Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

RESPONSE TO LETTER

Comment on the Review: Clarifying Steroid-Associated Glaucoma—from Association to an Actionable Closed-Loop [Response to Letter]

Rosario Izquierdo-Escamez[1], Matteo Belletti[2], Carolina Tornero[3], Otto M Olivas-Vergara[4], Diana Peiteado[3], Ester Carreño[3]

[1]Department of Ophthalmology, Hospital Universitario de Torrevieja, Alicante, Spain; [2]Department of Ophthalmology, Hospital Universitario La Paz, Madrid, Spain; [3]Department of Rheumatology, Hospital Universitario La Paz, Madrid, Spain; [4]Department of Rheumatology, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

Correspondence: Ester Carreño, Department of Rheumatology, Hospital Universitario La Paz, P.° de la Castellana, 261, Fuencarral-El Pardo, Madrid, 28046, Spain, Email carregnito@gmail.com

Dear editor

We sincerely appreciate the interest in our review, "Safe Use of Corticosteroids in Non-Infectious Uveitis",[1] and we would like to thank the authors for their thoughtful comments, particularly regarding the critical area of surveillance for steroid-associated glaucoma.[2]

We greatly value the closed-loop surveillance algorithm you propose. We agree that incorporating objective parameters and actionable thresholds substantially enhances the translational value of the information for clinicians.

We would like to take this opportunity to offer our point of view and constructively discuss your algorithm.

We appreciate your suggestion to use the term "association" rather than "causality" when discussing glaucoma progression with intraocular pressures (IOP) within the normal range. Indeed, in the context of non-infectious uveitis (NIU) when describing the long-term findings of the MUST trial, we have used terminology that reflects a clinical grounded probability that steroid exposure, beyond and not merely IOP-related, contributes to the observed damage, based on longitudinal data.[3–6] In other words, although formal and directed association of causality requires additional prospective and evidence-based research into the underlying mechanisms, we consider the MUST clinical evidence sufficiently compelling to treat steroid as an active contributing factor when progression occurs under controlled IOP. Nonetheless, we fully agree that prospectively elucidating these mechanisms remains a key priority for future research.

About the suggested algorithm, we consider the easy-to-consult scheme remarkable. Regarding retinal nerve fiber layer (RNFL) thinning progression thresholds, in NIU it reflects a complex interplay. First, the normal age-related loss of nerve fiber, which differs among decades. Usually, patients with NIU range between 20 and 50 years old, when median RNFL loss span between 0.24 µm/year and 0.54 µm/year.[7–9] Moreover, individual factors (ie axial length, RNFL baseline thickness and RNFL region) may influence this parameter. Second, the inflammatory activity which may mask the damage and paradoxically increase RNFL thickness.[10] Third, the RNLF thinning cause by steroid-related elevated IOP.

Weighing up these aspects, in the context of a high-risk inflamed eye exposed to long-acting steroids, we agree that it is appropriate to define progression as any rate of loss exceeding the "desired level" of stability (even lower than ≤1 µm/year). Notably, accepting such a low threshold implies treating even patients with normal progression of thinning, while avoiding undertreatment of patients who require treatment.

This threshold is intended as a sensitive trigger for early intervention, prioritizing neuroprotection in a risk-laden setting and prompting re-evaluation of whether the target IOP or the drug exposure are truly safe.

We would like to highlight the value of the structural sensitivity and the intensive schedule you propose, both of which are fundamental for neuroprotection in high-risk eyes.

Received: 1 December 2025
Accepted: 15 December 2025
Published: 21 December 2025

We wish to emphasize our concern that, in practice, both visual field (VF) testing and optical coherence tomography (OCT) may yield false-negative or difficult-to-interpret results in the presence of active inflammation or sequelae such as uveitic macular oedema. For this reason, critical structural and functional assessments of progression (OCT and VF) require direct clinical evaluation that allow for a complete clinical evaluation and ensure that active inflammation is not the underlying cause of reduced visual acuity or structural deterioration.

In this setting, we would highlight the challenging role of suprachoroidal triamcinolone acetonide as an alternative local route positioning implant. While it stands as a good lower-IOP-risk option for prior steroid responders or glaucoma suspects, further studies with longer follow-up are warranted to determine whether or not this route of administration is safer than others. Also it has limited availability worldwide nowadays and requires a steeper learning curve compared to other implants and specialized equipment.

