

379 Clinical virology

Tuesday, May 09, 2017 3:45 PM–5:30 PM

Exhibit/Poster Hall Poster Session

Program #/Board # Range: 3602–3614/B0161–B0173

Organizing Section: Immunology/Microbiology

Program Number: 3602 **Poster Board Number:** B0161

Presentation Time: 3:45 PM–5:30 PM

Efficacy and safety of dexamethasone/povidone-iodine ophthalmic suspension in adenoviral conjunctivitis

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Purpose: There are no approved treatments for acute, adenoviral conjunctivitis. The efficacy and safety of an ophthalmic suspension (0.1% dexamethasone/0.6% povidone-iodine [PVP-I]) in the treatment of acute adenoviral conjunctivitis was evaluated in a multicenter, randomized, double-masked parallel-group, active- and vehicle-controlled phase II study.

Methods: 176 patients \geq 18 years old were randomized 1:1:1 to dexamethasone/PVP-I suspension (n=59), PVP-I (n=59) or vehicle (n=58) after a positive Rapid Pathogen Screening Adeno Detector Plus test. One drop of study treatment was applied to both eyes four times daily x 5 days. The initial drop was administered in the office on Day 1. Additional office visits occurred on Day 3, 6, and 12 (+1 day window allowed). Safety measures included slit lamp biomicroscopy, visual acuity, and adverse events (AEs). Main efficacy measures included clinical resolution (defined as absence of watery conjunctival discharge and bulbar conjunctival redness) and adenoviral eradication (negative cell culture immunofluorescence assay [CC-IFA]). Efficacy endpoints were compared between treatment arms using Pearson's chi-square or Fisher's exact tests (in the case of expected counts $<$ 5) at two sided 0.05 significance level with missing data imputed by last observation carried forward method.

Results: The mean (SD) age of subjects was 34.5 (12.2). Most patients were male (66.3%) and all were Asian. A total of 124 patients completed the study. After 5 days of treatment, clinical resolution and adenoviral eradication in the primary study eye at the Day 6 visit were greater with dexamethasone/PVP-I (31.3% [15/48]; 79.2%[38/48]) compared with the vehicle (10.9% [5/46]; 56.5%[26/46]); $p <$ 0.05 for both). Resolution and eradication with PVP-I were 18.0% (9/50) and 62.0% (31/50), respectively; $p =$ NS compared with dexamethasone/PVP-I or with vehicle. Adenoviral eradication was evident as early as Day 3 in both dexamethasone/PVP-I and PVP-I. Thirty-seven patients withdrew owing to AEs (dexamethasone/PVP-I, n=9; PVP-I, n=12; vehicle, n=16). Proportion of subjects with treatment-emergent AEs was highest in the vehicle group (69.0% [40/58]) followed by PVP-I (62.7% [37/59]) and dexamethasone/PVP-I (53.4% [31/58]).

Conclusions: Study results suggest dexamethasone/PVP-I ophthalmic suspension was efficacious and safe to use in the treatment of adenoviral conjunctivitis in adults.

Commercial Relationships: Reza M. Haque, Shire (E);

Arjun Ahuja, None; Wenlei Liu, Shire (E); Abhijit Narvekar, Shire (E)

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Clinical Trial: NCT01470664

Program Number: 3603 **Poster Board Number:** B0162

Presentation Time: 3:45 PM–5:30 PM

Corneal subepithelial infiltrate in epidemic keratoconjunctivitis is associated with polymorphisms of group D human adenovirus E3 CR1 genes and fibrotic inflammation

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Yu-Chi Liu^{7,2}, Jay Stak^{4,1}, Florent Ginhoux⁵, Hidemi Watanabe⁸,

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Purpose: Subsets of group D human adenoviruses (HAdVs) are the main causes of epidemic keratoconjunctivitis (EKC). EKC is one of the most severe forms of virus-induced ocular surface inflammation that leads to persistent visual impairment due to corneal subepithelial infiltrate (SEI). Because several adenovirus proteins are known to have immunomodulatory effects, we investigated the association between polymorphisms of the virus proteins and the clinical and immunological manifestations of EKC to probe the mechanisms of this inflammation.

