AMERICAN UVEITIS SOCIETY
FALL MEETING
SUNDAY, NOVEMBER 5TH, 2023
6:00 PM

AMERICAN UVEITIS SOCIETY

AAO 2023
SAN FRANCISCO, CA

WAYNE AND GLADYS VALLEY CENTER FOR VISION
UNIVERSITY OF CALIFORNIA SAN FRANCISCO

SCHEDULE – AMERICAN UVEITIS SOCIETY – SUNDAY, NOVEMBER 5, 2023

6:00-7:00 PM	**Social Hour**
7:00-7:05 PM	**Introduction to the Plenary Session** Nisha Acharya, MD, MS Laura Kopplin, MD, PhD Program Chairs, AUS Fall Meeting
7:05-7:50 PM	**Plenary Session** Year in Review: Uveitis Basic and Clinical Science **Russell N. Van Gelder, MD, PhD** **Professor and Chair, Dept of Ophthalmology** **University of Washington School of Medicine**
	Case Competition
7:50 PM	**Renee Liu:** Shifting CAR Gears
7:54 PM	**Kevin Elwood**: Watch Out For That Tree!
7:58 PM	**Shani Pillar:** A Rare Bird
8:02-8:32 PM	**Business Meeting and Break**
	Free papers
8:32 PM	**Sumit Sharma:** A Novel Intravitreal Anti-IL-6 Monoclonal Antibody for Uveitic Macular Edema (UME): Preliminary Results from the Phase 1 DOVETAIL Study
8:38 PM	**Edmund Tsui:** Phase III Clinical Trial Insights on TRS01, a Non-Steroid Treatment with a Novel Mechanism of Action for Active Noninfectious Anterior Uveitis
8:44 PM	**Francesco Pichi:** The Humira In Ocular Inflammations Taper (HOT) Study
8:50 PM	**Jenny Shunyakova:** Therapeutic Drug Monitoring to Optimize TNF-alpha Inhibitor Treatment For Uveitis

SCHEDULE – AMERICAN UVEITIS SOCIETY – SUNDAY, NOVEMBER 5, 2023

8:56 PM	**Jullian Valadez:** Evaluating One, Two, and Three-year Outcomes Following Administration of Fluocinolone Acetonide Intravitreal Implant (FAi) in Patients with Uveitis
9:02 PM	**Amit Reddy:** Risk Factors for Failing sub-Tenon's Triamcinolone Acetonide for Uveitic Macular Edema
9:08 PM	**Fateme Montazeri:** Real-world Prescribing Patterns of Immunomodulatory Treatments among the Uveitis Specialists
9:14 PM	**Rayna Marshall:** Investigating Socioeconomic Barriers to Immunosuppressive Medication Compliance for the Treatment of Uveitis: A Prospective Multi-Center Study
9:20 PM	**Stanton Heydinger:** Treatment Delays in the Initiation of Immunomodulatory Therapy for Patients with Ocular Inflammatory Disease
9:26 PM	**Prithvi Ramtohul:** Multizonal Outer Retinopathy and Retinal Pigment Epitheliopathy (MORR). A Newly Recognized Entity or an Unusual Variant of AZOOR?
9:32 PM	**Shani Pillar:** Longitudinal Assessment of Change in Anterior Chamber Cells Among Children with Uveitis as Determined by Anterior Segment Optical Coherence Tomography Using Automated Quantification
9:38 PM	**Yu Xia:** Single-Cell RNA-Sequencing of Aqueous Immune Cells Reveals Distinctive Roles of CD4 and CD8 T cells in Human Uveitis
9:44 PM	**Jay Stewart:** Novel Transpupillary Technique for Retisert Implantation for Eyes with Pars Plana Fibrosis
9:48 PM	**Adjourn**

Shifting CAR Gears

Presenter: Liu, Renee
Position: Senior Research Assistant
Mentor: Sobrin, Lucia

Institution: Massachusetts Eye and Ear, Harvard Medical School

Purpose: To report cancer-associated retinopathy (CAR) after chimeric-antigen receptor T cell (CAR-T) therapy.

Case summary: A 71-year-old man with systemic lymphoma refractory to multiple chemotherapies underwent CAR-T therapy. Two weeks after CAR-T initiation, he developed rapid-onset decreased peripheral vision in both eyes. Fluorescein angiography showed no vasculitis and optical coherence tomography showed loss of ellipsoid zone except in the fovea. Electroretinography revealed nondetectable rod responses and severely prolonged and diminished cone responses.

