7/29/2023 12:00 am

Inflammatory & Infectious Disease Symposium

Prospective Imaging of the Intravitreal Fluocinolone Acetonide Implant Using Fluorescein Angiography and OCT in Uveitis (PANTHER)

- Sunil Srivastava, MD
- Abel Hamdan, MD
- Kimberly Baynes, RN MSN
- Danielle Burton, BS
- Sumit Sharma, MD, FASRS

Objective: To study the impact of intravitreal fluocinolone acetonide implant on imaging in patients with active non-infectious uveitis
Purpose: The intravitreal fluocinolone acetonide implant (iFA) was approved in 2018 for treatment of non-infectious uveitis affecting the posterior segment. There is limited imaging based outcome metrics for patients treated with iFA. This is a prospective investigator initiated study (IIS) evaluating the imaging outcomes in patients treated with the iFA implant utlizing ultrawide field fluorescein angiography (UWFFA) and optical coherence tomography (OCT). Advanced imaging metrics including leakage index on UWFFA and fluid index as measured on OCT.
Methods: 43 eyes of 29 adult non-infectious uveitis (NIU) patients were included in the 12-month prospective study if deemed active or recently active (6 months) by a uveitis specialist. All patients had standard clinical exams at baseline and imaging including optical coherence tomography (OCT), and ultra-wide field fluorescein angiography (UWFFA). Patients were treated with intravitreal fluocinolone acetonide implant and were eligible for rescue with standard treatment or reimplantation if they failed to respond to therapy. Patients were followed with standard clinical exams for 12 months with additional OCT, UWFFA imaging. An automated machine learning algorithm using a desktop-based software interface allowed quantification to identify changes over the yearlong study. OCT and UWFFA metrics were calculated at each visit. OCT metrics included Central Subfield Thickness (CST) and Fluid Index (Fl). UWFFA metrics included leakage measured within a macula centered area of 3 disc diameters (3DD), 6 Disc Diameter (6DD), and the total retinal Leakage.
Results: 43 eyes of 29 patients are included in this analysis. The mean age was 57 (23 - 79) years old. 18 of the 29 patients were women. 25 eyes had panuveitis and 17 had posterior uveitis. 20 eyes had idiopathic disease,12 eyes had sarcoidosis and 6 eyes had retinal vasculitis. 13 of 29 patients required rescue, with the vast majority occuring within the first 6 months. Mean central subfield thickness decreased from baseline from 345 um to 320 um by month 3 ($p < .001$) and continued to decrease through month 12 (310 um p= 002). Fluid index, the percentage of the intraretinal and subretinal fluid divided by total macular volume, reduced from on average 6.5% at baseline to 4.5% by month 9 ($p = .017$). On UWFFA all three metrics of leakage (3DD, 6DD, TRL) significantly reduced on average from baseline by month 3 and month 6 ($p < .02$). No eyes required glaucoma surgery during the 1 year and 9 of 12 phakic eyes at baseline required cataract surgery within 1 year. 40% of eyes were at baseline on drops for IOP and by 1 year 39% of eyes were on IOP drops
Conclusion: The intravitreal fluocinolone acetonide implant was well tolerated and significantly improved imaging metrics of inflammation by month 3. Improvements of these metrics continued through month 12. No patients required glaucoma surgery and the percentage of eyes on glaucoma drops did not change. 45% of patients required supplemental therapy during the study.

IRB APPROVAL Yes

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Inflammatory & Infectious Disease Symposium

A novel intravitreal anti-IL-6 monoclonal antibody for uveitic macular edema (UME): preliminary results from the phase 1 DOVETAIL study

- Sumit Sharma, MD, FASRS
- Eric Suhler, MD, MPH
- Phoebe Lin, PhD
- Meike Pauly-Evers, PhD
- Daniele Willen, PhD
- Robbie Peck, PhD
- Federica Storti, PhD
- Simone Rauhut, MsC
- Tatiana Gott, BsC
- Benedicte Passemard, PharmD
- Lachlan Macgregor, MBBS, MMedSc, MBios
- Zdenka Haskova, MD, PhD
- David Silverman, MSc, MBChB
- Sascha Fauser, MD
- Marina Mesquida, MD, MSc, PhD

Objective: The DOVETAIL phase 1 clinical trial assessed the safety, tolerability and efficacy of a novel anti–IL-6 monoclonal antibody (RG6179) specifically designed for IVT use in patients with DME and UME.

Purpose: Inflammation is a key pathway in retinal disease pathophysiology. However, standard-of-care anti-inflammatory corticosteroid use carries significant risk of side effects. RG6179 is a recombinant monoclonal antibody that potently inhibits all forms of IL-6 signaling. This abstract reports the preliminary data with RG6179 in patients with UME.

Methods: DOVETAIL is a phase 1, multicenter, non-randomized, open-label, multiple ascending dose study that investigates the safety, tolerability, efficacy, and PK/PD profile of RG6179 in both DME and UME patients. Patients ≥18 years with non-infectious uveitis and concurrent ME (CST ≥325 µm) were included (N=33). Patients were enrolled into 3 dose groups: 0.25 mg (n=10), 1 mg (n=10), and 2.5 mg (n=13), and received IVT RG6179 at Week 0, 4 and 8, followed by post-treatment observation until Week 36.

Results: Mean age was 62 years, 42% of patients were male, mean (range) baseline BCVA and CST were 64 (43-80) letters and 509 (271-893) µm, respectively. Mean (SE) BCVA change from baseline was +10.3 (2.6), +9.5 (2.1) and +8.4 (3.1) letters for the 0.25, 1 and 2.5 mg doses, respectively, with a combined mean of +9.3 (1.6) letters at 12 weeks. Mean CST change from baseline was -124 (44), -177 (59) and -184 (48) µm, respectively, with a combined mean of -161 (28) µm at 12 weeks. Of note, the BCVA and CST benefits were maintained during the post-treatment observation period. All doses of RG6179 were well tolerated across all 33 patients. Ocular AEs (n=27) were reported in the study eye of 16 of 33 patients. Of those AEs; 21 were mild, 5 were moderate, 1 was severe (worsening of uveitis; unrelated). Only 1 AE in 1 patient was reported as related to RG6179 (transient visual acuity loss). Two patients had a progression of pre-existing cataract; none developed new cataracts. There were no cases of treatment-related intraocular pressure increase, occlusive retinal vasculitis or systemic AEs.