Methods: Comparative genomic analysis among group D HAdV strains was performed to identify genetic variations in virus genes associated with EKC. Clinical severity, tear cytokine profiles, and virus whole-genome sequences were compared among HAdV strains. Tear cytokine profiles and conjunctival leukocyte profiles unique to SEI were investigated using the conjunctival brush cytology samples at the first clinical visit.

Results: E3 CR1b and fiber proteins had the highest number of variations associated with EKC-causing HAdV strains, and the EKC-associated polymorphisms of E3 CR1b were centered on the extracellular domains of the protein. Clinically, HAdV-D8- and -D37-infected eyes displayed more severe inflammation with SEI, whereas those infected with HAdV-D53 displayed milder inflammation without SEI. Notably, the E3 CR1 genes in HAdV-D53 were 96%–99% identical to the non-pathogenic HAdV-D69 strain, although most of the other HAdV-53 genomic regions showed the highest similarity to HAdV-D8 or -D37 strains. Corneal epithelial defects were significantly associated with high incidences of SEI. High levels of TGF- β 1 were detected in tear fluid with SEI, and high CD163 expression was found on the conjunctival macrophages in the eyes with SEI.

Conclusions: Considering that the group D HAdV E3 CR1 proteins bind to various immune receptors, such as CD45 and the LILRB receptor families expressed on lymphocytes and leukocytes, our results imply that particular polymorphisms of E3 CR1 proteins are primarily responsible for SEI-inducing inflammation in EKC. The increase in TGF- β 1 levels and the presence of CD163⁺ macrophages, in association with a high incidence of SEI with corneal epithelial defects, suggest that SEI is a form of fibrotic response in the anterior corneal stroma.

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Program Number: 3604 **Poster Board Number:** B0163
Presentation Time: 3:45 PM–5:30 PM
Evaluation of multiplex real-time polymerase chain reaction for the detection of HSV-1 & 2 and VZV in the diagnosis of viral keratitis

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Purpose: To evaluate the role of multiplex real time PCR in the diagnosis of viral keratitis by quantification of the herpes simplex virus and varicella zoster virus (HSV 1 & 2, VZV) DNA in the corneal scrapings of patients with clinical viral keratitis and normal controls.

Methods: After appropriate ethical approval, 50 corneal scrapings from 50 patients with suspected HSV keratitis were included in the study. Corneal epithelial cells from 33 eyes of 21 patients undergoing photorefractive keratectomy surgery in essentially normal eyes served as controls. DNA was extracted and analysed for the presence of HSV-1 (Glycoprotein D gene) by conventional PCR in all samples and for the presence of HSV 1 & 2 and/or VZV by real-time PCR (R-gene® kit, bioMérieux) in all samples. Corneal scraping of patients with clinical viral keratitis had also been tested for HSV-1 antigen by immunofluorescence assay (IFA). The results were compared and clinical records of all patients were reviewed.

Results: Very low copy numbers of HSV1 and VZV DNA were detected by real time PCR in 8/15 controls (HSV1, mean-14.3 ±7.96, range: 3 - 29.1 copies/mL) and 2/15 controls (VZV, mean-10.7 ±10.9, range 3 - 18.5 copies/ml). HSV2 however was not detected in any of the control samples. Copy numbers above the mean +1 SD of controls were considered significant in patient samples for HSV1 and VZV. Evaluation of corneal scrapings for HSV 1 from patients showed that 39/50 (78%) were positive (copy number mean-1.18 x 10⁶ ± 3.77 x 10⁶ copies/ml, range: 44.6 - 1.5 x 10⁷ /mL) by real time PCR, 11 out of 48 (23%) by IFA and 20/50 (40%) by conventional PCR. The mean copy number of HSV1 DNA was significantly higher in corneal samples from patients compared to controls (p<0.0001). Double infection with HSV-1 (1.5 x 10⁷ copies/ml) and HSV-2 (3.57 x 10⁴ copies/ml) in one case and VZV infection (1.03 x 10² copies/ml) in another was detected by real-time PCR.

Conclusions: Multiplex real-time PCR reliably detects high copy numbers of HSV1/2 and VZV DNA in patients with clinical viral keratitis and the DNA level is significantly higher than normal individuals who may harbor latent virus. Although expensive, real time PCR is easy to perform, is superior to conventional uniplex PCR and IFA and is ideal for the diagnosis of HSV and VZV keratitis in an ocular microbiology laboratory, either alone or in combination with IFA.

