ARVO 2017 Annual Meeting Abstracts

134 Uveitis therapeutics: remedy and Relief
Sunday, May 07, 2017 1:30 PM–3:15 PM
Exhibit/Poster Hall Poster Session
Program #/Board # Range: 500–527/B0055–B0082
Organizing Section: Immunology/Microbiology

Program Number: 500 Poster Board Number: B0055
Presentation Time: 1:30 PM–3:15 PM
Optical Coherence Tomography Angiography Assessment Of Choriocapillaris Ischemia In Amnigenous And Serpigenous Choroiditis And Its Response To Treatment
Dilraj S. Grewal1,2, Sophia L. Zagora1, Susan Lightman1, Oren Tomkins-Netzer2. 1Ophthalmology, Duke University, Durham, NC; 2Moorfields Eye Hospital, London, United Kingdom.
Purpose: To analyze the vascular alterations in the choriocapillaris (CC) using Optical Coherence Tomography Angiography (OCTA) in patients with Amnigenous and Serpigenous choroiditis and assessed the reversibility of CC ischemia in response to treatment.
Methods: Retrospective review of new and established inflammatory amnigenous choroiditis (n=3) and Quantiferon Gold Positive (QGold) serpigenous choroiditis (n=6) patients who underwent multimodal imaging with OCTA (6x6 mm scan section, Zeiss Angioplex, Carl Zeiss Meditec or Optovue RTVue XR Avanti; Optovue, Inc.), fundus autofluorescence (FAF), fluorescein angiography and indocyanine green angiography (ICG) where available. CC morphological changes visualized on OCTA were overlaid on ICG and FAF images. Areas of CC ischemia (defined as loss of speckled hyperreflectance homogenity or dark defects not compatible with artifact) were calculated prior to and following treatment.
Results: Fourteen eyes of 9 patients (mean age 41.5±5.6 years) were included. Mean baseline VA was 0.36±0.45 logMAR. Among treated patients there was a reduction in choriocapillaris ischemia from 3.7±1.59 mm² at presentation to 1.39±2.05 mm² (p=0.06) following 2.5±2 weeks of oral steroids suggesting its utility as a non-invasive surrogate in monitoring treatment response. Over time, there may be a superimposition of the larger choroidal vessels in such eyes.
Conclusions: CC ischemia correlates with hypofluorescent areas on ICG angiography and is larger than hyperfluorescent areas on OCTA. There was a 62.4% reduction in size of CC ischemia with adequate treatment. The CC ischemia size was significantly larger than in untreated patients. CC ischemia was initiated in eyes with QGold serpigenous choroiditis. The areas of decreased flow on CC colocalized with areas of hypofluorescence on ICG and were larger than the corresponding areas of hyperautofluorescence on FAF. CC alterations ranged from localized CC ischemia on acute presentation (n=5) to large areas of extensive loss of CC with deeper choroidal vessels visible in longstanding disease (n=4). The superficial migration of larger choroidal vessels to the CC slab level was measured by the increased (83.2) vessel density in eyes with longstanding disease compared to eyes imaged at acute presentation (59.3, p=0.01)

135 The effect of early systemic treatment on the decrease of choroidal thickness in birdshot retinochoroiditis
Natalia A. Skvortsova1, Bruno Jeannin2, Amel Gasc1. 1Center, Moscow, Russian Federation; 2Posterior Eye Segment Diagnostics and Surgery Center, Moscow, Russian Federation.
Purpose: Birdshot retinochoroiditis (BRC) is a rare autoimmune disease affecting the retina and choroid independently. Choroidal inflammation responses to systemic treatment rapidly. This retrospective study tested the hypothesis that early and sustained systemic treatment preserves choroidal thickness (ChT) in BRC.
Methods: Patients with a disease duration ≥10 years were divided into two groups depending on their treatment status: early and sustained therapy (treated patients) versus insufficient, late, or no treatment (untreated patients) and enhanced depth imaging optical coherence tomography (EDI-OCT) measurements of ChT were analyzed retrospectively. The exclusion criteria were high myopia or hyperopia (more than 6 diopters), substantial media opacities affecting visual acuity (i.e. cataract) and the quality of OCT-scans, and a history of other retinal or choroidal diseases. The OCT images were evaluated and ChT was calculated horizontally and vertically in the macula, the calculation was performed in blind manner by two independent observers. ChT was compared in treated and untreated groups along with the number of typical fundus BRC lesions.
Results: 13 patients (24 eyes) with BRC (5M/8F) were included in the study. The mean age at the moment of ChT measurement was 61.4±11.2 years. Mean disease duration was 13.7±3.7 years. The HLA-A29 antigen was positive in all patients. There were no significant differences in age, sex, disease duration, and refractive error between the two groups. A significant difference in ChT was observed between adequately treated (13 eyes) and untreated patients (11 eyes) (288.3 ± 76.9 µm vs 161.4 ± 39.2 µm; P≤0.0001, Mann-Whitney U test). In the group with insufficient therapy, 10 of 11 eyes presented typical fundus BRC lesions while only 2 of 13 eyes presented the same typical BRC lesions in the treated group (P≤0.0006, two-tailed F-test).
Conclusions: Choroidal thickness decreases significantly less during long term follow-up if patients are treated early and adequately when compared to untreated patients. In parallel BRC fundus lesions are significantly more numerous in the latter group.
Commercial Relationships: Natalia A. Skvortsova; Bruno Jeannin, None; Amel Gasc, None; Carl P. Herbort, None

Program Number: 501 Poster Board Number: B0056
Presentation Time: 1:30 PM–3:15 PM
OCT- Predictive Visual Threshold Sensitivity Predicts Visual Field Loss in Patients with Ocular Inflammatory Disease
James J. Peairs1, Michael D. Abramoff2,3, Kyungmoo Lee1, Zhihui Guo2, Amel Gasc1. 1Ophthalmology and Visual Sciences, University of Iowa Hospital and Clinics, Iowa City, IA; 2University of Iowa, Iowa City, IA; 3Electrical and Computer Engineering, University of Iowa, Iowa City, IA.
Purpose: Patients with ocular inflammatory disease often develop slowly progressive visual field loss. Visual fields, however, have inter-test variability and can be affected by media opacities and refractive errors. This study tested whether our automated OCT-Predictive Visual Threshold Sensitivity (OCT-PVST) can predict field loss compared to the Humphrey 24-2 (HVF 24-2).
Methods: 13 patients with idiopathic ocular inflammatory disease, confirmed by an uveitis expert and with known visual field defects on HVF 24-2 underwent pre-dilation Standard Humphrey 24-2 SITA perimetry. After dilution, our standard 9-field Spectralis OCT protocol was used, sequentially fixating on areas of retina 12.5° apart using a 3 x 3 grid pattern. This protocol entirely covers the 54° area tested with HVF. Using our automated pre-trained machine learning

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OCT-PVTS algorithm, which achieves 0.74 correlation with HVF 24-2 in patients with glaucoma, each 9-field OCT was co-registered and the nerve fiber, ganglion cell, and inner plexiform layers were co-segmented and each of the 52 HVF 24-2 testpoint thresholds was predicted and compared to HVF 24-2 measured thresholds.

**Results:** Average correlation between actual and predicted HVF 24-2 thresholds was 0.53. As demonstrated in figure 1, predicted visual field corresponded reasonably well in most subjects. In several cases, the actual HVF 24-2 was abnormal while the prediction was relatively normal (i.e. the neuroretina had normal thickness), although the outer retina did appear thinner (as demonstrated in figure 2).

**Conclusions:** Automated prediction of HVF 24-2 from 9-field OCT may have a role in management of patients with ocular inflammatory disease, if combined with analysis of the outer retina.