Conclusion: This phase 1 trial provides preliminary data on the safety and efficacy of the novel anti–IL-6 antibody RG6179 in patients with UME. Two phase 2 studies in DME (mono and combo) and two phase 3 trials in UME are currently underway to further assess the clinical potential of RG6179.

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Inflammatory & Infectious Disease Symposium

Outcomes and Clinical Features Predictive of Fungal Endophthalmitis

- Mark Breazzano, MD, FACS
- Peng Huang, PhD
- Aaron Priluck, MD

Objective: What factors can predict a confirmed case of fungal endophthalmits versus a masquerade, as well as the prognosis at the time a patient receives intravitreal antifungal injection, and is there a role for routinely screening those with a fungal bloodstream infection?
Purpose: To review intravitreal antifungal injections performed at a tertiary center to determine: 1) risk factors increasing fungal endophthalmitis likelihood at time of patient presentation, 2) prognostic factors at presentation, and 3) validity of American Academy of Ophthalmology (Academy) ophthalmologic *Candida* septicemia (candidemia) screening guidelines.
Methods: Clinical course, visual outcome, and final diagnosis were reviewed for 75 patients (81 eyes) receiving intravitreal antifungal injections between 2014-2021 with this single-center, retrospective chart review. Features were compared between fungal endophthalmitis and clinically similar diseases (masquerades).
Results: Fungal endophthalmitis was more likely than masquerade based on injection in emergency department or inpatient setting ($p = 0.0002$) versus outpatient, greater visual acuity ($p = 0.049$), artificial indwelling line present ($p = 0.0004$), sepsis within past 6 months ($p = 0.0002$), prior/current hepatitis C diagnosis ($p = 0.044$), total parenteral nutrition ($p = 0.0028$), complicated diabetes mellitus ($p = 0.035$), actively treated cancer ($p = 0.021$), immunosuppressive medication within past year ($p = 0.035$), immunocompromising condition number ($p = 0.031$), and delayed pain ($p = 0.0094$) and vision loss ($p = 0.020$) onset. Visual acuity at presentation correlated with visual outcome ($R^2 = 0.3524$, $p = 8.5 \times 10^{-7}$). No patients with fungal endophthalmitis were asymptomatic or identified by screening.
Conclusion: Many conditions can mimic fungal endophthalmitis, but certain risk factors should raise its suspicion. Regardless of diagnosis, presenting vision correlates with final vision. Lastly, no patients with fungal endophthalmitis were asymptomatic or identified by screening, further supporting current Academy candidemia screening guidelines.

IRB APPROVAL No - exempt

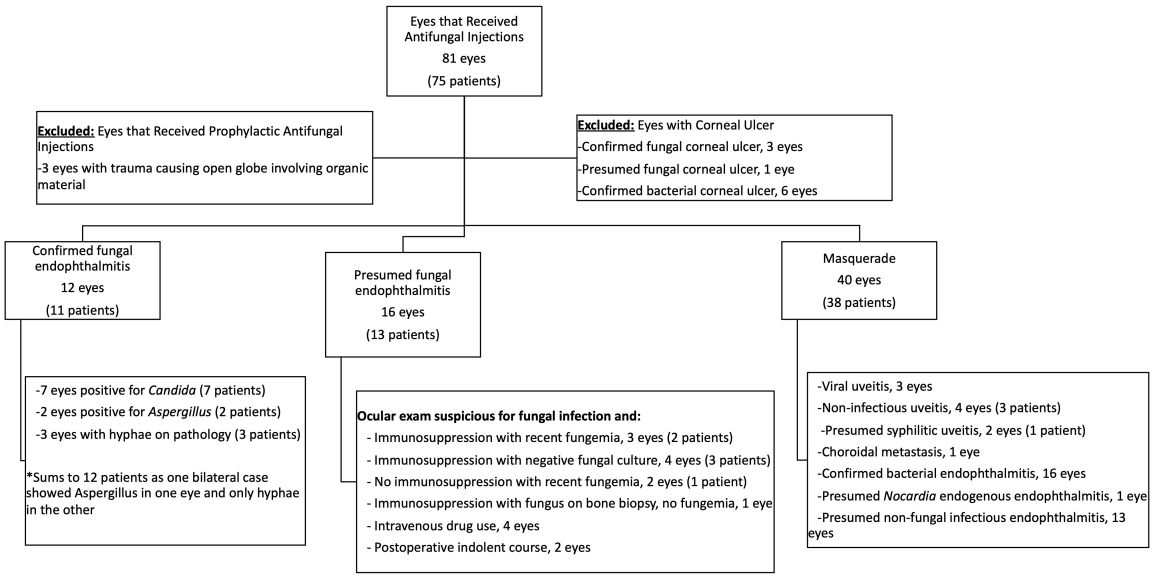

Figure 1. Summary of cases with intravitreal antifungal injection.