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Program Number: 3605 **Poster Board Number:** B0164
Presentation Time: 3:45 PM–5:30 PM
Ocular Features of Zika Virus in Infants with Microcephaly in Colombia and Venezuela

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Purpose: To report ocular features of Zika virus (ZIKV) in infants with microcephaly in Colombia and Venezuela. To April 2016, a total of 65,726 cases of ZIKV disease were reported in Colombia, and 723,550 cases in Venezuela.

Methods: We assessed the ophthalmological findings of 43 infants that had been clinically diagnosed with ZIKV-related microcephaly born between October 2015 and June 2016, and that presented ocular abnormalities in the cities of Maracaibo (Venezuela) and Cucuta (Colombia).

Results: No ophthalmological abnormalities were identified in the mothers and they did not report ocular symptoms during pregnancy. Serology was negative in all infants for toxoplasmosis, rubella, cytomegalovirus, syphilis and human immunodeficiency virus. Ocular manifestations were bilateral in all patients. Optic nerve findings in these infants consisted of hypoplasia with the double-ring sign, pallor, and increased cup-to-disk ratio, and were found in five (11.6%) patients. The macular abnormalities were mild to gross pigment mottling and lacunar maculopathy in 27 (62.8%) and 3 (6.9%) of the patients, respectively. Chorioretinal scarring was found in three (6.9%) patients. Congenital glaucoma was found in 5 (11.6%) patients characterized by the clinical triad of epiphora, photophobia and blefarospasm.

Conclusions: Forty-three infants with microcephaly had severe ocular abnormalities all patient with bilateral involvement; these infants were born after a ZIKV outbreak in Colombia and Venezuela. The posterior ocular findings were focal pigment mottling, chorioretinal atrophy with a predilection for the macular area, congenital glaucoma and optical nerve hypoplasia, as well as optic disc abnormalities. These findings can contribute to our understanding in the diagnosis of ZIKV congenital infection in children with congenital microcephaly. Further studies will assess the visual significance of these alterations.



An infant with microcephaly and ocular manifestations.

Commercial Relationships: J Fernando Arevalo, None; Juan B. Yopez, None; Felipe A. Murati, None; Michele Pettito, None; Carlos Peñaranda, None; Jazmin De Yopez, None; Gladys Maestre, None

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Presentation Time: 3:45 PM–5:30 PM

Prevalence and Diversity of Giant Viruses Among Contaminated Contact Lens Cases

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Purpose: Acanthamoeba polyphagia Mimivirus and other giant viruses are ubiquitous in nature. Free living amoebas serve as hosts and potential dissemination vectors. Although reported from a contact lens case of a patient with amoebic keratitis in 2011, they have also been recovered from other human samples since their discovery (respiratory secretions, feces, and blood). Their pathology, frequency, and diversity are still unknown.

Our purpose was to investigate the frequency, abundance, and diversity of giant viruses and associated virophages, in contact lens cases of patients presenting with microbial keratitis.

Methods: Shotgun proteomics coupled with mass spectrometry was used to determine quantity and diversity of proteins associated with 4 giant virus families in contaminated contact lens cases (CTL) of 8 patients presenting with both cornea (K) positive (n=5) and negative (n=3) microbial keratitis. Contact case cases were separated into 3 groups according to culture results; Group 1, (CTL+, Acanthamoeba, N=3), Group 2 (CTL +, bacteria, N=2) and Group 3 (CTL-, n=3).

The correlation between corneal and contact lens cultures was 62.5%. Viral identification was determined using a blast searches of NCBI giant viruses proteins. Chi-square statistics were used to compare differences between the groups.

Results: A total 1545 proteins from 4 different viral families (Mimiviridae (56.2%, n=869), Pandoraviridae (30.2% n=467), Marseilleviridae (10.6%, n=164) and Pithoviruses (Phycodnaviridae) - (2.9%, n=45) were found among our samples.

Of these 687 (44.5%) were mapped to known viral proteins. The highest number of characterized viral proteins were found in group 2 (92.8%, average, n=635) followed by group 1 (86.6%, average, n=593), and group 3 (82%, average=563).

The frequency of giant viruses found in all samples was Pandora (88.3%), Marseille (87%), Pithoviruses(86%) and Mimi (85%).

