Abstract (MUST be submitted as a separate file)

Purpose: To evaluate outcomes in birdshot chorioretinopathy following intravitreal implantation of a fluocinolone acetonide containing drug delivery device.

Design: Retrospective, multi-center, interventional case study.

Methods: University and community-based tertiary care. 22 HLA-A29+ birdshot patients (36 eyes) were implanted with a sustained-release corticosteroid device and followed for up to 3 years. Main outcome measures were Snellen acuity, intraocular inflammation, adjunctive therapy, cataract, ocular hypertension or glaucoma. Paired Wilcoxon statistics were used to analyze visual acuities; paired McNemar statistics were used to analyze presence or absence of other outcomes.

Results: 19 of 22 patients (32 eyes) completed 12 months follow-up with improvement in median visual acuity ($P = .015$). Prior to implantation,18 of 22 (82%) patients received immunosuppressive therapy vs. 1 of 19 (5%) by 12 months ($P < .001$). Eyes with zero vitreous haze increased from 7 of 27 scored eyes (26%) at baseline to 30 of 30 eyes (100%) by 12 months ($P < .001$). Cystoid macular edema decreased from 13 of 36 eyes (36%) at baseline to 2 of 32 eyes (6%) at 12 months ($P = .006$). Five of 24 phakic eyes at baseline exited the study before surgery; all other eyes received cataract surgery. 100% of study eyes had ocular hypertension, required intraocular pressure lowering therapy, or had glaucoma surgery by 12 months.

Conclusions: Implantation of a fluocinolone-acetonide containing intraocular device in birdshot chorioretinopathy can improve vision, control inflammation, and eliminate systemic therapy. There is a high incidence of cataract progression and intraocular hypertension or glaucoma.

Outcomes of Birdshot Chorioretinopathy Treated with an Intravitreal Sustained Release Fluocinolone Acetonide Containing Device

Ryan B. Rush [1], Debra A. Goldstein [2], David G. Callanan [3], Beeran Meghpara [2], William J. Feuer [1], and Janet L. Davis [1]

1 Bascom Palmer Eye Institute
University of Miami Miller School of Medicine
900 NW 17th ST
Miami FL 33136

2 University of Illinois at Chicago
Department of Ophthalmology
1855 W Taylor St
Chicago 60612

3 Texas Retina Associates
Suite 101, 801 W. Randol Mill Rd.
Arlington TX 76012

Corresponding Author:

Janet L. Davis
Bascom Palmer Eye Institute
900 NW 17th ST
Miami FL 33136

FAX 305 326 6071
PHONE 305 326 6377
jdavis@med.miami.edu

Short Title: Intraocular Drug Delivery in Birdshot Chorioretinopathy

Birdshot chorioretinopathy was identified in 1980[1] and accounts for approximately 8% of posterior uveitis in the US.[2] It is associated with the HLA-A29 allele with one of the highest odds ratios for a histocompatibility allele although it is rarely familial.[3-5] Factors that lead to disease initiation are unknown; autoimmunity to retinal antigens in a genetically predisposed individual has been proposed.[5, 6]

Early stage disease is characterized by retinal vascular leakage, while the mid-phase shows increasing prominence of "birdshot" choroidal lesions. The late stage is typified by cystoid macular edema (CME), vascular attenuation, and retinal pigment epithelial (RPE), choroidal and optic nerve atrophy. Although 20% of patients may achieve remission without treatment, most have a relentlessly progressive course. Birdshot can remain active and produce severe vision loss over two to three decades.[7,8]

Disease course is monitored by visual acuity, anterior chamber and vitreous cellular reaction, retinal vascular leakage, and the appearance of the chorioretinal lesions. Ancillary testing such as fluorescein angiography (FA), indocyanine green angiography (ICG), optical coherence tomography (OCT), perimetry and electroretinography are also often used to monitor disease activity. [9-12]

Immunosuppressive treatment is reported to reduce vision loss from cystoid macular edema [8] and to lessen visual field loss.[12] Regional or systemic corticosteroids can reduce retinovascular leakage and improve vision. [13-16] Corticosteroids are often combined with cyclosporine or replaced from the outset by immunosuppressive drugs. [17, 18] Since there are no known or suspected systemic associations with birdshot chorioretinopathy, intraocular drug delivery provides a potentially useful alternative to immunosuppressive medication or systemic corticosteroids.