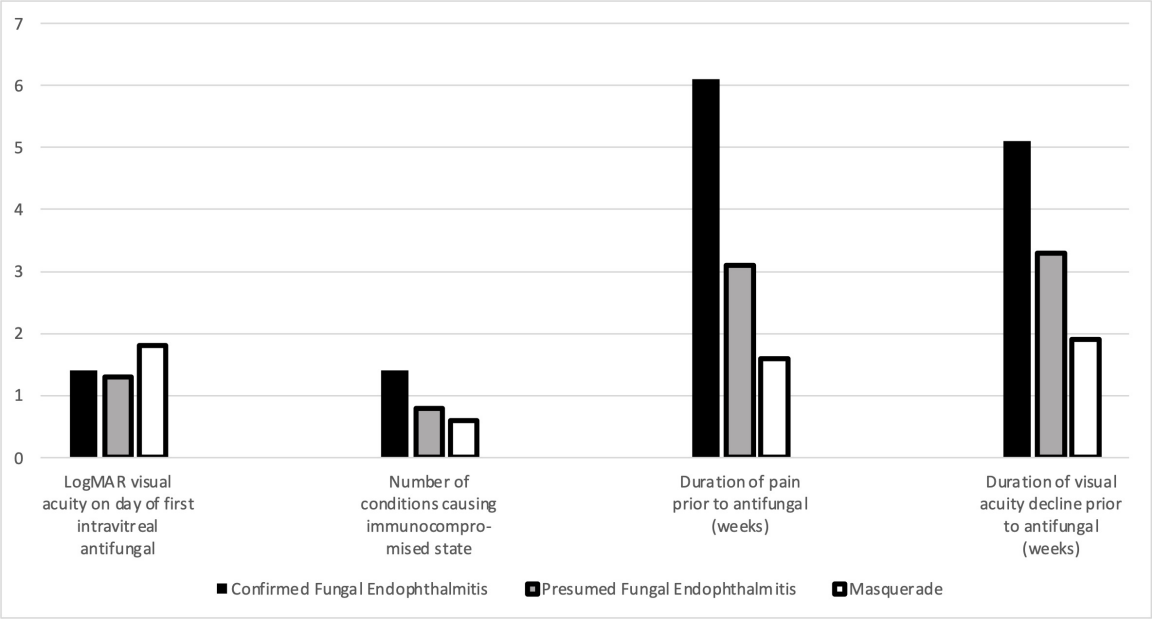

FIgure 2. Categorical variables differing based on final diagnosis.

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Inflammatory & Infectious Disease Symposium

Rates of Post Intravitreal Anti-VEGF Injection Endophthalmitis: Management Strategies and Visual Acuity Outcomes From the AAO IRIS Registry

- Alia Durrani, MD
- Sabin Dang, MD
- Shriji Patel, MD, MBA
- Flora Lum, MD

Objective: To Investigate risk factors for and rates of post anti-vascular-endothelial growth factor injection endophthalmitis across a large, national database.
Purpose: We used the American Academy of Ophthalmology's (AAO) Intelligent Research in Sight (IRIS) Registry to investigate rates of endophthalmitis post anti-vascular endothelial growth factor injection. Secondarily, we reviewed socioeconomic factors and management strategies in relation to endophthalmitis development and visual acuity (VA) outcomes
Methods: Retrospective cross-sectional study using the IRIS registry database from 2013-2020. Eyes diagnosed with endophthalmitis within 10 days of anti-VEGF injection with no other intraocular surgeries in preceding 27 days were included. Demographic and VA data, use of steroids, and performance of pars plana vitrectomy (PPV) were noted. Multivariable analysis was used to evaluate predictors of development of endophthalmitis and VA outcomes
Results: 6,175 total injections of 6,175 eyes and 6,131 patients were included out of 20.1 million injections (incidence, 0.03%). Aflibercept, Bevacizumab, and Ranibizumab comprised 47%, 36%, and 17% of injections, respectively. Mean VA prior to endophthalmitis was 20/59, and at 6 months was 20/98. Mean days from injection to diagnosis of endophthalmitis was 4 (SD 2.1, 1-10). Mean number of injections preceding endophthalmitis was 12.7 (SD 12.7, 0-90). Matched controls were randomly selected from the IRIS registry based on gender, age and date of injection. Prior or active smokers were found to have odds ratio (OR) of 1.21 and 1.26 ($p<0.00$) for development of endophthalmitis. Bilateral same-day injections did not confer higher odds of development of endophthalmitis (OR 1.00, $p=0.99$).Using multivariable analysis, a significant difference in 6 month VA based on anti-VEGF drug injected (Aflibercept, $p=0.04$, Ranibizumab, $p=0.02$) was found compared to Bevacizumab. Eyes managed with PPV within 10 days of diagnosis of endophthalmitis did not have significant improvement in VA at 6 or 12 months when controlling for baseline vision and demographics. Each day between initial injection of anti-VEGF agent and diagnosis of endophthalmitis was associated with decreased VA of 1/2 Snellen letter at 6 months and 1 year ($p=0.02$, $p=0.04$). Oral/intravitreal steroid use within 10 days of diagnosis of endophthalmitis did not result in significant difference in VA at 6 months or 1 year ($p=0.09$, $p=0.25$)
Conclusion: To date, this is the largest published dataset to investigate rates of endophthalmitis post anti-VEGF injection,facilitating exploration of potential risk factors for development of disease. Prior or active smokers may have higher odds of developing endophthalmitis post anti-VEGF injection. Performing bilateral, same-day injections did not increase odds of development of endophthalmitis. Management of post anti-VEGF injection endophthalmitis with PPV did not demonstrate clear VA benefit at 1 year. Delay in diagnosis of post anti-VEGF injection endophthalmitis results in visual acuity loss.

IRB APPROVAL No - no IRB

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Inflammatory & Infectious Disease Symposium