The differences between group 1 and 2 were significant for Mimi(p<0.0001), Marseille (p=0.0023) and total proteins (p=0.0005), between group 1 and 3 was significant for total proteins only (p=0.0401) and between group 2 and 3 was significant for, Pandora (p=0.034), Mimi (p<0.0001), Marseille (p=0.0186) and total proteins (p<0.0001).

Conclusions: We confirmed a high prevalence and diversity of giant viruses in contact lens cases of patients presenting with microbial keratitis. Pathogenicity and their role in microbial keratitis is unknown.

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Presentation Time: 3:45 PM–5:30 PM

Bilateral Acute Retinal Necrosis Shown in Patients with Viral Encephalitis: a Possible Potential Pathogen Related with Pig

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Purpose: To investigate the ocular and neurologic characteristics of a series of ARN closely following viral encephalitis which might be associated with occupational exposure to pigs.

Methods: Detailed medical history, clinical and imaging data as well as laboratory results of the patients in our case series in both eye and neurologic clinic were retrospectively analyzed.

Results: Totally 11 patients (medium 33 years old, range 24-53 years) with 7 males and 4 females were included in our study. All of the patients were bilaterally affected at the initial visit at the eye clinic. Nine out of the 11 patients complained of visual loss immediately after awaking from unconsciousness. Only 1 eye preserved central vision with best corrected visual acuity (BCVA) of 20/100, while all of the other eyes were worse than counting finger, and moreover 14 eyes of 9 patients displayed no light perception (NLP). All of the patients showed vitreous haze and 12 eyes of 7 patients were with dense opacity and fundi were not visible. The major ocular changes included pale optic disk (8/10), extensive narrowing and whitening of retinal arteries (5/10) and peripheral retinal necrosis (4/10). Retinal detachment (RD) was detected in 20 eyes in the 10 patients. The neurological manifestations were exhibited as high fever and persistent unconsciousness (medium 21 days, range 0-75 days). Laboratory analysis of cerebrospinal fluid (CSF) suggested probable viral infection in 9 patients, while no evidence of specific pathogens detected in CSF and ocular fluid. All the patients except one unknown

had occupational exposure to pigs, and in 9 cases the encephalitis occurred from Feb to Apr.

Conclusions: Symmetrically involved ARN with poor visual prognosis was found closely related to encephalitis and occupational exposure to pigs, which was different from the previously reported ARN. The etiology of the case series needs further investigation as it may be associated with pathogen other than herpetic viruses.



The right fundus imaging of ARN patient

Commercial Relationships: Xiaoyan Peng, None; Feng Hu, None; Ningli Wang, None

Program Number: 3608 **Poster Board Number:** B0167

Presentation Time: 3:45 PM–5:30 PM

Ebola Virus Persistence in Ocular Tissues and Fluids (EVICT) II Study: Cataract Surgery and RT-PCR Outcomes in Ebola Virus Disease Survivors

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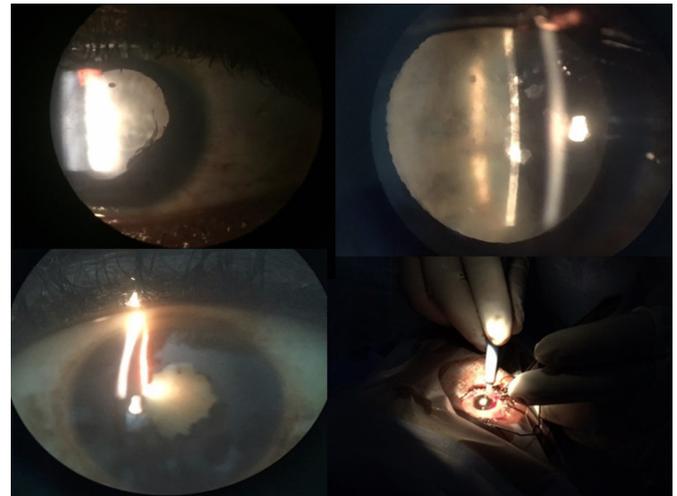
Purpose: Ebola virus (EBOV) persistence after acute illness has been previously reported in the aqueous humor, which suggests the eye could be a potential reservoir for EBOV transmission. We report the baseline characteristics and visual outcomes of Ebola virus disease (EVD) survivors undergoing cataract surgery.

