Ophthalmol Ther (2023) 12:2781–2792
https://doi.org/10.1007/s40123-023-00749-2

BRIEF REPORT

Fluocinolone Acetonide Implant Injected 1 Month after Dexamethasone Implant for Diabetic Macular Oedema: the ILUVI1MOIS Study

Nicolas Rousseau · Olivier Lebreton · Hélène Masse · Yann Maucourant · Valentin Pipelart · Manon Clement · Marie-Laure Le Lez · Raoul Kanav Khanna · Maxime Pepin · Yannick Eude · Guylène Le Meur · Michel Weber · Jean-Baptiste Ducloyer

Received: May 5, 2023 / Accepted: June 2, 2023 / Published online: June 27, 2023

ABSTRACT

Introduction: The aim of this study was to assess the efficacy and safety of fluocinolone acetonide implant (FAci) injected 1 month after the last dexamethasone intravitreal implant (DEXi) in chronic diabetic macular oedema (DME) patients.

Methods: Retrospective multicentric study conducted in pseudophakic patients with chronic DME frequently treated with dexamethasone intravitreal implant (DEXi; time to DME recurrence $\leq$ 6 months), receiving FAci 1 month after the last DEXi, with at least a 6-month follow-up. Best-corrected visual acuity (BCVA), central macular thickness (CMT) on optical coherence tomography, intraocular pressure (IOP) and additional treatments were assessed on the day of FAci injection (M0), 1 (M1) and 3 months (M3) later and then every 3 months.

Results: A total of 41 eyes from 34 patients were included. At M0, patients' mean age was 68.7 ± 9.8 years, the mean DME duration was 63.9 ± 22.9 months, the mean interval between two DEXi was 14.2 ± 3.3 weeks. M12 data were available for 71% of patients. At baseline, the mean BCVA, CMT and IOP were 63.2 ± 16.6 letters, 299.4 ± 103.3 µm, and 16.2 ± 4.5 mmHg, respectively, and remained stable during the follow-up. At M12, 14% of patients required additional intravitreal treatments.

Conclusion: In pseudophakic patients with chronic DME showing good response to DEXi but requiring repeated injections every < 6 months, switching to FAci 1 month after the last DEXi was effective and safe. Further prospective randomized controlled studies are needed to confirm these findings, and to determine the best interval between the last DEXi and the first FAci.

N. Rousseau · O. Lebreton · H. Masse · M. Clement · Y. Eude · G. Le Meur · M. Weber · J.-B. Ducloyer (✉)
Nantes Université, CHU Nantes, Service d'ophtalmologie, 1 Place Alexis Ricordeau, 44093 Nantes, France
e-mail: Jean-baptiste.ducloyer@univ-nantes.fr

Y. Maucourant
Centre Hospitalier Universitaire de Rennes, Service d'ophtalmologie, Rennes, France

V. Pipelart
Centre Hospitalier Le Mans, Service d'ophtalmologie, Le Mans, France

M.-L. Le Lez
Hôpital Universitaire Bretonneau, Service d'ophtalmologie, Tours, France

R. K. Khanna
Hôpital Universitaire Bretonneau, Service d'ophtalmologie, UMR 1253, iBrain, Tours, France

M. Pepin
Centre Hospitalier Universitaire d'Angers, Service d'ophtalmologie, Angers, France

Keywords: Corticosteroid implant; Dexamethasone; Diabetes complications; Diabetic macular oedema; DME; Fluocinolone acetonide; Intravitreal injection; Retinal diseases

Key Summary Points

Why carry out this study?

Fluocinolone acetonide implant (FAci) is effective in treating chronic diabetic macular oedema (DME), and its effect lasts longer than that of dexamethasone implant (DEXi; 24–36 months versus 3–6 months, respectively).

A FAci is therefore a relevant option to reduce the burden of care in pseudophakic eyes with chronic DME requiring frequent DEXi in the absence of ocular hypertension.

But the best time to switch implants needs to be investigated since waiting for the end of the effect of DEXi could result in a visual loss and injecting both FAci and DEXi could increase the risk of ocular hypertension.

What was learned from the study?

In this retrospective multicentric study including pseudophakic patients with chronic DME treated with frequent DEXi, switching to FAci injection 1 month after the last DEXi permitted the maintenance of control of the DME and best-corrected visual acuity, while limiting the use of additional therapies, without significantly increasing the intraocular pressure (IOP).

The positive predictive value of the event "IOP > 21 mmHg" during the first 6 months of follow-up was 14.6% (6 of 41). These events were treated by local IOP-lowering monotherapy or dual-therapy eye drops. No eye had IOP > 30 mmHg, and no eye required additional triple local therapy or incisional surgery.

This study provides reassuring data and paves the way for further randomized controlled studies to determine the best interval between the last DEXi and the first FAci.

INTRODUCTION

The number of diabetic patients is expected to reach 700 million in 2050 [1]. Diabetes is the fourth cause of visual impairment in the world and the leading cause in the active population [2]. Diabetic macular oedema (DME) affects the central vision and leads to a heavy medico-economic impact due to the burden of care, especially in working populations [3]. The pathophysiology of DME is complex and involves vascular [4] and inflammatory [5] mechanisms.

Repeated intravitreal injections of anti-vascular endothelial growth factor (VEGF) is the gold standard treatment for decreased vision associated with DME [6]. Intraocular dexamethasone implant (DEXi) also plays an important role in the management of DME due to its longer duration of action (3–6 months) [7] compared with anti-VEGFs (1–2 months) [6], allowing for the the burden of care to be reduced [8]. In addition, DEXi allows a complete DME regression to be achieved in almost half of the patients 2 months after the first injection [9]. However, the use of DEXi is associated with the occurrence of ocular hypertension (OHT) in 20% of cases [10], cataracts requiring surgery in 67% of cases [6], a lack of effect on the activity of peripheral diabetic retinopathy, as well as a need for repeated injections to maintain its efficacy on DME [11]. Overall, DEXi is used as a second-line therapy in the absence of response to anti-VEGF therapy, or as a first-line therapy in patients with a significant cardiovascular history or in pseudophakic patients, especially in the absence of peripheral diabetic retinopathy.