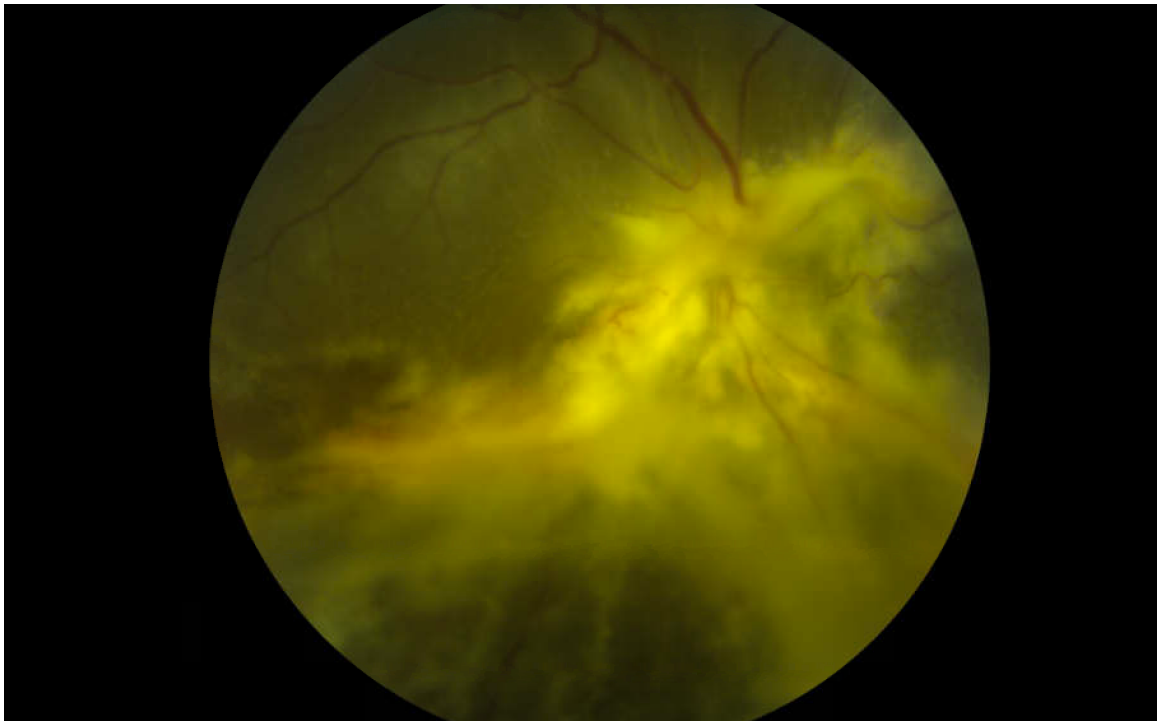
Long-Term Visual and Surgical Outcomes in 35 Eyes With Infectious Retinitis Requiring Retinal Detachment Repair

- Sruthi Arepalli, MD
- Albert Liao, MD/MS
- Steven Yeh, MD
- Andrew Zheng, MD
- Jiong Yan, MD

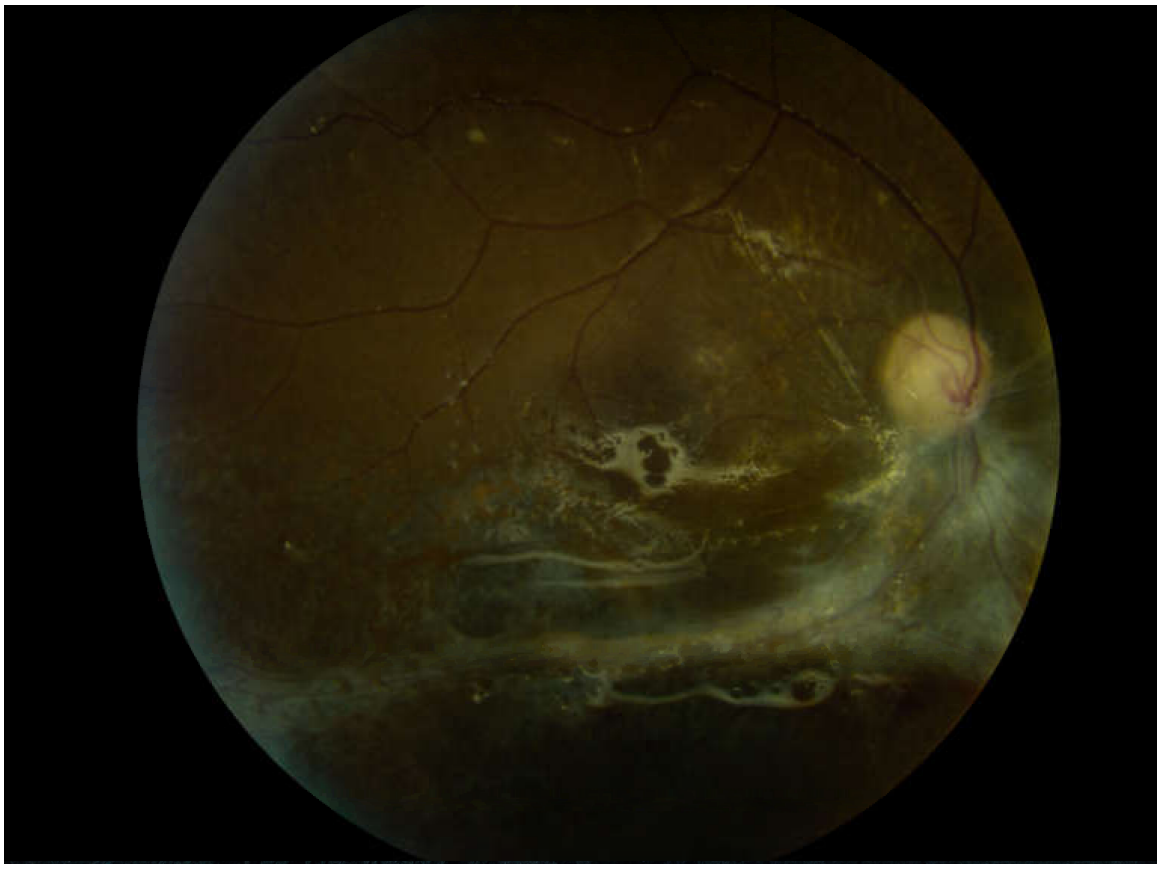
Objective: To describe the long-term visual and surgical outcomes following retinal detachment repair in 35 eyes with infectious retinitis.
Purpose: A paucity of long-term data exists regarding the visual acuity and sugical outcomes of infectious retinitis detachments, especially in cases of infetious retinitis caused by etiologies other than acute retinal necrosis. Our report reviews these in 35 eyes with infectious retinitis related detachments presenting to a single center over 10 years.
Methods: This is a single-center, retrospective observational study of patients diagnosed with infectious retinitis who developed retinal detachment and were repaired between 1/1/10 to 5/1/20. Inclusion criteria included patients with infectious retinitis who subsequently developed retinal detachment requiring surgical intervention. Exclusion criteria included age less than 18, prior detachment or previous intraocular surgeries except for cataract removal. Best corrected visual acuity (BCVA) was converted to logarithm of the minimum angle of resolution (LogMAR). Data collected included age, demographics, type of infection, type of primary surgery, type of secondary surgery if applicable, and presence of proliferative vitreoretinopathy (PVR). All cases were classified into surgery with vitrectomy (PPV), combined vitrectomy and scleral buckle (PPV+SB), or scleral buckle (SB). This yielded 35 eyes in 31 patients.

