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ARTICLE

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Clinical efficacy and safety of intravitreal fluocinolone acetonide implant for the treatment of chronic diabetic macular oedema: five-year real-world results

Emilie Dobler[1]✉, Bashar Raouf Mohammed[1], Randhir Chavan[1], Peck Lin Lip[1], Arijit Mitra[1] and Bushra Mushtaq[1]

BACKGROUND/AIM: To report 5-year real-world efficacy and safety data following the treatment of chronic diabetic macular oedema (DMO) with the intravitreal 0.19 mg fluocinolone acetonide implant(ILUVIEN).
METHODS: Retrospective cohort study of 31 eyes treated with ILUVIEN for chronic DMO at a tertiary centre in Birmingham (UK). Best corrected visual acuity (BCVA) and central retinal thickness (CRT) were recorded at baseline, and then at 1-,2-,3-, and 5-years. Safety was assessed based on intraocular pressure (IOP) -lowering medication, surgery, and other complications.
RESULTS: BCVA significantly improved 1-year post-ILUVIEN (+4.2 letters, $p < 0.05$) and gradually reverted to baseline levels over the 5-year period of follow-up (+0.2 letters at year-5). A significant and sustained CRT reduction was observed throughout the 5-years. The proportion of eyes on IOP-lowering medication increased from 16% at baseline, to 70% at 5-years ($p < 0.001$) with eyes on a mean of 1.3 medications. Laser trabeculoplasty ($n = 2$), cyclodiode laser ($n = 1$), and trabeculoplasty and trabeculotomy ($n = 1$, in the same eye; 3.2%) were required for uncontrolled IOP. Other complications included endophthalmitis ($n = 1$) and vitreous haemorrhage ($n = 1$). 58% of eyes required additional intravitreal injections, with a mean 29.2 months to first injection. We observed a 69% reduction in treatment burden following treatment with ILUVIEN implant.
CONCLUSIONS: Our real-world results confirm the efficacy of the ILUVIEN implant over 5 years, with two-thirds of eyes having improved or stable visual acuity 5 years after ILUVIEN, and an overall sustained improvement in anatomical outcome. Although the rate of IOP-lowering medications use was higher than previously reported, the rate of incisional IOP-lowering surgery and other complications remained low and in keeping with rates reported in larger studies.

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INTRODUCTION

Diabetic macular oedema (DMO) is a leading cause of visual loss in young adults in developed countries. It is a multifactorial condition, which directly impairs central vision, affecting 12% of Type 1 and 28% of Type 2 diabetics within 9 years of diagnosis [1]. Its treatment used to be limited to focal/grid macular laser photocoagulation and sub-Tenon or intravitreal short-acting corticosteroid injections, such as the off-label use of triamcinolone acetonide [2, 3]. In recent years, anti-VEGF agents, such as Ranibizumab and Aflibercept, have transformed the treatment of DMO and become first-line options [4]. Nevertheless, for an estimated 40% of patients, response to anti-VEGF remains sub-optimal [5]. In such cases, intravitreal corticosteroids remain a valuable alternative pharmacological option by targeting alternative pathways to VEGF, in particular sustained-release implants of dexamethasone (Ozurdex®, Allergan Inc., Irvine, California) and fluocinolone acetonide (ILUVIEN®, Alimera Sciences Ltd.; Alpharetta GA, USA) [6–9].

ILUVIEN provides a slow-release preparation of fluocinolone acetonide 0.19 mg and is approved by regulators in the UK for the treatment of chronic DMO that is insufficiently responsive to alternative therapies in eyes with a pseudophakic lens and it offers the advantage of prolonged clinical effects lasting for up to three years [10, 11]. Its effectiveness and safety have been well established in several clinical trials, with the most common adverse effect reported being cataract formation and elevated intraocular pressure (IOP) [12, 13]. Several reports of real-world outcomes of chronic DMO treatment with ILUVIEN have been published with 3 years of follow-up reported [14–17]. To our knowledge, this is the first long-term report of real-world safety and efficacy of intravitreal ILUVIEN implant over a 5-year follow-up period in a cohort of 31 eyes at a tertiary ophthalmology centre in Birmingham, United Kingdom.