The 0.19 mg fluocinolone acetonide implant (FAci) is the newest corticosteroid implant. This polymer device is inserted into the vitreous

cavity using a 25-gauge needle, where it releases 0.2 μg/day of FAci for up to 36 months [12, 13]. As with the DEXi, the use of a FAci is associated with the occurrence of OHT in 20% of cases [14, 15], cataracts requiring surgery in 80% of cases 12–18 months after the injection [12] and an absence of effect on diabetic retinopathy activity. According to its French Marketing Authorization, FAci is currently indicated for treatment of chronic DME as a third-line therapy [16]. In clinical practice, and in line with expert opinions [17], this indication is extended to cases treated with effective, well-tolerated DEXi injections but for which a very short injection interval is needed for three reasons: (a) the risk of OHT associated with FAci is limited in patients who did not experience OHT with DEXi [18], (b) patients with DME well controlled with DEXi (good responders) are likely to respond well to FAci [19, 20] and (c) the efficacy of FAci lasts much longer than that of DEXi and allows for less frequent intravitreal injections [21].

However, the modalities for switching from DEXi to FAci are poorly described in the literature, and it remains unknown whether FAci should be injected during or after the end of the efficacy period of DEXi (6 months after the injection). It is important to study this transition phase because the kinetics of action of FAci are slower than that of DEXi, with complete anatomical and functional efficacy reached 11 months after the injection [14]. Indeed, the visual improvement may be delayed with FAci, and 30% of patients require additional treatment during their follow-up [14], mainly during the first year [17, 18, 22]. It appears essential to optimize this transition to minimize DME variation because: (a) a visual discomfort in daily life (decreased visual acuity and metamorphopsia) directly correlates with the presence of DME; (b) the shorter the duration of DME progression is, the better the response to treatment is [14]; and (c) the long-term visual acuity is worse in the case of longer progression and greater DME variations [23].

The aim of this study was to assess the efficacy and safety of a FAci injection on chronic DME, when the FAci was injected 1 month after the last DEXi injection in patients adequately controlled with frequent DEXi injections and to confirm if an early switch permitted the maintaining of control of the DME and visual acuity, without increasing the risk of OHT.

METHODS

The ILUVI1MOIS study was a regional, multicentric, open-label, non-randomized, retrospective phase IV study involving ophthalmology departments in five French centres: the university hospitals (CHU) of Nantes, Tours, Angers and Rennes, and the hospital of Le Mans.

The study population included patients injected with a FAci in the participating centres between March 2019 and September 2021. Inclusion criteria were: being a patient with chronic DME who had been injected with a FAci 1 month after the last DEXi injection and in whom mean time to DME recurrence after DEXi was available, with a minimum follow-up $\geq$ 6 months, and who did not oppose participating in the study after oral and written information.

Data collected were: age, gender, type of diabetes, DME duration, history of panretinal photocoagulation (PRP), history of focal macular laser, number of anti-VEGF and DEXi injections received before inclusion, mean time to DME recurrence after DEXi (in weeks) and previous intraocular pressure (IOP)-lowering therapy. The following data were collected at each standardized follow-up visit: best-corrected visual acuity [BCVA, Early Treatment Diabetic Retinopathy Study (ETDRS) scale], central macular thickness (CMT; 1000 μm diameter) measured on optical coherence tomography (OCT), IOP and IOP-lowering therapy and additional treatment. For eyes requiring additional treatment during the follow-up, OCT and indocyanine green angiography (ICGA) performed prior to FAci injection were analysed, if available, to detect telangiectatic capillaries (TELCAPS) responsible for a focal component of DME. TELCAPS were considered accessible to focal argon laser treatment if they were colocated with a focal component of DME and located outside an area centred on the fovea and measuring 1500 μm in diameter.

As part of the follow-up protocol standardized in our five centres, patients treated with FAci attended the following consultations: on the day of the FAci injection (M0), 1 month (M1) and 3 months (M3) after the injection, and then every 3 months.

The study was approved by a regional ethics committee (Groupe Nantais d'Ethique dans le Domaine de la Santé – GNEDS, Decision 9,112,021) and was conducted in compliance with the Declaration of Helsinki of 1964 and its later amendments. According to the French law for retrospective studies, patients' non-opposition is sufficient to process retrospective data. All patients received information and gave oral consent to participate in the study. Quantitative data were compared using a Student's *t*-test or a Mann–Whitney U test (for parametric and non-parametric data, respectively). The positive predictive value of the event "IOP > 21 mmHg" during the first 6 months of follow-up was calculated as follows: number of eyes that experienced IOP > 21 mmHg during the first 6 months of follow-up divided by the number of eyes followed up on during the first 6 months.

RESULTS

Among the 47 patients (55 eyes) injected with FAci during the study period, 34 patients (41 eyes) were included and analysed (Fig. 1). The mean follow-up duration after the FAci injection was 13.1 ± 4.4 months (range: 6–-22 months): 29 out of 41 eyes had a 12-month follow-up, and 9 out of 41 eyes had an 18-month follow-up (Table 1).

Best-Corrected Visual Acuity

The mean BCVA was 63.2 ± 16.6 letters at M0 and was not significantly different at M1 (63.0 ± 17.5 letters), M9 (65.2 ± 14.8 letters) and M12 (62.1 ± 20.3 letters). The BCVA was significantly higher at M3 (64.3 ± 14.7 letters) and M6 (64.6 ± 15.7 letters) compared with M0 ($p = 0.0208$ and $p = 0.0377$, respectively, Fig. 2).