Results: A total of 35 eyes in 31 patients were included. 16 were male (51.6%), and average age was 46 years; the longest follow was 12.5 years. The most common infection was cytomegalovirus (13, 37%) (Fig. 1), followed by toxoplasmosis (7, 20%). 29 eyes (82.9%) presented with a rhegmatogenous detachment and 6 (17.1%) had tractional detachments. The macula was off in 22 eyes (62.9%). 23 eyes were initially treated with pars plana vitrectomy (PPV), 11 with a combination of PPV and scleral buckle (PPV+SB), and 1 eye received a scleral buckle (SB). Of these, primary reattachment occured in 12 of PPV only group (52.2%), 7 of PPV+SB group (63.6%) (Fig. 2), and 0 of the SB group (0%). Overall, single surgery success was achieved in 19 eyes (54.2%).With multiple surgeries, final attachment occured in 28 eyes (80%).
18 of the 35 eyes (51.4%) presented with PVR; 11 of these were repaired with primary PPV, 6 with combined PPV+SB, and 1 with sole SB. Of these, 3 of the primary PPV group were successful (27.3%), 3 of the PPV+SB were successful (50%), and none of the SB group were successful (0%).There was no significant difference in single surgery reattachment or visual outcome between surgical techniques. The final VA also did not significantly differ between the macula involving and macula sparing detachments.
Conclusion: While difficult to treat surgically, final attachment rates of patients with multiple etiologies of infectious retinitis was obtained in 80%, with the highest success seen in the combined PPV+SB group for primary surgery and those presenting with PVR. Final visual acuity does not differ significantly between macula sparing and macula involving detachments.

IRB APPROVAL Yes



38 year old male presenting with HIV, CMV retinitis and retinal detachment



Attached retina in the same 38 year old male after SB/PPV/SO

Visual Outcomes and Foveal Fluid Dynamics in Patients Treated With Steroid Injections for Postoperative Macular Edema

- Scott Walter, MD, MSc, FASRS
- Christopher Edwards

Objective: To evaluate the efficacy of steroid injections for postoperative macular edema (ME) following intraocular surgery.

Purpose: Postoperative ME is a common complication following vitreoretinal and anterior segment surgery. While postoperative ME resembles uveitic ME angiographically, patients with postoperative ME have generally been excluded from FDA labeling trials. There are now three FDA-approved steroid injections for uveitic ME: Ozurdex (0.4mg dexamethasone implant; Allergan), Yutiq (0.19mg intravitreal flucinolone implant; EyePoint), and Xipere (4mg/0.1mL suprachoroidal triamcinolone acetonide suspension; Bausch + Lomb). This study sought to validate the use of these agents in eyes with postoperative ME.

Methods: Consecutive case series of patients treated with injections of Ozurdex, Yutiq, and/or Xipere for the management of postoperative ME. This study focused specifically on eyes with ME following intraocular surgery, excluding patients with a pre-operative diagnosis of ME, uveitis, or systemic inflammatory disease. All patients were treated by SDW at RCPC and received an initial injection between June 5th, 2018 and November 11th, 2022 (4.5 years). The primary outcome measures were visual acuity (VA) and intraocular pressure (IOP). Secondary outcome measures included microanatomic changes on optical coherence tomography (OCT) including assessment of central subfield thickness (CST), macular volume (MV), as well as the presence or absence of intraretinal fluid (IRF) and subretinal fluid (SRF) on foveal line scans. These clinical endpoints were assessed at 6 weeks and 3 months following the initial administration of each agent.

Results: A total of 146 injections (N=90 Ozurdex, 37 Yutiq, 19 Xipere) were analyzed. A significant improvement in VA was observed at 6 weeks (+4.8 letters, $p=7 \times 10^{-5}$) and at 3 months (+3.6 letters ($p=0.003$). Approximately 5.5% of patients had IOP elevation ≥25 mm Hg at 6 weeks (N=6/107) and 3 months (N=5/91). However, there was no significant rise in mean IOP at 6 weeks (+1.0 ETDRS letters, $p>0.05$) or at 3 months (-0.0 letters, $p>0.05$), allowing for topical IOP management at the discretion of the treating physician. Highly significant anatomic improvements in CST (-129 µm, $p\sim10^{-13}$) and MV (-0.88 mm , $p\sim10^{-11}$) were observed at 6 weeks with a persistent treatment effect at 3 months (CST: -75 µm; $p\sim10^{-6}$, MV: -0.59 mm, $p\sim10^{-7}$). The majority of foveal OCT scans were "dry" at 6 weeks with no IRF in 74% and no SRF in 97% of patients. However, 50% of patients demonstrated IRF on their foveal OCT lines scans at 3 months.

Conclusion: This study supports the efficacy of three FDA-approved steroid injections for patients with postoperative ME. There was significant improvement in visual and anatomic outcomes at 6 weeks and 3 months following the initial injection. A small minority of patients experienced IOP elevation and these were adequately managed with topical antihypertensive therapy. The recurrence of intraretinal fluid at 3 months and trend towards increasing MV and CST suggests that some patients with postoperative ME may require retreatment sooner than 3 months following the first injection.

IRB APPROVAL No - no IRB

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Inflammatory & Infectious Disease Symposium

Demographic and Socioeconomic Predictors of Visual Outcomes in Pediatric Uveitis: An IRIS Registry Study

- Akshay Thomas, MD, MS
- Laura Kopplin
- Sruthi Arepalli, MD
- Eric Suhler, MD, MPH
- Phoebe Lin, MD, PhD

Objective: To identify socioeconomic or demographic predictors of visual outcomes for patients with pediatric uveitis.