MATERIALS AND METHODS

Study design

This a retrospective study of a cohort of patients who have been treated for chronic DMO with an intravitreal ILUVIEN implant (fluocinolone acetonide 0.19 mg) over a three-year period (2014–2016) at the Birmingham and Midland Eye Centre (UK). Clinical records were used to identify patients meeting these criteria and $n = 60$ treated eyes were identified as part of this real-world cohort. No ethics committee approval was required, as this data was collected retrospectively for departmental

[1]Birmingham and Midland Eye Centre, Birmingham, UK. ✉email: emilie.dobler@gmail.com

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Table 1. Baseline characteristics of 31 eyes included in this analysis.

Baseline characteristics		Eyes ($n = 31$ from 25 patients)
Age in years, mean ± SD		67 ± 8.0
Gender, *n* (%)	Male	12 (39%)
	Female	19 (61%)
Ethnicity, *n* (%)	Asian	13 (42%)
	White	9 (29%)
	Afro-caribbean	7 (23 %)
	Mixed	2 (6%)
Diabetes type, *n* (%)	Type 1	3 (10%)
	Type 2	28 (90%)
DMO duration in years, mean ± SD		5.9 ± 3.5
BCVA (ETDRS letters)	BCVA mean ± SD	48.1 ± 16.2
	Patients with <60 letters, *n* (%)	22 (71%)
	Patients with ≥60 letters, *n* (%)	9 (29%)
Central retinal thickness, µm (mean ± SD)		477.1 ± 159.5
Prior treatment, *n* (%)	Vitrectomy	4 (13%)
	Macular/focal/grid laser	21 (68%)
	Any intravitreal therapy	30 (97%)
	Mean number of treatments ± SD	9.7 ± 6.3
	Any anti-VEGF	30 (97%)
	Mean number of treatments ± SD	8.2 ± 5.6
	Bevacizumab	24 (77%)
	Mean number of treatments ± SD	4.3 ± 2.5
	Ranibizumab	24 (77%)
	Mean number of treatments ± SD	6.0 ± 3.4
	Any intravitreal corticosteroid	18 (58%)
	Mean number of treatments ± SD	3.0 ± 2.8
	Ozurdex intravitreal implant	2 (6%)
	Mean number of treatments ± SD	1.0 ± 0.0
	Triamcinolone acetonide intravitreal injection	16 (52%)
	Mean number of treatments ± SD	3.3 ± 2.9
On IOP-lowering medication, *n* (%)		5 (16%)

clinical effectiveness purposes. This analysis was conducted in accordance with the Declaration of Helsinki and the UK's Data Protection Act. Patients gave informed consent for all investigations and treatments.

Due to the retrospective nature of this study, the COVID-19 pandemic caused some disruption to the timing of 5-year follow-up visits for patient treated in 2015. Eyes were included in the analysis only if they had documented Best-Corrected Visual Acuity (BCVA) and an Optical Coherence Tomography (OCT) scan both at baseline and at the 5-year follow-up visit (accepted from a minimum of 4.5 years following ILUVIEN implant). Data was collected from case notes, clinical letters, and Topcon OCT (3D OCT-2000; Topcon Corporation, Tokyo, Japan). BCVA was measured at the last clinic visit prior to ILUVIEN implant injection, and patients were excluded if there was any other intravitreal injection or macular laser in the interval between the last measured BCVA and ILUVIEN implant.

In order to observe the safety profile of ILUVIEN in a real-world setting, patients were included in this study regardless of any prior history of IOP steroid response, past or current IOP-lowering medication, or any diagnosis of OHT. The clinical decision to use ILUVIEN in those situations rested with the treating clinician and the patient. ILUVIEN product characteristics specify that it is contraindicated in the presence of pre-existing glaucoma.

Individual clinical decisions regarding the use and timing of any rescue intravitreal injections, macular laser, and IOP-lowering therapy following ILUVIEN rested with the clinician's judgement and the patient's informed choices.

Twenty-nine eyes were excluded as they missed 5-year follow-up data due to death ($n = 21$), discharge from clinic ($n = 2$), and loss to follow-up ($n = 6$). Therefore, 31 eyes were included in this analysis, which belonged to 25 individual patients (6 patients had both eyes included in this analysis).