We report our experience with implantation of an FDA-approved, sustained-release intraocular implantable drug delivery device containing fluocinolone acetonide in one or both eyes of 22 patients with birdshot chorioretinopathy. [21]

Methods

Surgical logs were reviewed to identify patients with birdshot chorioretinopathy who were implanted with fluocinolone acetonide containing drug delivery devices (Retisert®, Bausch & Lomb, Rochester, New York) from 2002 to 2008 at Bascom Palmer Eye Institute, the University of Illinois at Chicago, and Texas Retina Associates. Clinical diagnoses were based on typical choroidal inflammatory lesions associated with vitritis and past or current retinal vasculitis. Patients were excluded from the study if they were not HLA-A29 positive. Inclusion in the study was not dependent on a required length of follow-up. Both eyes were considered for the study if both were implanted. All eligible patients and eyes were included in the study.

Baseline data was recorded for one month (+/- 2 weeks) before implantation. Follow-up data was collected at 4 months (+/- 1 month), 1 year (+/-2 months), 2 years (+/- 4 months), and 3 years (+/- 4 months) after implantation, the expected duration of effect of the implant. Clinical information collected included age, local and systemic therapies for uveitis or glaucoma, best-corrected Snellen visual acuity, lens status (no, mild, moderate or severe opacity), intraocular pressure, glaucoma history, anterior chamber and vitreous inflammation, [22] and the presence of CME and epiretinal membranes.

The fluorescein angiographic findings, Humphrey visual field mean deviation in decibels, ERG cone B flicker amplitude, and ERG cone B flicker latency were recorded if available. Fluorescein angiograms were graded according to the following scale: 0 = no retinal vascular leakage, 1 = large vessel leakage, 2 = small vessel leakage in the posterior pole, 3 = CME, 4 = RPE atrophy in the posterior pole.[11]

Treatment with the device was provided according to the clinician's best medical judgment based on subjective complaints, visual acuity, clinical assessment of the degree of inflammation response to prior treatment, and the individual patient's preference for treatment or participation in a clinical trial. Information ascertained from Humphrey visual fields, fluorescein angiography (FA), indocyanine angiography (ICG) and electroretinography (ERG) were also used in management decisions.

The main outcome measures were Snellen visual acuity, the need for either local or systemic therapy to control intraocular inflammation, control of intraocular inflammation, cataract progression, and the development or progression of glaucoma. Paired Wilcoxon statistics were used to analyze visual acuities; paired McNemar statistics were used to analyze presence or absence of other outcomes.

Results

Twenty-two patients met eligibility criteria and were included in this series. Fourteen patients were bilaterally implanted and 8 were unilaterally implanted for a total of 36 eyes. All patients had bilateral disease. The age at implantation of the first eye averaged 59.7 years (SD=10.1, range: 39 to 78). Median [range] of follow-up was 24 [4, 36] months. Seven (35%) patients were taking antihypertensive medications and one (5%) was receiving medical therapy for diabetes mellitus. Median [range] of best-corrected Snellen visual acuity was 20/50 [20/20, 20/400] at baseline. Best-corrected Snellen visual acuity improved at a statistically significant level at all follow-up points (Table 1).

Eighteen (50%) eyes were treated with local therapy at baseline (Table 1). Eleven (31%) were receiving topical corticosteroids, 5 (14%) topical non-steroidal anti-inflammatories, 5 (14%) had received intravitreal triamcinolone acetonide, and 2 (6%)

received posterior sub-Tenon triamcinolone acetonide. Table 1 summarizes the statistically significant decrease in local therapy during the study.

Seventeen of 22 patients (82%) were receiving systemic immunosuppressive therapy prior to implantation (Table 1). Seven patients (32%) were taking oral prednisone; 2 as a single agent, 2 with cyclosporine, 1 with tacrolimus,1 with mycophenolate mofetil, and 1 with both cyclosporine and mycophenolate. Five patients (23%) were taking mycophenolate mofetil as a single agent, 2 patients (9%) were taking cyclosporine, and 2 patients (9%) were taking tacrolimus. One patient (5%) was taking methotrexate and infliximab. There was a statistically significant decrease in the proportion of patients receiving immunosuppressive therapy at 4, 12, and 24 months compared to baseline, $P < 0.001$, with no patients taking immunosuppressive medication by 24 months.