Key concept: This patient developed CAR soon after receiving CAR-T therapy which depletes B cells. This suggests that CAR pathophysiology may not be purely auto-antibody-mediated.

Disclosures: None
Support: None

Watch Out For That Tree!

Presenter: Elwood, Kevin
Position: Resident
Mentor: Kopplin, Laura

Institution: University of Wisconsin Department of Ophthalmology & Visual Sciences

Purpose: Solve a case of progressing scleritis with broad range PCR.

Case summary: A patient developed scleritis after a tree branch injury. Initial surgical exploration, culture, imaging for intraocular foreign body & rheumatologic testing were unrevealing. Therapy with NSAIDs, prednisone & periocular Kenalog resulted in worsening scleritis and panuveitis, prompting referral. He underwent vitrectomy & scleral debridement due to concern for infectious scleritis and endophthalmitis. Repeat cultures/gram stain were negative; however, broad-range vitreous PCR was Aspergillus fumigatus positive & antifungals started. The eye did not recover & was enucleated.

Key concepts: Molecular diagnostics are key in assessing intractable ocular inflammation.

Disclosures: None
Support: Unrestricted Grant from Research to Prevent Blindness, Inc. to the UW-Madison Department of Ophthalmology and Visual Sciences

A Rare Bird

Presenter: Pillar, Shani
Position: Fellow
Mentors: Tsui, Edmund

Institution: Stein Eye Institute, Department of Ophthalmology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California

Purpose: To report a case of HLA-A29+ birdshot chorioretinopathy in a Hispanic patient.

Case summary: A 55-year-old female of Mexican ancestry presented with decreasing vision, preceded by 4 years of floaters. Both fundi were noted to have a heavily pigmented appearance, disrupted by lightly pigmented areas, and few small atrophic lesions, in a birdshot chorioretinopathy distribution. Imaging and workup were consistent with birdshot chorioretinopathy. Vascular leakage responded well to systemic treatment.

Key concepts: It is important to consider birdshot chorioretinopathy in the differential in Hispanic patients. Racial pigmentary changes may obscure fundus findings and result in an atypical clinical presentation or delayed treatment.

Disclosures: None
Support: None

A Novel Intravitreal Anti-IL-6 Monoclonal Antibody for Uveitic Macular Edema (UME): Preliminary Results from the Phase 1 DOVETAIL Study

Sharma, Sumit[1]; Suhler, Eric[2]; Lin, Phoebe[3]; Pauly-Evers, Meike[4]; Willen, Daniela[4]; Peck, Robbie[4]; Storti, Federica[4]; Rauhut, Simone[4]; Gott, Tatiana[4]; Passemard, Benedicte[4]; Macgregor, Lachlan[4]; Holmes, William[4]; Barekati, Zeinab[4]; Haskova, Zedenka[5]; Silverman, David[4]; Fauser, Sascha[4]; Mesquida, Marina[4]

Affiliations:
1. Cole Eye Institute, Cleveland Clinic, Cleveland, OH, USA; 2. Casey Eye Institute, Oregon Health & Science University, Portland, OR, USA; 3. Cole Eye Institute, Cleveland Clinic, Cleveland, OH, USA; 4. F. Hoffmann-La Roche AG, Basel, Basel-Stadt, Switzerland; 5. Genentech, Inc., South San Francisco, CA, USA.

Purpose: RG6179 is a recombinant monoclonal antibody that potently inhibits all forms of IL-6 signaling. This abstract reports preliminary RG6179 data in patients with UME.

Methods: DOVETAIL is an ongoing 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 diabetic macular edema (DME) and UME patients. Patients ≥18 years with NIU 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% 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. CST change from baseline was -124 (44), -177 (59) and -184 (48) µm, respectively. 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 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.

Conclusions: 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 trials in DME (monotherapy and combination therapy) and two phase 3 trials in UME are currently underway to further assess the clinical potential of RG6179.

Disclosure: SS: Consultant for Roche, Genentech, Alimera, Abbvie, Eyepoint, Clearside, Regeneron, Bausch and Lomb, RegenxBio. Research support from Roche, Genentech, Eyepoint, IONIS, Gilead, Santen. ES: Consultant for Roche, Abbvie, Clearside, EyePoint, Gilead, Kriya. Research support from Roche, Abbvie, Clearside, EyePoint, Gilead. PL: Consultant for Roche/Genentech, Bausch and Lomb. MPE, DW, RP, FS, SR, TG, BP, LM, DS, SF, MM: Employees of Roche. ZH: Employee of Roche/Genentech. F. Hoffmann-La Roche Ltd. provided support for the study. Medical writing assistance provided by Adam Dagnall, DPhil, of Envision Pharma Group and funded by F. Hoffmann-La Roche Ltd.