BCVA was converted from Snellen visual acuity score to Early Treatment Diabetic Retinopathy Study letter score using the formula described by Gregori et al., in order to facilitate statistical analyses [18].

Study endpoints

Baseline demographic data was collected, including age, sex, ethnicity, diabetes mellitus type, duration of DMO, prior treatment (macular laser, vitrectomy, intravitreal corticosteroids, intravitreal anti-VEGF), and baseline IOP-lowering medication.

Primary outcome measures were the change from baseline in BCVA and Central Retinal Thickness (CRT) five years after starting treatment with the ILUVIEN implant.

Secondary outcome measures included the change in BCVA and CRT at 1-, 2- and 3-years post-ILUVIEN, number and type of complications following ILUVIEN, IOP-lowering treatments (number of IOP-lowering medications at 5-year follow-up visit, selective laser trabeculoplasty or cyclodiode laser treatment, incisional surgery), number and type of intravitreal injections or implants within 5 years post-ILUVIEN, and number of retinal laser photocoagulation treatments.

Statistical analyses

Statistical analyses were performed using Wilcox's signed rank paired *t*-test, with a level of $p < 0.05$ being accepted as statistically significant. Centre values are reported as mean ± standard deviation.

RESULTS

The mean follow-up period was 1867 (±122) days, which is equivalent to 5 years and 6 weeks. Two eyes (from a single patient) were missing 2- and 3- year follow-up data, and one eye was missing 1-year BCVA measurement, but as they all had adequate baseline and 5-year follow-up data, they were included in this analysis.

Baseline characteristics

Baseline characteristics are presented in Table 1. As per the UK national guidelines for treatment with ILUVIEN, all eyes were pseudophakic and had some form of prior treatment for DMO at baseline, with 97% having received prior anti-VEGF therapy, 58% having received prior intravitreal corticosteroids (intravitreal triamcinolone or intravitreal Ozurdex implant) and 68% having received prior macular laser photocoagulation. The mean interval between the last intravitreal injection and/or macular laser and ILUVIEN implant was 213 (± 289) days, with the shortest recorded interval being 54 days. No eye received Ozurdex within 6 months prior to ILUVIEN. No eye had a pre-existing diagnosis of glaucoma at baseline. Five eyes were on IOP-lowering medication at baseline, due to a diagnosis of ocular hypertension ($n = 3$) or previous steroid-related IOP elevation ($n = 2$).

BCVA

BCVA at baseline ranged from 0 to 76 letters, with a mean of 48.1 (±16) letters, which improved to 52.3 (±17) letters after one-year (a gain of +4.2 letters) before gradually reducing back down to 48.3 (±23) letters at 5 years. Compared to baseline, the difference

in BCVA at 1-year was statistically significant ($p < 0.05$), but it was not statistically significant at 2-, 3-, and 5-year follow-up.

The change in BCVA at baseline and at one, two, three, and five-year follow-up visits is shown in Fig. 1.

Five years after treatment with ILUVIEN, 13 eyes had an improved BCVA of 5 letters or more compared to baseline, 8 eyes had a similar BCVA as baseline (+/− 4 letters from baseline), and 10 eyes had a worse BCVA with a loss of 5 letters or more compared to baseline. This means that 68% of eyes had a similar or improved BCVA after 5 years when compared to baseline.

The proportion of eyes achieving a BCVA of 60 letters or more (6/18 Snellen equivalent) increased from 29% at baseline to 42% at 1-year, before reducing to 39% at 2- and 3-year, and 35% at 5-year post-ILUVIEN.

CRT

Baseline CRT ranged from 222 µm to 835 µm, with a mean of 477.1 µm (±160), which improved to 323.7 µm (±117) after 1 year (a 32% reduction), and remained stable thereafter, with a mean CRT of 310.2 µm (±116) after 5 years. The difference in CRT compared to baseline was statistically significant ($p < 0.001$) for all time points. Changes in CRT over 5 years following ILUVIEN are shown in Fig. 1.