Central Macular Thickness

The change in mean CMT between M0 (299.4 ± 103.3 µm), M1 (283.1 ± 101.6 µm), M3 (319.3 ± 125.8 µm), M6 (328.9 ± 131.7 µm), M9 (300.9 ± 79.9 µm) and M12 (322.9 ± 123.1 µm) was always less than 10% and was never significant.

Additional Treatments

In our cohort, 29 eyes had a complete follow-up of at least 12 months. Among them, 6 eyes (20.6%) received additional treatment during this period: a DEXi injection at M6 ($n = 3$), focal laser for TELCAPS at M6 ($n = 2$) or combined focal laser and DEXi injection at M9 ($n = 1$; Fig. 3). Thus, 4 eyes (13.8%) followed for at least 12 months required additional pharmacological treatment during the first year: recent ICGA findings were available for 3 eyes, showing TELCAPS centring a focal component of the DME, accessible to focal laser treatment (at least at 750 µm from the fovea). Among the 6 eyes that required early additional treatment, 5 had TELCAPS that maintained a focal component of DME visible on ICGA prior to FAci injection, 4 had TELCAPS at a distance of at least 750 µm from the fovea and 1 had TELCAPS between 500 and 750 µm from the fovea.

Intraocular Pressure

The mean IOP at M1 (17.05 ± 5.0 mmHg), M3 (16.7 ± 4.1 mmHg), M6 (16.3 ± 3.9 mmHg), M9 (15.9 ± 4.5 mmHg) and M12 (15.6 ± 4.3 mmHg) did not significantly differ from that measured at M0 (16.2 ± 4.5 mmHg). Out of 18 eyes treated with IOL-lowering therapy at M0, 4 had a transient IOP > 21 mmHg (Table 2). Three of them had an IOP of 22 or 23 mmHg that returned to a normal value without intervention, and the fourth had an IOP of 26 mmHg because he had stopped IOP-lowering eye drops: IOP returned to a normal value on resumption of treatment. Out of 23 eyes without any IOP-lowering therapy at M0, 6 had a transient IOP > 21 mmHg: all of them were treated with local IOP-lowering

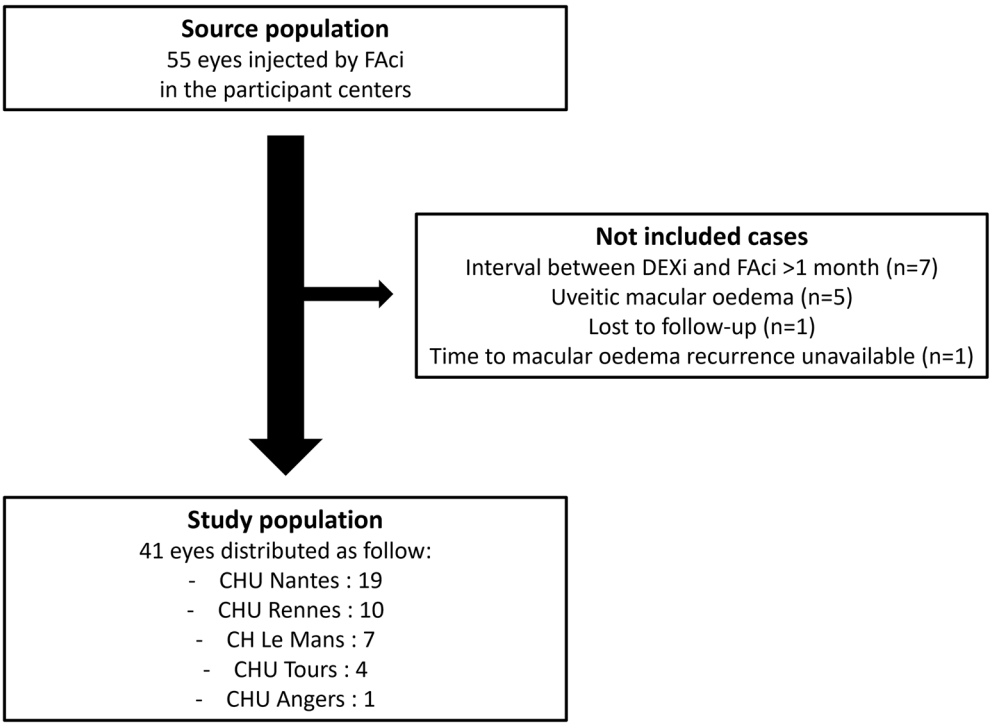


Fig. 1 Flow diagram. *DEXi* dexamethasone implant, *FAci* fluocinolone acetonide implant

monotherapy (n = 1) or dual-therapy (n = 5) eye drops. No eye had IOP > 30 mmHg during the follow-up. No eye required additional triple therapy or incisional surgery. Overall, the positive predictive value of the event "IOP > 21 mmHg" during the first 6 months of follow-up was 14.6% (6/41). Figure 4 shows the risk of an "IOP > 21 mmHg" event during a 12-month follow-up.

DISCUSSION

In patients with chronic DME requiring frequent DEXi injections, we found that injecting a FAci 1 month after the last DEXi effectively maintained stable BCVA and CMT, with a low rate of additional treatments required and minimal OHT concerns. To our knowledge, this was the first study to investigate the switch interval of 1 month between a DEXi and a FAci. Indeed, in most published large, real-life studies, the last molecule injected prior to FAci injection is usually not reported [14, 18, 21, 24, 25]. Similarly, the time between the last treatment and the injection of FAci is usually not mentioned. However, in these studies, the injection was mostly performed at the time of a recurrence of DME.