Methods: Baseline (cross-sectional) study from a prospective clinical cohort of EVD survivors with cataracts. Criteria for cataract surgery included: 1) negative EBOV RT-PCR anterior chamber paracentesis 2) visually significant cataract as determined by vision and ophthalmic exam. Patients were excluded if diagnosed with any ophthalmic condition that would preclude meaningful visual acuity improvement despite cataract surgery. Data collected consisted of demographic characteristics, ocular and medical history, and ophthalmic exam (slit lamp exam, dilated fundus exam, B-scan), serum EBOV IgG, and EBOV RT-PCR on intraocular fluid after removal of lens material. All surgeries were performed with strict infection control procedures for health care provider protection.

Results: Sixteen patients (EBOV IgG positive) met eligibility criteria for surgery: 62.5% were female with an average age of 31 years (range: 12–70). Mean time from discharge from an Ebola treatment unit was 21 months (range: 13–31); 14 (87.5%) eyes had a history of uveitis; and, median pre-op visual acuity (VA) was 20/1260

(range: 20/80–LP). 56.2% had cataracts in the right eye. Cataract types included age-related nuclear sclerotic (3), posterior subcapsular (3), cortical (2), uveitic white cataract (5), mature cataract (1), combination (2). Cataract extraction, synechiolysis and posterior chamber intraocular lens implantation was performed without complication in all eyes. The median post-operative day 1 (POD) VA was 20/60 (range: 20/20–hand motion, $p < 0.05$) with continued improvement at post-operative month 1 with median VA 20/30 ($n = 9$; $p < 0.05$). Two patients experienced transient elevated intraocular pressure on POD 1, which resolved with ocular hypotensives. Intraocular fluid immediately after cataract extraction tested negative for EBOV by RT-PCR in all eyes.

Conclusions: Cataract surgery, with strict infection control guidance, was safe, effective, and led to meaningful visual restoration in EVD survivors. Further studies are needed given the public health impact to eye care providers and patients.



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Support: Heed Foundation, Bayer Global Ophthalmology Awards Program

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Presentation Time: 3:45 PM–5:30 PM

Ebola Virus Persistence in Ocular Tissues and Fluids (EVICT) Study: Baseline Characteristics and Primary Findings from Ocular Fluid of Ebola Survivors in Sierra Leone

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Purpose: Thousands of West African Ebola virus disease (EVD) survivors are at-risk for sight-threatening uveitis, which has been associated with persistent Ebola virus (EBOV) in the aqueous humor of a U.S. survivor. The EVICT Study aims to determine the prevalence of EBOV persistence in ocular fluids and establish protocols for ocular fluid sampling of EVD survivors.

Methods: EVD survivors were prospectively enrolled into EVICT for visually significant cataract requiring surgery or active uveitis. Demographic and medical information, visual acuity (VA), and ophthalmic exam findings were collected. Serologies included HIV,

RPR, EBOV IgG/IgM and Lassa Fever (LASV) IgG/IgM. A high-level safety facility and ocular sampling protocols were established via multidisciplinary collaboration between infectious disease and eye care specialists. Aqueous or vitreous humor and conjunctival swabs (pre-, immediate post-, and post-procedure day 1) were collected. Patients were monitored at post procedure day 1, day 7, and monthly.

Results: Twenty-two patients were enrolled into the EVICT Study. Mean age was 30 years (range 12-70) and 15 were female (68%). Mean time from EVD diagnosis was 18 months (range 15-28). Mean VA was 20/1000 (range 20/40-HM). Cataracts were identified in 20 (91%) patients. Two enrollees (9%) had active anterior or intermediate uveitis. Cataracts were attributed to uveitis (18,90%), age (1,5%), and trauma (1,5%). Other structural complications included posterior synechiae (15, 8%), keratic precipitates (5,23%) and chorioretinal scars (5,23%). Serologies showed EBOV IgG positive in 21 (95%) patients, LASV IgG positive in 1 (5%), RPR positive in 1 (5%). LASV IgM, EBOV IgM and HIV were negative in all patients. 21 aqueous humor and 1 vitreous sample tested EBOV-negative by RT-PCR. Pre-, immediate post-, and post-procedure day 1 conjunctival specimens tested EBOV-negative in all 22 patients. Mean VA was stable at 2-months follow-up.