Left: actual field from HVF 24-2; center: predicted field from 9-field OCT; right: outer retinal layer thickness

Left: actual field from HVF 24-2; center: predicted field from 9-field OCT; right: outer retinal layer thickness

**Commercial Relationships:** James J. Peairs, None; Michael D. Abramoff, University of Iowa (P), IDx LLC (I), IDx LLC (C); Kyungmoo Lee, None; zihui guo, None; Douglas B. Critser, None; James C. Folk, IDx LLC (I)

**Support:** NIH Grants R01 EY019112, R01 EY018853; the Department of Veterans Affairs; Alimera Inc, The Robert C. Watzke MD Professorship for Retina Research

**Program Number:** 503 Poster Board Number: B0058

**Presentation Time:** 1:30 PM–3:15 PM

**Ocular toxicity and ocular tissue distribution of topically applied PP-001 in vivo**

Nadine Schuerer1, Romana Seda-Zehetner2, Aleksandra Inic-Kanada1, Elisabeth Stein1, Ehsan Ghasemian1, Franz Obermayr1, Talin Barisani-Aшенбауер1.

1Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria; 2Panoptes Pharma, Vienna, Austria.

**Purpose:** PP-001 is an inhibitor of dihydroorotate dehydrogenase and has a best-in-class pharmacological profile for autoimmune uveitis following oral and intravitreal administration. In Experimental Autoimmune Uveitis PP-001 has shown a profound effect on T cell proliferation and downregulation of IL-17 and IFN-γ. This study aimed to evaluate ocular toxicity in vitro and ocular tolerability as well as tissue distribution after topical administration of PP-001 in vivo.

**Methods:** In vitro cytotoxicity was measured by quantifying lactate dehydrogenase production in both human conjunctival epithelial (HCJE) and human corneal-limbal epithelial (HCLE) cells incubated with dilutions of PP-001 for 5, 15, and 30 minutes, as well as 24h after 30 minutes of exposure. New Zealand White rabbits (NZW) received instillations of 0.26% PP-001 or vehicle solution (control) 4 times per day over 4 days. 35µl were instilled in both eyes of each animal. Clinical signs and Draize’s scale were evaluated every day. Slit lamp and histopathology examination was performed on day 4. Ocular tissues (cornea, conjunctiva, retina, aqueous humor) and plasma samples were taken on day 1 (single dose) and day 4 and analyzed for PP-001 content with LC/MS.

**Results:** PP-001 was well tolerated in in vitro experiments with epithelial cells. Less than 4% and 10% cytotoxicity was determined for HCJE cells and HCLE cells, respectively. Clinical and ocular examination in NZW rabbits did not reveal test article or vehicle related ocular findings in all animals. Histological analysis confirmed that PP-001 was very well tolerated in albino rabbits. The exposure in tissues after administration of 0.26% PP-001 eye drops was highest in conjunctival tissue with 19283 ng/g, followed by cornea with 12141 ng/g. In plasma, a maximal concentration of 33 ng/ml was found at 0.5 h post dose. No accumulation of PP-001 was detected in plasma and ocular tissues.

**Conclusions:** PP-001 is well tolerated in vitro and in vivo when instilled 4 times daily over 4 days. The ocular distribution was highest in conjunctiva and cornea, suggesting a great potential for therapeutic use in inflammatory ocular surface diseases.

**Commercial Relationships:** Nadine Schuerer; Romana Seda-Zehetner, Panoptes Pharma (E); Aleksandra Inic-Kanada, None; Elisabeth Stein, None; Ehsan Ghasemian, None; Franz Obermayr, Panoptes Pharma (E); Panoptes Pharma (I); Talin Barisani-Aшенбауер, None

**Support:** Austrian Research Promotion Agency (FFG project number 822768)

**Program Number:** 504 Poster Board Number: B0059

**Presentation Time:** 1:30 PM–3:15 PM

**Association between ocular findings and preventive therapy with onset of central nervous system involvement in patients with primary vitreoretinal lymphoma**

Noriyasu Hashida, Kei Nakai, Norimitsu Saito, Kohji Nishida, Dept of Ophthalmology, Osaka University Graduate School of Medicine, Suita, Japan.

**Purpose:** To investigate if the site of ocular lesions and prophylactic treatment in patients with primary vitreoretinal lymphoma (PVRL) are associated with the time to onset of central nervous system (CNS) involvement.

**Methods:** We retrospectively studied 26 patients (seven men, 19 women; mean age, 67.0 ± 11.1 years) with a diagnosis of PVRL at our hospital between January 2001 and October 2011 and a minimum 2-year follow-up after treatment. We classified the PVRL lesions as: (1) the vitreous opacity type, vitreous opacity of 2+ or higher without retinal lesions, (2) the retina type, vitreous opacity of 1+ or less with retinal lesions only, or (3) the concomitant type, with both. We also evaluated whether prophylactic treatment of systemic chemotherapy such as high-dose methotrexate (HD-MTX) and intrathecal MTX (IT-MTX), or topical ocular treatments such as intravitreal injections of MTX and rituximab, inhibited the onset of CNS involvement in patients with PVRL without cerebral involvement.

**Results:** During a mean follow-up of 44.0±18.7 months, CNS involvement began in 14 patients (53.8 %), i.e., three (60 %) of five patients with retina-type lesions, five (41.7 %) of 12 patients with vitreous opacity-type lesions, and six (66.7 %) of nine patients with concomitant-type lesions. There was no significant (P=0.496) association between the site of the ocular lesions and the onset of brain lesions. In addition, CNS involvement occurred in eight of 11 patients receiving CNS prophylactic chemotherapy and six of

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15 patients receiving no prophylaxis; the difference between the two did not reach significance (P=0.131). The time to onset of cerebral involvement in the CNS prophylactic chemotherapy group (42.8±13.8 months) was significantly (P=0.0005) longer than in the group that did not receive prophylaxis (10.2±2.0 months). Preventive systemic chemotherapy, especially HD-MTX, significantly prolonged the time to the onset of brain lesions compared to IT-MTX and local ocular therapy. =

**Conclusions:** While prophylactic systemic chemotherapy did not inhibit the onset of CNS involvement in most of patients with PVRL, it significantly prolonged the time to cerebral involvement.

**Commercial Relationships:** Noriyasu Hashida, None; Kei Nakai, None; Norimitsu Saito, None; Kohji Nishida, None

**Program Number:** 505 Poster Board Number: B0060

**Presentation Time:** 1:30 PM–3:15 PM

**Evaluation of the glucocorticoid receptor as a biomarker of treatment response in Vogt-Koyanagi-Harada disease**

Cristhian A. Urzua1, Julia Guerrero2, Hector Gatica1, Victor Velasquez3, Annelise Goecke1.

1Ophthalmology, Universidade de Chile, Santiago, Chile; 2Universidad de Chile, Santiago, Chile.

**Purpose:** To investigate the role of glucocorticoid receptor (GR) isoforms in peripheral blood mononuclear cells (PBMC) as a biomarker of glucocorticoid (GC) resistance and to validate a set of clinical predictive factors in patients with Vogt-Koyanagi-Harada disease (VKH).

**Methods:** Prospective cohort study that included a total of twenty-one patients with VKH. A complete ophthalmologic evaluation was carried out at baseline that recorded the presence of any clinical predictive factors (visual acuity < 20/200, tinnitus, chronic disease and fundus depigmentation). Real-time quantitative PCR was performed to measure the mRNA levels of GR alpha isoform (GRα) and beta isoform (GRβ), at baseline and two weeks after prednisone initiation.