Anterior chamber cells and flare were present in 25 to 28% of eyes at baseline. There was a statistically significant decrease in anterior inflammation by the 4 month follow-up visit (Table 1) that persisted at 12 months. Similarly, a statistically significant decline in vitreous cell scores was seen at the 4 month, 12 month, and 24 month follow-up visits (Table 1). At the 12 month mark when 19/22 (86%) of patients were still being followed, all 30 eyes with available haze scores had vitreous haze of 0 compared to 7 of 27 eyes (26%) at baseline ($P = 0.001$).

At baseline there were 12 (33%) pseudophakic eyes (Table 1). The cumulative proportion of pseudophakic eyes rose to 75% by 12 months and was 100% by 3 years among eyes remaining in the study. Five eyes exited the study before cataract surgery was performed, one at 4 months and 4 at 12 months. Five of 24 phakic eyes (21%) underwent surgery by 4 months, and 10 of phakic 18 eyes (56%) by 12 months. All 4 remaining phakic eyes were operated by 24 months.

Mean intraocular pressure was in the normal range throughout the study (Table 1). Prior to implantation, 30 eyes of eighteen patients (83%) had an IOP less than 25 mmHg without IOP-lowering medical therapy and 6 eyes of 4 patients had either higher pressure or were using pressure-lowering medication (Table 1). The proportion of eyes with normal pressures steadily declined during the study (Table 1). Twenty-six of the 30 eyes (87%) without high pressure at baseline developed pressures greater than 25 mmHg or required medical pressure lowering therapy during the study and 23 had done so by the 12 month visit. Seven of the initially normal eyes (28%) required surgical glaucoma treatment as did 5 of the 6 eyes (83%) with initially elevated pressures. By 3 years, all 9 eyes were being treated medically or had received glaucoma surgery. Although relatively few patients completed the three-year follow-up visit, only 4 of 36 (11%) eyes were lost to follow-up before either the medical or surgical glaucoma endpoint was reached. Two eyes (1 patient) with no ocular hypertension or glaucoma surgery were lost at the 4 month visit and 2 eyes (2 patients) were lost at the 24 month

visit, therefore, glaucoma status was ascertainable for 32 of 36 (89%) of study eyes; however, there were 2 patients on glaucoma medication at 4 months, 10 patients on medication at 12 months, and 4 patients at 24 months with no follow-up, and these patients were at risk for further glaucoma surgery.

The prevalence of CME decreased from 13 of 36 eyes (36%) to 6 of 36 (17%) eyes and 2 of 32 eyes (7%) at 4 and 12 months (P = 0.16 and 0.006) (Table 1). The cumulative proportion of epiretinal membrane formation was higher by the end of the study, but the results were not statistically significant.

Fluorescein angiography results were available for 25 (69%) study eyes at baseline (Table 2). Eyes with baseline angiograms had repeat angiograms at follow-up visits if they continued in the study. Angiography scores at each time point are given in Table 2. The proportion of eyes with retinal vascular leakage decreased during follow-up whereas RPE atrophy became more prevalent. By month 12 80% of eyes had either no leakage or had atrophy, increasing to 90% by month 24, and 100% by month 36.

Table 2 also reports the Humphrey visual field mean deviations, and the cone B wave flicker amplitudes and latencies. Group means were abnormal at all time points; statistical analysis was not attempted because of the wide variation among patients.

Discussion

Similar to this study, results from treatment of 8 patients with sympathetic ophthalmia demonstrated a reduction in the need for systemic immunosuppression after implantation. [23] Whether local suppression of inflammation without systemic immunosuppression is adequate is of interest because both birdshot chorioretinopathy and sympathetic ophthalmia are assumed to result from a systemic autoimmune response. Sympathetic ophthalmia can involve other pigmented tissues, whereas disease expression in birdshot is confined to the eye.