Conclusions: EVD survivors presented with severe VA impairment or blindness largely due to cataracts associated with uveitis. No evidence of EBOV persistence in ocular fluid was identified at approximately 18-months. These findings are relevant to patients anticipating cataract surgery and have public health implications for eye care providers due to the potential risk of EBOV persistence in ocular fluid.

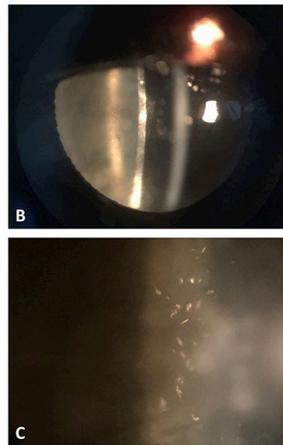
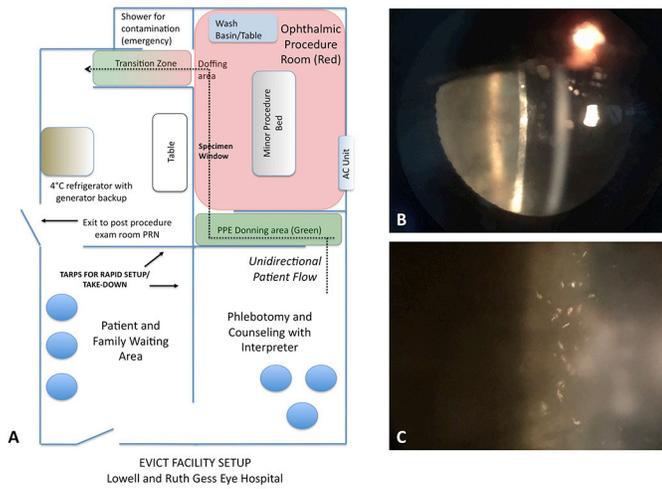


Figure. Blueprint diagram of EVICT setup including unidirectional patient flow, donning and doffing areas for infection control, specimen handling, and patient counseling (A). Cortical and posterior subcapsular cataract in a 39-year-old patient (B) with crystalline lens deposits at high magnification (C).

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Program Number: 3610 **Poster Board Number:** B0169

Presentation Time: 3:45 PM–5:30 PM

Merkel cell polyomavirus detection by next-generation sequencing of the anophthalmic socket

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Purpose: Microbiome characterization of the ocular surface in subjects with ocular prosthesis has not been investigated using high-throughput DNA sequencing. We characterized the ocular surface microbiome by applying biome representational *in silico* karyotyping (BRiSK) deep DNA sequencing to conjunctival samples.

Methods: Conjunctival swab samples from 20 anophthalmic volunteers were analyzed by bacterial culture and biome representational *in silico* karyotyping (BRiSK, n = 20). 16S rDNA gene quantitative PCR was used to calculate the bacterial load in each sample. BRiSK data were analyzed for presence of fungi and viruses. DNA tags were cross-referenced to a comprehensive database for taxonomic classification. Quantitative PCR was used to confirm presence of specific potential pathogens.

Results: The distribution of non-human sequences differed significantly between anophthalmic and control contralateral eyes. BRiSK revealed presence of Merkel cell polyomavirus (MCPyV) in all samples collected from the anophthalmic conjunctiva, but only a minority of contralateral samples. Quantitative PCR demonstrated an average of 894 MCPyV copies/ng DNA on the anophthalmic ocular surface compared to 193 MCPyV copies/ng DNA on the healthy contralateral conjunctiva (two-sample t-test and paired t-test p < 0.0001).

Conclusions: We find the ocular surface microbiome of anophthalmic conjunctiva is distinct from the healthy contralateral eye. Merkel cell polyomavirus is a regular constituent of the anophthalmic microbiome and present in significantly higher quantities compared to contralateral control. The results from this study will inform further investigation aimed at the understanding of the role of this viral community in ocular health and disease.

