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Post-operative outcomes following fluocinolone acetonide implant surgery in patients with Birdshot chorioretinitis and other types of posterior and panuveitis.

Bryn M. Burkholder, M.D.¹, Jiangxia Wang, M.S.², James P. Dunn, M.D.¹, Quan D. Nguyen, M.D.¹, and Jennifer E. Thorne, M.D., Ph.D.^{1,3}

¹The Wilmer Eye Institute, The Johns Hopkins University School of Medicine, Baltimore, MD

²Department of Biostatistics, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

³Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Abstract

Purpose—To evaluate outcomes following placement of fluocinolone acetonide (FA) implants in eyes with Birdshot chorioretinitis (BSCR) and to compare these outcomes with eyes with posterior and panuveitis.

Methods—This is a retrospective cohort study of 48 eyes from patients with posterior and panuveitis treated with FA implants from 2006 through 2010. Outcome measures include visual acuity, intraocular pressure (IOP), need for glaucoma surgery, postoperative complications, and control of inflammation.

Results—All eyes treated with FA implants achieved improved control of inflammation and decreased reliance on adjunctive therapy. BSCR eyes had a statistically significant increase in IOP in the first four months after FA implantation ($p = 0.04$) as compared to baseline IOP. A higher percentage of eyes with BSCR required glaucoma surgery and after a shorter time period following FA implantation than did eyes with other forms of posterior and panuveitis (0.42/EY versus 0.11/EY; median time to glaucoma surgery: 15.5 vs. 31.5 months respectively, hazard ratio = 3.4, 95% CI 1.0-10.8, $p = 0.04$).

Conclusions—Although the FA implant is effective in controlling inflammation and reducing the need for systemic immunosuppressive therapy, eyes of patients with BSCR tended to have a more robust IOP response to the FA implant than eyes with other types of posterior and panuveitis.

Keywords

Birdshot chorioretinitis; fluocinolone acetonide implant; posterior uveitis

Corresponding Author: Jennifer E. Thorne, M.D., Ph.D. **Address:** 600 N. Wolfe St. Woods Building, Room 476 Baltimore, MD 21287 **Tel:** 410-955-1966 **Fax:** 410-955-0629 jthorne@jhmi.edu.

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Introduction

The fluocinolone acetonide (FA) implant (Retisert; Bausch & Lomb, Rochester, NY, USA) is an intravitreal corticosteroid delivery device used to treat severe, sight-threatening noninfectious intermediate, posterior, and panuveitis.¹⁻³ The implant contains 0.59 mg of fluocinolone acetonide, which is a low-solubility corticosteroid with slow-release kinetics that produce sustained release of drug into the vitreous cavity over a period of approximately 30 months.^{1, 3} Advantages of this drug delivery system over topical, periocular, and oral corticosteroids include more consistent, targeted drug delivery over a longer time period and the avoidance of systemic corticosteroid side effects.^{1, 2, 4, 5} A randomized controlled trial showed that the implant provides comparable improvement in mean visual acuity over a two year period to systemic immunomodulatory therapy.⁶

The FA implant has been shown to reduce inflammation, decrease the risk of uveitis recurrence, and decrease reliance on adjunctive therapy in patients with noninfectious posterior uveitis.^{2, 4-8} However, the FA implant is associated with a few well-known complications, including cataract formation and elevation of intraocular pressure (IOP).^{2, 4, 5, 9, 10} In one study,⁹ 75% of patients receiving the fluocinolone implant require IOP-lowering therapy within three years of implantation, and 37% required IOP-lowering surgery.

Birdshot chorioretinitis (BSCR) is a type of posterior uveitis characterized by vitritis and multiple ovoid, hypopigmented, choroidal lesions radiating from the posterior pole to the mid-peripheral retina.^{11, 12} First described by Ryan and Maumenee in 1980, BSCR is a rare cause of uveitis, compromising only about 1-2% of all uveitis cases and about 8% of posterior uveitis cases, specifically.¹²⁻¹⁴ BSCR has a strong association with the HLA-A29 allele, and although the precise etiology of the disease is unknown, it may involve an autoimmune reaction to retinal antigens.¹⁵⁻¹⁷ BSCR is typically a chronic, progressive disease with the potential for visual impairment from either recurrent cystoid macular edema or from progressive atrophy of the retina and optic nerve.^{11, 18, 19} Because visual impairment can occur without obvious clinical evidence of active inflammation, these patients often require chronic immunosuppressive drug therapy to control their disease.^{11, 18-21}

It has been our clinical impression that patients with BSCR respond well to treatment with FA implants but may have a different IOP response to the FA implant than patients with other types of posterior and panuveitis. The objective of our study was to evaluate the clinical outcomes in eyes with posterior and panuveitis after placement of an FA implant. Specifically, we assess vision and IOP outcomes, as well as the need for IOP-lowering drops and surgery. We hypothesized that eyes with BSCR would have a greater elevation in IOP and subsequent need for glaucoma medication and/or surgery following FA implantation than eyes of patients with other types of posterior and panuveitis.