**Results:** There were no differences between GC-sensitive and GC-resistant patients in GRα and GRβ levels at baseline before treatment initiation. After two weeks of prednisone treatment, GC-sensitive patients had a median 5.5-fold increase in the levels of GRα, while GC-resistant patients had a median 0.7-fold decrease in the levels of this isoform (p=0.003). GRβ expression increased in both groups, with a significantly higher increment in GC-sensitive patients (6.6-fold versus 4.6-fold, p=0.01). The mRNA levels of GR isoforms were independent of disease activity. Fundus depigmentation and chronic disease at diagnosis were associated with GC-resistance (p=0.03, OR=21.0 and p=0.008, OR=37.8, respectively). However, associations with visual acuity or tinnitus were not confirmed in this study.

**Conclusions:** The evaluation of clinical predictive factors and the determination of the change in expression of GR isoforms as potential biomarkers can contribute to the early identification of GC-resistant patients with VKH.

**Commercial Relationships:** Cristhian A. Urzua, CAU is named inventor on a patent application in Chile (no. 2015-001420) that includes the glucocorticoid receptor as a predictive factor for treatment refractoriness in inflammatory diseases (P); Julia Guerrero, None; Hector Gatica, None; Victor Velasquez, None; Annelise Goecke, AG is named inventor on a patent application in Chile (no. 2015-001420) that includes the glucocorticoid receptor as a predictive factor for treatment refractoriness in inflammatory diseases (P)

**Support:** FONDECYT, Santiago, Chile (grant number: 1080529).

**Program Number:** 506 Poster Board Number: B0061

**Presentation Time:** 1:30 PM–3:15 PM

**Hypermethylation of Interferon Regulatory Factor 8 (IRF8) confers risk to Vogt-Koyanagi-Harada Disease**

Yingqiu Qiu1, Hongsong Yu1, Yunyun Zhu1, Zi Ye1, Jing Deng1, Wencheng Su2, Qingfeng Cao2, Gangxiang Yuan2, Aize Kijlstra2, Peizeng Yang1.

1Department of Ophthalmology, the First Affiliated Hospital of Chongqing Medical University, Chongqing Key Laboratory of Ophthalmology, Chongqing Eye Institute, Chongqing, China; 2University Eye Clinic Maastricht, Maastricht, Netherlands.

**Purpose:** To investigate the methylation change of IRF8 in monocyte-derived dendritic cells (DCs) obtained from Vogt-Koyanagi-Harada (VKH) patients, and in the DCs incubated with conventional drugs, thus to study the effect of IRF8 demethylation on the in vitro function of DCs, and Th1/Th17 cell responses in patient group.

**Methods:** Monocyte-derived DCs from VKH patients were cultured with or without the presence of 5-Aza-2'-deoxycytidine (DAC), cyclosporin a (CsA) or dexamethasone (DEX). The mRNA expression of IRF8 was determined by real-time PCR. The methylation level of IRF8 promoter was detected by mass spectrometry. The demethylation effect of DAC on DCs and on Th1/Th17 responses was evaluated by ELISA and flow cytometry. Two-tailed Student’s t-test, Wilcoxon’s matched-pairs test or paired-samples t-test were used for the statistical analysis.

**Results:** A decreased IRF8 mRNA expression in association with a higher methylation level was observed in active VKH patients compared to controls (*p<0.05, **p<0.01). Inactive VKH patients that responded to treatments showed a down-regulated methylation level and increased mRNA expression of IRF8 compared to active VKH patients (*p<0.05, **p<0.01). The DCs from active untreated VKH patients which were incubated with CsA or DEX also showed a lower methylation and higher mRNA expression of IRF8 than untreated DCs (*p<0.05, **p<0.01, ***p<0.001). DAC showed a notable demethylation effect as evidenced by increasing the mRNA expression and reducing the methylation level of IRF8 (*p<0.05, **p<0.01, ***p<0.001). It also suppressed the Th1 and Th17 responses through down-regulating the expression of co-stimulatory molecules (CD86, CD80, and CD40), and reducing the expression of pro-inflammatory cytokines (IL-6, IL-1β, IL-23 and IL-12) secreted by DCs (*p<0.05, **p<0.01, ***p<0.001). The frequencies of Th1, Th17 cells and the production of INF-γ, IL-17 were also decreased with the treatment of DAC (*p<0.05, **p<0.01).

**Conclusions:** These findings show that hypermethylation of IRF8 in DCs confers risk to VKH disease. Demethylation of IRF8 may offer a novel therapeutic opportunity in the treatment of VKH disease.

**Commercial Relationships:** Yiguo Qiu, None; Hongsong Yu, None; Yunyun Zhu, None; Zi Ye, None; Jing Deng, None; Wencheng Su, None; Qingfeng Cao, None; Gangxiang Yuan, None; Aize Kijlstra, None; Peizeng Yang, None

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In the current study, the majority of patients with non-infectious uveitis and scleritis in the Japanese population were Hispanic. The mean age was 36.0 years (range 15-58) and average follow-up was 3.8 years. Over the course of treatment, 100% of patients had bilateral involvement. At final follow-up, persistently active disease was seen in 25.0% of eyes. At first presentation, visual acuity was 20/100 or better in 50.0% of eyes, which improved to 69.4% of eyes at final follow up (p=0.042). The majority of patients required immunomodulatory therapy (IMT) consisting of azathioprine, cyclosporine, infliximab, methotrexate or mycophenolate mofetil: 80.6% of patients received both oral steroids and IMT, 13.9% received oral steroids alone, and 5.6% of patients received only topical treatment. At final follow-up, ocular manifestations included: retinal pigment epithelium clumping (61.1%), fundus depigmentation (55.6%), nummular scars (45.8%), chronic anterior uveitis (12.5%), chronic posterior uveitis (12.5%), and serous retinal detachment (4.2%). Additional findings included: cataracts/intracocular lens implantations (55.6), glaucoma (47.2%), subretinal fibrosis (12.5%), and choroidal neovascular membranes in (5.6%).

Conclusions: In the current study, the majority of patient with chronic VKH were of Hispanic ethnicity with a female predominance. Despite chronic complications, the majority of patients retained visual acuity of 20/100 or better with a combination of corticosteroids and steroid sparing agents.

Commercial Relationships: On-Tat Lee, None; Philip Storey, None; Jeffrey Tan, None; Hassan A. Aziz, None; Jiun Do, None; Brandon J. Wong, None; Anna Ter-Zakarian, None; Damien C. Rodger, None; Narsing A. Rao, None

Efficacy of low-dose methotrexate for non-infectious uveitis and scleritis in the Japanese population

Yosuke Harada, Yoshiaki Kiuchi. Department of ophthalmology, Hiroshima University, Hiroshima, Japan.

Purpose: The use of methotrexate to control ocular inflammation is not common in Japan. This study elucidated the efficacy of methotrexate for non-infectious uveitis and scleritis in a Japanese population.

Methods: We performed a chart review of patients with non-infectious uveitis and scleritis who were treated with methotrexate at Hiroshima University from February 2016 to November 2016. Demographic and clinical characteristics, including the type of uveitis, dosage of methotrexate, control of inflammation after starting methotrexate, and corticosteroid-sparing effect were obtained. The reason for starting methotrexate, and incidence of and reason for discontinuation of therapy were also elucidated. Statistical significance was evaluated with the Wilcoxon signed-rank test.

Results: Seventeen patients were included. There were 8 males and mean age at start of therapy was 47.7±17.9 years (range, 16–68 years). Fourteen patients (82.4%) had non-infectious uveitis and 3 patients (17.6%) had scleritis. All patients had multiple episodes of recurrence of inflammation with reduced dose or stopping of topical or oral steroid. Four patients (23.6%) had elevated intraocular pressure or developed glaucoma and two (11.8%) had cataract formation during steroid therapy. After starting methotrexate therapy, three patients (17.6%) discontinued the therapy due to pancytopenia, fatigue, and elevated liver enzymes, respectively. The mean dose of methotrexate was 8.9 ± 3.3 mg/week (range, 6–16 mg). Among eight patients who had received oral prednisolone before methotrexate therapy and were followed more than 6 months after starting methotrexate, corticosteroid-sparing effect was obtained in all patients. Mean dose of prednisolone was decreased from 16.25 ± 6.4 mg/day to 5.5 ± 4.4 mg/day (P<0.01). No patient had deteriorated inflammation after starting therapy.