Anatomical and Functional Efficacy

Since our patients were injected with a FAci during the efficacy period of the DEXi, in the absence of DME recurrence, their BCVA and CMT were already improved at M0 and thus evolved very differently from those observed in previous studies in which the FAci was injected at the time of a recurrence of DME. The MEDISOFT study has shown a mean CMT reduction of 97 µm during the follow-up and a mean BCVA improvement of 5.3 letters at 24 months [21]. A meta-analysis has shown a mean BCVA improvement of 8.7 letters at 11.3 months and a mean CMT reduction of 184 µm (34.3%) at 16.6 months [14]. This meta-analysis has also shown a good anatomical and functional correlation (CMT reduction of at least 20% associated with a BCVA gain of at least 5 letters) in

Table 1 Baseline demographics and ocular characteristics

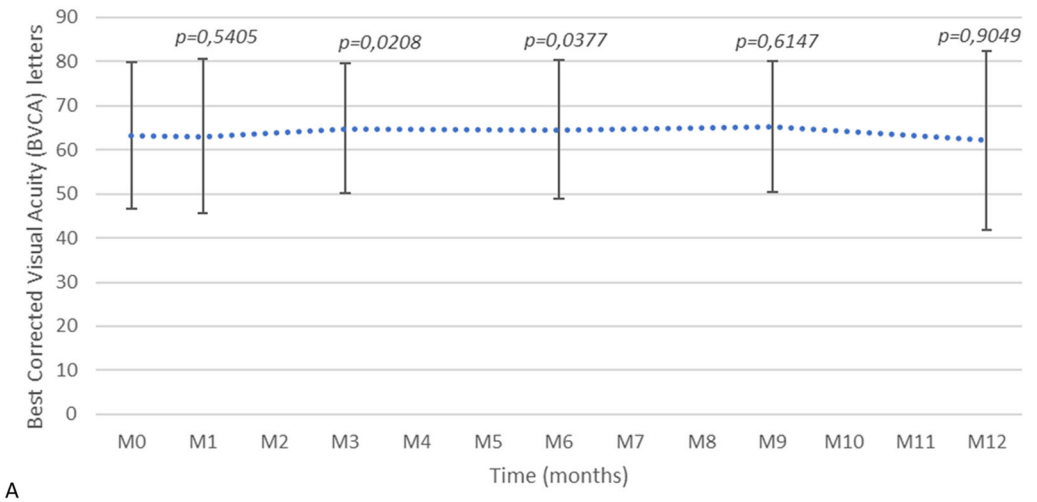
Patient characteristics	
Number of eyes (number of patients)	41 (34)
Sex	
Male	20
Female	14
Age in years, mean ± SD [range]	68.7 ± 9.8 [44; 85]
Type of diabetes	
Type 1, *n* (%)	2 (4.8)
Type 2, *n* (%)	39 (95.2)
Ocular characteristics	
Pseudophakic, *n* (%)	41 (100)
Diabetic macular oedema duration (months)	63.9 ± 22.9 [18; 120]
Panretinal photocoagulation	28 (68.3)
Macular laser therapy	9 (21.9)
Number of anti-VEGF injections per eye	7.6 ± 5.8 [0; 21]
Number of DEXi injections per eye	6.1 ± 4.5 [2; 21]
Time between two DEXi injections (weeks)	14.2 ± 3.3 [8; 24]
CMT (µm)	299.4 ± 103.3
BCVA (ETDRS letters)	63.2 ± 16.6
IOP (mmHg)	16.2 ± 4.5
IOP-lowering medications	18 (43.9)
Monotherapy	8 (19.5)
Dual therapy	7 (17.1)
Triple therapy	1 (2.4)
Incisional surgery	2 (4.8)
Follow-up duration after FAci (months)	13.1 ± 4.4 [6; 22]

BCVA best-corrected visual acuity, *CMT* central macular thickness, *ETDRS* early treatment diabetic retinopathy study, *IOP* intraocular pressure, *SD* standard deviation

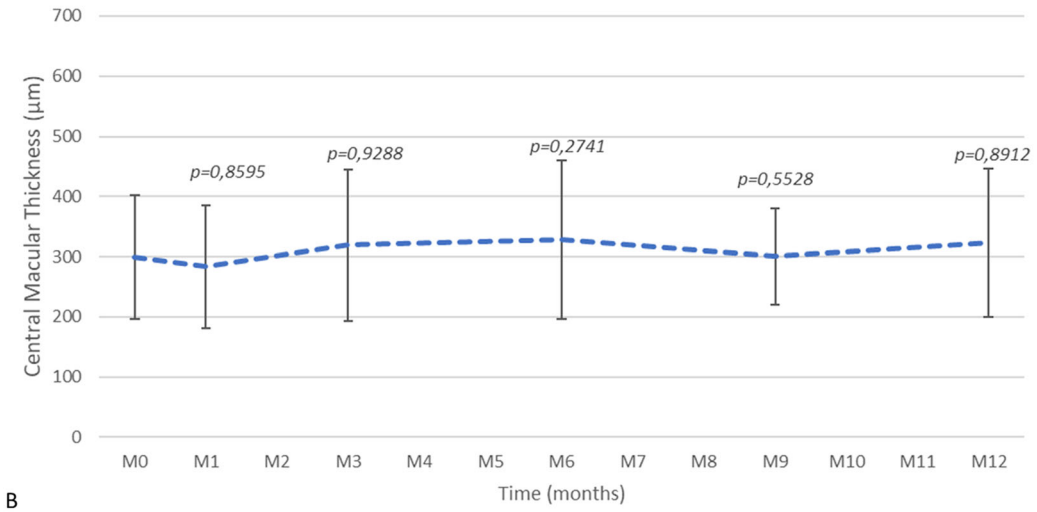
77.0% of analysed studies. In our study, the mean BCVA gain was 1.1 letter and the mean CMT change was < 10% after a 12-month follow-up. Our results are consistent with other studies if we consider the stability period following the FAci ramp-up. Indeed, the MEDISOFT study has found a mean BCVA change of only 1.0 letter between 6 and 24 months. Similarly, the PALADIN study has found a mean BCVA change of 2.1 letters and a mean CMT change < 5.0% between 6 and 18 months [18].