Methods

Study Population

We retrospectively reviewed the medical records of all patients with posterior and panuveitis undergoing placement of an FA implant at the Wilmer Eye Institute between 2006 and 2010. All surgeries were performed by four attending surgeons. We defined posterior and panuveitis based on the Standardization of Uveitis Nomenclature (SUN) criteria.²² The patient's specific uveitis diagnosis was obtained from the medical record and was based on the physician's clinical impression and supported by laboratory and radiologic data, when indicated. Prior to treatment with the FA implant, patients had received treatment according

to best medical judgment that has been summarized previously by published guidelines.²³ Indications for placement of the FA implant were inadequate control of inflammation or intolerance of the current treatment regimen. Patients were excluded from the study if a complete medical record (including preoperative visit, operative note, and postoperative follow-up note) was not available for review. No other exclusion criteria were used. This study was approved by the Johns Hopkins University School of Medicine's Institutional Review Board and was conducted in accordance of the Declaration of Helsinki.

The procedure for FA implantation at our institution was similar to what has been described in the literature.^{1, 2, 4} A limited conjunctival peritomy was first performed. The FA implant was then inserted through a pars plana incision, typically in one of the inferior quadrants, and anchored to the sclera using 8-0 or 9-0 prolene suture. The conjunctiva was closed with 6-0 plain gut suture.

Data Collection

Demographic data collected from the preoperative visit included age, gender, and ethnicity. Each patient's uveitis diagnosis and medication history prior to treatment with the FA implant were documented. For the preoperative visit and all subsequent postoperative visits, data were collected from the patient's clinical chart. All patients were seen post-operatively at one day, one week, one month, and every three months thereafter at a minimum until the end of follow-up. The chart contains a flow sheet with clinical information that includes visual acuity, IOP, grade of inflammation in the anterior chamber and in the vitreous (based on SUN criteria²²), current medications, and slit lamp and fundus examination findings. IOP was measured by applanation tonometry, and a single measurement was obtained for each eye at every visit. Surgical complications and need for additional surgery were also documented. Uveitis disease status was noted as either active or inactive at each visit, depending on whether active anterior cells (anterior chamber cells 0.5+ being active disease), active vitreous cells (vitreous cells 1+ in the liquid phase of the vitreous), new or active chorioretinal lesions, and/or macular edema was present.²²

Main Outcome Measures

Visual acuity, intraocular pressure, and control of inflammation were assessed. Visual acuity outcomes included vision loss to the 20/50 or worse and 20/200 or worse thresholds, and a doubling or halving of the visual angle (equivalent to loss of or gain of 3 or more lines of visual acuity on a logarithmic Early Treatment of Diabetic Retinopathy Study [ETDRS] chart, respectively). Refraction to determine best-corrected visual acuity was performed as clinically indicated. When refraction was not available, a pinhole vision (if available) was used. Other outcome measures included incidence of glaucoma surgery and presence of structural complications such as cataract, macular edema, and vitreous hemorrhage. Cystoid macular edema (CME) was defined as the presence of macular thickening as seen on clinical examination, fluorescein angiography, or optical coherence tomography (OCT) according to SUN recommendations.²²

Statistical Analyses

Fisher's exact tests and Students' t-tests were used to compare baseline patient-level characteristics between the BSCR and Other groups. Logistic and linear regression models with general estimating equations (GEE) were performed to compare baseline eye-level characteristics between the BSCR and Other groups. The models accounted for the correlation among measurements of eyes from the same patient. Poisson regression models with robust variance were used to calculate the incidence rate ratios for the visual acuity outcomes, and the secondary outcome measures.²⁴ Cox regression models, with robust variance estimator accounting for correlation between the eyes from the same patient, were

used to compare the times to the clinical events between the BSCR and Other groups.²⁵ Generalized linear mixed models were performed to compare clinical characteristics over time. The models accounted for the correlation among measurements of eyes from the same patient, and the correlation among the repeated measures of the same eye at different clinic visits.²⁶ Statistical significance evaluations were reported as p-values and 95% confidence intervals (CIs). P-values were two-sided and nominal with a value of 0.05 or less considered statistically significant. Data analysis was performed using STATA version 11.0 (Stata Statistical Software; College Station, TX 2010).