Commercial Relationships: Yosuke Harada, None; Yoshiaki Kiuchi, None

Comparing Prednisone and Methotrexate to Off-label Infliximab for the Management of Posterior Uveitis and Panuveitis: A Cost-Effectiveness Analysis

William V. Padula 1, Taygan Yilmaz 2, Miguel Cordero-Coma 3, Michéal J. Gallagher 1, Michael E. Migliori 1. 1Health Policy & Management, Johns Hopkins Bloomberg School of Public Health, BALTIMORE, MD; 2Department of Ophthalmology, Brown University, Providence, RI; 3Uveitis Unit, University Hospital of León, León, Spain; 4Instituto de Biomedicina (IBIOMED), University of Leon, León, Spain; 5Department of Ophthalmology, Hermitage Medical Clinic, Dublin, Ireland.

Purpose: Approximately 3.75% of cases of blindness in the U.S. are caused by uveitis. Incurred clinical costs and lost productivity related to vision loss totals $3.58 billion annually. We evaluated whether infliximab, a modern off-label biologic, is cost-effective for treating posterior uveitis and panuveitis compared to current standards of care, methotrexate and prednisone.

Methods: A cost-effectiveness analysis was performed using a Markov model to simulate a patient cohort with posterior uveitis or panuveitis. The model followed patients’ therapy from onset of posterior uveitis or panuveitis from the U.S. societal perspective. The lifetime model simulated health states that could lead to successful reversal of uveitis with standard or intensified treatment with prednisone, methotrexate, or infliximab. Probabilities, health utilities, and cost were included in the model based on published literature. We conducted univariate sensitivity analyses and a Bayesian multivariate probabilistic sensitivity analysis to estimate uncertainty. Outcomes were measured in terms of costs ($US, 2010) and effects (quality-adjusted life years; QALYs), discounted at 3%/year. An incremental cost-effectiveness ratio (ICER) for pairwise results was interpreted assuming a predetermined willingness-to-pay threshold of $100,000/QALY.
**Program Number:** 510  
**Poster Board Number:** B0065  
**Presentation Time:** 1:30 PM–3:15 PM

**INFLIXIMAB versus ADALIMUMAB for uveitis-related refractory macular edema**

**Raphael Lejoyeux, Christine Fardeau, david saudoun, sophie Tezenas Du Montcel, Eleonore Diwo, Bahram Bodaghi, Phuc Lehouang.**

**Purpose:** To compare the efficacy of infliximab (IFX) versus adalimumab (ADA) for the treatment of non infectious uveitis-related refractory macular edema (ME).

**Methods:** Patients diagnosed with non infectious uveitis related refractory ME and treated with IFX or ADA at Pitie Salpetriere hospital between 2006 and 2016 were included in this retrospective study. All patients were assessed including best corrected visual acuity (BCVA), clinical inflammatory parameters, multimodal imaging with fluorescein angiography, ICG and SD-OCT. Central foveal thickness (CFT) and retinochoroidal architecture were analysed with SD-OCT at baseline, 6 and 24 months after treatment initiation. Findings of patients treated with IFX were compared with those of patients treated with ADA.

**Results:** Twelve patients with a mean age of 40 years and 13 patients with a mean age of 46 years were treated with ADA and IFX, respectively. At baseline, the mean BCVA of ADA patients was 0.59 logMAR (0; 1); median=0.54; SD=0.41) and the mean BCVA of IFX patients was 1.01 logMAR (0.30; 1.3) median=1; SD=0.30. The mean CFT of ADA patients was 417µ (247; 732); median=350; SD=171) and the mean CFT of IFX patients was 450.4µ (202; 617); median=521; SD=145).

At 6 months (M6), the average decrease of CFT was more important in the IFX group in comparison to the ADA group (132.8 µ and 78µ). The average BCVA improved for both groups. The gain of BCVA was -0.10logMAR in the ADA group (SD=0.20) and -0.11logMAR in the IFX group (SD=0.21).

A 24-month follow-up was possible for only 9 patients of the IFX group (3 discontinued IFX because of inefficacy, 1 had a follow-up less than 24 month and 5 patients of the ADA group (4 patients discontinued IFX because of inefficacy, 1 for a minor side effect, 2 were lost to follow-up). The average BCVA improved between M6 and M24 (from 0.48 to 0.33 log MAR) for the 5 eyes (ADA), but decreased for the 9 eyes (IFX) (from 0.89 to 0.99 log Mar). The average CFT decreased for the 5 eyes of the ADA group (from 339 µ to 250 µ).
at M6 to 321 µ at M24) and increased (from 317.6 µ at M6 to 342.5 µ at M24) for the 9 eyes of the IFX group. **Conclusions:** Anti TNF alpha therapy seems to be an efficient treatment at 6 month for uveitis related refractory macular edema. No difference in efficacy was observed between IFX and ADA.

**Commercial Relationships:** Raphael Lejoyeux, None; Christine Fardeau; david saadoun, None; sophie Tezenas Du Montcel, None; Eleonore Diwo, None; Bahram Bodaghi, None; Phuc Lehoang, None.

**Program Number:** 512 **Poster Board Number:** B0067  
**Presentation Time:** 1:30 PM–3:15 PM  
**The Efficacies of Anti TNF-alpha and Interferon alpha-2a Therapies for Patients Diagnosed with Posterior or Panuveitis Associated with Behcet Disease  
Ozlem Gurses¹, Eda Karaismailoglu³, ¹Ophthalmology, DunyaGoz Eye Hospital, Oran Ankara, Turkey; ³Biostatistics, Kastamonu University, Kastamonu, Turkey.  
**Purpose:** Anti TNF-alpha and interferon alpha-2a therapies have been considered for uveitis associated with Behcet disease. The purpose of this study is to compare the efficacy of anti TNF-alpha and interferon alpha-2a therapies for patients diagnosed with posterior or panuveitis associated with Behcet disease.

**Methods:** This was an observational study including 18 eyes of 11 patients treated with interferon alpha-2a, and 15 eyes of 8 patients treated with anti TNF-alpha. The follow-up time for both groups was 36 months. The primary outcome was time inducing remission. The secondary outcomes included change in visual acuity in logMAR, and change in the vitreous haze and haze. Statistical analysis was done by using Mann Whitney U test. (SPSS 21.0) p-value < 0.05 was considered as statistically significant.

**Results:** The median (min-max) time inducing remission for anti TNF-alpha group was significantly shorter (12.0(6-20) months, p=0.001) compared to interferon alpha-2a group. (18 (11-30) months) There was no statistically significant difference of change in the median (min-max) visual acuity between anti TNF-alpha group (0.22 (0-1.78) logMAR) and interferon alpha-2a group. (0.26(0-2) logMAR, p=0.509) There was no statistically significant difference of change in the median (min-max) vitreous cell between anti TNF-alpha group 1 (0-2) and interferon alpha-2a group (1.50 (0-3), p=0.307) There was no statistically significant difference of change in the median (min-max) vitreous haze between anti TNF-alpha group (1 (0-2)) and interferon alpha-2a group. (1.50 (0-3), p=0.220)

**Conclusions:** Our results disclosed no statistically significant difference between interferon alpha-2a and anti TNF-alpha therapies for efficacy of reducing inflammation and improving visual acuity in patients with posterior or panuveitis associated with Behcet disease. However; time inducing remission for anti TNF-alpha therapy was significantly shorter than interferon alpha-2a therapy. Further observational studies will be needed to compare time for maintaining remission between interferon alpha-2a and anti TNF-alpha therapies for uveitis patients associated with Behcet disease.