Additional Treatments

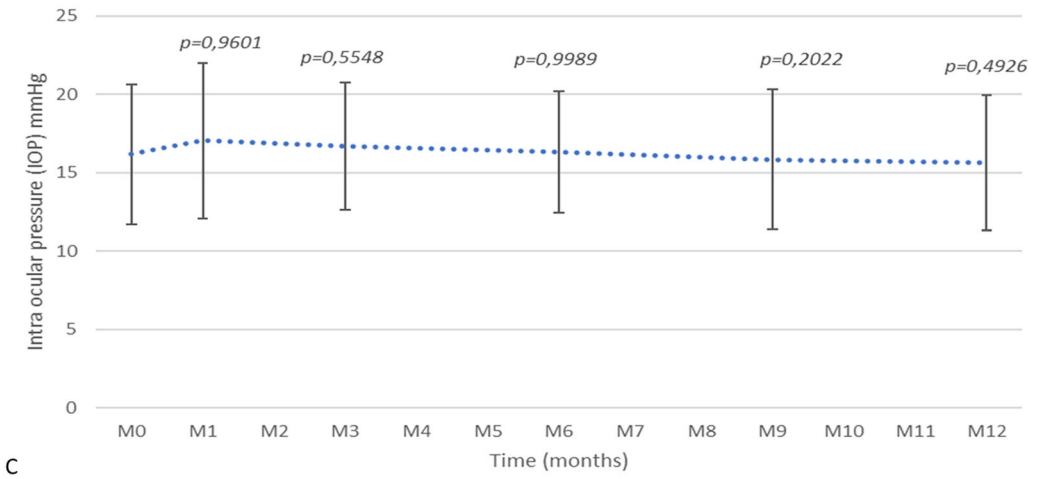
The data available in the literature on additional treatments have shown that about 30% of patients require additional treatment during their follow-up, with a mean time to retreatment of 15.4 months [14]. In the IRISS study [26], 22.4% of eyes were treated with anti-VEGF, 6.6% with DEXi and 9.6% with focal laser during the follow-up. In the MEDISOFT study [21], a retreatment rate of 35.7% was reported during the follow-up, and 32.2% of eyes were retreated with intravitreal injections (DEXi or anti-VEGF) and 6.4% with focal laser. The PALADIN study [18] has investigated the likelihood of using additional early treatment and has found that 48.1% of patients received additional treatment during the first 12 months. This is a relatively high proportion of patients, although this study has clearly shown a decrease in the number of treatments per year required after FAci compared with before FAci. In their study, Baillif et al. have found a rate of additional treatments of 32.7% during the first 12 months with a mean time to retreatment of 113.27 days [22]. In our study, only 6 out of the 29 eyes (20.9%) with a complete follow-up at 12 months required additional treatment during the first year, and only 4 eyes required additional pharmacological treatment (13.8%). A retrospective analysis of pre-FAci angiograms has found that 4 out of the 6 retreated eyes had visible TELCAPS easily accessible to laser treatment (at least at 750 µm from the fovea) and 1 had visible TELCAPS relatively close to the fovea (between 500 and 750 µm from the fovea). This finding suggests that many patients could have



A



B



C

Fig. 2 Mean best-corrected visual acuity **A**, central macular thickness **B** and intraocular pressure **C** during the 12-month follow-up after fluocinolone acetonide implant injection

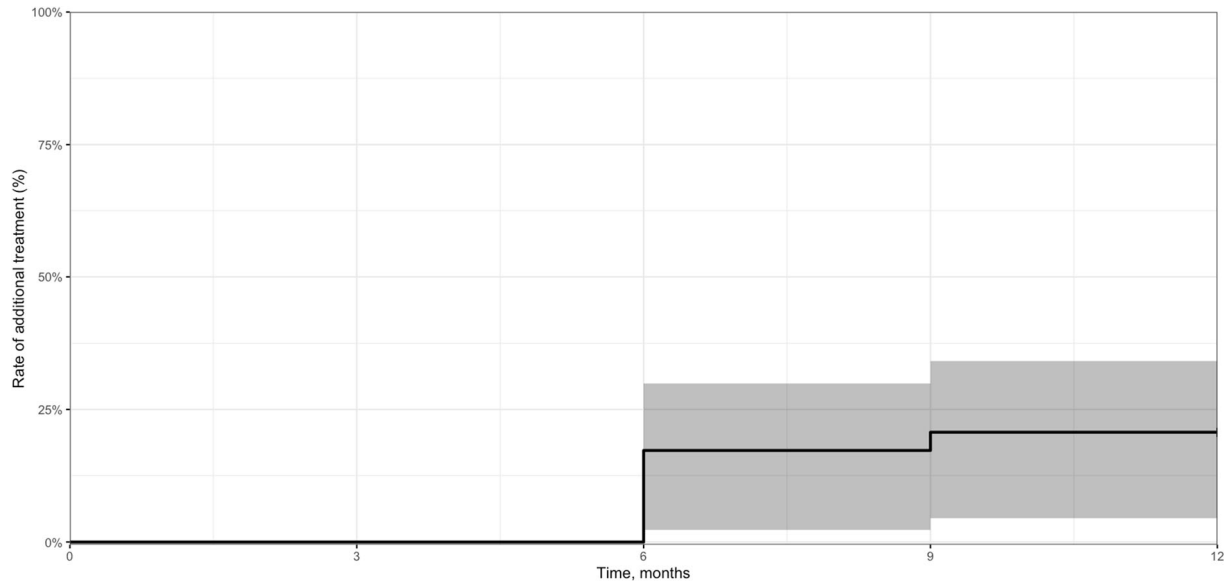


Fig. 3 Rate of additional treatment during the 12-month follow-up after fluocinolone acetonide implant injection. The 95% confidence interval is in grey. Edited with R version 1.2.5019 with the survminer package