Results

Study Population

A total of 50 FA implants were placed in 48 eyes of 28 patients with posterior or panuveitis from 2006 through 2010. Three eyes required a second implant; all others had a single, primary implant. Seventy-one percent of the patients were female and 64% were Caucasian. At the time of surgery, mean ($\pm$ SD) patient age was 55 ± 15 years (range, 27-89 years, Table 1). Of this group, 11 patients or 20 eyes (42% of eyes) had BSCR; 17 patients or 28 eyes had another type of posterior or panuveitis. Multifocal choroiditis and panuveitis (MFCPU) was the most represented diagnosis from the 'Other' group (14 eyes). Other diagnoses included sarcoidosis-associated uveitis (5 eyes), serpiginous choroidopathy (2 eyes), idiopathic uveitis (3 eyes), Vogt-Koyanagi-Harada syndrome (2 eyes), HLA B27-associated anterior and intermediate uveitis (1 eye), and sympathetic ophthalmia in 1 eye. Four patients (8 eyes) from the Other group and one patient (2 eyes) from the BSCR group were involved in the Multicenter Uveitis Steroid Treatment (MUST) Trial.⁶ Additionally one patient (1 eye) in the Other group participated in a Bausch and Lomb study.²

Comparing the BSCR group with the rest of the posterior and panuveitis group (Other group) at the preoperative visit before FA implant surgery, there was a significantly higher percentage of Caucasian patients in the BSCR vs. Other group (100% vs. 41%; $p=0.002$) (Table 1). There were no differences in mean age and gender distribution between the groups at the preoperative visit. Mean (SD) logMAR visual acuity was better preoperatively in the BSCR group (0.3 (0.3) vs. 0.7 (0.5); $p=0.007$). Among all eyes in the study group, 56% had visual acuity of 20/50 or worse and 23% had visual acuity 20/200 or worse. The frequencies of 20/50 or worse vision at the preoperative visit did not differ significantly ($P=0.29$) between the two groups. However, 11 eyes in the Other group (39%) had a visual acuity of 20/200 or worse (the majority of which were attributable to previous chorioretinal scarring) whereas no BSCR eyes had visual acuity of 20/200 or worse at the preoperative clinical visit.

Mean (SD) IOP at the preoperative visit was 14.5 (5) mm Hg for all eyes in the study, with no significant differences between the groups. Similarly, no significant differences were noted in the percentage of eyes using at least one glaucoma medication at the preoperative visit.

A trend was observed in the percentage of eyes with macular edema at the preoperative visit (40% BSCR vs. 14% Other), but this did not achieve significance ($p=0.14$). A high percentage of eyes in both groups had active uveitis immediately before placement of the FA implant (80% BSCR vs. 75% Other).

Prior to treatment with the FA implant, seventeen (35%) eyes had used topical corticosteroids. Forty-two eyes (88%) had used oral corticosteroids, 27 (56%) had received posterior sub-Tenon's triamcinolone acetonide injections, and 14 (29%) had received intravitreal triamcinolone acetonide injections. Thirty-eight (79%) eyes had been treated

with systemic immunomodulatory therapy (Table 1). A higher percentage of eyes in the Other group had been treated with topical corticosteroids than in the BSCR group (54% vs. 10%, respectively; $p=0.05$). The median (range) follow-up time after FA implantation was 37 (4-51) months for the BSCR group and 41 (1-112) months for the Other group (data not shown). Median length of follow-up was not statistically significantly different between the two groups ($p=0.5$). Additionally among patients with 6 months or greater of follow-up, the differences in follow-up were not statistically significant.

Outcomes

The incidence rates of events and the median times to those events after FA implant placement are summarized as Tables 2 and 3, respectively. During the study period, we found a higher incidence rate of loss of at least 3 lines of visual acuity in eyes in the Other group when compared to the BSCR group (0.39/eye-year (EY) versus 0.16/EY, respectively). Visual acuity remained relatively stable in BSCR eyes in the follow-up period. However, there were no significant differences in the median time to gain or loss of at least three lines of acuity between the two groups (Table 3).

A higher rate of IOP increase of 10 mm Hg or more was seen in BSCR eyes (0.46/EY versus 0.28/EY). Also, BSCR eyes had a higher overall incidence of glaucoma surgery (0.42/EY versus 0.11/EY) and progressed more rapidly to glaucoma surgery (i.e., trabeculectomy, tube shunt, trabectome) with median time to surgery of 15.5 months vs. 35.5 months for the Other group (hazard ratio 3.4, 95% CI 1.0-10.8, $p=0.04$) (Table 3; Figure).