Patients with a thicker baseline CRT (≥400 µm) had a more pronounced decrease in CRT after 1 year (−234.7 µm), which was maintained after 5 years (−257 µm), whereas there was no significant change in CRT in the group with thinner baseline CRT (<400 µm) at any timepoint. However, this was not reflected in the BCVA changes in those two groups. The group with thin baseline CRT had a statistically significant increase in BCVA at 2-years (+10.3 letters, $p < 0.05$), and the group with thick baseline CRT had a statistically significant increase in BCVA at 1-year (+5.7 letters, $p < 0.05$), although both groups had no significant change in BCVA at 5 years compared to baseline. Results are summarised in Table 2.

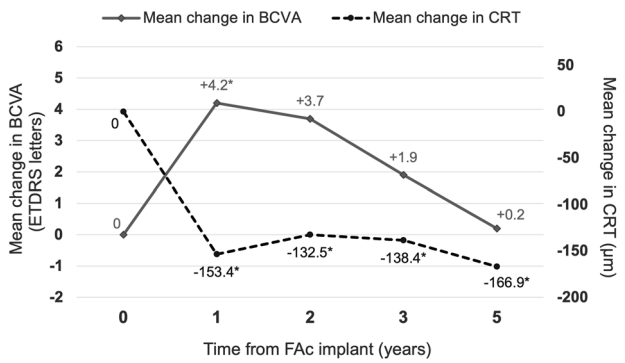

Fig. 1 Functional and anatomical outcomes over five years following ILUVIEN. Change in BCVA (ETDRS letters) and CRT (µm) over 5 years following treatment with Fluocinolone Acetonide (FAc) ILUVIEN implant. *$p < 0.05$.

Rescue therapy

After 5 years post-ILUVIEN, 42% of patients remained free of any rescue intravitreal injection. Eighteen eyes required rescue intravitreal therapy over 5 years, with a mean time to first rescue injection of 29.2 ± 14 months. Sixteen eyes received rescue anti-VEGF therapy (mean 6.4 ± 4.8 injections over 5 years), two eyes received an Ozurdex implant (mean 1.0 ± 0.0 implants over 5 years) and five eyes received a repeat ILUVIEN implant. Two eyes received intravitreal triamcinolone injections, which were given peri-operatively for epiretinal membrane surgery and retinal detachment surgery.

Eyes that did not require any rescue intravitreal injections were found to have received less macular laser at baseline than eyes that received rescue intravitreal injections (46% vs. 83%, respectively).

Two eyes received PRP laser and three eyes received macular laser over 5 years post-ILUVIEN.

Repeat ILUVIEN implant

Five eyes received one repeat ILUVIEN implant, with a mean time to repeat ILUVIEN of 38 ± 4 months. One of these five eyes suffered a rhegmatogenous retinal detachment affecting the macula 20 months after the initial ILUVIEN implant (eye number 18), which was surgically repaired, and ILUVIEN implant was removed during the vitrectomy, before receiving a second implant 41 months after the first one. This eye had a predictably poorer outcome. Mean change in BCVA from baseline is summarised in Table 3. No eye received more than one repeat ILUVIEN during this study's 5-year follow-up period.

Treatment burden

Eyes required a mean of 2.5 intravitreal injections per year prior to ILUVIEN, vs. 0.78 intravitreal injections per year in the 5 years post-ILUVIEN, representing a reduction in treatment burden of 69%.

Safety

IOP-related events. Five eyes (16%) were on IOP-lowering drops at baseline, versus 22 eyes (70%) on IOP-lowering drops at the 5-year follow-up visit. Eyes received an average of 0.2 (± 0.6) IOP-lowering topical medications at baseline, versus 1.3 (±1.1) IOP-lowering medications at the 5-year follow-up visit.

No eye had a prior diagnosis of glaucoma. The 5 eyes on IOP-lowering medication at baseline had either a diagnosis of OHT ($n = 3$) or prior steroid-response ($n = 2$). One of these eyes had poorly controlled IOP following ILUVIEN and required SLT and incisional surgery; the other four eyes continued to have well-controlled IOP on topical medication following ILUVIEN.