Support: The DOVETAIL study was funded by F. Hoffmann-La Roche Ltd.

Clinical Trials Statement: This research IS a clinical trial and is registered at www.clinicaltrials.gov

Phase III Clinical Trial Insights on TRS01, a Non-Steroid Treatment with a Novel Mechanism of Action for Active Noninfectious Anterior Uveitis

Tsui, Edmund; Chu, David; Rifkin, Lana; Wang, Robert; Foster, Stephen; McDonald, Frank; Crowell, Eric; Gangaputra, Sapna; Korenfeld, Michael; Palestine, Alan; Spencer, Doran; Tawansy, Khaled; Abrams, David; Dacey, Mark; Scales, David; Deuter, Christoph; Finger, Robert; Meleth, Annal; Guthoff, Rainer; Ness, Thomas; Shah, Rajiv; Thurau, Stephan; Ben-Ghezala, Inès; Brézin, Antoine; Sheppard, John; Weber, Michel; Tarsier Pharma Research Group

Affiliations: UCLA Stein Eye Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Purpose: This study evaluated the safety and efficacy of TRS01, an eye drop formulation of dazdotuftide (formerly known as TRS), a novel bio-inspired immunomodulator based on a peptide conjugate of Tuftsin-Phosphorylcholine, in patients with active noninfectious anterior uveitis, including cases of Uveitic Glaucoma (UG) and pediatric patients of all ages.

Methods: In a randomized, double-masked, active-controlled phase III trial conducted across 30 sites in the United States, France, and Germany, 142 patients with active noninfectious anterior uveitis were randomized in a 2:1 ratio to receive either TRS01 or potent steroid eye drop administered four times daily for four weeks, with a subsequent two-week follow-up period. The trial assessed efficacy based on anterior chamber cell (ACC) count, pain, and flare after 28 days of treatment. A post-hoc analysis examined the prolonged resolution of inflammation and potential rebound effects two weeks after treatment cessation. Intraocular pressure (IOP) changes were also investigated, along with an assessment of the overall safety of TRS01.

Results: TRS01 demonstrated efficacy in resolving inflammation. The change from baseline in pain and flare was comparable between the TRS01 and steroid groups, with rapid pain relief observed within the first week of treatment. In a post-hoc analysis, nearly a third of responders in the steroid group experienced a rebound of inflammation within two weeks of treatment cessation, while a quarter of patients in the steroid group exhibited a significant elevation in IOP after only four weeks of treatment (four drops per day). In contrast, TRS01 exhibited a sustained anti-inflammatory effect following treatment cessation and maintained stable IOP levels in both the general uveitis patient population and specifically in the UG subgroup. The safety and tolerability profile of TRS01 remained favorable, consistent with previous trial findings.

Conclusions: TRS01 eye drops emerged as a safe and effective treatment for active noninfectious anterior uveitis, including cases of Uveitic Glaucoma. The favorable blend of safety and efficacy exhibited by TRS01 has the potential to redefine the management of UG patients, offering new prospects for improving their quality of life.

Disclosure: Site PI of TRS4Vision Clinical Trial. This trial was sponsored by Tarsier Pharma

Support: Tarsier Pharma

Clinical Trials Statement: This research IS a clinical trial and is registered at www.clinicaltrials.gov

The Humira In Ocular Inflammations Taper (HOT) Study

Francesco Pichi[1,2]; Scott D Smith[1,2]; Debra A Goldstein[3]; Dina Baddar[4,5]; Terese K A Gerges[4]; Timothy M Janetos[3]; Matilde Ruiz-Cruz[6]; Luz Elena Concha-del-Río[6]; Kazuichi Maruyama[7,8]; Josianne Carina ten Berge[9]; Saskia M Rombach[10]; Luca Cimino[11,12]; Elena Bolletta[12]; Elisabetta Miserocchi[13,14]; Pierluigi Scandale[13,14]; Massimiliano Serafino[15]; Paola Camicione[15]; Sofia Androudi[16]; Julio J Gonzalez-Lopez[17]; Lyndell L. Lim[18]; Nandini Singh[18]; Vishali Gupta[19]; Nikita Gupta[19]; Radgonde Amer[20]; Emilio M Dodds[21]; Sebastian Inchauspe[21]; Marion R Munk[22-24]; Emilia Donicova[22]; Ester Carreño[25]; Masaru Takeuchi[26]; Soon-Phaik Chee[27-30]; Milton C Chew[27,28]; Aniruddha Agarwal[1,2]; Ariel Schlaen[31,32]; Ramiro A Gómez[32]; Cristobal A. Couto[32]; Moncef Khairallah[33]; Piergiorgio Neri[1,2]