Aside from IOP-related complications, the most frequent complication observed after FA implant was the development of cataract. A large majority of phakic eyes underwent cataract surgery during the study period (incidence 0.75/EY and 0.88/EY for BSCR and Other groups, respectively). Vitreous hemorrhage was seen in 7 eyes and cleared spontaneously in all cases. None of the FA implants became exposed during the observed follow up period.

A high percentage of eyes had active uveitis at their preoperative visit, prior to FA implant surgery. The rate of control of uveitis was high in both groups (3.84/EY and 2.37/EY in BSCR and Other groups, respectively) with a median time to control of intraocular inflammation of 2 months. This time period was not significantly different between groups. Recurrence of uveitis activity was seen in only one patient over the study period. Time to resolution of macular edema was not significantly different between the two groups.

Finally, we looked at trends in clinical outcomes over time, from the preoperative visit to postoperative month 4 (+/- 1 month), month 12 (+/- 2 months), month 24 (+/- 4 months), and month 36 (+/- 4 months) (Table 4). We found no statistically significant change in mean visual acuity from the preoperative visit in either group. We did note a significant increase in mean IOP from the preoperative visit to month 4 in the BSCR group (14.73 to 20.07; $p=0.04$). Similarly, there was a significant increase in the percentage of eyes requiring glaucoma surgery in the BSCR group by months 24 and 36 ($p=0.02$ for both time points).

Regarding control of uveitis, we observed a significant decrease in percentage of patients requiring systemic immunosuppressive therapy at almost all time points after FA implantation in both groups ($p=0.001-0.05$). Additionally, a significant decrease in number of BSCR eyes with macular edema was observed at month 24 ($p=0.004$).

Discussion

The BSCR patient group in our study had similar characteristics to those reported in other studies of BSCR patients.^{11, 18, 19, 27} Of note, mean logMAR visual acuity in our study was

0.3 at the preoperative visit, which corresponds to a Snellen equivalent of 20/40. This is significantly better than eyes with other types of posterior and panuveitis and is consistent with the observation that BSCR patients often maintain good central visual acuity, despite other signs of retinal dysfunction, including visual field loss and abnormal ERG.²⁸ The Other group had higher frequencies of 20/200 of worse visual acuity which was primarily due to either chorioretinal scarring from treated and inactive choroidal neovascularization occurring prior to FA implantation or due to severe CME prior to implantation. Mean visual acuity in our BSCR group remained relatively stable throughout the study period, and only five eyes lost acuity to the 20/200 level.

Preoperative medications and medication history were similar in the BSCR and Other groups. A lower percentage of BSCR eyes were treated with topical corticosteroids than the Other group, which reflects the relative paucity of anterior chamber inflammation in BSCR compared to other causes of panuveitis.^{18, 29} It is possible that because patients with BSCR are not habitually treated with topical corticosteroids, that some patients who would be “steroid responders” were not discovered prior to FA implantation whereas some of the “steroid responders” in the Other group were not considered for FA implantation due to this reason (e.g. bias of selection). There was a trend toward increased frequency of oral beta blocker use ($p=0.06$) in the BSCR group. There is a questionable association of BSCR with cardiovascular disease and systemic hypertension, with previous studies reporting incidences of hypertension in 20-46% of BSCR patients.^{19, 29} The higher percentage of BSCR patients vs. Other patients using oral beta blockers may reflect an increased incidence of hypertension in the BSCR group, although this requires further study.

Our results support the findings of previous randomized clinical trials, which showed that the FA implant reduced inflammation and decreased the need for adjunctive therapy in patients with noninfectious posterior uveitis.^{2, 4, 6} In one large, multi-center, randomized controlled trial, eyes with the FA implant had a higher incidence of elevated IOP (> 10 mm Hg) than non-implanted eyes ($p<0.01$), and glaucoma surgery was performed in 40% of implanted eyes vs. 2% of nonimplanted eyes ($p<0.01$).⁴ Data from three such studies showed that the increase in IOP was dramatic in many cases, with 55.1%, 24.7%, and 6.2% of eyes reaching IOPs of 30, 40, and 50 mm Hg, respectively.^{2, 4, 9} As many as three quarters of these patients required IOP-lowering medications, and more than a third required IOP-lowering surgery within the three year study period.⁹ Similarly, a recent retrospective review of patients with noninfectious posterior uveitis receiving FA implants reported 45% of eyes requiring glaucoma surgical intervention.¹⁰