**Commercial Relationships:** Ozlem Gurses, None; Eda Karaismailoglu, None  
**Clinical Trial:** Dunya Eye Hospital, CT-065

**Program Number:** 513 **Poster Board Number:** B0068  
**Presentation Time:** 1:30 PM–3:15 PM  
**Treatment of scleritis and uveitis in granulomatosis with polyangiitis using cyclophosphamide or rituximab  
Aseef Ahmed¹, ², C. Stephen Foster¹, ³, Massachusetts Eye and Research Surgery Institution, Wakefield, RI; ²University of New England College of Osteopathic Medicine, Biddeford, ME; ³Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA.  
**Purpose:** Vision-threatening ocular inflammation can be a complication of granulomatosis with polyangiitis (GPA) that is difficult to control. Here we performed a retrospective observational study to describe the safety and efficacy of treating scleritis and uveitis seen in patients with GPA with either cyclophosphamide or rituximab.

**Methods:** A chart review of patients with GPA-associated scleritis or uveitis, refractory to steroids and treated with either cyclophosphamide or rituximab as final therapy, was conducted. Patients were searched from the Massachusetts Eye Research and Surgery Institution database between 2006 and 2016. A total of six months of follow up visits was required for inclusion in the study. Demographic dates, serology, previous therapy, and treatment outcomes were individually assessed. Remission was defined as showing no signs of active ocular inflammation on exam, in the presence or absence of therapy.

**Results:** Thirteen patients (19 eyes) suffering from GPA-associated scleritis or uveitis, refractory to steroids and treated with either cyclophosphamide or rituximab as final therapy, was conducted. Patients were searched from the Massachusetts Eye Research and Surgery Institution database between 2006 and 2016. A total of six months of follow up visits was required for inclusion in the study. Demographic dates, serology, previous therapy, and treatment outcomes were individually assessed. Remission was defined as showing no signs of active ocular inflammation on exam, in the presence or absence of therapy.

**Results:** Of the 13 patients (19 eyes) suffering from GPA-associated scleritis or uveitis, refractory to steroids and treated with either cyclophosphamide or rituximab, 10 patients (15 eyes) were treated with cyclophosphamide, and 7 patients (9 eyes) were treated with rituximab. The follow-up time for both groups was 36 months. The primary outcome was time inducing remission. The secondary outcomes included change in visual acuity in logMAR, and change in the vitreous cell and haze. Statistical analysis was done by using Mann Whitney U test. (SPSS 21.0) p-value < 0.05 was considered as statistically significant.

**Results:** The median (min-max) time inducing remission for anti TNF-alpha group was significantly shorter (12.0(6-20) months, p=0.001) compared to interferon alpha-2a group. (18 (11-30) months) There was no statistically significant difference of change in the median (min-max) visual acuity between anti TNF-alpha group (0.22 (0-1.78) logMAR) and interferon alpha-2a group. (0.26(0-2) logMAR, p=0.509) There was no statistically significant difference of change in the median (min-max) vitreous cell between anti TNF-alpha group 1 (0-2) and interferon alpha-2a group (1.50 (0-3), p=0.307) There was no statistically significant difference of change in the median (min-max) vitreous haze between anti TNF-alpha group (1 (0-2)) and interferon alpha-2a group. (1.50 (0-3), p=0.220)

**Conclusions:** Our results disclosed no statistically significant difference between interferon alpha-2a and anti TNF-alpha therapies for efficacy of reducing inflammation and improving visual acuity in patients with posterior or panuveitis associated with Behcet disease. However; time inducing remission for anti TNF-alpha therapy was significantly shorter than interferon alpha-2a therapy. Further observational studies will be needed to compare time for maintaining remission between interferon alpha-2a and anti TNF-alpha therapies for uveitis patients associated with Behcet disease.

**Commercial Relationships:** Aseef Ahmed, None; C. Stephen Foster, None

**Program Number:** 514 **Poster Board Number:** B0069  
**Presentation Time:** 1:30 PM–3:15 PM  
**Comparison of visual acuity improvement by vitrectomy for vitreous opacity between infections and non-infectious uveitis  
Yuka Hasegawa, Tomohito Sato, Rina Kinoshita, Yutaka Sakurai, Kozo Hartimoto, Masaru Takeuchi. ophtalmology, National Defense Medical College, Tokorozawa, Japan.  
**Purpose:** To evaluate outcome of diagnostic or therapeutic vitrectomy for vitreous opacity (VO) by comparing of the best corrected visual acuity (BCVA) before and after surgery between infectious and non-infectious uveitis patients.

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Fourteen cases were identified from the uveitis clinic at Vanderbilt University Hospital, Nashville, TN. None; 1:30 PM–3:15 PM

B0070 Optometry

Heather Tamez

This cohort of patients with ocular inflammation included a variety of conditions, such as endophthalmitis, retinitis, and acute retinal necrosis. Two patients had positive serology results. Eleven of the fourteen patients had no recurrence of inflammation after starting antiviral therapy. Two patients experienced recurrent inflammation after antiviral therapy was stopped and one patient suffered recurrent inflammation despite antiviral therapy. The mean length of follow-up was 14.6 months (range one to 39 months).

Conclusions: This cohort of patients with ocular inflammation was recalcitrant to anti-inflammatory therapy and elevated HSV-IgM showed a timely clinical response to the addition of anti-herpes virus therapy. Since HSV may play a role (direct or indirect) in ocular inflammation and its replication may be promoted by standard anti-inflammatory therapies, routine testing of recalcitrant cases for HSV may be beneficial since its suppression may have a favorable effect on disease course.

Commercial Relationships: Heather Tamez, None; Stephen Kim, None

Program Number: 516 Poster Board Number: B0071
Presentation Time: 1:30 PM–3:15 PM

Vitreous density estimation by Spectral-domain-OCT as a sensitive measure of uveitis activity: defining the technical limits of reliability

Christopher M. Way1, Hussein Ibrahim1, Wei Bi2, Robert Carmichael3, David P. Crabb1, Pearse A. Keane4, Alastair K. Denniston2, 5

1University of Birmingham, Woking, United Kingdom; 2Academic Unit of Ophthalmology, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom; 3NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom; 4Department of Ophthalmology, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; 5Optometry and Visual Science, School of Health Science, City, University of London, London, United Kingdom.

Purpose: Quantitative measurement of the vitreous by Optical Coherence Tomography (OCT) has been shown to be an objective way of measuring changes in vitreous density such as may occur in inflammation, infection or haemorrhage. This has the potential to transform the monitoring of disease activity in routine clinical practice and to provide a much needed sensitive endpoint for therapeutic trials.

In order to take this technique to the next stage for clinical adoption it is important to assess the limits of reliability of the technique, specifically to assess whether variations in the way the images are taken could introduce error into the vitreous density readings. We tested the extent to which changes in a novel image acquisition technique might alter the reflectivity signal and cause inaccurate estimations of Vitreous:Retinal Pigment Epithelium (Vit:RPE) signal intensity. Inter- and intra-patient repeatability was also analysed.

Methods: Spectral-domain OCT images were collected prospectively from 40 eyes of 20 visually healthy patients. Isolated adjustments to retina position, Automatic Real Time (ART) level and focus level were made before scans were acquired. Intra-patient repeatability was tested based on 3 repeats of each scan type performed, as was inter-patient repeatability across the 20 participants.