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Purpose: To assess factors that impact the risk of relapse in patients with non-infectious uveitis (NIU) who undergo adalimumab tapering after achieving remission.

Methods: This multicenter retrospective study enrolled patients with NIU treated with adalimumab and subsequently tapered.Patient demographics, type of NIU, onset and duration of disease, period of inactivity before tapering adalimumab and tapering schedule were collected.Independent predictors of the rate of uveitis recurrence after adalimumab tapering were assessed, including age, time from diagnosis to initiation of adalimumab, time of inactivity before tapering of adalimumab, and tapering schedule.

Results: 328 patients were included (54.6% female) with a mean age of 34.3 years. The mean time between disease onset and initiation of adalimumab therapy was 35.2±70.1 weeks. Adalimumab tapering was commenced after a mean of 100.8±69.7 weeks after initiation. Recurrence was observed in 39.6% of patients at a mean of 44.7±61.7 weeks. Patients who experienced recurrence were significantly younger than those without recurrence (mean 29.4 years vs. 37.5 years, p=0.0005) and the rate of recurrence was significantly higher in younger subjects (HR=0.88 per decade of increasing age, p=0.01). The lowest rate of recurrence was among Asian subjects. A faster adalimumab taper was associated with an increased recurrence rate (HR=1.23 per unit increase in speed, p<0.0005). Conversely, a more extended period of remission prior to tapering was associated with a lower rate of recurrence (HR=0.97 per 10-weeks longer period of inactivity, p=0.04).

Conclusions: When tapering adalimumab, factors that should be considered include patient's age, race, and duration of adalimumab treatment. A slow tapering schedule is advisable.

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Support: None

Therapeutic Drug Monitoring to Optimize TNF-alpha Inhibitor Treatment For Uveitis

Shunyakova, Jenny; Chen, Howard ; Hassman, Lynn

Affiliations: Washington University- St. Louis, Colorado University, University of Missouri-Kansas City

Purpose: We examined the impact of low serum adalimumab levels on treatment outcomes, and explored whether serum adalimumab levels and the presence of anti-drug antibodies could guide treatment decisions.

Methods: 33 patients who partially responded or experienced secondary failure to adalimumab had serum adalimumab and anti-adalimumab antibody levels measurements. If serum adalimumab was >6 ug/ml, the dose was increased. If serum adalimumab was <6 ug/ml, and anti-drug antibodies were present, patients were switched to an alternative TNF-inhibitor (infliximab). The primary outcome was success, defined as inactive uveitis 12 months after therapy change with low-dose corticosteroids. We also assessed patient characteristics, such as BMI, that have previously been linked with success of TNF-inhibitors.

Results: 18 patients did not have evidence of neutralizing anti-drug antibodies and had adalimumab increased to weekly. Of these, 12 successfully achieved remission at 12 months, while 6 failed therapy. Of 10 patients who were switched to infliximab due to the presumed presence of neutralizing anti-drug antibodies, 4 achieved remission, and 6 failed. The odds of treatment success for patients with serum adalimumab >6 ug/ml were 3x higher than with serum adalimumab levels ≤ 6 ug/ml and anti-drug antibodies ($p=0.1785$). Of 5 patients switched to infliximab despite adequate adalimumab levels and no anti-drug antibodies, 3 succeeded, and 2 failed. Lower BMI was positively correlated ($p=0.045$) with success after switching to infliximab. No relation with antimetabolite use was found in the dose-increase group.

Conclusions: For patients experiencing suboptimal therapeutic response to adalimumab dosed every 2 weeks, an increase to weekly dosing may be warranted when neutralizing anti-drug antibodies are absent. Additionally, consideration of BMI may be warranted when dosing infusion-based TNF-inhibitors for patients who have failed an initial empirically dosed TNF-inhibitor.