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Program Number: 3611 **Poster Board Number:** B0170

Presentation Time: 3:45 PM–5:30 PM

Similar outcomes for oral and intravenous treatment of acute retinal necrosis

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Purpose: Acute retinal necrosis (ARN) is a rare form of herpetic uveitis which requires intensive systemic anti-viral treatment. There are different treatment approaches to ARN, but their clinical outcome remains unclear. We reviewed a large retrospective case series to compare the clinical outcome of patients treated with either intravenous (IV) acyclovir or oral valaciclovir therapy.

Methods: Patients were identified from records at Moorfields Eye Hospital, London, UK. Data was collected regarding presentation and subsequent visits including: signs, symptoms, treatments, LogMAR visual acuity (VA), development of retinal detachment (RD), and ocular complications. Cases of ARN were diagnosed clinically and confirmed by vitreous biopsies, where available. Only cases

with a minimum of 6 months follow-up were selected for analysis. Multivariate linear regression and logistic regression methods were used to test for differences in outcomes between the two treatment groups.

Results: 50 eyes with ARN were identified (average age 52 years) in a total of 46 patients from 1992-2014. ARN was diagnosed clinically in 16 cases (32%), biopsies confirmed 30 eyes with varicella zoster (60%) and 4 with herpes simplex (8%). Forty two percent of cases were female. Twenty six cases (52%) were treated with oral valaciclovir and 24 (48%) with IV acyclovir. Intravitreal foscarnet was used as adjunctive treatment in 65% of oral cases (17/26) and 25% of IV cases (6/24). Mean VA at diagnosis was slightly worse for the IV group (1.1 vs 0.9 LogMAR, p value, p=0.38). At 1 month VA improved to 0.9 LogMAR for the IV group and remained 0.9 LogMAR in the oral group (p=0.08). Mean VA worsened in both groups at 6 months (to 1.1 vs 1.2 LogMAR respectively, p=0.13) and 1 year (to 1.2 and 1.5 LogMAR respectively, p=0.17). Both groups recorded poor visual outcomes, with severe vision loss (VA \geq 1.0 LogMAR) observed in 50% of the IV group and 54% of the oral group at final review within 1 year (p=0.79). 66% of eyes developed RD at a mean of 116 days post diagnosis, occurring in 67% (16/24) of the IV cases and 65% (17/26) of the oral treatment group (p=0.85).

Conclusions: ARN results in significant deterioration in vision in a majority of patients, with up to two thirds developing retinal detachment. Systemic treatment with oral valaciclovir resulted in outcome comparable to IV acyclovir and can be considered as an alternative treatment approach.

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Presentation Time: 3:45 PM–5:30 PM

A comparison of visual outcomes and clinical management of CMV retinitis in HIV and non-HIV positive patients

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Purpose: The purpose of this study is to investigate differences in therapy, visual outcomes, and ocular complications between HIV positive and negative patients with active CMV retinitis.

Methods: Retrospective record review from 2000-2016 of CMV retinitis patients at UIC. Demographic information, medical history, medications, logMAR visual acuity (VA) (presentation, 1, and 6 months), and ocular complications were recorded.

Results: Fourteen patients (23 eyes) had confirmed CMV retinitis; 8 patients (13 eyes) were HIV positive with mean CD4 count of 37 cells/mm³ at initial presentation (1-110) and 89 cells/mm³ at 6 month follow up (20-220). Of the 6 non-HIV patients (10 eyes), 3 were on immunosuppressive medications (2 solid organ transplants, 1 CLL), 1 had diabetes and neutropenia, 1 aplastic anemia, and 1 congenital CMV.

Zone 1 retinitis occurred in 60% of HIV eyes compared to 50% of non-HIV eyes (p=0.44); mean clock hours involved per eye were 9.9 in HIV and 6.0 in non-HIV (p=0.02). The mean number of intravitreal antiviral injections in HIV eyes was 1.75 compared to 8.0 in non-HIV eyes (p=0.007). Intravitreal treatments in HIV group: 5 eyes combined Foscarnet/Ganciclovir, 3 eyes Ganciclovir (GCV) alone, 4 eyes GCV implant. Treatments in non-HIV group included: 7 eyes combined Foscarnet/GCV, 2 eyes GCV alone, 1 eye Foscarnet

alone, and 3 eyes GCV implant. 6 non-HIV and 4 HIV patients received combined systemic and local therapies. 1 HIV patient received only systemic therapy.