Results: Vitreous:RPE ratio showed good repeatability under standard conditions with a low coefficient of variation (mean (SD) = 0.356 (0.139)). Variation in the vitreous:RPE ratio was seen (mean (SD) = 0.0482 (0.0186)) between individuals which primarily arose due to variation in vitreous reflectivity (mean (SD) = 9.11 (3.83)) rather than RPE reflectivity (mean (SD) = 183.5 (14.71)). Alterations in acquisition settings can significantly alter the absolute measures of reflectivity, with higher vitreous:RPE scores being seen where retina position was lower, where the ART score was higher, and where a positive focus had been applied.

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**Conclusions:** This technique shows good repeatability in estimating Vitreous:RPE ratio within the same patient under standard acquisition conditions. Systematic error can be introduced if there are major deviations in acquisition parameters, but these would be easily avoided in both routine clinical and trial use.

**Commercial Relationships:** Christopher M. Way; Hussein Ibrahim, None; Wei Bi, None; Robert Carmichael, None; David P. Crabb, Allergan (R), Novartis (R); Pearse A. Keane, Novartis (S), Heidelberg (R), Novartis (R), Haag-Streit (R), Bayer (R), Allergan (R), Topcon (R), DeepMind (C); Alastair K. Denniston, None

**Program Number:** 517 **Poster Board Number:** B0072 **Presentation Time:** 1:30 PM–3:15 PM

**Efficacy and Safety Results From the SAKURA Program:** Two Phase III Studies of Intravitreal Sirolimus Every Other Month for Non-infectious Uveitis of the Posterior Segment

**Quan Dong Nguyen,1 Pauline Merrill,2 W. Lloyd Clark3. 1Byers Eye Institute, Stanford University, Palo Alto, CA; 2Ophthalmology, Rush University Medical Center, Chicago, IL; 3Palmetto Retina Center, West Columbia, SC.

**Purpose:** The SAKURA Program – two Phase III, multinational, multicenter, randomized, double-masked studies – assessed the safety and efficacy of every-other-month intravitreal (IVT) sirolimus for treating active non-infectious uveitis of the posterior segment (NIU-PS).

**Methods:** SAKURA Study 1 enrolled subjects through March 31, 2013 (N=347) and SAKURA Study 2 enrolled subjects on/after April 1, 2013 (N=245). All subjects had vitreous haze (VH) ≥1.5+ at baseline. Subjects from both studies comprised the integrated Intent-to-Treat (ITT) population evaluating sirolimus 440 µg vs 44 µg active control, n=208 for each group. 81% of subjects in the SAKURA Program (n=171), 440 µg; n=163, 44 µg were considered to have more severe disease at baseline, defined as VH ≥1.5+ and ≥1 markers of disease: systemic corticosteroids at an overall prednisone-equivalent dose >5 mg/day, best-corrected visual acuity ≤75 ETDRS letters, macular edema (central retinal thickness ≥300 µm on optical coherence tomography). VH was analyzed at Month 5 and safety at Month 6.

**Results:** Study 1 demonstrated the efficacy of every-other-month IVT injections of 440 µg sirolimus over 44 µg. Although the results of Study 2 were not statistically significant (Figure), in the integrated ITT population, 21.2% and 13.5% of subjects (in 440 µg and 44 µg, p=0.0381) achieved the primary endpoint of VH=0 and 50% and 40.4% (in 440 µg and 44 µg, p=0.0488) achieved the pre-specified key secondary endpoint of VH score of 0 or 0.5+. In the integrated subgroup of subjects with more severe disease, 21.1% and 8% of subjects (in 440 µg and 44 µg, p=0.0007) achieved VH=0 and 48% and 37.4% (in 440 µg and 44 µg, p=0.0519) achieved VH 0 or 0.5+. Occurrences of serious adverse events were similar among treatment groups in both the integrated ITT population and more severe disease subgroup.

**Conclusions:** The integrated analysis of the SAKURA Program demonstrated the efficacy and safety of the 440 µg dose of every-other-month IVT sirolimus in NIU-PS, including in those subjects with more severe disease.

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**SAKURA Program: Primary and Key Secondary Endpoints at Month 5**

**Intent-to-Treat (ITT) Population**

**Vitreous Haze (VH) = 0**

- **44 µg (Active Control):**
  - Study 1: 21.2%
  - Study 2: 16.8%
  - Integrated: 20.9%

- **440 µg:**
  - Study 1: 24.8%
  - Study 2: 23.6%
  - Integrated: 24.0%

**VH = 0 or 0.5+**

- **44 µg (Active Control):**
  - Study 1: 17.4%
  - Study 2: 16.1%
  - Integrated: 16.8%

- **440 µg:**
  - Study 1: 19.1%
  - Study 2: 17.9%
  - Integrated: 18.3%

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The efficacy results from the SAKURA Program: Primary endpoint of vitreous haze (VH)=0 at Month 5 and key secondary endpoint of VH = 0/0.5+ at Month 5 in Study 1, Study 2, and Integrated Intent-to-Treat populations.

**Commercial Relationships:** Quan Dong Nguyen, Santen (S), Regeneron (F), Santen (R), Xoma (C), Santen (C), Genentech (R), Abbvie (S), Regeneron (C), Genentech (F), Regeneron (R), AbbVie (C), Santen (F), Genentech (F), Xoma (S), Abbvie (F), Xoma (F); Pauline Merrill, AbbVie (R), AbbVie (F), Santen (F), Santen (R); W. Lloyd Clark, Santen (F), Regeneron (F), Bayer (C), Allergan (F), Santen (C), Genentech/Roche (C), Regeneron (C), Genentech/Roche (F)

**Clinical Trial:** NCT01358266

**Program Number:** 518 **Poster Board Number:** B0073 **Presentation Time:** 1:30 PM–3:15 PM

**Adalimumab in non-infectious uveitis – efficacy across different etiologies in the VISUAL I and VISUAL II trials**

Pauline Merrill1, Albert T. Vitale2, Manfred Zierhut3, Eric Fortin4, Hiroshi Goto5, Martina Kron6, Samir R. Tari7, Sophia Pathai8, 1Rush University Medical Center, Oak Park, IL; 2University of Utah, Utah, UT; 3University of Tuebingen, Tuebingen, Germany; 4University of Montreal, Montreal, QC, Canada; 5Tokyo Medical University, Tokyo, Japan; 6AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany; 7AbbVie Inc, North Chicago, IL; 8AbbVie Ltd, Maidenhead, United Kingdom.

**Purpose:** To assess adalimumab (ADA) efficacy in active and inactive, non-infectious uveitis across different etiologies in patients who were recruited as part of the VISUAL program.

**Methods:** Exploratory data analyses from two global phase 3, double-masked trials: VISUAL I (patients with active uveitis despite ≥2 weeks of prednisone 10–60 mg/day) and VISUAL II (patients with inactive disease dependent on 10–35 mg/day of prednisone to maintain inactivity) were performed. Patients received placebo (PBO) or ADA subcutaneously (80 mg week 0, followed by 40 mg every other week from week 1 up to 80 weeks). In VISUAL I, all patients received a prednisone burst followed by taper to 0 mg by week 15. In VISUAL II, prednisone taper to 0 mg was mandatory by week 19. The primary endpoint was time to treatment failure (TF) at or after week 6 for VISUAL I; and at or after week 2 for VISUAL II. For this analysis, patients were categorized into different uveitis etiologies which they presented at study entry. Hazard ratios (HR) for time to TF were obtained for each uveitis etiology.
**Results:** The efficacy of ADA was significantly greater than PBO in the largest subgroup of patients with idiopathic/other uveitis (VISUAL I: 103 and VISUAL II: 90) etiology in both VISUAL I and VISUAL II trials. All other subgroups showed a trend in favor of ADA, except for sarcoidosis subgroup in the VISUAL II trial (Figure). Overall safety for both trials has been previously reported 1, 2.