Table 2 Distribution of eyes with ocular hypertension during follow-up

	IOP-lowering therapy at M0	No IOP-lowering therapy at M0	Total
Intraocular pressure (IOP)			
IOP > 21 and ≤ 25 mmHg	3 of 18 (16.7%)	3 of 23 (13.0%)	6 of 41 (14.6%)
IOP > 25 and ≤ 30 mmHg	1 of 18 (5.6%)	3 of 23 (13.0%)	4 of 41 (9.8%)
IOP > 30 mmHg	0	0	0 of 41 (0%)
Positive predictive value of the event "IOP > 21 mmHg" during the first 6 months of follow-up	3 of 18 (16.7%)	3 of 23 (13.0%)	6 of 41 (14.6%)

benefited from macular focal laser earlier. Further studies are needed to confirm that diagnosing and treating TELCAPS before FAci injection could decrease the need for additional treatment. Other publications support the need to diagnose and treat TELCAPS as part of the management of DME. A study has found that 63% of eyes with DME had TELCAPS on ICGA, at a median distance of 2700 μm from the fovea, and thus accessible to laser treatment in most cases [27]. Another study of chronic macular oedema (secondary to diabetes and vein occlusion) has found that 66.3% of patients had macular TELCAPS [28]. Furthermore, treating these TELCAPS allowed for the reduction of the interval between intravitreal injections [29].

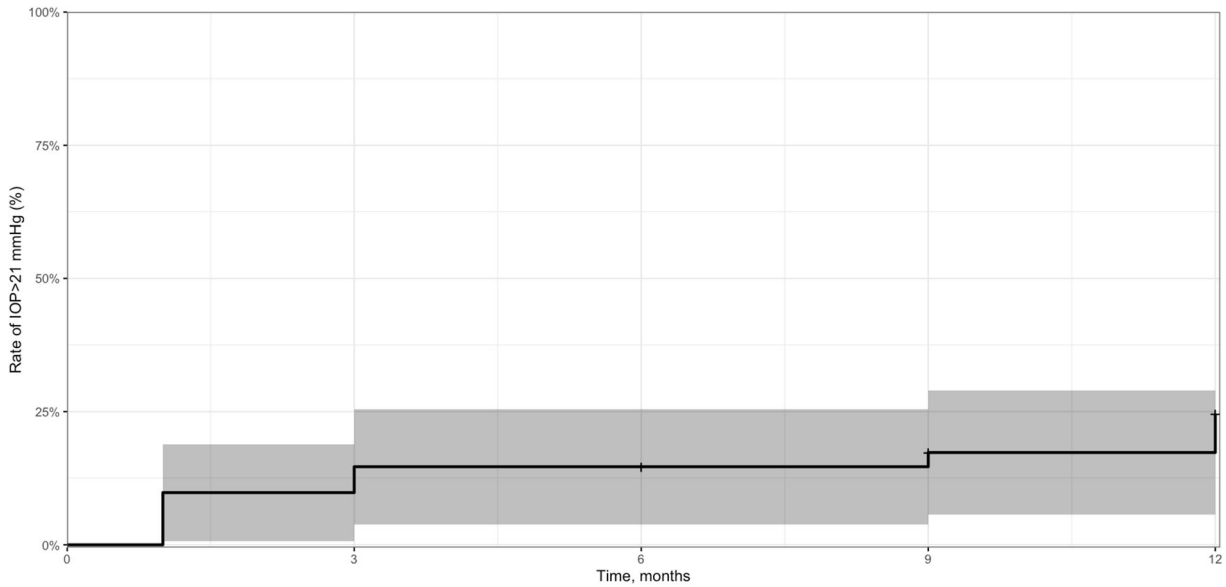


Fig. 4 Rate of the event "Intra ocular pressure (IOP) > 21 mmHg" during the 12-month follow-up after fluocinolone acetonide implant injection. The 95% confidence interval is in grey. Edited with R version 1.2.5019 with the survminer package

Intraocular Pressure

OHT concerns were remarkably low in our study. As mentioned above, no patient had OHT > 30 mmHg and no patient required triple IOP-lowering therapy nor incisional surgery. The 24% of eyes that required IOP-lowering therapy were all well controlled thereafter. Baillif et al. have found similar results [22]. Conversely, in the RETRO IDEAL study [24] conducted in 81 eyes, 12.3% of patients had an IOP peak > 30 mmHg at some point during the follow-up, and 3.7% of them required filtering surgery. In the MEDISOFT study [21], 7.2% of eyes had an IOP peak > 30 mmHg. A major difference between these two studies and our study is that a minority of patients had received a DEXi injection before injecting a FAci. Indeed, in the RETRO IDEAL study [24], only 24.1% of eyes had received a DEXi injection within the year before FAci injection. In the MEDISOFT study [21], only 32.8% of eyes had received a corticosteroid intravitreal injection before FAci injection, and the authors have pointed out that eyes that did not experience any increase in IOP under DEXi and did not experience a severe increase (> 30 mmHg) in IOP under FAci. These data suggest that it is more prudent to inject DEXi to identify patients at risk of OHT before considering injecting a FAci. Indeed, the PALADIN study [18] has shown that patients who do not experience OHT related to corticosteroids are at low risk of OHT under FAci, unlike those with a history of OHT with corticosteroids (positive predictive value of 79.6% of having an IOP < 25 mmHg after FAci injection in the absence of a history of IOP rise under corticosteroids).