Purpose: To assess the impact of age, race, gender, demographic region and insurance on outcomes in pediatric non-infectious uveitis

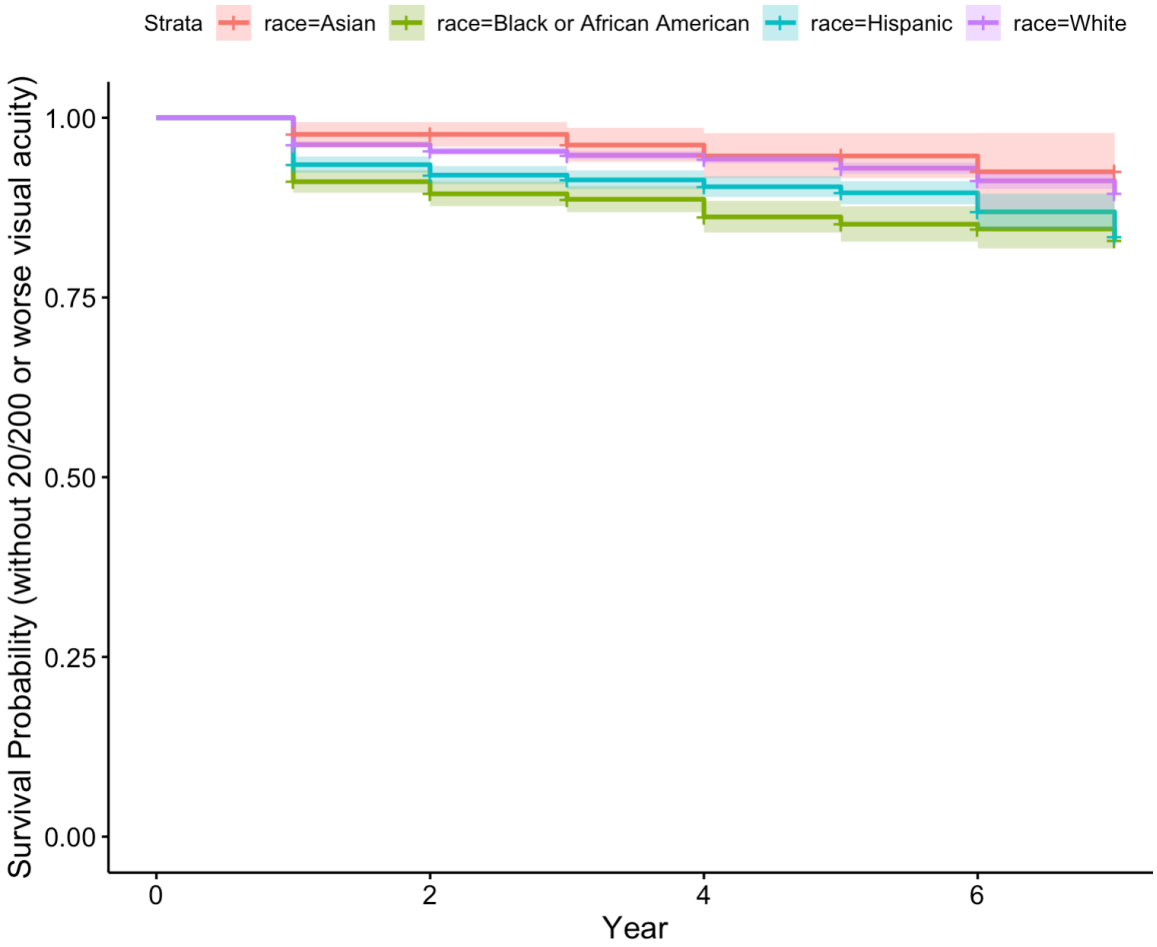
Methods: Patients diagnosed with non-infectious uveitis at the age of 18 or younger between 1/1/2013 and 12/31/2019 and with ≥1 year of follow-up were identified using the IRIS registry. Patients with incomplete demographic and socioeconomic data (age, gender, race, region and insurance type) were excluded. Multivariate regression was used to determine if age, gender, race, region and insurance type were associated with higher risk of (i) poor visual acuity outcomes (20/200 or worse in the affected eye) at final follow-up, (ii) complications (cataract, glaucoma, amblyopia, synechiae, cystoid macular edema, band keratopathy) and (iii) requirement for ocular surgery.

Results: Data from 7,541 unique patients (representing 11,268 eyes) were included. The most common form of uveitis was anterior uveitis (67.7%) followed by intermediate uveitis (11.4%), posterior uveitis (10.2%), panuveitis (5.6%) and retinal vasculitis (2%). 16.7% of eyes had a documented ocular complication related to uveitis. On multivariate regression, Black children were more likely than Caucasian children to have a final visual acuity of 20/200 or worse and develop glaucoma ($p<0.05$). Compared to children with private insurance, those with Medicaid were more likely to have a final visual acuity of 20/200 or worse, suffer from cataract, amblyopia, posterior synechiae and band keratopathy and require cataract surgery, glaucoma surgery and retinal detachment surgery ($p<0.05$ for all). Children from the Midwest were more likely than children from other regions to suffer from cataract, glaucoma, amblyopia and require cataract and glaucoma surgery ($p<0.05$ for all). Children with uveitis onset at ≤12 years were more likely to develop cataracts, glaucoma, amblyopia and band keratopathy than those 13-18 years old at uveitis diagnosis ($p<0.05$ for all).

Conclusion: The most pronounced socioeconomic and demographic predictors for poorer visual outcomes in pediatric uveitis include younger age of presentation, Black race and belonging to a low-income family (qualifying for Medicaid). Awareness of these prognosticators may impact our approach to uveitis management for such at-risk groups.