Disclosure: None
Support: None

Evaluating One, Two, and Three-year Outcomes Following Administration of Fluocinolone Acetonide Intravitreal Implant (FAi) in Patients with Uveitis

Valadez, Jullian; Xiangyu, Ji; Chen, Qingxia; Gangaputra, Sapna

Affiliations: Vanderbilt University School of Medicine

Purpose: FAi trials have shown efficacy in quelling inflammation and reducing steroid burden. However, data is scarce regarding long term efficacy in real-world application. Here we evaluate "failure" in 105 eyes on FAi, measured by an increase in oral corticosteroid use above the clinically significant 10mg/d threshold. This marks the largest and longest retrospective case series looking at FAi's effectiveness.

Methods: A retrospective chart review was performed on 105 eyes treated with FAi at an academic uveitis center including 3 years of post-injection data. Outcome variables were average oral corticosteroid use and number of eyes on >10mg/d of oral corticosteroid. The difference in the number of occurrences between the primary outcomes was analyzed with Pearson's Chi-squared test. The impact of age on the primary outcomes was analyzed with Wilcoxon rank sum test and Peason's Chi-squared test was used for the impact of gender, race, and uveitis type.

Results: In eyes treated with FAi, there is a decrease in average oral corticosteroid dose across all three years, with a consistent downward trend year to year. The proportion of eyes who were on an oral corticosteroid regimen greater than 10mg/d also consistently decreased year to year following FAi implantation, with nearly all eyes below this threshold at the third year. Our covariate analysis showed that female eyes ($p=0.028$) and eyes with posterior uveitis ($p=0.026$) were more significantly likely to relapse to >10 mg/d of steroid.

Conclusions: Our analysis of 105 eyes treated with FAi shows a reduction in both average steroid dose and proportion of eyes on clinically significant dose of steroid across a three year period. Notably, the reduction in medication burden remains consistent across all three years with a stable downward trend. Our cohort's results implicate utility of FAi to a three-year period in real world clinical settings.

Disclosure: None
Support: None

Risk Factors for Failing sub-Tenon's Triamcinolone Acetonide for Uveitic Macular Edema

Reddy Amit; Patnaik, Jennifer; Palestine, Alan

Affiliations: Department of Ophthalmology, University of Colorado School of Medicine, Aurora, Colorado, USA

Purpose: To identify risk factors for failing sub-Tenon's triamcinolone acetonide (STA) for the treatment of uveitic macular edema (ME).

Methods: A retrospective cohort study was performed. Medical records were reviewed of patients who underwent STA for the treatment of uveitic ME between January 1, 2013, and July 31, 2022, at the University of Colorado Hospital. Uveitic ME was defined by a central subfield thickness (CST) greater than 320 µm or the presence of intra-retinal cystoid spaces on optical coherence tomography (OCT), or by the presence of petaloid macular leakage on fluorescein angiography (FA). Data collected included age, race/ethnicity, sex, history of diabetes mellitus, anatomic classification of uveitis, use of corticosteroids, use of immunomodulatory therapy, presence of intra-retinal fluid on OCT, CST on OCT, and presence of petaloid macular leakage on FA. STA failure was defined as the need for additional therapy within 12 weeks of STA due to persistent or worsening uveitic ME.

Results: 180 eyes from 131 patients were included. 138 eyes (76.7%) were considered treatment successes. In univariate and multivariable analysis, higher baseline CST was associated with a higher likelihood of failing STA (OR 1.17 for each 30 µm increase in CST, $P = 0.016$).

Conclusions: STA, while not as potent as intravitreal corticosteroids for the treatment of uveitic ME, was still an effective therapy, particularly for patients with lower baseline CST. Given its lower side effect profile and cost compared to intravitreal treatments, clinicians could consider STA as an initial treatment for mild uveitic ME.

Disclosure: None
Support: Support for this work was provided in part by an unrestricted grant to the University of Colorado Department of Ophthalmology from Research to Prevent Blindness, New York, NY, and by the Center for Ocular Inflammation at the University of Colorado. The sponsor or funding organization had no role in the design or conduct of this research.

