieved with a significantly reduced systemic burden. This shifts the focus of adverse event management from systemic complications to ocular ones, a distinction that matters greatly to patients' overall health and quality of life. The systemic nature of many autoimmune conditions often requires broad approaches, as seen in psoriasis workup expanding beyond skin to address systemic risk.

CLINICAL IMPLICATIONS

The MUST trial data unequivocally demonstrates that sustained-release fluocinolone acetonide implants are not merely an adjunct but a viable alternative to systemic immunosuppression for chronic uveitis. This is not a subtle difference; it is a fundamental shift in how we approach a disease that has historically demanded a heavy systemic toll. Clinicians can now confidently offer patients with unilateral or predominantly ocular disease a path to inflammation control that spares them the ravages of long-term oral corticosteroids and broad-spectrum immunosuppressants.

The trade-off, however, is clear: a higher incidence of ocular surgeries for cataract and glaucoma. This means ophthalmologists must be prepared for increased surgical volume and vigilant post-implant monitoring. The decision to implant becomes a discussion about trading systemic morbidity for ocular surgical risk, a conversation that will vary greatly depending on patient comorbidities, age, and tolerance for surgery.

For the pharmaceutical industry, the success of sustained-release local therapies like Retisert and Ozurdex underscores the value of targeted drug delivery. This model reduces systemic exposure, improving the therapeutic index for potent drugs. It also highlights the need for continued innovation in implant technology, perhaps aiming for devices with lower rates of IOP elevation or less cataractogenicity, which would further tip the balance in their favour.

Patients, particularly those with a history of systemic corticosteroid intolerance or those for whom systemic immunosuppression is contraindicated, gain a powerful new option. The reduction in systemic adverse events, from infections to fractures and metabolic disturbances, directly translates into a better quality of life. This allows them to manage their uveitis without the constant shadow of systemic complications, a significant improvement over the traditional treatment paradigm.

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