Intravitreal fluocinolone acetonide 0.19 mg (ILUVIEN ® ) in patients with non-infectious uveitis: real-world effectiveness and safety outcomes at 12 months

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Abstract

Purpose

This assessed the effectiveness of the 0.19 mg flucinolone acetonide (FAc) implant by multimodal measurements in patients with non-infectious uveitis (NIU) in a real-world setting in Spain.

Methods

A prospective study of patients who had NIU including uveitic macular oedema (UME) with ≥ 12 months follow-up was done. Exclusion criteria include infectious uveitis and uncontrolled glaucoma or ocular hypertension requiring more than 2 medications. Effectiveness was assessed using a multicomponent outcome measure that included nine outcomes, with effectiveness defined as all components being met at every timepoint. Secondary outcome measures: onset or progression of glaucoma and investigator-reported adverse events.

Results

Twenty-six eyes from 22 patients were included, with 96.2% having an indication including UME. During the 12-month study, the FAc implant was effective in 15 (57.7%) eyes, reaching effectiveness as soon as 2 weeks post-implantation. Mean best-corrected visual acuity and mean central macular thickness (CMT) were significantly improved vs. baseline at all timepoints (all comparisons \( p < 0.01 \)). During the 12-month study, markers of inflammation (anterior chamber cells and vitreous haze) also significantly declined. Factors predicting effectiveness at month 12: systemic corticosteroid dose pre-FAc, higher immunomodulatory therapy (IMT) load at baseline and thicker retinal nerve fiber layer (RNFL) at baseline (all \( p < 0.05 \)). Factors predicting failure: male, thinner RNFL at baseline and treatment ineffective at 1 month (all \( p < 0.05 \)). In parallel, corticosteroid and IMT use also declined significantly. No significant increases in IOP.

Conclusion

The FAc implant is safe and effective at treating NIU over 12 months in a real-world setting in Spain.

Introduction

Non-infectious uveitis (NIU) is a clinically heterogenous group of inflammatory disorders of the eye responsible for ~15% of adult visual disability in the developed world[1]. Often affecting individuals of working age, NIU is associated with a substantial socioeconomic impact in terms of both direct (e.g., clinic visits, treatment) and indirect costs (e.g., productivity loss due to impaired vision)[1][2]. Currently, in the absence of a curative therapy, patients with NIU often require long-term care to manage the condition.

Macular oedema (ME) – defined as macular thickening due to fluid accumulation – is a complication of uveitis. It is a leading cause of visual impairment (quantity and quality loss of central vision)[3][4] which is found in approximately 40–44% of patients with uveitis[5][6]. ME is the results from the breakdown of the outer and/or inner blood-retina barrier(s) caused by inflammatory mediators[4].

Despite progress in recent years, the pathophysiological mechanisms behind NIU and associated ME (termed uveitic macular oedema [UME]) are poorly understood, yet are known to be dependent on an array of inflammatory pathways[7][8]. Chronic inflammation leads to structural and functional changes within the eye, cumulative ocular tissue damage and, ultimately, visual impairment[8][9].

Targeting and controlling chronic inflammation in NIU is the basis for current treatment approaches[8]. Disease-modifying anti-rheumatic drugs (DMARDs), topical and periocular corticosteroids are used in the treatment of NIU with variable success rates and heterogeneous side effects[10][11][12]. Systemic corticosteroids can be effective but are associated with ocular side effects (glaucoma, cataracts, ocular hypertension) and, as with DMARDs, systemic side effects (hypertension, diabetes, osteoporosis, gastrointestinal disturbances, etc.) when given in moderate-high doses and/or in the long term[4][13].
A post-hoc analysis from the VISUAL-1 and VISUAL-2 studies suggested that the incidence rates of corticosteroid-related adverse events (AEs) increase systematically with corticosteroid dose[14]. And, despite systemic treatments being effective at controlling inflammation, UME can persist in 50% of patients[5].

An alternative to these approaches in NIU is the implantation of sustained-release corticosteroid implants, which minimize the risk of systemic side effects as compared with their systemic counterparts. Moreover, intravitreal treatment can be a good option when systemic immunomodulatory therapy is contraindicated (e.g., recent cancer, severe osteoporosis).