The patients in our study appeared to be typical of birdshot patients described in other series in terms of retinal vascular leakage, CME, abnormal ERG and visual fields, and relatively preserved Snellen visual acuity.[24] The baseline prevalence of glaucoma and cataract also appeared to be similar to other studies.[25]

Implantation demonstrated beneficial effects by maintaining or improving visual acuity and vitreous clarity, reducing cellular inflammation and retinal vascular leakage on fluorescein angiography, and by preserving Humphrey visual field mean deviation and ERG cone B flicker amplitude and latency throughout the course of the study. Outcomes for the birdshot patients appeared similar to those with other types of non-infectious posterior uveitis who were treated with the fluocinolone-containing device.[21, 23, 26, 27]

Implantation permitted the successful discontinuation of systemic immunosuppressive therapy in all but one of the 19 patients who remained under follow-up at 12 months. This benefit should be weighed against the high rate of progression of cataract and elevation of intraocular pressure since all phakic patients continuing under follow-up required cataract surgery and nearly all patients required either medical or surgical management for high IOP at two years follow-up.

IOP elevation has been recognized as a common complication of regional corticosteroid use. In 278 patients with non-infectious causes of posterior uveitis prospectively followed for three years after implantation of the fluocinolone-acetonide containing intravitreal device, 78% of implanted eyes required topical IOP-lowering therapy and 40% of implanted eyes required IOP-lowering surgery.[21] In a larger series of 584 eyes, including many of the same patients, topical IOP-lowering medications were required in 74.8% of implanted eyes, and IOP-lowering surgeries were performed in 36.6% of implanted eyes by three years.[28] Of the 31 patients in our study with ascertainable outcomes, all required medical therapy (100%), and 12 required glaucoma surgery (33%). Both new medical treatment and new surgeries peaked at 12 months when most patients were still being followed. Long-term clinical follow-up outside the period of formal data collection revealed that 6 more eyes subsequently required glaucoma surgery, a proportion (50%) higher than that reported in the randomized clinical trials. Patients who entered the study already on medical therapy or with elevated eye pressure were most likely to require glaucoma surgery.

Birdshot patients may have a higher risk for developing optic nerve damage from glaucoma compared to other patients with uveitis. Since there is a minimal anterior inflammatory component, protective ciliary body hyposecretion is less likely to occur. Also, the circulation to the optic nerve may diminish as a sequela of reduced choroidal circulation associated with birdshot. Indeed, the end-stage of birdshot is often similar in appearance to advanced glaucoma with optic nerve cupping and pallor. Nonetheless, visual fields remained stable throughout the study and ocular hypertension and glaucoma were treatable.

The risk of cataract surgery following implantation in this study is similar to prior published results in which 93% of phakic eyes were operated by three years after implantation, with most surgeries occurring between week 34 and month 24 after implantation. [21] Birdshot appears to confer no special risk for cataract formation, which is nearly universal following implantation, and the lack of clinically significant anterior segment inflammation favors uncomplicated cataract surgery.

Weaknesses of this study include its retrospective nature, the lack of a treatment comparator other than the baseline status, and the small number of study participants. Three patients (four eyes) did not have data collection after 4 months, although 1 of 2

eyes at risk for cataract had already required surgery and 2 of 4 eyes at risk had already started glaucoma medications by 4 months. Although we report a higher incidence of glaucoma than prior studies, some patients who entered into the study already had elevated eye pressure and may therefore have been more prone to develop glaucoma. No data was collected regarding other risk factors for glaucoma such as family history or myopia.

Candidates for implantation must be willing to undergo cataract surgery, be available for frequent IOP monitoring, and be prepared to have IOP-lowering surgery if necessary. Despite these limitations, birdshot chorioretinopathy is a purely ocular disease that may not need systemic immunosuppression, and the patients in this series appeared to have improved vision, excellent control of inflammation and stabilization of global measures of retinal function such as visual field and ERG. Given the possible side effects of systemic immunosuppression, implantation of a corticosteroid containing drug delivery device may be a good therapeutic choice in selected patients with birdshot chorioretinopathy.

ACKNOWLEDGEMENTS

A. Funding/Support: This study was supported by National Eye Institute, Bethesda, Maryland, Core Center Grant No. P30 EY014801 (Bascom Palmer Eye Institute, Miami, Florida), and NEI Core Grant for Vision Research P30 EY001792 (University of Illinois at Chicago); and unrestricted funds from Research to Prevent Blindness, New York, New York (Bascom Palmer Eye Institute and University of Illinois at Chicago).