Real-world Prescribing Patterns of Immunomodulatory Treatments among the Uveitis Specialists

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Affiliations: Department of Ophthalmology & Vision Science, Tschannen Eye Institute, University of California, Davis, Sacramento, CA; Eastern Virginia Medical School, Norfolk, VA; Department of Ophthalmology & Vision Science, Tschannen Eye Institute, University of California, Davis, Sacramento, CA

Purpose: Uveitis accounts for an estimated 10-15% of all US blindness cases. Non-infectious uveitis (NIU) presents a challenge for effective treatment while limiting adverse effects commonly associated with long-term corticosteroid use. This study evaluated the real-world prescribing patterns of corticosteroid-sparing treatments among uveitis specialists in the US.

Methods: We comprehensively analyzed Medicare's Part D prescription data by cross-referencing it with uveitis specialists' identifiers. Our study focused on common immunomodulatory therapy (IMT) drugs including methotrexate, mycophenolate mofetil, azathioprine, cyclophosphamide, cyclosporine, etanercept, golimumab, infliximab, adalimumab, rituximab, sirolimus, tacrolimus, tocilizumab, and tofacitinib and their associated costs.

Results: IMTs represented 3.9% (60,973) of all uveitis specialists' prescriptions. From 2013 to 2021, there was a notable expansion in IMT prescriptions, growing from 4,115 (3%) to 10,701 (5.1% of all drugs, $p<0.001$). Interestingly, during COVID-19 pandemic, IMT prescriptions grew 11% annually in 2020-2021. While prescriptions for methotrexate (-0.65, $p=0.049$), mycophenolate mofetil (-1.55, $p<0.001$), and azathioprine (-0.28, $p=0.02$) declined, adalimumab's utilization markedly increased from 0.93% in 2013 to 18.5% of IMT prescriptions in 2021, particularly post-FDA approval in 2016 (4.81, $p=0.002$). Adalimumab was the most expensive IMT, averaging $6,683/prescription and making up 73.5% of total IMT expenditure. The average costs for other drugs ranged from $52 (methotrexate) to $148.3 (mycophenolate mofetil). During the study period, adalimumab's costs rose substantially (571.55, $p<0.001$), while methotrexate declined (-3.3, $p=0.003$).

Conclusions: Uveitis specialists' preferences for managing NIU in elderly patients are evolving and may be influenced by drug efficacy, FDA approvals, costs, and insurance. Effective management requires evaluating treatment patterns and cost-effectiveness.

Disclosure: None
Support: None

Investigating Socioeconomic Barriers to Immunosuppressive Medication Compliance for the Treatment of Uveitis: A Prospective Multi-Center Study

Rayna Marshall[1], Karen Sun[2], Cynthia Montana[3], Eric Crowell[4], Karen Armbrust[5], Laura Kopplin[6], Meghan Berkenstock[1,2]

Affiliations: 1. Drexel University College of Medicine; 2. Johns Hopkins Wilmer Eye Institute; 3. Washington University School of Medicine in St. Louis; 4. The University of Texas at Austin; 5. University of Minnesota; 6. University of Wisconson School of Medicine and Public Health

Purpose: To shed light on socioeconomic reasons for non-compliance with therapy by assessing what patient barriers lead to non-compliance with immunosuppressive medication (IMT) for the treatment of uveitis.

Methods: This was a prospective, 6-center, cohort study. A 44-question survey was created about demographics and barriers limiting IMT use. The survey was distributed at follow-up clinic visits over a period of 4 weeks at each site. Participants were established patients who spoke English and had a diagnosis of uveitis or ocular inflammation. The project was approved by the Johns Hopkins IRB.

Results: The survey was completed by 76 subjects, of whom were 64% white, 68% female, and 52% had a college or advanced degree. 47% were on one or two IMT, the most common were mycophenolate (18%) or adalimumab (15%). 36% of patients took BID dosing with 16% taking 8 or more meds in addition to the IMT.

Limitations to getting lab work included difficulty remembering lab draws (5%), finding time for lab draws (12%), and getting rides to labs (2%). 22% of patients reported cost as a limitation to getting labs.

54% of patients required reminders to take their medications. 23% of patients found it difficult to take IMT regularly, and 12% struggled to take medications multiple times a day. 40% of patients admitted to not taking their medication as prescribed.

14% of patients missed doses due to lack of refills, and 2% missed doses due to refill costs. Costs of IMT refills monthly were less than 5 dollars (24%), 5-20 dollars (30%), over 100 dollars (7%), and over 1000 dollars (4%). No patients were unable to take medications due to insurance loss.