In this setting, the 0.70 mg dexamethasone implant (Ozurdex® [DEX]) is associated with a significant gain in best-corrected visual acuity (BCVA [Log minimum angle of resolution]) vs. sham injection that is maintained up to 26 weeks[15]. Additionally, greater improvements in BCVA and central macular thickness (CMT) were noted when DEX was compared with periocular triamcinolone up to 24 weeks[12]. However, UME relapses frequently after 4–6 months from DEX implantation, leading to the necessity of reinjections[16][17], cumulative structural macular damage, and unstable visual functional oscillations over time. Longer term effectiveness (up to 30 months) can be achieved with the 0.59 mg fluocinolone acetonide (FAc) implant (Retisert®), but, whilst it is licensed in the USA[18], it is not currently licensed in Europe due to the high risk of ocular complications. Ocular hypertension, glaucoma and cataract surgery have been described[19].

Conversely, the 0.19 mg FAc implant (ILLUVIEN®), which is an intravitreal, non-bioerodible implant that releases the drug steadily and continuously into the vitreous cavity for up to 3 years, is licensed in Europe for the prevention of relapse in recurrent NIU affecting the posterior segment (NIU-PS) of the eye[20].

A Phase 3, prospective study of the 0.19 mg FAc implant vs. sham injections in NIU-PS demonstrated encouraging results, including lower rates of recurrence, time to first recurrence and number of recurrences per eye and greater sustained improvements in mean change in BCVA[21].

Here, we describe the effectiveness of the 0.19 mg FAc implant by multimodal measurements in patients treated for NIU over ≥ 12 months.

**Materials and methods**

**Study design**

A prospective, 2-year study of NIU cases treated with the 0.19 mg FAc implant from November 2018 to November 2020 in a single referral uveitis unit in Spain (Clinic Hospital of Barcelona). The study was approved by the institutional review board (HCB/0440) and followed the tenets of the Declaration of Helsinki with all patients providing written informed consent.

**Patients**

Patients were included if they were ≥ 18 years, had NIU (intermediate, posterior, panuveitis or anterior-intermediate) affecting the posterior segment of the eye including macular oedema as activity criteria, had ≥ 12 months follow-up and provided informed consent. The Standardization of Uveitis Nomenclature (SUN) Working Group recommendations were used to anatomically classify and grade each case[22]. Inflammatory activity as per vitreous haze (VH) score was based on the National Eye Institute (NEI) grading scale[23]. Exclusion criteria were infectious uveitis, uncontrolled glaucoma or ocular hypertension requiring more than 2 medications, low-quality optical coherence tomography imaging (Q < 7/10), pregnant or breast-feeding women and persons with a disability.

OCT scans (spectral-domain OCT; Cirrus HD-OCT®, Carl Zeiss Meditec, California, USA) were obtained in all patients after pupillary dilation. CMT, macular volume (MV), retinal nerve fiber layer (RNFL) and vertical cup/disc ratio were determined automatically by the manufacturer’s built-on software as quantitative data.

**Outcomes**

Effectiveness was assessed at week 2 and months 1, 3, 6 and 12 using a multicomponent outcome measure, encompassing: BCVA (Log Minimum Angle of Resolution [LogMAR]) ≥ baseline; anterior chamber cells (ACC) (SUN) ≤ 0.5+; VH (NEI) ≤ 0.5+; no active chorioretinal or vascular lesions; CMT < baseline; immunomodulatory therapy score (IMTS) ≤ baseline based in Nussenblatt score[24]; oral prednisone or equivalent ≤ 7.5 mg/d; no new-onset or dosage increase in IMT; and no adjuvant intravitreal therapy
The FAc implant was defined as effective if all components were met at every timepoint; correspondingly, patients failed when any of the components were not met at any timepoint.

Secondary outcome measures were survival of FAi until the first failure and, due to a potential incomplete effect at 2 weeks, the survival of FAi until the first failure after 2 weeks of injection. Regarding safety outcomes: onset or progression of glaucoma (depends on IOP, RNFL, vertical cup/disc ratio, fundus image of optic disc and visual field testing when necessary) recorded at any timepoint, along with final evaluation by a glaucoma specialist; investigator-reported adverse events (AE) at any timepoint.

**Statistical analyses**

Statistical analyses were conducted using IBM SPSS V.28. McNemar's test was used to analyse paired categorical data; for other data, the non-parametric signed-rank test, independent mean t-test, Mann-Whitney median test for comparisons were used, as indicated along with the data. To predict treatment failure, a multivariate general estimating equations (GEE) model was applied at patient level to control for possible bias due to repeated measurements of both eye inclusion in the analysis, with logit link function, binomial distribution, and an independent correlation matrix structure. The Kaplan-Meier method was used to estimate the survival rate of FAc until failure. For all tests, p < 0.05 was considered statistically significant.