B. Financial Disclosures: Dr. Davis received grant support from Novartis, the Jaime Marti Foundation (>10,000), the Len-Ari Foundation (>10,000), and consulting fees from Centocor and Alcon (<10,000). Dr. Goldstein received honoraria, consulting fees, and grant support from Bausch & Lomb (<10,000), Allergan, Lux (<10,000). Dr. Callanan is a consultant for Bausch & Lomb and Allergan (<10,000), and received lecture fees from Novartis (<10,000). Dr. Rush, Mr. Feuer and Dr. Meghpara have no financial disclosures.

C: Contributions of Authors: Design and conduct of the study (JLD, DAG, DGC); collection, management, analysis and interpretation of data (RBR, JLD, WJF, DAG, DGC, BM); preparation, review, or approval of the manuscript (RBR, JLD, DAG, DGC, WJF).

D. Statement about Conformity with Author Information: The Medical Sciences Institutional Review Board at the University of Miami Miller School of Medicine, the IRB at the University of Illinois at Chicago (UIC), and the Western Institutional Review

Board, Olympia, Washington, approved retrospective review of data and waiver of authorization for this study, which was conducted in accordance with the principles of the Declaration of Helsinki.

References

1. Ryan SJ, Maumenee AE. Birdshot retinochoroidopathy. Am J Ophthalmol 1980; 89(1):31-45.

2. Rodriguez A, Calonge M, Pedroza-Seres M, et al. Referral patterns of uveitis in a tertiary eye care center. Arch Ophthalmol 1996;114(5):593-599.

3. LeHoang P, Ozdemir N, Benhamou A, et al. HLA-A29.2 subtype associated with birdshot retinochoroidopathy. Am J Ophthalmol 1992; 113(1):33-35.

4. Trinh L, Bodaghi B, Fardeau C, et al. Clinical features, treatment methods, and evolution of birdshot chorioretinopathy in 5 different families. Am J Ophthalmol 2009;147(6):1042-1047.

5. Nussenblatt RB, Mittal KK, Ryan S, Green WR, Maumenee AE. Birdshot retinochoroidopathy associated with HLA-A29 antigen and immune responsiveness to retinal S-antigen. Am J Ophthalmol 1982(2); 94:147-158.

6. de Smet MD, Yamamoto JH, Mochizuki M, et al. Cellular immune responses of patients with uveitis to retinal antigens and their fragments. Am J Ophthalmol 1990;110(2):135-142.

7. Rothova A, Berendschot TT, Probst K, van Kooij B, Baarsma GS. Birdshot chorioretinopathy: long-term manifestations and visual prognosis. Ophthalmology 2004; 111(5):954-959.

8. Thorne JE, Jabs DA, Peters GB, Hair D, Dunn JP, Kempen JH. Birdshot retinochoroidopathy: ocular complications and visual impairment. Am J Ophthalmol 2005;140(1):45-51.

9. Zacks DN, Samson CM, Loewenstein J, Foster CS. Electroretinograms as an indicator of disease activity in birdshot retinochoroidopathy. Graefes Arch Clin Exp Ophthalmol 2002; 240(8): 601-607.

10. Holder GE, Robson AG, Pavesio C, Graham EM. Electrophysiological characterisation and monitoring in the management of birdshot chorioretinopathy. Br J Ophthalmol 2005; 89(6):709-718

11. Sobrin L, Lam BL, Liu M, Feuer WJ, Davis JL. Electroretinographic monitoring in birdshot chorioretinopathy. Am J Ophthalmol 2005;140(1):52-64.

12. Thorne JE, Jabs DA, Kedhar SR, Peters GB, Dunn JP. Loss of visual field among patients with birdshot chorioretinopathy. Am J Ophthalmol 2008;145(1):23-28.

13. Martidis A, Duker JS, Puliafito CA. Intravitreal triamcinolone for refractory cystoid macular edema secondary to birdshot retinochoroidopathy. Arch Ophthalmol 2001;119(9):1380-1383.

14. Fuerst DJ, Tessler HH, Fishman GA, Yokoyama MM, Wyhinny GJ, Vygantas CM. Birdshot retinochoroidopathy. Arch Ophthalmol 1984(3); 102:214-219.

15. Oosterhuis JA, Baarsma GS, Polak BC. Birdshot chorioretinopathy--vitiliginous chorioretinitis. Int Ophthalmol 1982; 5:137-144.