Conclusions: Socioeconomic barriers to IMT treatment include lab work costs, difficulty with medication administration, and issues with remembering medication schedules. The cost of medications was not reported to be a significant barrier. Addressing these barriers to compliance can increase IMT adherence for uveitis patients.

Disclosure: None
Support: None

Treatment Delays in the Initiation of Immunomodulatory Therapy for Patients with Ocular Inflammatory Disease

Heydinger, Stanton; Cao, Jennifer

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Purpose: To characterize time to treatment delays for immunomodulatory therapy (IMT) in patients with chronic non-infectious uveitis and ocular inflammatory disease.

Methods: A retrospective chart review of patients with non-infectious uveitis or ocular inflammatory disease evaluated at the UTSouthwestern Medical Center Department of Ophthalmology and Children's Medical Center of Dallas Uveitis Clinics between 3/1/2023 and 9/1/2023 in which the uveitis specialist attempted initiation of a new IMT. Demographics included age, gender, type of uveitis, and insurance coverage. Primary outcome was time to treatment delay. Secondary outcomes included: rate of primary insurance approval and number of appeals.

Results: There were 66 independent occurrences for 55 patients that met inclusion criteria. The mean age was 51 (range 12-83), predominantly female (61%). Primary indications for IMT were: panuveitis (32, 48%), pemphigoid (20, 30%), anterior uveitis (5, 8%), intermediate uveitis (4, 6%), scleritis (4, 6%), and posterior uveitis (1, 2%). Medications prescribed included methotrexate (12, 18%), mycophenolate mofetil (11, 17%), adalimumab (25, 38%), baricitinib (10, 15%), tofacitinib (6, 9%), and tocilizumab (2, 3%). There were 15 (23%) requests for "on-label" (ON-L) medication (adalimumab every 2 weeks), the remainder (51, 77%) of requests were "off-label" (OFF-L). Average time to initiation was 10.3 days for ON-L and 38.3 days for OFF-L (p=0.02). Approval rates were 100% for ON-L and 64% for OFF-L (p=0.01). The average number of insurance appeals required per initiation was significantly greater for OFF-L patients (0.65 vs 0.13; p=0.03). In the OFF-L cohort, private insurance approval rates were significantly higher than medicare approval rates (82% vs 43%; p=0.03).

Conclusions: Insurance prior authorizations and denials for use of IMT in the treatment of uveitis and ocular inflammatory diseases pose significant delays in initiating vision-saving treatment.

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Multizonal Outer Retinopathy and Retinal Pigment Epitheliopathy (MORR). A Newly Recognized Entity or an Unusual Variant of AZOOR?

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Purpose: To describe specific clinical, multimodal imaging, and natural history features of an unusual variant of acute zonal occult outer retinopathy (AZOOR).

Methods: Retrospective, observational, longitudinal, multi-center case series. Patients exhibiting this unusual clinical condition among cases previously diagnosed with AZOOR were included. Multimodal imaging, laboratory evaluations and genetic testing for inherited retinal diseases were reviewed.

Results: Twenty eyes from 10 patients (8 females and 2 males) with a mean age of 54.1±13.3 years (range, 38-71 years) were included. The mean follow-up duration was 13.1±5.3 years (range, 8-23 years). Presenting symptoms were bilateral in 7 patients (85% of eyes) and included scotomata and photopsia. All patients had bilateral lesions at presentation involving the peripapillary and far peripheral retina. Baseline optical coherence tomography showed alteration of both the retinal pigment epithelium (RPE) and photoreceptor layers corresponding to zonal areas of fundus autofluorescence abnormalities. Centrifugal and centripetal progression of the peripapillary and far-peripheral lesions, respectively, occurred over the follow-up resulting in areas of complete outer retinal and RPE atrophy.

Conclusions: Initial alteration of both photoreceptors and RPE and a stereotypical natural course, that includes involvement of the far retinal periphery, characterize this unusual condition. It may represent a variant of AZOOR or may be a new entity. We suggest to call it multizonal outer retinopathy and retinal pigment epitheliopathy (MORR).

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Longitudinal Assessment of Change in Anterior Chamber Cells Among Children with Uveitis as Determined by Anterior Segment Optical Coherence Tomography Using Automated Quantification

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Purpose: To compare anterior chamber cell (ACC) counts determined by automated quantification using anterior segment (AS) optical coherence tomography (AS-OCT) to clinical grades of ACC using SUN criteria during longitudinal follow-up of children with uveitis; and to compare change in automated quantification to clinical improvement of active disease on two sequential visits.