Our study has several limitations. The first is the retrospective collection of data, which does not give our conclusions the same strength as a prospective study. However, the robustness of our study relies on the common decision to apply a systematized care and follow-up protocol for all patients. Similarly, the absence of a control group with a different injection interval is explained by the retrospective design of the study, the relatively small number of eligible patients, and the collegiate care protocol implemented given the scientific findings presented above. The follow-up duration was relatively short and heterogeneous, but the inclusion criterion requiring a follow-up of at least 6 months for all patients allowed the

transition period of interest to be properly investigating. Furthermore, a 12-month follow-up was available for 71% of cases (29 out of 41 eyes) and allowed relevant secondary results to be obtained.

CONCLUSION

In conclusion, in pseudophakic patients with chronic DME showing a good response to DEXi in the absence of OHT but requiring repeated injections every < 6 months, we showed the efficacy and safety of injecting a FAci 1 month after the last DEXi injection. Further prospective randomized studies are needed to confirm this result, to determine the best interval between the DEXi and FAci injections, and to confirm that diagnosing and treating TELCAPS before initiating FAci injection could further reduce the need for additional treatment.

ACKNOWLEDGEMENTS

We thank the ophthalmologists who performed the injections and followed the patients in accordance with the standardized care protocol. We thank the patients who consented to participate.

Funding. We thank Horus Pharma© for funding the English proofreading of the manuscript and publication, including the journal's Rapid Service Fee. Horus Pharma© did not fund the study itself.

Medical Writing/Editorial Assistance. We thank Sophie Pegorier (EURL Pegorier Traductions) for her careful English proofreading. This assistance was funded by Horus Pharma©.

Author Contributions. Nicolas Rousseau, Olivier Lebreton, Hélène Massé, Manon Clément, Michel Weber and Jean-Baptiste Ducloyer contributed to the study conception and design. Material preparation and data collection were performed by Nicolas Rousseau, Olivier Lebreton, Hélène Massé, Manon Clément, Yann Maucourant, Valentin Pipelart, Marie-Laure Le Lez, Raoul Khanna, Maxime Pépin, Michel Weber and Jean-Baptiste Ducloyer. Data analysis was performed by Nicolas Rousseau, Olivier Lebreton, Hélène Massé, Yannick Eude, Guylène Le Meur, Michel Weber and Jean-Baptiste Ducloyer. The first draft of the manuscript was written by Nicolas Rousseau, and all authors reviewed the previous versions of the manuscript. All authors read and approved the final manuscript.

Disclosures. Nicolas Rousseau, Olivier Lebreton, Hélène Massé, Yann Maucourant, Valentin Pipelart, Manon Clément, Marie-Laure Le Lez, Raoul Khanna, Maxime Pépin, Yannick Eude, Guylène Le Meur, Michel Weber and Jean-Baptiste Ducloyer declare they have no competing interests.

Compliance with Ethics Guidelines. The study was approved by a regional ethics committee (Groupe Nantais d'Ethique dans le Domaine de la Santé – GNEDS, Decision 9,112,021) and was conducted in compliance with the Declaration of Helsinki of 1964 and its later amendments. According to the French law for retrospective studies, patients' non-opposition is sufficient to process retrospective data. All patients received information and gave oral consent to participate in the study.

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

REFERENCES

1. Home, Resources, diabetes L with, et al. 9th edition | IDF Diabetes Atlas. https://diabetesatlas.org/atlas/ninth-edition/ (Accessed 20 Jun 2022).

2. GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Health 2021;9:e144–60. https://doi.org/10.1016/S2214-109X(20)30489-7

3. Cooper OAE, Taylor DJ, Crabb DP, et al. Psychological, social and everyday visual impact of diabetic macular oedema and diabetic retinopathy: a systematic review. Diabet Med J Br Diabet Assoc. 2020;37:924–33. https://doi.org/10.1111/dme.14125.

4. Haritoglou C, Neubauer AS, Kernt M. Fluocinolone acetonide and its potential in the treatment of chronic diabetic macular edema. Clin Ophthalmol Auckl NZ. 2013;7:503–9. https://doi.org/10.2147/OPTH.S34057.

5. X Z, H Z, S B, et al. Diabetic macular edema: new concepts in patho-physiology and treatment. Cell Biosci 2014; https://doi.org/10.1186/2045-3701-4-27

6. Schmidt-Erfurth U, Garcia-Arumi J, Bandello F, et al. Guidelines for the management of diabetic macular edema by the European Society of Retina specialists (EURETINA). Ophthalmol J Int Ophtalmol Int J Ophthalmol Z Augenheilkd. 2017;237:185–222. https://doi.org/10.1159/000458539.

7. Boyer DS, Yoon YH, Belfort R, et al. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. Ophthalmology. 2014;121:1904–14. https://doi.org/10.1016/j.ophtha.2014.04.024.

8. Weiss M, Sim DA, Herold T, et al. Compliance and adherence of patients with diabetic macular edema to intravitreal anti-vascular endothelial growth factor therapy in daily practice. Retina Phila PA. 2018;38:2293–300. https://doi.org/10.1097/IAE.0000000000001892.

9. Bonnin S, Dupas B, Sanharawi ME, et al. Efficacy of dexamethasone intravitreal implant for the treatment of diabetic macular edema. Eur J Ophthalmol. 2015;25:448–53. https://doi.org/10.5301/ejo.5000581.

10. Malclès A, Dot C, Voirin N, et al. Safety of intravitreal dexamethasone implant (OZURDEX): the SAFODEX study. Incidence and risk factors of ocular hypertension. Retina Phila Pa 2017;37:1352–9. https://doi.org/10.1097/IAE.0000000000001369

11. Bellocq D, Akesbi J, Matonti F, et al. The pattern of recurrence in diabetic macular edema treated by dexamethasone implant: the PREDIAMEX study. Ophthalmol Retina. 2018;2:567–73. https://doi.org/10.1016/j.oret.2017.10.016.