16. Ladas JG, Arnold AC, Holland GN. Control of visual symptoms in two men with birdshot retinochoroidopathy using low-dose oral corticosteroid therapy. Am J Ophthalmol 1999; 128(1):116-118.

17. Vitale AT, Rodriguez A, Foster CS. Low-dose cyclosporine therapy in the treatment of birdshot retinochoroidopathy. Ophthalmology 1994; 101(5):822-831

18. Jabs DA, Rosenbaum JT, Foster CS, et al. Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. Am J Ophthalmol 2000(4);130:492-513.

19. Kempen JH, Gangaputra S, Daniel E, et al. Long-term risk of malignancy among patients treated with immunosuppressive agents for ocular inflammation: a critical assessment of the evidence. Am J Ophthalmol 2008(6);146:802-812.

20. Kempen JH, Daniel E, Dunn JP, et al. Overall and cancer related mortality among patients with ocular inflammation treated with immunosuppressive drugs: retrospective cohort study. BMJ Jul 3 2009;339:b2480.

21. Callanan DG, Jaffe GJ, Martin DF, Pearson PA, Comstock TL. Treatment of posterior uveitis with a fluocinolone acetonide implant: three-year clinical trial results. Arch Ophthalmol 2008(9); 126: 1191-201.

22. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005; 140(3): 509-516.

23. Mahajan VB, Gehrs KM, Goldstein DA, Fischer DH, Lopez JS, Folk JC. Management of sympathetic ophthalmia with the fluocinolone acetonide implant. Ophthalmology 2009(3);116:552-557.

24. Oh KT, Christmas NJ, Folk JC. Birdshot retinochoroiditis: long term follow-up of a chronically progressive disease. Am J Ophthalmol 2002; 133(5):622-629.

25. Kiss S, Ahmed M, Letko E, Foster CS. Long-term follow-up of patients with birdshot retinochoroidopathy treated with corticosteroid-sparing systemic immunomodulatory therapy. Ophthalmology 2005(6); 112: 1066-1071.

26. Jaffe GJ, Ben-Nun J, Guo H, Dunn JP, Ashton P. Fluocinolone acetonide sustained drug delivery device to treat severe uveitis. Ophthalmology 2000; 107(11): 2024-2033.

27. Jaffe GJ, McCallum RM, Branchaud B, Skalak C, Butuner Z, Ashton P. Long-term follow-up results of a pilot trial of a fluocinolone acetonide implant to treat posterior uveitis. Ophthalmology 2005; 112(7): 1192-1198.

28. Goldstein DA, Godfrey DG, Hall A, et al. Intraocular pressure in patients with uveitis treated with fluocinolone acetonide implants. Arch Ophthalmol 2007; 125(11): 1478-1485.

Table 1

Table 1. Comparison of the clinical characteristics of eyes with birdshot chorioretinopathy at baseline vs. 4 to 36 months after implantation of a fluocinolone-containing intravitreal device

	Baseline	Month 4	Month 12	Month 24	Month 36
Number of Eyes	36	36	32	16	9
Snellen Acuity Median [range]	20/50 [20/20, 20/400]	20/40 [20/20,20/200]	20/40 [20/15, 20/200]	20/30 [20/20, 20/200]	20/30 [20/20, 20/150]
P value[a]		0.003	0.015	0.018	0.011
Intraocular pressure Mean (SD) [range]	16.2 (6.5) [9,47]	17.6 (5.6) [6, 27]	17.1 (6.8) [4, 32]	14.7 (4.8) [7, 22]	16.7 (6.9) [8, 29]
Local anti-inflammatory therapy Eyes (%)	18 (50%)	1 (3%)	4 (13%)	4 (25%)	4 (44%)
P value[b]		<0.001	0.006	0.29	1.0
Immunosuppressive therapy n/N Patients (%)	18/22 (82%)	5/22 (23%)	1/19 (5%)	0/12 (0%)	0/6 (0%)
P value[b]		<0.001	<0.001	<0.001	0.031
AC cells, 0.5 – 2+_[c] Eyes (%) [c]	9 (25)	1 (3)	0	1 (6)	0
P value[b]		0.021	0.016	0.38	0.50
AC flare, 1 – 2+ [c] Eyes (%)	10 (28)	2 (6)	5 (16)	1 (6)	0