**Results**

**Patients**

A total of 26 eyes from 22 patients were included. Patient demographics and baseline characteristics are shown in Table 1. The majority of eyes (25; 96.2%) had an indication involving UME. Noteworthy, 10 (45.5%) patients suffered from an underlying condition (recent cancer, psychiatric disorders, severe osteoporosis, and gastro-duodenal perforated ulcer) limiting systemic treatment with immunomodulators, including systemic corticosteroids (SCS).

Table 1. Patient demographics and baseline characteristics
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N = 26 eyes (22 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>65.0±14.4</td>
</tr>
<tr>
<td>Range</td>
<td>33 – 90</td>
</tr>
<tr>
<td><strong>Sex, % Female</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>69.2%</td>
</tr>
<tr>
<td><strong>Underlying condition limiting systemic therapy, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (38.6%)</td>
</tr>
<tr>
<td><strong>Single functioning eye, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (15.4%)</td>
</tr>
<tr>
<td><strong>Duration of uveitis, months</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>69.5±58.4</td>
</tr>
<tr>
<td>Range</td>
<td>6–216</td>
</tr>
<tr>
<td><strong>Type of uveitis, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Anterior-intermediate uveitis</td>
<td>7 (26.9%)</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>7 (26.9%)</td>
</tr>
<tr>
<td>Posterior uveitis</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Panuveitis</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td><strong>Diagnosis of uveitis, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>BCG HLA-B27+</td>
<td>1 (3.8%)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4 (15.4%)</td>
</tr>
<tr>
<td>Sympathetic ophthalmia</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Birdshot chorioretinitis</td>
<td>3 (11.5%)</td>
</tr>
<tr>
<td>Post-surgical uveitis</td>
<td>4 (15.4%)</td>
</tr>
<tr>
<td>Tubulointerstitial nephritis and uveitis</td>
<td>1 (3.8%)</td>
</tr>
<tr>
<td>IRVAN</td>
<td>1 (3.8%)</td>
</tr>
<tr>
<td>Blau syndrome-associated uveitis</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>8 (31.0%)</td>
</tr>
<tr>
<td><strong>Endogenous uveitis, n (%)</strong></td>
<td>21 (81%)</td>
</tr>
<tr>
<td><strong>Affected bilaterally, n (%)</strong></td>
<td>17 (65.4%)</td>
</tr>
<tr>
<td><strong>Corneal thickness, µm</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>557±38.2</td>
</tr>
<tr>
<td>Range</td>
<td>485–609</td>
</tr>
<tr>
<td><strong>Prior glaucoma surgery, n (%)</strong></td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td><strong>Lens status, pseudophakic, n (%)</strong></td>
<td>23 (88.5%)</td>
</tr>
<tr>
<td><strong>Indication for FAc implant, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Central macular oedema (isolated)</td>
<td>18 (69.2%)</td>
</tr>
</tbody>
</table>
Centra macular oedema in association with:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitreous haze</td>
<td>3 (11.5%)</td>
</tr>
<tr>
<td>Optic disk swelling</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Vitreous haze + optic disk swelling</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Vitreous haze (isolated)</td>
<td>1 (3.8%)</td>
</tr>
</tbody>
</table>

BCG, bacillus Calmette-Guérin; HLA, human leukocyte antigen; FAc, fluocinolone acetonide; IRVAN, Idiopathic Retinitis, Vasculitis, Aneurysms and Neuroretinitis; SD, standard deviation

**Effectiveness**

As shown by the multicomponent endpoint, over the course of the 12-month study, the FAc implant was effective at every timepoint in 15 (57.7%) eyes, reaching effectiveness as soon as 2 weeks post-implantation. From month 1 onwards, 19 (73.1%) of eyes achieved effectiveness at every timepoint. The FAc implant was effective in a minimum of 69.2% (week 2) and maximum of 84.6% of eyes (Months 3 and 6) (Fig. 1).

Mean BCVA (LogMAR) was significantly improved vs. baseline at all timepoints (all comparisons \( p < 0.01 \); Fig. 2). Mean CMT was significantly reduced vs. baseline at all timepoints (all comparisons \( p < 0.01 \); Fig. 3A), with the greatest reduction of 72.2 µm between baseline and week 2 reaching a maximum reduction of 105.5 µm at month 6. Similarly, significant reductions vs. baseline in mean MV were noted at all timepoints (all comparisons \( p < 0.01 \); Fig. 3B).