We once again appreciate your valuable contribution, which undoubtedly enriches the discussion on clinical practice guidelines and helps shift the focus from mere association towards an actionable risk-management strategy.

Data Sharing Statement

Data availability is not applicable as no new data was generated or analyzed in this communication.

Author Contributions

Conceptualization: Rosario Izquierdo-Escamez, Matteo Belletti, Carolina Tornero, Otto M. Olivas-Vergara, Diana Peiteado & Ester Carreño.

Writing – Original Draft: Matteo Belletti, Rosario Izquierdo-Escamez, Ester Carreño.

Writing – Review & Editing: Carolina Tornero, Otto M. Olivas-Vergara, Diana Peiteado, Ester Carreño.

All authors agreed to the final version of the communication accepted for publication; agreed to submit to this journal; and agreed to be accountable for the contents of this communication.

Funding

No funding was received for this communication.

Disclosure

Ester Carreño reports personal fees from Roche, Active Biotech, Santen outside the submitted work. The other authors have no relevant financial or non-financial competing interests to report.

References

1. Belletti M, Izquierdo-Escamez R, Tornero C, Olivas-Vergara O, Peiteado D, Carreño E. Safe use of corticosteroids in non-infectious uveitis. *J Inflamm Res*. 2025;18:14441–14455. doi:10.2147/JIR.S540821
2. Xu L, Chen X, Liu G. Comment on the review: clarifying steroid-associated glaucoma—from association to an actionable closed-loop [Letter]. *J Inflamm Res*. 2025;18:17073–17075. doi:10.2147/JIR.S581607
3. Kempen JH, Van Natta ML, Friedman DS, et al. Incidence and outcome of uveitic glaucoma in eyes with intermediate, posterior, or panuveitis followed up to 10 years after randomization to fluocinolone acetonide implant or systemic therapy. *Am J Ophthalmol*. 2020;219:303–316. doi:10.1016/j.ajo.2020.06.038
4. Group MUSTMTF-uSR. Quality of life and risks associated with systemic anti-inflammatory therapy versus fluocinolone acetonide intraocular implant for intermediate uveitis, posterior uveitis, or panuveitis: fifty-four-month results of the multicenter uveitis steroid treatment trial and follow-up study. *Ophthalmology*. 2015;122(10):1976–1986. doi:10.1016/j.ophtha.2015.06.043
5. Friedman DS, Holbrook JT, Ansari H, et al. Risk of elevated intraocular pressure and glaucoma in patients with uveitis: results of the multicenter uveitis steroid treatment trial. *Ophthalmology*. 2013;120(8):1571–1579. doi:10.1016/j.ophtha.2013.01.025
6. Kempen JH, Altaweel MM, Holbrook JT, et al. Association between long-lasting intravitreous fluocinolone acetonide implant vs systemic anti-inflammatory therapy and visual acuity at 7 years among patients with intermediate, posterior, or panuveitis. *JAMA*. 2017;317(19):1993–2005. doi:10.1001/jama.2017.5103
7. Maghsoudlou P, Epps SJ, Guly CM, Dick AD. Uveitis in adults: a review. *JAMA*. 2025. doi:10.1001/jama.2025.4358
8. Peng PH, Hsu SY, Wang WS, Ko ML. Age and axial length on peripapillary retinal nerve fiber layer thickness measured by optical coherence tomography in nonglaucomatous Taiwanese participants. *PLoS One*. 2017;12(6):e0179320. doi:10.1371/journal.pone.0179320

9. Mansoori T, Balakrishna N. Effect of aging on retinal nerve fiber layer thickness in normal Asian Indian eyes: a longitudinal study. *Ophthalmic Epidemiol*. 2017;24(1):24–28. doi:10.1080/09286586.2016.1255762
10. Asrani S, Moore DB, Jaffe GJ. Paradoxical changes of retinal nerve fiber layer thickness in uveitic glaucoma. *JAMA Ophthalmol*. 2014;132 (7):877–880. doi:10.1001/jamaophthalmol.2014.954