12. Campochiaro PA, Brown DM, Pearson A, et al. Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. Ophthalmology. 2012;119:2125–32. https://doi.org/10.1016/j.ophtha.2012.04.030.

13. Campochiaro PA, Brown DM, Pearson A, et al. Long-term benefit of sustained-delivery fluocinolone acetonide vitreous inserts for diabetic macular edema. Ophthalmology. 2011;118:626-635.e2. https://doi.org/10.1016/j.ophtha.2010.12.028.

14. Kodjikian L, Baillif S, Creuzot-Garcher C, et al. Real-world efficacy and safety of fluocinolone acetonide implant for diabetic macular edema: a systematic review. Pharmaceutics. 2021;13:72. https://doi.org/10.3390/pharmaceutics13010072.

15. Parrish RK, Campochiaro PA, Pearson PA, et al. Characterization of intraocular pressure increases and management strategies following treatment with fluocinolone acetonide intravitreal implants in the FAME trials. Ophthal Surg Lasers Imag Retina. 2016;47:426–35. https://doi.org/10.3928/23258160-20160419-05.

16. ILUVIEN (acétonide de fluocinolone), corticoïde en implant intravitréen. Haute Aut. Santé. https://www.has-sante.fr/jcms/c_1622369/fr/iluvien-acetonide-de-fluocinolone-corticoide-en-implant-intravitreen (Accessed 2 Aug 2022).

17. Kodjikian L, Bandello F, de Smet M, et al. Fluocinolone acetonide implant in diabetic macular edema: international experts' panel consensus guidelines and treatment algorithm. Eur J Ophthalmol. 2022;32:1890–9. https://doi.org/10.1177/11206721221080288.

18. Mansour SE, Kiernan DF, Roth DB, et al. Two-year interim safety results of the 0.2 μg/day fluocinolone acetonide intravitreal implant for the treatment of diabetic macular oedema: the observational PALADIN study. Br J Ophthalmol. 2021;105:414–9. https://doi.org/10.1136/bjophthalmol-2020-315984.

19. Cicinelli MV, Rosenblatt A, Grosso D, et al. The outcome of fluocinolone acetonide intravitreal implant is predicted by the response to dexamethasone implant in diabetic macular oedema. Eye Lond Engl. 2021;35:3232–42. https://doi.org/10.1038/s41433-020-01373-1.

20. Adán A, Cabrera F, Figueroa MS, et al. Clinical-decision criteria to identify recurrent diabetic macular edema patients suitable for fluocinolone acetonide implant therapy (ILUVIEN®) and follow-up considerations/recommendations. Clin Ophthalmol Auckl NZ. 2020;14:2091–107. https://doi.org/10.2147/OPTH.S252359.

21. Bailey C, Chakravarthy U, Lotery A, et al. Real-world experience with 0.2 μg/day fluocinolone acetonide intravitreal implant (ILUVIEN) in the United Kingdom. Eye Lond Engl. 2017;31:1707–15. https://doi.org/10.1038/eye.2017.125.

22. Baillif S, Staccini P, Weber M, et al. Management of patients with diabetic macular edema switched from dexamethasone intravitreal implant to fluocinolone acetonide intravitreal implant. Pharmaceutics. 2022;14:2391. https://doi.org/10.3390/pharmaceutics14112391.

23. Sadda SR, Campbell J, Dugel PU, et al. Relationship between duration and extent of oedema and visual acuity outcome with ranibizumab in diabetic macular oedema: a post hoc analysis of Protocol I data. Eye Lond Engl. 2020;34:480–90. https://doi.org/10.1038/s41433-019-0522-z.

24. Augustin AJ, Bopp S, Fechner M, et al. Three-year results from the Retro-IDEAL study: real-world data from diabetic macular edema (DME) patients treated with ILUVIEN® (0.19 mg fluocinolone acetonide implant). Eur J Ophthalmol. 2020;30:382–91. https://doi.org/10.1177/1120672119834474.

25. Holden SE, Kapik B, Beiderbeck AB, et al. Comparison of data characterizing the clinical effectiveness of the fluocinolone intravitreal implant (ILUVIEN) in patients with diabetic macular edema from the real world, non-interventional ICE-UK study and the FAME randomized controlled trials. Curr Med Res Opin. 2019;35:1165–76. https://doi.org/10.1080/03007995.2018.1560779.

26. Chakravarthy U, Taylor SR, Koch FHJ, et al. Changes in intraocular pressure after intravitreal fluocinolone acetonide (ILUVIEN): real-world experience in three European countries. Br J Ophthalmol. 2019;103:1072–7. https://doi.org/10.1136/bjophthalmol-2018-312284.

27. Castro Farías D, Matsui Serrano R, Bianchi Gancharov J, et al. Indocyanine green angiography for identifying telangiectatic capillaries in diabetic macular oedema. Br J Ophthalmol. 2020;104:509–13. https://doi.org/10.1136/bjophthalmol-2019-314355.

28. Chaperon M, Kodjikian L, Agard E, et al. Screening of telangiectatic capillaries in chronic macular edema based on multimodal imaging: a study of 101 eyes. LyoMAC1 study. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol. 2022;260:2501–8. https://doi.org/10.1007/s00417-022-05592-y.

29. Séjournet L, Kodjikian L, Elbany S, et al. Focal photocoagulation as an adjunctive therapy to reduce the burden of intravitreal injections in macula edema patients, the LyoMAC2 Study. Pharmaceutics. 2023;15:308. https://doi.org/10.3390/pharmaceutics15020308.