In a categorical analysis, the percentage of patients with a preserved ellipsoid layer was found to be significantly greater than baseline (50.0%) at all timepoints from week 2 (\( p < 0.05 \)), ranging from 73.1% (week 2) to 76.9% (all other timepoints; data not shown). As assessed using SUN grading, mean ACCs were reduced vs. baseline at all timepoints, with significance reached from month 6 and maintained to month 12 (\( p < 0.05 \); Fig. 4A). ACC \( \geq 0.5 \) increased from 27% of the eyes at baseline to 23%, 23%, 19%, 11% and 8% at weeks 2, and months 1, 3, 6, and 12, respectively. Mean VH score was significantly reduced vs. baseline at all timepoints (\( p < 0.05 \); Fig. 4B). Mirroring mean ACCs results, VH \( \geq 0.5 \) decreased from 23% of the eyes at baseline to 15%, 11%, 0%, 0% and 0% at weeks 2, and months 1, 3, 6, and 12, respectively.

Eleven eyes, 42.3% failed, at least once, during the course of the study. The Kaplan-Meier curve until first failure, estimated a survival (initial efficacy) of 84.6% at 2 weeks, 69.2% at months 1, 3 and 6, and 57.7% at 12 months. However, 3 (11.5%) eyes did not meet efficacy criteria at 2 weeks, but they continued to improve, reaching efficacy at 1 month, which was maintained at all the following time points. Survival curve until first failure after 2 weeks post-FAc injection, showed 96.2% survival at 1 month, 80.8% at 3 and 6 months, whereas it declined to 69.2% at 12 months. There were 8 (30.8%) of the eyes failing, at least once, at some point from 1 month to 12 months of follow-up.

In a univariate risk analysis, a higher systemic corticosteroid dose pre-FAc, higher IMT load (Nussenblatt score) at baseline and thicker RNFL at baseline were all found to be significant predictors of FAc implant efficacy at month 12 (Fig. 5). Further, using general estimating equations (GEE) modelling, it was shown that the factors predicting treatment failure were being male, having a thinner RNFL at baseline and treatment being ineffective at 1 month (all \( p < 0.05 \)).

**Safety**

There were no significant increases in IOP at any timepoint (Fig. 6A). IOP over 21 mmHg was recorded in 5 (19.2%) of the eyes at 2 weeks, in 3 (11.5%) eyes at 1, 3 and 6 months, and in 2 (7.7%) eyes at 12 months. This IOP increase occurred in different eyes at each timepoint, and IOP was normalized by adding appropriate topical medication in all of them. No eye achieved IOP \( \geq 30 \) mmHg at any timepoint. A tendency towards an increase in use of topical IOP-lowering medications was noted over the course of the study, but none of these changes reached significance (at any timepoint; Fig. 6B). In the OCT, the mean RNFL decreased significantly vs. baseline (114.81 µm) at every timepoint of the study, declining by 7.4% and 14.9% from baseline at months 6 and 12, respectively (all \( p < 0.001 \)). The OCT-measured mean vertical cup/disc ratio significantly increased vs. baseline at each timepoint of the study, with an increasing trend to month 6 (27.5% change vs. baseline) and falling slightly at month 12 (17.5% increase vs. baseline; all \( p < 0.01 \)).
After a case-by-case evaluation by a glaucoma specialist (M.P.), including visual field testing when necessary, from baseline to month 12, true glaucomatous progression or new glaucoma onset was not recorded in any eye. One eye showed less than 80 µm of RNFL at baseline, which was maintained to 12 months follow-up. Other adverse events noted during the study were: two of cataract, one of transient post-injection subconjunctival hemorrhage, and one of transient post-injection hypotony.

**Additional therapies**

Mean IMT load (Nussenblatt Score) was significantly reduced vs. baseline at all timepoints ($p < 0.05$; Fig. 7A); this was mirrored by significant reductions in systemic corticosteroid use vs. baseline over the course of the study ($p < 0.05$ all timepoints; Fig. 7B). From week 2 to month 3, no patient received an adjuvant intravitreal injection; this rose to a mean of 0.04 injections per eye at month 6 to 0.2 injections per eye at month 12 (Fig. 7C).