We observed a similar IOP phenomenon in our study, and the BSCR group appeared to have a more robust IOP response than other eyes with posterior and panuveitis. The elevation of IOP in FA implanted BSCR eyes occurred earlier in the preoperative period, with a significant increase in IOP between the preoperative visit and four months after surgery, which was not observed in the Other group. We feel that it is notable that 70% of BSCR eyes in our study required glaucoma surgery after FA implantation. This is a considerably higher percentage than reported in previous studies of patients with posterior uveitis who had been treated with FA implants, although our study is small in size.^{2, 5, 9, 10, 30} Similarly, BSCR patients progressed to glaucoma surgery faster than other patients with posterior and panuveitis. Compiled data from three previous studies showed a mean time of 870 days (29 months) from FA implantation to glaucoma surgery.⁹ This time period was similar to what we found for the Other group, which had a median duration of 31.5 months to glaucoma surgery. The BSCR group, however, progressed to glaucoma surgery at a significantly faster rate, with median time to glaucoma surgery of only 15.5 months. Further, we observed that two eyes from the BSCR group and two eyes from the Other group required glaucoma surgery more than 30 months after FA implant surgery. Additionally, one of these BSCR

eyes had an IOP increase of greater than 10 mm Hg in this time period, indicating that the risk of glaucoma may persist even as the FA implant becomes exhausted of corticosteroid. It is possible that limited follow-up time after FA implantation could prevent us from ascertaining all cases of IOP-lowering surgeries and differential follow-up between the two groups could bias the findings. However greater than 50% of the patients in each group had greater than 30 months of follow-up after FA implant surgery and the differences in follow-up were not statistically significant between the two groups.

Our findings support the results of the study by Rush and colleagues, which looked at a cohort of 22 BSCR patients (36 eyes) who had been treated with FA implants.²⁷ In this study, all eyes had been treated either medically or surgically for elevated IOP by 12 months of follow up. Unlike our study, no comparison group was reported in this study, yet the findings of ocular hypertension and the need for IOP-lowering interventions were compelling.

The reason for the observed IOP response in BSCR patients is unclear. Uveitis is associated with elevated IOP in approximately 8-26% of patients with acute uveitis and 11-46% with chronic uveitis, and the risk of IOP elevation appears to increase with duration of uveitis.³¹⁻³³ The mechanisms of IOP elevation are varied, and include occlusion of aqueous outflow with inflammatory debris or peripheral anterior synechiae, as well as angle closure and pupillary block.^{34, 35} Importantly the use of corticosteroids can result in elevated IOP and is associated with reduced aqueous outflow.^{36, 37} Of all the modalities of corticosteroid delivery, intraocular corticosteroid is associated with the greatest risk of IOP elevation.³⁸⁻⁴⁰ The magnitude of IOP elevation is dependent on multiples variables, including potency of the corticosteroid, dose and duration of treatment, and the patient's innate susceptibility to an IOP response.⁴¹ Regarding BSCR patients in particular, Rush and colleagues proposed that the lack of significant anterior chamber inflammation precludes the development of ciliary body hyposecretion, which may be protective against an IOP rise; thus, a more healthy ciliary body in eyes of patients with BSCR could explain the more robust IOP response to the FA implant.²⁶ This could explain the differences observed in our study as the patients with other forms of posterior and panuveitis were largely MFCEU and sarcoidosis-associated panuveitis, both of which have anterior chamber inflammation and can cause ciliary body hyposecretion. We were not able to compare each of the different uveitis types in the Other group due to the small sample size and therefore it is possible that there are other forms of uveitis such as serpiginous choroiditis or punctate inner choroidopathy that do not affect the ciliary body that may also manifest a more severe IOP response after FA implantation. Interestingly though, neither of the two eyes of patients with serpiginous choroiditis developed elevated IOP during the study period.

Rush also postulated that BSCR patients may be at increased risk of glaucoma, due to decreased optic nerve perfusion from reduced choroidal circulation. Indeed, we believe that there may be additional factors inherent to BSCR that may magnify the IOP response to fluocinolone acetonide. It is unclear whether this marked IOP response can be generalized to other modalities of corticosteroid delivery (e.g., topical or periocular corticosteroids), but this topic may be amenable to further study, particularly in a larger cohort of BSCR patients.