IRB APPROVAL No - no IRB

Kaplan-Meier Survival Curve showing time to 20/200 or worse vision


Strata
race=Asian
race=Black or African American
race=Hispanic
race=White
Survival Probability (without 20/200 or worse visual acuity)
1.00
0.75
0.50
0.25
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2
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Inflammatory & Infectious Disease Symposium

Comparison of Originator and Biosimilar Medications for Pediatric Noninfectious Uveitis

- Nita Valikodath, MD, MS
- Jay Rathinavelu
- Jordan Deaner, MD
- Dilraj Grewal, MD, FASRS

Objective: Is there a difference in the frequency of flares between biosimilar and originator tumor necrosis factor-alpha (TNF-alpha) inhibitors for non-infectious uveitis in pediatric patients?
Purpose: Biosimilar tumor necrosis factor-alpha (TNF-alpha) inhibitors are increasingly being used to treat pediatric uveitis due to expiring patents of originator medications and lower costs, but little is known regarding its effects on ocular disease activity compared to the originator medications. We aimed to review our data comparing the efficacy of TNF-alpha inhibitor biosimilars to the originator medications in pediatric non-infectious uveitis.
Methods: Retrospective case series at a single pediatric tertiary care center from January 1, 2019 to November 1, 2022. We included patients ≤ 18 years old treated with a biosimilar agent for non-infectious uveitis, had history of active uveitis, and had at least 9 month follow up with ophthalmology. Demographics, uveitis anatomical location and phenotype, originator and biosimilar medication, dose, frequency, and duration were documented. Number of flares, additional immunomodulatory therapy (IMT), and reason for switching to a biosimilar agent were noted. Descriptive statistics including mean, standard deviation and ranges were reported for continuous variables and frequency and percentages for categorical variables.
Results: Of the 80 pediatric patients who were on biosimilar TNF-alpha inhibitors, 72 were excluded for having no history of uveitis. 8 patients met the inclusion criteria. 62.5% had anterior uveitis and 37.5% had panuveitis. Mean age was 9.7 ± 4.0 years (range 4.6 – 16.6). Six patients were initiated on originator adalimumab and switched to biosimilar infliximab-dyyb. None of the patients were initiated on originator infliximab and two patients had therapy initiation with biosimilar infliximab-dyyb. Mean duration was 4.87 ± 3.28 years for originator adalimumab (n = 6), 0.76 years for infliximab-dyyb as the initial medication (n=1, other was lost to follow-up), and 0.78 ± 0.42 years for infliximab-dyyb after switching from adalimumab (n = 6). All six patients had flares while on adalimumab, prior to switching. Two (33%) of these six patients had a repeat flare even after switching to biosimilar infliximab-dyyb. Mean flares per year were 1.0 ± 0.3 on originator adalimumab (n = 6) and 0.4 ± 0.7 after switching to biosimilar infliximab-dyyb (n = 6). Other IMT medications included prednisone, methotrexate, leflunomide, and tocilizumab. Reasons for switch included insurance mandate (37.5%) and/or worsening disease activity (83.3%).
Conclusion: After switching to the biosimilar, infliximab-dyyb, pediatric patients had fewer number of flares per person compared to the originator, adalimumab, however 33% continued to have a repeat flare. Our sample is limited in that direct comparison of the same TNF-alpha inhibitor agent was not possible. Further studies are required to characterize the efficacy of the biosimilars directly compared to the originator drug in pediatric non-infectious uveitis.

IRB APPROVAL Yes

Variable	Mean ± standard deviation (range)/ N (%)
Age (y) when started on initial TNF inhibitor (n=8)	9.68 ± 3.97 (range 4.6 – 16.6)
Sex (n = 8)	
Female	3 (37.5%)
Diagnoses (n = 8)	
Anterior uveitis	5 (62.5%)
Panuveitis	3 (37.5%)
Initial medication (n = 8)	
Adalimumab	6 (75%)
Infliximab	0 (0%)
Biosimilar infliximab–dyyb	2 (25%)
Duration (y)	
Originator adalimumab (n =6)	4.87 ± 3.28
Initial biosimilar infliximab-dyyb (n=1) *	0.76
After biosimilar infliximab-dyyb switch (n=6) *	0.78 ± 0.42
Flares/year	
Originator adalimumab (n=6)	1.05 ± 0.34
Initial biosimilar infliximab-dyyb (n=1)	0
After biosimilar infliximab-dyyb switch (n=6)	0.39 ± 0.66
*Currently on medication y = years; IMT = immunomodulatory therapy	

Table 1: Characteristics of study sample

Patient #	Primary diagnosis	Medication	Age (y)	Weight (kg)	Dose (mg)	Dosing interval (weeks)	Duration (m)	Other IMT	# of Flares	Active flaring prior to switch	Reason for switch
1	Panuveitis	Originator (Adalimumab)	10.5	40.1	40	2	34	MTX 25 mg/w, Pred 20 mg/d†	3	No	Insurance
		Biosimilar (infliximab-dyyb)	13.4	49	490	4	8.3*	MTX 20 mg/w	0		
2	Anterior uveitis	Originator (Adalimumab)	11.8	45	40	2	13.4	MTX 25 mg/w	1	Yes	Insurance, clinical, and other logistical concerns
		Biosimilar (infliximab-dyyb)	12.9	57	500	4	12.9*	MTX 20 mg/w	0		
3	Anterior uveitis	Originator (Adalimumab)	10.3	35.3	20	2	92.7	MTX 25 mg/w, Toc 162 mg/w†	5	Yes	Clinical
		Biosimilar (infliximab-dyyb)	18.0	78	500	4	1.1*	MTX 25 mg/w	0		
4	Anterior uveitis	Originator (Adalimumab)	11.6	60.3	20	1	28.6	MTX 17.5 mg/w	4	Yes	Insurance
		Biosimilar (infliximab-dyyb)	14.0	83	500	4	15.6*	MTX 17.5 mg/w	1		
5	Anterior uveitis	Originator (Adalimumab)	6.2	6.7	20	2	69.1	MTX 15 mg/w†, LEF 20 mg/d,	6	Yes	Insurance, clinical
		Biosimilar (infliximab-dyyb)	12	47	470	4	10.3*	LEF 20 mg/d	0		
6	Anterior uveitis	Originator (Adalimumab)	5.8	40.6	40	2	112.5	MTX 25 mg/w†, LEF 10 mg/d	9	Yes	Clinical
		Biosimilar (infliximab-dyyb)	15.1	72	360	4	7.6*	LEF 10 mg/d	1		
7	Panuveitis							Pred 2.5 mg/d		Yes	Insurance
		Biosimilar (infliximab-dyyb)	4.6	18	180	4	LTFU	MTX 17.5 m/w, Pred 2.5 mg/d	N/A		
8	Panuveitis							Pred 60 mg/d		Yes	Clinical
		Biosimilar (infliximab-dyyb)	16.6	58.9	589	4	9.2*	MTX 7.5 mg/w, Pred 15mg/d†	0		

