SUPPLEMENTARY INFORMATION

CONTENTS

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METHODS

Study design

Appendix S1

To be included, patients had to be eligible for treatment with the FAc implant according to the prescribing indication. The 0.2 µg/day FAc implant was administered intravitreally following the method described in the prescribing information.[1] The eye receiving treatment was referred to as the study eye; if patients had both eyes treated, they were included as separate study eyes. All patients in the study underwent assessments at baseline (treatment with the FAc implant), day 1, day 7, month 2, month 3, and then every 3 months thereafter, over a 3-year period. The study design and schedule of assessments are summarised in **table S1**.

Table S1 Study design and schedule of assessments

Assessment	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**
Study period	**0**	**Day 1**	**Day 7**	**Mo 2**	**Mo 3**	**Mo 6**	**Mo 9**	**Mo 12**	**Mo 15**	**Mo 18**	**Mo 21**	**Mo 24**	**Mo 27**	**Mo 30**	**Mo 33**	**Mo 36**
Medical history	X															
Ophthalmic history*	X															
Prior steroid use†	X															
Ophthalmic exam‡	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
SD-OCT	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant treatments	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Injection procedure	X															
Telephone contact		X														

*Ophthalmic history includes treatments for DMO, VA, retinal thickness, macular volume, cup-to-disc ratio, IOP and IOP-lowering medications and procedures for the preceding 3 years in eye(s) receiving ILUVIEN®.

†The ocular steroid used to qualify the eye(s) for the administration of ILUVIEN®.

‡Ophthalmic examination includes BCVA, IOP, slit lamp examination and dilated ophthalmoscopy.

BCVA, best-corrected visual acuity; DMO, diabetic macular oedema; IOP, intraocular pressure; mo, month; SD-OCT, spectral-domain optical coherence tomography; VA, visual acuity.

Investigational methods

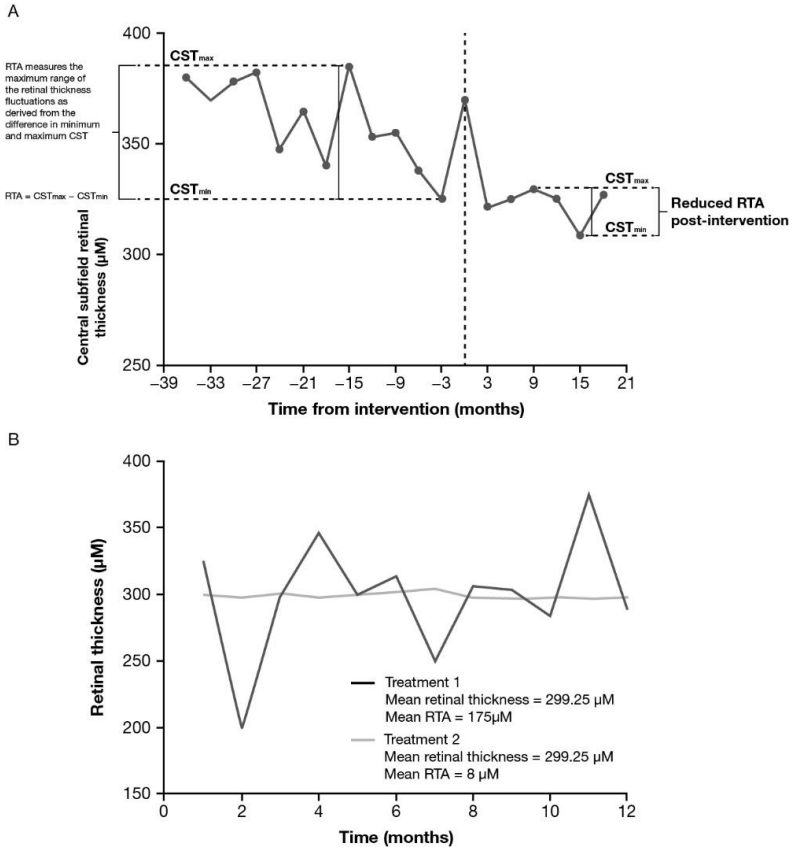
Appendix S2

IOP-lowering procedures were recorded across the duration of the study. IOP was measured using the investigator's standard procedure and analysed as mean IOP over time. IOP elevations (≥25 and ≥30 mmHg) and IOP-lowering medications were also recorded. VA measured by the investigator's standard procedure was collected pre-FAc implant and BCVA post-FAc implant was measured using the standard procedure developed for the Early Treatment Diabetic Retinopathy Study (ETDRS) at 4 metres[2] or electronic-ETDRS at 3 metres.[3] Change in BCVA was compared using two defined patient populations: baseline BCVA ≥20/40 and baseline BCVA <20/40. Both IOP and VA were collected for 36 months before, and, in the current analysis, for 24 months after the FAc implant.

In a subgroup analysis, treatment frequency for 24 months pre- and post-FAc implant was calculated using a categorical shift analysis of the number of eyes receiving additional treatments for DMO in the 24 months post- compared with 24 months pre-FAc implantation; this standardised any differences in pre- and post-FAc implant follow up. Treatments were defined as any intravitreal anti-VEGF, intraocular steroid or laser therapies for the treatment of DMO. Treatment frequencies were reported as number of eyes receiving 0–1, >1–4 or >4 treatments per year. Time to rescue treatment and re-treatments over time were evaluated using Kaplan-Meier analysis for the full population.

CST was analysed using the investigator's standard procedure for spectral-domain optical coherence tomography (SD-OCT). Mean CST, the percentage of patients with CST ≤300 µm and mean retinal thickness amplitude (RTA) were measured for 36 months pre- and 24 months post-FAc implant. **Figure S1** provides hypothetical scenarios that illustrate how RTA can be beneficial when evaluating oedema control over time. Cataract-related events were also documented. Safety analyses included ocular and systemic safety evaluation and a summary of AEs.

Figure S1 The use of RTA to evaluate oedema control **(A)** illustrating how RTA is measured and **(B)** how it can compare two treatments.



A small RTA indicates that fluctuation in retinal thickness is minimal over a specified period, whereas a large RTA indicates that retinal thickness was subject to substantial peaks and troughs during the specified period. CST, central subfield thickness; RTA, retinal thickness amplitude.

RESULTS

Frequency distribution of maximum observed IOP

The frequency distribution of maximum observed IOP following the last steroid administered pre- and post-FAc implant are shown in **table S2** for patients that completed 24 months of treatment following FAc implant.

Table S2 Frequency distribution of maximum observed IOP

		IOP response post-FAc implant (n=97)			
		≤25 mmHg n (%)	**>25 mmHg n (%)**	**Total n (%)**	
IOP response to last steroid pre-FAc implant (test)	**≤25 mmHg n (%)**	74 (76.3)	19 (19.6)	93 (95.9)	PPV 79.6%
	>25 mmHg n (%)	1 (1.0)	3 (3.1)	4 (4.1)	NPV 75.0%
	Total n (%)	75 (77.3)	22 (22.7)	97 (100)	
		Sensitivity 98.7%	Specificity 13.6%		

FAc, fluocinolone acetonide; IOP, intraocular pressure; n, number; NPV, negative predictive value; PPV, positive predictive value.

REFERENCES

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3. Beck RW, Moke PS, Turpin AH, et al. A computerized method of visual acuity testing: adaptation of the early treatment of diabetic retinopathy study testing protocol. *Am J Ophthalmol* 2003;135:194–205. doi:10.1016/s0002-9394(02)01825-1