**Discussion**

Using a multicomponent outcome measure, this prospective study assessed the effectiveness of the 0.19 mg FAc implant at treating a series of NIU cases from November 2018 to November 2020 at a single referral unit for uveitis in Spain (Clinic Institute of Ophthalmology, Barcelona, Spain). The composite endpoint demonstrated the 0.19 mg FAc implant to be effective in 15 (57.7%) eyes across the initial 12 months of the study, including at an initial 2-week timepoint. However, effectiveness fluctuated between timepoints (16 (69.2%) eyes at week 2 to 22 (84.6%) eyes at months 3 and 6). Safety data showed generally tolerable and non-significant changes across a variety of measures (mean IOP, mean IOP-lowering medication use, mean RNFL and mean vertical cup/disc ratio). The multicomponent outcome measure used in this study covers a broad spectrum of outcomes, which were monitored in all patients throughout the initial 12 months of this study. In our study, we used nine outcome measures to assess treatment failure. Combined, these outcome measures provide a robust assessment of the effectiveness of the FAc implant that covers inflammatory activity, therapeutic requirements, structural changes, and functional measures. Indeed, given that these outcomes are frequently recorded in the clinic, such multicomponent assessments of treatment failure could be used to provide a more complete picture of treatment effectiveness in this setting.

In the current study, we observed a rapid improvement in BCVA, which reached significance (vs. baseline) 2 weeks post-implantation and remained relatively stable over the following 12 months. A similarly rapid and sustained improvement was noted in the trial by Jaffe et al., where mean gains of ~ 4 and 7 ETDRS letters were observed after 1 and 3 months, respectively[21]. Our data are also somewhat in line with those of Battista et al., who report a steady and sustained improvement in BCVA with the FAc implant over 12 months; although, these results were only significant from month 6. However, the population included in the study by Battista et al., had posterior uveitis only with a mean ± SD duration of 8 ± 5 years (range 3–20); in the current study, included patients had uveitis of any locale with a mean ± SD duration of 5.8 ± 4.9 (range: 0.5–18) years, indicating that earlier treatment may be beneficial[25].

Functional improvements were mirrored by those associated with structural outcomes. For instance, significant reductions compared with baseline (433.5 µm) in mean CMT were noted from as early as week 2 (-72.2 µm) and sustained to month 12 (-92.4 µm). This reduction is in agreement with the data from Jaffe et al., who observed an 82.5 µm reduction over 12 months from a baseline of 368.0 ± 145.0 µm[21]. The slightly greater decrease (~ 10 µm) in our study is likely due to the baseline CMT being higher. In the study by Studsgaard et al., mean CMT at 12 months following treatment with the FAc implant was reduced by 45 µm vs. baseline (314 µm [189–459 µm]). Again, the smaller reduction can likely be accounted for by the lower baseline CMT – Studsgaard et al., report that they conventionally pre-treat patients with standard treatment prior to administering the FAc implant to reduce the NIU recurrence rate, thus accounting for the lower baseline CMT[26].

Further, the percentage of patients with a preserved ellipsoid layer was significantly greater after FAc implantation at all timepoints. Integrity of the ellipsoid layer has been defined as a marker of better visual prognosis in UME with DEX implantation[27]. However, it is not clear whether cystoid spaces in UME may result in artefacts in the ellipsoid layer analysis, mimicking a loss of its integrity and recovering after UME resolution.

In the current study, following FAc implantation, measures of inflammation (ACC, VH) gradually declined over time, which corroborates the beneficial effect of the implant at controlling underlying inflammation in NIU[21]. Further, there is a marked absence...
of inflammatory relapse in our study up to month 12; this data reflect evidence that the FAc implant reduces NIU recurrence through reductions in underlying inflammation[21]. Throughout the course of our study, IMT and SCS dosage significantly decreased from week 2, which is a clinical manifestation of the reduced levels of inflammation discussed. The data suggest that, with the FAc implant, clinicians can reduce the burden of treatment on patients. Conversely, from month 6 there was a slight increase in the requirement for IVT.

The univariate risk analysis showed that a higher systemic corticosteroid dose pre-FAc, higher IMT load at baseline and thicker RNFL at baseline to all be significant predictors of FAc implant efficacy at month 12. GEE modelling demonstrated that the factors predicting treatment failure at month 12 were being male, having a thinner RNFL at baseline and treatment being ineffective at month 1. Together, these data show potential subgroups of patients that may be more amendable to treatment with the FAc implant.