The information provided by this study may be useful for physicians considering various treatment options for BSCR patients. Such patients should be informed that an additional glaucoma procedure that may be likely within the first year after FA implant surgery. Additionally, the FA implant may be a poor choice for patients with preexisting glaucomatous damage, depending on the degree of damage or if such glaucomatous damage exists, it may be prudent to perform the FA implantation in conjunction with a glaucoma surgery as has been described previously.⁴²

The main limitations of this study include its retrospective design and relatively small numbers of patients which make multivariate analyses difficult and increase the likelihood of type 2 errors. It is possible that more significant differences between the BSCR and Other group would be detected with a larger study population. Referral bias may also be present, as all patients were seen at a tertiary care medical center and may represent more severe cases of posterior and panuveitis. Additionally, the study population comprises of patients specifically selected to receive an FA implant—typically due to treatment failure or intolerance—and may not be representative of the broad population of BSCR, posterior and panuveitis patients. Lastly, although no specific exclusion criteria existed for IOP prior to FA implantation, the 4 surgeons who performed the implant surgeries required IOP control prior to implantation as part of standard of care.

In conclusion, our study demonstrates that excellent control of intraocular inflammation and decreased reliance on systemic immunosuppressive therapy can be achieved by treatment with an intravitreal FA implant in eyes with posterior and panuveitis. However, eyes with BSCR may have a more pronounced intraocular pressure response to the FA implant, necessitating glaucoma surgery sooner and more frequently than eyes with other types of posterior and panuveitis. Clinicians should be aware of these risks and counsel patients appropriately before proceeding with implantation of a fluocinolone acetonide device.

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Summary Statement

The fluocinolone implant is effective in controlling inflammation and reducing the need for systemic immunosuppressive therapy in eyes with posterior and panuveitis; however, eyes of patients with birdshot chorioretinitis appeared to have a more robust IOP response to the implant than patients with other types of posterior and panuveitis.

1. .

Kaplan-Meier curve of time to glaucoma surgery in eyes treated with fluocinolone implants: comparison of Birdshot chorioretinitis (BSCR) vs. other posterior/panuveitis (Other). Log rank p-value = 0.006

Table 1

Characteristics of Birdshot and Other Groups at the Preoperative Visit before Fluocinolone Implant Surgery

Characteristics		BSCR	Other [*]	Total	P value [†]
Patient level	Number of patients, N	11	17	28	
	Female gender, N(%)	6 (55)	14 (82)	20 (71)	0.2
	Caucasian ethnicity, N(%)	11 (100)	7 (41)	18 (64)	0.002
	Age (years), mean $\pm$ SD [‡]	60 $\pm$ 13	52 $\pm$ 16	55 $\pm$ 15	0.18
	Medication History ^{**} , N(%)				
	Oral steroids	9 (82)	15 (88)	24 (86)	0.52
	Immunomodulatory therapy	9 (82)	13 (76)	22 (79)	0.56
	Oral beta blockers	5 (45)	2 (12)	7 (25)	0.06
	Current Medications ^{††} , N(%)				
	Oral steroids	9 (82)	10 (59)	19 (68)	0.20
	Immunomodulatory therapy	9 (82)	12 (67)	21 (72)	0.67
	Methotrexate	1 (9)	0 (0)	1 (4)	0.39
	Mycophenolate mofetil	10 (91)	9 (53)	19 (68)	0.04
	Cyclosporine	2 (18)	2 (12)	4 (14)	0.52
	Adalimumab	0 (0)	1 (6)	1 (4)	0.61
	Tacrolimus	1 (9)	1 (6)	2 (7)	0.64
	Cyclophosphamide	0 (0)	1 (6)	1 (4)	0.61
Eye level	Number of eyes, N	20	28	48	
	Visual acuity 20/50, N(%)	9 (45)	18 (64)	27 (56)	0.29
	Visual acuity 20/200, N(%)	0	11 (39)	11 (23)	0.001 ^f
	LogMAR visual acuity, mean $\pm$ SD	0.3 $\pm$ 0.3	0.7 $\pm$ 0.5	0.5 $\pm$ 0.5	0.01
	IOP, mean $\pm$ SD	14.7 $\pm$ 4	14.3 $\pm$ 6	14.5 $\pm$ 5	0.69
	IOP<5, N(%)	0	2 (7)	2 (4)	0.67 ^f
	IOP>20, N(%)	2 (10)	1 (4)	3 (6)	0.38
	Macular edema, N(%)	8(40)	4 (14)	12 (25)	0.08
	Active uveitis, N(%)	16 (80)	21 (75)	37 (77)	0.51
	Medication History ^d , N(%)				
	Topical steroids	2 (10)	15 (54)	17 (35)	0.03
	PST triamcinolone	8 (40)	19 (68)	27 (56)	0.20
	Intravitreal triamcinolone	7 (35)	7 (25)	14 (29)	0.73
	IOP-lowering drops	5 (25)	11 (39)	16 (33)	0.57
	Intravitreal anti-VEGF	0 (0)	5 (18)	5 (10)	0.11 ^f
	Current Medications ^e , N(%)				
	Topical steroids	3 (16)	15 (60)	18 (41)	0.06
	IOP-lowering drops	4 (20)	9 (32)	13 (27)	0.74