Over the five years following ILUVIEN, two eyes had selective laser trabeculoplasty (SLT) only, one eye had cyclodiode laser, and one eye had both SLT and incisional glaucoma surgery. As detailed above, the eye requiring SLT and incisional surgery had a prior history of ocular hypertension (OHT). The other three eyes requiring SLT or cyclodiode laser had no prior history of OHT or glaucoma, and one received a diagnosis of steroid-induced OHT, while the other two were diagnosed with OHT and glaucoma in

Table 2. Change in CRT (µm) compared to baseline for two categories of baseline CRT (<400 µm and ≥400 µm).

		Number of eyes	Change from baseline (in um) after			
			1 year	2 years	3 years	5 years
CRT ≥ 400 um	CRT	20	−234.7*	−225.4*	−239.5*	−257*
	BCVA		5.7*	1.4	2	0.3
CRT < 400 um	CRT	11	−5.5	39.9	52	−2.9
	BCVA		2	10.3*	3.3	0.2

*$p < 0.05$.

both eyes several years after ILUVIEN and were not deemed to be steroid-induced by their glaucoma specialist.

Eyes receiving repeat ILUVIEN ($n = 5$) were not found to be at any significantly increased risk of IOP-related complications, with eyes receiving a mean of 1.5 IOP-lowering medications after year-5 and 1 eye receiving SLT.

Other complications. One eye developed rubeotic glaucoma (unilateral, occurred 4 years and 2 months after treatment with ILIUVIEN), which was managed with panretinal photocoagulation and topical IOP-lowering medication.

Other significant complications included one case of endophthalmitis presenting 3 days post-ILUVIEN implant (confirmed by vitreous tap), which was treated with intensive intravitreal antibiotic therapy and made a good recovery, with a 5-year BCVA of 61 letters (vs. 55 letters at baseline); one case of vitreous haemorrhage presenting 6 days post-ILUVIEN; and one case of rhegmatogenous retinal detachment 20 months post-ILUVIEN. One patient required epiretinal membrane surgery and vitrectomy 32 months post-ILUVIEN.

Safety-related outcomes are summarised in Table 4.

DISCUSSION

This is the first report of real-world outcomes of patients over 5 years following treatment with intravitreal ILUVIEN implant for chronic DMO and it confirms the safety and efficacy of ILUVIEN demonstrated in FAME and PALADIN trials, as well as other real-world studies. Although our cohort had a lower baseline BCVA than in FAME and PALADIN studies (48.1 vs. 53.3 and 61.3 respectively), we still observed a statistically significant BCVA gain of +4.2 letters one year after ILUVIEN, which is in keeping with BCVA gains reported those studies (+4.4 letters in FAME study low-dose group after 2 years, and +3.71 in PALADIN study after 1 year), as well as in real-life studies such as the Medisoft audit study and IRISS study (+3.6 letters and +3.7 letters respectively after 1 year) [12–15]. Gains in BCVA were observed over 3 years post-ILUVIEN, although there was a gradual return to baseline BCVA at year 5, which is in keeping with the estimated duration of action of ILUVIEN of up to 3 years. The FAME, PALADIN, and Medisoft audit studies all demonstrated a sustained improvement in BCVA over three years, whereas in our small cohort we observed a peak improvement at 1-year, followed by a gradual decline towards baseline [13, 15, 19]. This could be in part due to the fact that our cohort had a higher mean baseline CRT than in FAME and Paladin studies (477 µm vs. 461 µm and 386 µm, respectively), a factor which has been shown to be associated with DMO persistence or earlier recurrence [20]. Anatomically, there was a significant improvement in CRT observed after 1 year and sustained throughout the 5-year follow-up period. Interestingly, this did not translate into sustained BCVA gains, a phenomenon which has been reported in several studies and may be attributable to other factors, such as neural and glial cell loss, disorganisation of the inner retinal layers, and macular ischaemia associated with DMO [21–23]. Further studies investigating different anatomical characteristics on OCT other than CRT and their predictive value on functional outcomes would be required, in order to better understand the differing functional responses to treatment and to better tailor individual treatment plans for different patients.