Mean IOP was stable throughout this study (i.e., change from baseline was not significant), which differs from other reports showing mean IOP increases with FAc implantation[28][21][26][29]. For instance, Studsgaard et al. report a mean IOP increase of 3 mmHg, with an absolute peak increase of 45 mmHg[26]. It is well known that inflammatory glaucoma benefits from low-dose corticosteroid therapy, which is able to better control a raised IOP, along with anti-hypertensive medications. In fact, a pivotal clinical trial of the FAc in uveitis with 36 months of follow-up found less chance of glaucoma surgery in FAc eyes versus simulated injection (sham). In two patients enrolled in the current study who had received prior surgery for glaucoma, IOP rises were negligible. These results are in agreement with a recent case report by Reddy et al., and the study by Studsgaard et al. (2 eyes), in which previous receipt of glaucoma surgery did not correspond to a higher rise in IOP[30][26].

The RNFL decreased significantly at every timepoint. Uveitis has been described as a major confounding factor in assessing the thickness of the RNFL. Patients with active inflammation have a greater RNFL thickness due to swelling of the optic nerve. Moore et al., observed in 19 non-glaucomatous active uveitic eyes that the mean global and sectorial RNFL measurements were greater than the normative 95th percentile. Moreover, in glaucomatous eyes with active or quiescent uveitis, the mean global RNFL was higher than the mean global RNFL reported in eyes with same stage of non-uveitic glaucoma[31]. Therefore, after successful control of inflammation, RNFL and other OCT measurements can be reduced as it occurred in our cohort, without meaning true glaucomatous progression. In these situations, or in cases of doubt, visual field test assessment can be a good alternative to monitor glaucomatous changes.

The strengths of the current study include use of a broad-spectrum multicomponent outcome measure to assess effectiveness. This measure covers structural, functional and inflammatory assessments (along with the need for additional treatments) as the basis for determining treatment failure. The study’s prospective design allows tailoring of the study to collect the data of interest. Further, the study was conducted in a real-world population that was reflective of care in the clinic setting. The study was limited by the relatively small number of eyes included (26 eyes); however, this is similar to some recent reports such as those from Studsgaard et al., (22 eyes) and Battista et al., (10 eyes)[25][26]. The single center design may hinder interpretation of the results in other countries/regions.

CONCLUSIONS

The 0.19 mg FAc implant is effective at 12 months of follow-up in the majority of patients treated for NIU in our clinic. A significant number of treated eyes reached a sustained functional and structural improvement from 2 weeks through 12 months after implantation as assessed by a multicomponent endpoint. No major safety concerns were raised during the course of the study.

Declarations

Funding

Funding was not received for the conduct of this study.

Acknowledgments

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Competing Interests
The authors have no relevant financial or non-financial interests to disclose.

**Authorship confirmation**

Conceptualization and data curation were performed by Aina Moll-Udina, Inés Hernanz and Victor Llorenç. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Ethics approval**

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Hospital Clinic of Barcelona (HCB/0440).

**Consent to participate**

Informed consent was obtained from all individuals participants included in the study.

**References**


Figures
Figure 1

Effectiveness of the FAC implant assessed by multicomponent outcome measure at 2 weeks to 12 months after FAC implantation (n=26).
Figure 2

Mean BCVA (LogMAR) at baseline to 12 months after FAc implantation (n=26).

p-values versus baseline using a non-parametric sigrank test; significance at p<0.05
BCVA, best-corrected visual acuity; FAc, fluocinolone acetonide; MAR, minimum angle of resolution
Figure 3

Mean CMT (A) and mean MV (B) at baseline to 12 months after Fac implantation (n=26).

p-values versus baseline using a non-parametric sign rank test; significance at p<0.05
CMT, central macular thickness; FA, fluocinolone acetonide; MV, macular volume
Figure 4

Mean ACCs (SUN grading; A) and VH (NEI scale; B) at baseline to 12 months after FAc implantation (n=26).
Figure 5

Univariate risk analysis of factors predicting treatment failure at 12 months after FAc implantation (n=26).
**Figure 6**

Mean IOP (A) and number of IOP-lowering medications (B) at baseline to 12 months after FAc implantation (n=26).

*p*-values versus baseline using non-parametric sign rank test; significance at *p*<0.05

FAc, fluocinolone acetonide; IOP, intraocular pressure
Figure 7

Mean IMT load (Nussenblatt Score; A), SCS use (B) and number of IVT (C) at baseline to 12 months after FAc implantation (n=26).