BSCR= Birdshot chorioretinitis

Other= Other Posterior and Panuveitis patients

PST= posterior sub-tenon's

IOP= intraocular pressure

VEGF= vascular endothelial growth factor

* Other group is comprised of patients with the following diagnoses: 14 multifocal choroiditis and panuveitis (29%), 5 sarcoidosis-associated (10%), 2 serpiginous choroidopathy (4%), 3 idiopathic (6%), 2 Vogt-Koyanagi-Harada syndrome (4%), 1 HLA B27-associated uveitis (2%), 1 sympathetic ophthalmia (2%).

[†] For patient level characteristics, p values are from Fisher's exact test. For eye level characteristics, p values are from logistic or linear regressions with generalized estimating equations account for correlation between eyes from the same patient, unless otherwise specified.

[‡] Students' t-test

^{**} Medication history refers to medications used prior to the fluocinolone implant.

^{††} Current medications refer to medications used at time of the preoperative visit.

Table 2

Incidence of Events after Fluocinolone Acetonide Implantation

Event	BSCR (N=20)			Other (N=28)		
	N (%)	Incidence Rate (per Eye Year)	95% CI	N (%)	Incidence Rate (per Eye Year)	95% CI
IOP <5	1 (5)	0.02	0.003, 0.16	7 (25)	0.07	0.03, 0.18
IOP > 20	16 (80)	0.99	0.43, 2.28	15 (54)	0.29	0.13, 0.67
IOP increase 10 mm Hg	12 (60)	0.46	0.25, 0.85	13 (46)	0.28	0.13, 0.61
Visual acuity 20/50	18 (90)	1.27	0.32, 4.96	24 (86)	0.83	0.35, 1.98
Visual acuity 20/200	5 (25)	0.10	0.03, 0.31	17 (61)	0.22	0.09, 0.56
Loss of 3 lines of visual acuity	6 (30)	0.16	0.07, 0.29	15 (54)	0.39	0.29, 0.82
Gain of 3 lines of visual acuity	4 (20)	0.10	0.03, 0.30	11 (39)	0.19	0.09, 0.40
Glaucoma surgery	14 (70)	0.42	0.27, 0.86	8 (29)	0.11	0.04, 0.26
Cataract	4 (44)	0.35	0.07, 1.83	10 (71)	0.67	0.22, 2.04
Cataract surgery	7 (78)	0.75	0.56, 1.00	11 (79)	0.88	0.46, 1.67
Exposure of implant	0 (0)	-	-	0 (0)	-	-
Vitreous hemorrhage	4 (17)	0.08	0.03, 0.22	3 (10)	0.03	0.01, 0.10
Control of uveitis	16 (100)	3.84	2.57, 5.74	21 (100)	2.37	1.13, 4.99
Resolution of macular edema	7 (88)	1.6	0.33, 7.80	2 (100)	1.28	0.48, 3.42
IMT discontinued	11 (58)	0.45	0.17, 1.17	9 (38)	0.15	0.06, 0.43