**Conclusions:** These exploratory analyses from the VISUAL I and VISUAL II trials show significantly higher efficacy in ADA-treated patients over PBO in ‘idiopathic/other’ diagnoses of patients with both active and inactive non-infectious uveitis. Furthermore, across different uveitis etiologies, these analyses suggest that ADA-treated patients had a prolonged time to treatment failure compared to PBO.

References:

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**Program Number:** 519
**Poster Board Number:** B0074
**Presentation Time:** 1:30 PM - 3:15 PM

**Uveitis Clinical Trials Analysis 2000-2015**

Theodora Gkika, Shaista Giny, Andrej Kidess, Helen Palmer, Alastair K. Denniston, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom.

**Purpose:** To analyse the trends in the subject and design of clinical trials in uveitis from 2000-2015.

**Methods:** We conducted a systemic registry review of the NIH clinical trials registry (clinical trials.gov) for all trials categorised under uveitis. Data analysed included study design, type of uveitis included, source of funding; for interventional studies the phase, endpoint classification and type of intervention were also noted.

**Results:** A total of 216 studies were identified increasing from an average of 2 studies per year for 2000-2003 to 19 studies per year for 2012-2015. During the study period the proportion of studies that were interventional remained fairly constant at around 70%. The proportion of trials receiving industry funding increased from 14% (2000-2003) to 47% (2012-2015). Studies of intermediate/posterior/panuveitis (n=33) were almost twice as common as anterior uveitis (n=18), although most studies either specified by syndrome (n=54) or did not restrict by anatomical subtype (n=127). Of the 157 interventional trials, the intervention was a drug in 146, a device in 6, and surgery/other in 5. The number of phase 2/3 or later phase trials increased from <1/yr (2000-2003) to 7/yr (2012-2015), with randomised controlled trials increasing from <1/yr (2000-2003) to 5/yr (2012-2015).

**Conclusions:** There has been an increase in research investment in uveitis over the last 16 years, with greater engagement from industry and improved progression through the drug-development pipeline to later phase trials, and which is now providing benefit to patients through regulatory approval of therapeutics such as Ozurdex and adalimumab.

**Commercial Relationships:** Theodora Gkika, None; Shaista Giny, None; Andrej Kidess, None; Helen Palmer, None; Alastair K. Denniston, None

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**Program Number:** 520
**Poster Board Number:** B0075
**Presentation Time:** 1:30 PM - 3:15 PM

**Corticosteroid Tapering Success With Every-Other-Month Intravitreal Sirolimus for Non-infectious Uveitis of the Posterior Segment: Results of the SAKURA Program**

Raj Maturi. Midwest Eye Institute, Indianapolis, IN.

**Purpose:** The SAKURA Program was designed to be a monotherapy study assessing the efficacy and safety of every-other-month intravitreal (IVT) sirolimus in subjects with active non-infectious uveitis of the posterior segment (NIU-PS). The proportion of subjects in whom systemic corticosteroids (CSTs) were successfully tapered alongside improvements in vitreous haze (VH) was examined.

**Methods:** The SAKURA Program comprised two Phase III, multinational, multicenter, randomized, double-masked studies. Study 1 included subjects enrolled through March 31, 2013 (N=347) and Study 2 enrolled subjects on/after April 1, 2013 (N = 245). Subjects from both comprised the integrated Intent-to-Treat (ITT) population evaluating sirolimus 440 µg vs 44 µg active control, n=208 for each group. VH was assessed at Month 5. Non-CST systemic immunosuppressants and topical CSTs were discontinued before baseline. 46 subjects from the 440 µg group and 32 from the 44 µg group in the integrated ITT population formed the Intent-to-Taper population (overall prednisone-equivalent dose >5 mg/day at baseline). Subjects achieving an overall prednisone-equivalent dose ≤5 mg/day at Month 5 without any rescue therapy were classified as CST tapering successes. Tapering success with...
High-dose chemotherapy with autologous hematopoietic stem cell transplantation in relapsing Vitreoretinal Lymphoma. A LOC network study

Amin Bennedjai', Caroline Houillier', Sylvain Choquet', Nathalie Cassoux', hervé guesquières', jean-pierre marroleau', Bahram Bodaghi', Phuc LeHoang', Ibrahim Jdid', Cécile Chabrot', Carole Soussain', Khe Hoang Xuan', Valérie Touitou', 'Pitié Salpetrière, Paris, France; 'CHU Lyon, Paris, France; 'CHU Amiens, Amiens, France; 'CH ORléans, Oréans, France; 'CHU Clermont-ferrand, Paris, France.

Purpose: Because of the rarity of the disease, the management of isolated vitreoretinal lymphoma (VRL) remains controversial. VRL prognosis remains severe, mainly because of the risk of central nervous system lymphoma development. The objective of this study is to evaluate the efficacy and safety of high-dose chemotherapy with autologous hematopoietic stem cell transplantation (HCT-ASCT) for the treatment of recurrent relapsing VRL.

Methods: We retrospectively reviewed medical records of patients seen by the French LOC network between 2007 and 2016 with isolated vitreoretinal relapse of either primary vitreoretinal lymphoma, oculocephalor lymphoma, or systemic lymphoma and treated with HCT-ASCT.

Results: 18 patients (8 F/10 M), all immunocompetent, were included in the study. Mean age at HCT-ASCT was 59.17 (range 41 years-73 years). Median Karnofsky Performance status before HCT-ASCT was 90. At diagnosis, 8/18 had PVRL, 9/18 Primary Central Nervous Cells Lymphoma (PCNCL), 1/18 systemic lymphoma. Before HCT-ASCT, patients had received a median number of 1 line of treatment including high-dose methotrexate for all patients. All the patients received a thiopeta-based HCT. After HCT-ASCT, 14 patients experienced a complete response. Noc toxic death occurred. After a mean follow-up of 34.5 months (range: 8-82), 7/18 patients had recurrences (3 VRL relapses, 1 cerebral relapse, 3 ocular and cerebral relapses). The 1 year survival rate was 94.4%.

Conclusions: Intensive chemotherapy followed by autologous stem cell transplant is an aggressive therapeutic approach but appears to give interesting results in young and fit patients with recurrent refractory vitreoretinal lymphoma.

Commercial Relationships: Amin Bennedjai, None; Caroline Houillier, Sylvain Choquet, None; Nathalie Cassoux, None; hervé guesquières, None; jean-pierre marroleau, None; Bahram Bodaghi, None; Phuc LeHoang, None; Ibrahim Jdid, None; Cécile Chabrot, None; Carole Soussain, None; Khe Hoang Xuan, None; Valérie Touitou, None

Program Number: 522 Poster Board Number: B0076
Presentation Time: 1:30 PM–3:15 PM

Poster Sub–Tenon Triamcinolone Acetonide Injection For Treatment of Intraocular Inflammation and Macular Edema Associated with Uveitis

Maria S. Ormaechea', Marilina Ingolotti', Cristobal A. Couto', Mario J. Saravia', Ariel Shlaimer', Hospital Universitario Austral, Buenos Aires, Argentina; 'Hospital de Clinicas Jose de San Martin, Buenos Aires, Argentina.

Purpose: To assess the effectiveness of posterior sub–Tenon (PST) triamcinolone acetonide injection in the treatment of intraocular inflammation and macular edema associated with uveitis.

Methods: Clinical data from patients with diagnosis of uveitis who were treated with PST triamcinolone acetonide injection at the uveits department from Hospital Universitario Austral was reviewed. Information collected consisted in age, gender, anamnestic and clinical course classification according to the SUN study group criteria. Best corrected visual acuity (BCVA) before and 1 and 3 months after injection, anterior chamber inflammation grade, vitreous haze, posterior segment inflammation signs (retinal vasculitis, papillitis, choroidal thickening at EDI OCT, and choroiditis) before and 1, 3 and 6 months after the injection were reviewed. When macular edema was identified, central retinal thickness (CRT) before and at 1 month after injection was recorded. Development of complications such as ocular hypertension and cataract were consigned.