P value[b]		0.039	0.51	0.63	1.0
Vitreous Cells [d]					
Eyes (%)					
0 – trace	10 (28)	24 (67)	29 (91)	13 (81)	9 (100)
1	10 (28)	11 (31)	3 (9)	3 (19)	0
2	15 (42)	1 (3)	0	0	0
3	1 (3)	0	0	0	0
P value[b]		0.001	<0.001	0.031	0.38
Vitreous Haze Score [c]					
Eyes (%)					
0	7 (26)	34 (94)	30 (100)	16 (100)	8 (89)
0.5	2 (7)	2 (6)	0	0	1 (11)
1	14 (52)	0	0	0	0
2	4 (15)	0	0	0	0
Unavailable	9	0	2	0	0
P value[b]		<0.001	<0.001	0.004	0.25
Cataract status, Eyes (%)					
Mild or no cataract	18 (50)	11 (31)	3 (9)	0	0
Moderate cataract	5 (14)	7 (19)	3 (10)	0	0
Severe or mature cataract	1 (3)	1 (3)	2 (6)	0	0
Pseudophakia	12 (33)	17 (47)	24 (75)	16 (100)	9 (100)
New pseudophakia		5	10	4	0
Intraocular Pressure					
Mean (SD) [range]	16.2 (6.5) [9,47]	17.6 (5.6) [6, 27]	17.1 (6.8) [4, 32]	14.7 (4.8) [7, 22]	16.7 (6.9) [8, 29]
Glaucoma status, Eyes (%)					
IOP<25, no medical therapy	30 (83)	18 (50)	5 (16)	2 (12)	0

IOP>25 or medical therapy	6 (17)	16 (44)	19 (59)	10 (63)	4 (44)
New medical therapy		11	11	3	0
Trabeculectomy or GDI	0	2 (6)	8 (25)	4 (25)	5 (56)
New glaucoma surgery		2	6	2	2
Cystoid macular edema					
Eyes (%)	13 (36)	6 (17)	2 (6)	0	0
P value[b]		0.016	0.006	0.016	0.13
Epiretinal membrane					
Eyes (%)	8 (23)	9 (25)	11 (34)	6 (38)	5 (56)
P value[b]		1.0	0.5	1.0	0.5

a Paired Wilcoxon test. Compared to baseline.

b Paired McNemar test (none versus any). Compared to baseline.

c Inflammatory scores recorded according the Standard Uveitis Nomenclature consensus document. [22]

d Vitreous cells were recorded according to the conventions of the individual investigators.

GDI=glaucoma drainage implant

Table 2

Table 2. Comparison of the results of ancillary testing of eyes with birdshot chorioretinopathy at baseline and 4 to 36 months after implantation of a fluocinolone-containing intravitreal device

	Baseline	Month 4	Month 12	Month 24	Month 36
Number of Eyes	36	36	32	16	9
Fluorescein Angiography Score, Eyes (%)					
0 No leakage	0 (0)	4 (24)	4 (27)	1 (10)	1 (17)
1 Large vessel leakage	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)
2 Small vessel leakage	11 (44)	4 (24)	2 (13)	1 (10)	0 (0)
3 CME	12 (48)	5 (29)	1 (7)	0 (0)	0 (0)
4 Atrophy in posterior pole	1 (4)	4 (24)	8 (53)	8 (80)	5 (83)
Number of Eyes Evaluated	25	17	15	10	6
Visual Field Mean Deviation					
Mean (SD) [Range]	-7.6 (6.5) [-24.7, -0.9]	-9.8 (7.5) [-28.7, -1.1]	-7.6 (7.9) [-26.5, 1.0]	-4.4 (3.1) [-11.9, -1.0]	-4.5 (4.2) [-13.7, -0.1]
Number Eyes Evaluated	28	11	20	10	9
Cone B wave flicker					
Mean (SD [range])					
Amplitude	53.9 (37.9) [7.6, 111.5]	53.4 (16.8) [38.3, 71.5]	47.9 (31.7) [19.8, 97.5]	37.0 (26.5) [20, 76]	44.8 (13.3) [29, 53]
Latency	40.8 (13.6) [31.8, 71.0]	34.6 (3.6) [32.3, 38.8]	40.9 (15.0) [31, 67]	35.0 (2.8) [32.7, 38.6]	44.2 (19.8) [31.7, 67.0]

Number Eyes Evaluated	12	3	5	4	3

SD = Standard deviation