*currently on medication; † discontinued prior to initiation of biosimilar
d, day; IMT, immunomodulatory therapy; kg, kilogram; LEF, leflunomide; m, months; MTX, methotrexate; Pred, prednisone, Toc, tocilizumab; y, years;

Table 2: Comparison of originator adalimumab and biosimilar infliximab-dyyb

7/29/2023 12:00 am

Inflammatory & Infectious Disease Symposium

Outcomes of Children With Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy

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- Ilaria Maccora, MD
- Grant Schulert, MD
- Jennifer Huggins, MD
- Cameron Sapp, BS
- Tiffany Nguyen
- Alexandra Duell
- Megan Quinlan-Waters
- Sunil Srivastava, MD
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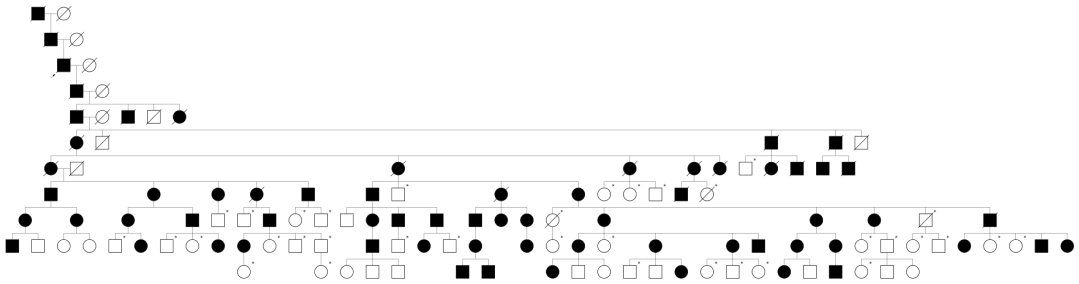
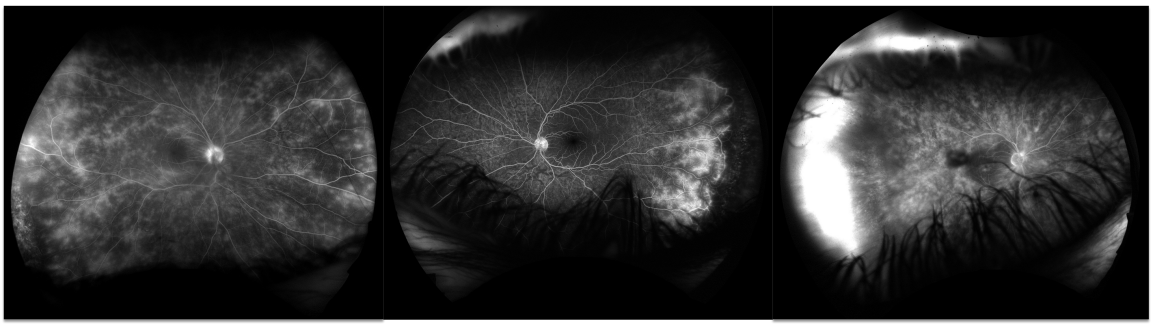
Objective: To determine the efficacy of systemic immunosuppressive therapy in children with Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy
Purpose: Autosomal Dominant Neovascular Inflammatory Vitreoretinopathy (ADNIV) is a rare inherited condition typically diagnosed in adults and characterized by inflammation, retinal degeneration and neovascularization. In early stages, children are asymptomatic, and exhibit occult retinal vasculitis on ultra-widefield fluorescein angiography (UWFA). Corticosteroids improve retinal vascular inflammation, but long-term use can lead to steroid related side effects. Proteomic studies of the vitreous show elevations in IL-6 and other pro-inflammatory cytokines, suggesting a possible role for targeted therapy. In this study, we present the short-term outcomes of the first cohort of children diagnosed with ADNIV and treated with systemic immunosuppressive therapy (IMT).
Methods: Cohort study of patients ≤ 18 years old at diagnosis with CAPN5 mutation (c.731 T>C, p.Leu244Pro), ocular findings consistent with ADNIV and a minimum follow-up of 6 months. Treatment response was defined as a decrease in retinal vascular leakage on UWFA.
Results: Of 21 children with a family history ADNIV, 10 were positive for CAPN5 mutation and 8 children (16 eyes) met inclusion criteria. Sixty-two percent were female (5/8) and 6 children were asymptomatic at presentation. At diagnosis, UWFA revealed retinal vascular leakage in 16/16 eyes, peripheral ischemia in 11/16 eyes, and neovascularization in 4/16 eyes. Initial treatment was oral steroids (n=5), local corticosteroids (n=4) and anti-VEGF therapy (n=2). Systemic IMT was initiated in 7/8 patients. First-line treatment was Methotrexate 25mg subcutaneous weekly that is still ongoing in all (median duration 11 months, R6-16). Because of absent response, Infliximab (anti-TNF) 10mg/kg intravenous every 4 weeks was added in all patients after median time from diagnosis of 3.2 months and continued for a median time of 7 months (R 3.5-10). Infliximab/Methotrexate combination therapy failed to decrease retinal vascular leakage in all patients. Five patients were transitioned to Tocilizumab (anti-IL6) 10mg/kg intravenous every 2 weeks after a median time from diagnosis of 9 months (R1-12). Three patients received Tocilizumab for ≥ 4 months and thus far have not shown any improvement in leakage.

Conclusion: We report on the largest series of children with ADNIV treated with systemic immunosuppression. Early testing for CAPN5 gene in at risk children, and regularly scheduled screening for uveitis and vasculitis will lead to prompt intervention. Methotrexate/Infliximab failed to decrease retinal vascular leakage, and early results suggest Tocilizumab/Methotrexate may also be ineffective. Long-term Fluocinolone Acetonide implants may be the next step in managing children with ADNIV.

IRB APPROVAL Yes



Pedigree of an 11-generational family with ADNIV



Ultra-widefield fluorescein angiography of 3 children with ADNIV