Results: One hundred and one eyes from 70 patients (26 males y 44 females) were found. Average age was of 40,56 ± 18,35 years (women: 40,52 ± 18,35 años, men: 40,62 ± 18,71 years). A total of 242 PST injections were performed. Macular edema was the main indication in 71 injections, intraocular inflammation was the main indication in 183 injections, while 19 injections were performed for both reasons. BCVA in macular edema before injection was less than 20/60 in 24 procedures (36,36%), 20/60 to less than 20/40 in 18 procedures (27,27%), and 20/40 or better in 24 procedures (36,36%).
BCVA at 1 month of follow up after injection was less than 20/60 in 18 procedures (27.27%), 20/60 to less than 20/40 in 7 procedures (10.6%), and 20/40 or better on 41 procedures (62.12%) (chi square = 10.14, P<0.01). Average CRT before injection was 388.40 ± 94.61 microns, and average central retinal thickness 1 month after injection was 266.11 ± 62.10 microns (t student test for paired samples: 6.629, P < 0.001).

**Conclusions:** PST injection was effective for improving best corrected visual acuity and decreasing CRT in macular edema. It was also effective in improving intraocular inflammation parameters in uveitis.

**Commercial Relationships:** Maria S. Ormaechea, None; Mariana Ingolotti, None; Cristobal A. Couto, None; Mario J. Saravia, None; Ariel Shlaen, None

**Program Number:** 523 **Poster Board Number:** B0078 **Presentation Time:** 1:30 PM–3:15 PM

### The role of calprotectin in uveitis

**Zai-Long Chi, Fan Lu, Jia Qu. Laboratory of Neurovascular Biology, The Eye Hospital of Wenzhou Medical University, Wenzhou, China.**

**Purpose:** Uveitis and its sequelae remain an important cause of blindness worldwide. Acute anterior uveitis (AAU) is generally recognized as the most common form of uveitis. Calprotectin (also known as heterodimers of S100A8/S100A9) is a calcium-binding protein which mainly expresses in myeloid cells and plays a prominent role in the regulation of inflammatory processes and immune response. To date, there have been few studies on this protein and uveitis, and the extracellular function of this protein in AAU remains unclear. Here, we report the role of calprotectin in endotoxin-induced uveitis (EIU) rat model and patients with uveitis.

**Methods:** All animal experiments were conducted in compliance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. All patients involved in this study were treated according to the tenets of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of institutions. LPS (lipopolisaccaride) was injected intraperitoneally in male rats to produce anterior uveitis and keratitis. DEX (Dexamethasone) and BAY 11-7085 (an inhibitor of I-kB phosphorylation) was injected intraperitoneally. Serum samples were collected from different types of uveitis patients. The mRNAs and protein levels were measured by real-time PCR, flow cytometry, Immunohistochemistry, and enzyme-linked immunosorbent assay (ELISA).

**Results:** In rat models of EIU, S100A8 and S100A9-positive granulocytes and monocytes increased significantly in the iris-ciliary body and cornea as well as in the blood. Interestingly, Glucocorticoids slightly increased S100A8 and S100A9 levels in leukocytes, but reduced its presence significantly in the iris-ciliary body after LPS injection. Moreover, inhibition of NF-kB activation remarkably suppressed both progression of AAU and total S100A8 and S100A9 levels in leukocytes and the iris-ciliary body after LPS administration. Additionally, S100A8 and S100A9 protein level was also found to be elevated in the serum of AAU patients parallel with the progression of AAU through the designated clinical stages.

**Conclusions:** Calprotectin plays a pivotal role in the processes of AAU through involvement in migration and infiltration of S100A8 and S100A9-positive cells. Our findings suggest that serum levels of calprotectin protein can be used to monitor inflammatory activity in AAU.

**Commercial Relationships:** Zai-Long Chi, None; Fan Lu, None; Jia Qu, None

**Program Number:** 524 **Poster Board Number:** B0079 **Presentation Time:** 1:30 PM–3:15 PM

### Delayed Acceleration of Severity in Recurrent Acute HLA-B27 Associated Anterior Uveitis

**Karen Small, Jing Hua, Alexander Cohn, Stephen D. Anesi, C. Stephen Foster. Ophthalmology, Massachusetts Eye Research & Surgery Institution, Waltham, MA; Ocular Immunology & Uveitis Foundation, Waltham, MA.**

**Purpose:** Steroid treatment responses to acute flares of anterior uveitis are titrated to the level of inflammation observed when the patient presents. We performed a chart review to investigate the phenomenon whereby mild flares in HLA-B27 patients may become more severe despite topical steroid treatment.

**Methods:** Patients included in this study were evaluated at Massachusetts Eye Research and Surgery Institution (MERSI) from January 1, 2004 until November 30, 2016. Inclusion criteria were individuals who were HLA-B27 positive and who developed acute anterior uveitis. The authors evaluated the clinical records to identify uveitis flares where the subsequent exam documented worse anterior inflammation than at initial presentation despite treatment with topical steroids. Patients were excluded if they were diagnosed with any other significant ocular inflammatory condition.

**Results:** There were 218 HLA-B27 positive patients identified. Of these, 22 eyes of 22 patients (10.1%) were found to exhibit delayed acceleration. The average interval from initial presentation was 9.1 days with standard deviation of 6.7 days. The phenomenon exhibited no gender preference, consisting of 11 males, and 11 females, with the average age of 42.4 years (ranging from 20.7 to 65.1 years). Two patients (9.1%) were on immunomodulatory therapy, and 1 patient (4.5%) was taking oral prednisone. Patients had an average of 1.7 other flares while a patient at MERSI, and 9 patients (40.9%) had no other flares. None of the other documented flares exhibited the delayed inflammatory acceleration.

**Conclusions:** HLA-B27 patients in this study were observed to have a unique characteristic during intervals of breakthrough where the disease process becomes active again. These patients may require more frequent and higher doses of steroid treatment at initial presentation of a flare to avoid subsequent aggressive inflammatory acceleration.

**Commercial Relationships:** Karen Small, None; Jing Hua, None; Alexander Cohn, None; Stephen D. Anesi, None; C. Stephen Foster, None

**Program Number:** 525 **Poster Board Number:** B0080 **Presentation Time:** 1:30 PM–3:15 PM

### Long-term outcomes in Juvenile idiopathic arthritis-associated uveitis

**Sarah Syeda, Nakhoul Nakhoul, Buraa Kubaisi, C. Stephen Foster. 1Massachusetts Eye Research and Surgery Institute, Waltham, MA; Department of Ophthalmology, Harvard Medical School, Cambridge, MA; 2Ocular Immunology & Uveitis Foundation, Waltham, MA.**

**Purpose:** Juvenile idiopathic arthritis (JIA)-associated uveitis is an indolent yet serious condition with poor visual prognosis. Our purpose is to present long-term clinical outcomes in patients treated with immunomodulatory therapy (IMT) in the long-term.

**Methods:** A retrospective analysis of JIA-associated uveitis patients presenting between 2005 to 2016 with a minimum of 3 years follow-up was conducted. Information collected included presenting and final visual acuities (VA), development of band keratopathy, cataract and glaucoma, IMT used as well as side effects. Remission was defined as successful inflammation-free weaning off of IMT.
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3 randomized, masked, controlled trial is currently underway as part of continued developmental efforts.

**Commercial Relationships:** Milan Shah, Clearside Biomedical (F)

**Clinical Trial:** NCT02255032