The proportion of eyes on topical IOP-lowering medication at the 5-year endpoint (70% after 5 years vs. 16% at baseline) was significantly higher than that reported in other studies: in the PALADIN study 22% of eyes were on IOP-lowering medication at year-3; in the FAME study 23.9% of eyes required treatment-emergent IOP-lowering medication over 3 years; in the IRISS study 23.3% of eyes required treatment-emergent IOP-lowering medication over 3 years; and in the Medisoft Audit study 29.7% of eye required treatment-emergent IOP-lowering medication over 2 years [13–15, 19]. Nevertheless, most eyes had well-controlled IOP on topical treatment alone, with the proportion of eyes receiving

Table 3. Change in BCVA (ETDRS letters) compared to baseline in eyes receiving no further intravitreal injections, eyes receiving repeat ILUVIEN implant (results shown including and excluding one eye which had a retinal detachment 20 months post-ILUVIEN), and eyes receiving other rescue intravitreal injections (anti-VEGF and/or Ozurdex implant).

Rescue intravitreal injection		Number of eyes	Mean change in BCVA compared to baseline (ETDRS letters)			
			1 year	2 years	3 years	5 years
None		13	+6	+5.1	+2	+3.8
ILUVIEN	Including all eyes	5	+4.6	+6.4	+4.2	−5.8
	Excluding 1 eye with retinal detachment at 20 months	4	+5.8	+14.5	+8	+1.5
Anti-VEGF and/or Ozurdex implant		13	+2.5	+1.1	+0.9	−1

Table 4. Summary of IOP-related outcomes and other significant complications occurring within 5 years following ILUVIEN.

Adverse events		Eyes ($n = 31$)	Further details
IOP-related events	On IOP-lowering medication at baseline, *n* (%)	5 (16%)	
	On IOP-lowering medication after 5 years, *n* (%)	22 (70%)	
	Number of IOP-lowering agents after 5 years, mean ± SD	1.3 ± 1.1	
	SLT laser only, *n* (%)	2 (6.5%)	
	Cyclodiode laser only, *n* (%)	1 (3%)	
	Incisional glaucoma surgery, *n* (%)	1 (3%)	Trabeculotomy
Other complications	Endophthalmitis	1 (3%)	3 days post-ILUVIEN
	Vitreous haemorrhage	1 (3%)	6 days post-ILUVIEN
	Rhegmatogenous retinal detachment	1 (3%)	20 months post-ILUVIEN
	Epiretinal membrane surgery	1 (3%)	32 months post-ILUVIEN
	Rubeotic glaucoma	1 (3%)	49 months post-ILUVIEN

trabeculoplasty alone (6.5%) and incisional IOP-lowering surgery (3.2%) over 5 years post-ILUVIEN being in keeping with rates reported in other studies (1.3% and 4.8%, respectively in FAME study over 3 years) [19]. This suggests that the majority of eyes have well-controlled IOP on topical medication alone [19]. Therefore, the higher proportion of patients we observed on IOP-lowering eye drops may not be an accurate surrogate measure for the true rate of persistent OHT and glaucoma. In a real-world busy clinical practice, patients may not be as closely monitored as in clinical trials, particularly during the covid-19 pandemic period, which limited face-to-face assessments and may have impacted the regular monitoring required for patients receiving sustained-release intravitreal corticosteroids. Clinicians may therefore have a more cautious approach, using a lower threshold to start IOP-lowering therapy than in clinical trials. We can also hypothesise that there may be less of an emphasis in real-world practice to stop IOP-lowering drops in a timely manner, even when IOP has been well-controlled for several months, and while collecting the data for this study we did observe patients remaining on IOP-lowering treatment with well-controlled IOP for several years, without an attempt to stop treatment. This may represent sub-optimal clinical practice and, moving forward will be the object of an internal departmental review to improve the care of patients receiving sustained-release corticosteroid implants. The high proportion of patients already on IOP-lowering eye drops at baseline (16%) also sets this real-world study apart from the FAME (patients with any history of glaucoma or OHT were excluded) and PALADIN studies (9.6% of patients were on IOP-lowering medication at baseline) and may have an impact on the proportion of patients on IOP-lowering drops after 5 years [13]. Nevertheless, our findings reinforce the idea that patients receiving sustained-release intravitreal corticosteroid preparations require ongoing regular monitoring of IOP. Further research would be required to investigate the true impact of ILUVIEN on IOP and data on serial IOP measurements, optic disc cupping, and visual fields may be more informative in establishing the true adverse effects of ILUVIEN.