BSCR = birdshot chorioretinitis

Other = other posterior and panuveitis

IOP = intraocular pressure

IMT= immunomodulatory therapy

Table 3**Median Time to Events After Fluocinolone Acetonide Implantation**

Event	Median durations (25 th , 75 th quartile), months		Hazard ratio (BSCR vs. Other)	95% Confidence Interval	P value
	BSCR	Other			
IOP <5	33.5 (12, 41)	40 (12.5, 46)	0.24	0.03, 2.1	0.19
IOP > 20	5.5 (3.5, 10)	11.5 (2, 31)	2.2	0.9, 5.2	0.08
IOP increase 10 mm Hg	9.5 (4.5, 2.6)	11.5 (4.5, 31)	1.3	0.6, 2.8	0.54
Visual acuity 20/50	1 (0.5, 2.5)	0.5 (0, 4.5)	1.02	0.5, 2.1	0.96
Visual acuity 20/200	31.5 (7.5, 36.5)	2 (0, 39)	0.4	0.1, 1.6	0.21
Loss of 3 lines of visual acuity	25 (5, 36)	10 (3, 31)	0.45	0.2, 1.2	0.11
Gain of >3 lines of visual acuity	31 (7, 36)	19 (7, 41)	0.56	0.2, 2.1	0.39
Glaucoma surgery	15.5 (4.5, 32)	31.5 (9.5, 44)	3.4	1.0, 10.8	0.04
Cataract	9 (5, 22)	8.5 (1, 11)	0.5	0.1, 2.3	0.41
Cataract surgery	15 (6, 17)	10.5 (6, 17)	0.7	0.2, 2.1	0.53
Vitreous hemorrhage	33 (5, 41)	40 (19, 47)	1.8	0.4, 8.0	0.45
Control of uveitis	2 (2, 4)	2 (1, 4)	1.2	0.6, 2.6	0.63
Resolution of macular edema	2 (0, 6)	10 (3, 15)	1.8	0.7, 4.9	0.24
IMT discontinued	8 (4, 23)	34 (3.5, 42)	1.9	0.6, 6.3	0.31

BSCR= birdshot chorioretinitis

Other= other posterior and panuveitis

IMT= immunomodulatory therapy

Table 4

Clinical Characteristics from Time of Fluocinolone Acetonide Implantation

Clinical Characteristics	Time from FA implant	BSCR		Other	
Number of eyes		N		N	
	Baseline	20		28	
	Month 4	15		22	
	Month 12	16		23	
	Month 24	15		22	
	Month 36	13		20	
LogMAR Acuity		Mean (SD)	P value *	Mean (SD)	P value
	Baseline	0.30 (0.3)		0.67 (0.5)	
	Month 4	0.33 (0.3)	0.49	0.66 (0.5)	0.63
	Month 12	0.25 (0.3)	0.67	0.72 (0.4)	0.43
	Month 24	0.21 (0.2)	0.55	0.67 (0.5)	0.74
	Month 36	0.36 (0.3)	0.34	0.67 (0.6)	0.99
Intraocular Pressure		Mean (SD)	P value	Mean (SD)	P value
	Baseline	14.73 (4.4)		14.29 (5.8)	
	Month 4	20.07 (8.2)	0.04	16.80 (9.9)	0.15
	Month 12	16.66 (8.1)	0.51	13.96 (7.9)	0.91
	Month 24	15.87 (10.2)	0.81	12.27 (8.2)	0.34
	Month 36	14.19 (6.2)	0.55	14.80 (10.7)	0.88
IOP increase ≥ 10 mm Hg		N(%)	P value	N(%)	P value
	Month 4	4 (27)		2 (9)	
	Month 12	3 (18)	0.48	1 (4)	0.29
	Month 24	2 (13)	0.49	3 (14)	0.7
	Month 36	1 (8)	0.29	4 (20)	0.38
Glaucoma surgery		N(%)	P value	N(%)	P value
	Baseline	1 (5)		3(11)	
	Month 4	4 (27)	0.08	0	-
	Month 12	5 (31)	0.06	0	-
	Month 24	9 (60)	0.02	2 (9)	-
	Month 36	10 (77)	0.02	0	-
Immunomodulatory Therapy		N(%)	P value	N(%)	P value
	Baseline	19 (95)		24 (86)	
	Month 4	9 (60)	0.01	15 (68)	0.05
	Month 12	7 (44)	0.002	18 (78)	0.32
	Month 24	4 (27)	0.001	15 (68)	0.05
	Month 36	3 (23)	0.001	13 (65)	0.03
Active uveitis		N(%)	P value	N(%)	P value

Clinical Characteristics	Time from FA implant	BSCR		Other	
	Baseline	16 (80)		21 (75)	
	Month 4	2 (13)	<0.001	4 (18)	0.003
	Month 12	0	-	2 (9)	0.001
	Month 24	0	-	3 (14)	0.01
	Month 36	1 (8)	0.05	0	-
Cystoid Macular Edema		N(%)	P value	N(%)	P value
	Baseline	8 (40)		4 (14)	
	Month 4	4 (27)	0.24	3 (14)	0.79
	Month 12	4 (25)	0.27	4 (17)	0.92
	Month 24	1 (7)	0.004	3 (14)	0.82
	Month 36	2 (15)	0.18	3 (15)	0.83

- indicates model did not achieve convergence.

Baseline represents the preoperative visit, typically less than one month prior to fluocinolone acetonide implantation.

FA= fluocinolone acetonide

BSCR= Birdshot chorioretinitis

IOP= intraocular pressure

*

P values are from generalized mixed effects models and compare each visit with the preoperative visit.