Methods: We conducted a prospective study of 21 children (40 eyes) <18 years of age who had uveitis involving the AS and ≥3 follow-up visits. Single cross-sectional line scans centered on the AC were obtained using the Optovue Avanti RTVue XR AS-OCT. An automated algorithm was developed to quantify the number of hyperreflective foci in each image. Results were compared to SUN grades using a mixed-effects linear regression model. A subset analysis was conducted using data from eyes with active inflammation and improvement by clinical criteria at the following visit; change in median ACC was compared between visits using the Wilcoxon rank-sum test.

Results: Median age of patients was 11 years (range 4-16 years). Median number of visits per eye was 6 (range 3-8 visits). Median follow-up duration was 508 days (range 85-1030 days). The majority of eyes had JIA-associated uveitis (21 eyes [53%]). SUN clinical grades were 2+ or lower in 98% of eye-visits (n=183). A one-step increase in SUN grade was associated with a 43% increase in the number of ACC by automated quantification ($p<0.001$). In the subset analysis (36 visit-sets, 27 eyes), clinical improvement was associated with a 44% decrease in number of ACC by automated quantification ($p=0.014$).

Conclusions: Automated quantification of ACC can identify improvement in anterior segment inflammation. Further development of this technique, with validation against definitive clinical outcomes, may provide an objective and reproducible means of monitoring disease course and response to treatment in children with uveitis involving the anterior segment.

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Single-Cell RNA-Sequencing of Aqueous Immune Cells Reveals Distinctive Roles of CD4 and CD8 T cells in Human Uveitis

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Purpose: Non-infectious uveitis (NIU), which accounts for the majority of uveitis cases in the US, is a heterogeneous group of diseases classified by clinical features and a common cause of blindness due to high treatment failure rate. While immune dysregulation is known to play a role, a deep understanding of the immunopathogenesis of different types of NIU is lacking, hindering the development of targeted therapies.

Methods: Aqueous humor in a healthy eye has no detectable immune cells, but it contains immune cells in a uveitis flare. To understand the immune landscape of uveitis, we biopsied aqueous humor from 23 patients with various types of uveitis and performed paired single-cell RNA-sequencing and TCR sequencing on those samples.

Results: Conventional CD4 and CD8 T cells were the most abundant cell types in the aqueous immune infiltrate. CD4 T cells are of Th1 and Th17 phenotypes and demonstrate signs of antigen-specific stimulation. CD4 clones detected at high frequency in the eye are detected at low frequency in the peripheral blood, suggesting a local antigen-driven clonal expansion. Clonally expanded CD4 T cells are mainly observed in granulomatous uveitis. On the other hand, CD8 T cells express cytotoxic genes at high levels, show features of antigen-independent activation, and clones of high frequency in the eye also exist at high frequency in the blood. Clonally expanded CD8 T cells are found in both granulomatous uveitis and non-granulomatous uveitis.

Conclusions: Using single-cell analyses of ocular immune infiltrate, we find strong evidence of antigen-specific clonal expansion of CD4 T cells in the eye, especially in patients with granulomatous uveitis. In contrast, CD8 T cell expansion occurs in both granulomatous and non-granulomatous uveitis, where they likely get activated not in an antigen-driven manner but as bystanders. Our findings provide insight into the immune landscape of different uveitis types, which might inform targeted therapies.

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Support: None

Novel Transpupillary Technique for Retisert Implantation for Eyes with Pars Plana Fibrosis

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Purpose: To describe a novel technique for Retisert implantation in which the device is introduced into the posterior chamber through the pupil. This avoids the complications associated with transscleral incisions in eyes with fibrovascular membranes on the pars plana.

Methods: The surgical technique will be demonstrated during the presentation. The Retisert is introduced into the eye at the limbus. Fixation sutures tied to the device's plate are externalized through the pars plana using 27g forceps. As the sutures are pulled up, the Retisert is delivered posteriorly through the pupil via a posterior capsulotomy.

Results: Two pediatric and one adult patient, all with panuveitis and hypotony in association with extensive epiciliary and pars plana membranes, underwent Retisert implantation using the novel technique in conjunction with pars plana vitrectomy and silicone oil injection. No complications associated with the surgical procedure were noted. Improved control of intraocular inflammation and intraocular pressure was achieved.

Conclusions: Transpupillary Retisert implantation can be a useful technique to avoid the need for an incision through fibrovascular tissue at the pars plana.

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