This study demonstrates a significant reduction in the number of intravitreal treatments required following ILUVIEN, with a remarkable 69% reduction in treatment burden and nearly half of eyes remaining free of intravitreal injections for 5 years. This is comparable with the 70.5% reduction in treatment frequency reported in the PALADIN study over 3 years following treatment with ILUVIEN [13]. The reduction in treatment burden we observed translates to nearly 9 fewer injections per eye on average over the 5 years following treatment with ILUVIEN; a very positive outcome for both patients, with a reduced risk of possible injection-related infection and discomfort, and providers, with a reduction in the ever-growing demand for intravitreal injections. This may be an important consideration for ophthalmology service providers proactively planning the delivery of diabetic eye disease care, which includes the use of long-term therapies, in accordance with the Royal College of Ophthalmologists Way Forward report. Further research would be needed to establish the optimum type and timing of rescue interventions following treatment with ILUVIEN.

Our study's main strength is its long duration of follow-up in a real-world setting, including patients with previous OHT, previous vitrectomy, and where patients were reinjected with a second ILUVIEN. Potential limitations of this study include a small sample size, its retrospective nature, the lack of comparator arm, and use of IOP-lowering medication and laser/surgical intervention as a surrogate measure for IOP-related adverse events. The use of rescue treatments following ILUVIEN is also a potential confounding factor, but this study shows the long-term outcomes of real-life patients treated with ILUVIEN, for whom rescue intravitreal injections and laser treatment are commonly used adjunctive treatments.

CONCLUSION

This real-life study suggests that intravitreal ILUVIEN fluocinolone acetonide 0.19 mg sustained-release implant is a safe and effective treatment option for the treatment of chronic DMO in patients with a pseudophakic lens. We observed a significant improvement in both functional and anatomical outcomes one year after treatment, and after 5 years around two-thirds of eyes had the same or better visual acuity than at baseline, with a sustained reduction in CRT. The most commonly observed adverse effect was IOP elevation, which we found was higher than reported in other studies, although this may be due to confounding factors and the rate of serious adverse events remains low and in keeping with published literature. Larger studies are required to corroborate these findings.

Summary

What was known before

- ILUVIEN is effective for the treatment of chronic diabetic macular oedema in pseudophakic eyes with effects lasting up to 3 years.
- Main adverse effects include cataract formation in phakic eyes and intraocular pressure elevation.

What this study adds

- This real-world study confirms the efficacy of the ILUVIEN implant over 5 years, with two-thirds of eyes having improved or stable visual acuity 5 years after ILUVIEN, and an overall sustained improvement in anatomical outcome.
- Intraocular pressure elevation is a common adverse effect of ILUVIEN, but appears to be well controlled on topical therapy in this real-world setting, which includes a variety of patients, and also after repeated treatment with the ILUVIEN implant. Over 5 years following treatment with the ILUVIEN implant, the rate of serious adverse events, such as incisional IOP-lowering surgery, remains low and in keeping with rates reported in clinical trials.
- This study demonstrates a 69% reduction in intravitreal treatment frequency following treatment with the ILUVIEN implant in a real-world setting.

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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AUTHOR CONTRIBUTIONS

ED contributed to the study's planning, data collection, data analysis, creation of tables and figures, and writing of the manuscript. BM contributed to the study's conceptualisation and planning, data analysis, and critically reviewing and editing the manuscript. BRM, RC, PLL, and AM critically reviewed and edited the manuscript.

COMPETING INTERESTS

E Dobler—none. BR Mohammed—received educational travel sponsorship from Bayer and Novartis and attended educational meeting sponsored by Alimera. R Chavan–received speaker fees and travel grants from Novartis, Bayer, and Allergan. PL Lip—none. A Mitra—consultant for Roche, Novartis, Alimera Sciences, and Allergan. B Mushtaq - advisory board member and consultant for Novartis, Bayer, Allergan, and Alimera sciences.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Emilie Dobler.