Mean VAs at initial presentation (1.67 vs. 0.8, p=0.07) and one month follow up (1.32 vs. 0.59, p=0.02) were worse in HIV eyes compared to non-HIV eyes. There was no significant difference in VA at 6 month follow up (1.19 vs. 1.3, p=0.47) but sample sizes were small. Mean follow up times were 12.8 months (HIV) and 22.1 months (non-HIV) (p=0.18), but 4 HIV patients had <1 month follow up. Retinal detachment occurred in 6/13 (46%) HIV eyes and in no non-HIV eyes.

Conclusions: In this small series of CMV retinitis, HIV patients had a higher rate of retinal detachment, more total clock hours of retinitis, and worse initial VA, suggesting more severe disease; however, there was no difference in VA over time between groups. Long-term visual and anatomic outcomes were limited by significant loss to follow up, especially in HIV patients.

Commercial Relationships: Seema Ghelani, None; Pooja Bhat, None; Yannek I. Leiderman, None; Jennifer I. Lim, None; Lawrence J. Ulanski, None; William F. Mieler, None; Debra A. Goldstein, None; Ann-Marie Lobo, None
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Presentation Time: 3:45 PM–5:30 PM

Variation of Ophthalmic Manifestations in Congenital TORCH Infection: A 5-Year Review

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Purpose: To describe the variability of clinical presentation of the ophthalmic manifestations in congenital TORCH infection at a single institution (Queen Sirikit National Institute of Child Health) in Thailand.

Methods: Retrospective review of medical records of patients diagnosed with congenital TORCH infection between 2012-2016. The birth weight, gestational age, organism of infection, ophthalmic findings, and treatment were recorded.

Results: 146 cases were diagnosed with congenital TORCH infection. There were 76 with congenital cytomegalovirus infection, 29 with congenital toxoplasmosis, 33 with congenital rubella, 3 congenital herpes simplex, 2 with congenital syphilis, 1 congenital hepatitis B virus, and 2 congenital mycobacterium tuberculosis. There were 9 cases with multiple organisms: 3 cases with both CMV and HSV, which mostly presented with severe tractional retina detachment; 1 case with CMV and Rubella had bilateral total retina detachment; 3 cases with combined CMV, toxoplasmosis and HSV presented with macular scar and no active retinitis; 1 case with HSV, CMV and Rubella had severe bilateral occlusive pupil and microphthalmos; and 1 case with TB and Toxoplasmosis infection had active macular retinitis.

All preterm cases had no ROP noted on presentation.

Conclusions: Congenital TORCH infections, involving multiple organisms, in our study had severe systemic infection and were significant causes of blindness. Ophthalmic manifestations of these infections are variable with an unpredictable presentation that may be unique for each organism. The clinical characteristics of active eye infection are important to recognize and may lead to better

identification of the active organisms. This is critical for proper systemic treatment.

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OKG-0301, a Novel Ribonuclease, Demonstrates Antiviral Activity against Adenovirus in the Ad5/NZW Rabbit Ocular Model

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Purpose: At present, there is no FDA approved antiviral therapy available for the treatment of adenovirus (Ad) ocular infections. OKG-0301 is a novel ribonuclease which preferentially degrades tRNA leading to an inhibition of protein synthesis. It has been previously shown to have antiviral activity against HIV. The goal of the current study was to evaluate the anti-adenoviral efficacy of topical OKG-0301 in the Ad5/NZW rabbit ocular model.

Methods: 39 NZW rabbits were inoculated in both eyes with 1.5×10^6 PFU/eye of Ad5 after corneal scarification. On day 1, the rabbits were divided into 4 topical treatment groups: 1) 25 μ M OKG-0301 (n=9); 2) 2.5 μ M OKG-0301 (n=10); 3) Saline (Negative Control) (CON) (n=10); 4) 0.5% Cidofovir (Positive Antiviral Control) (CDV) (n=10). Rabbits were treated topically in both eyes 8x/day for 9 days

except for CDV (2X/day for 7 days). All eyes were cultured for virus on Days 0, 1, 3, 4, 5, 7, 9, 11, and 14. Viral titers and positive cultures were determined on A549 cells.

Results: 25 μ M OKG-0301, 2.5 μ M OKG-0301, and CDV reduced viral titers compared with CON on Days 3, 4, 5, 7, 11 ($P \leq 0.05$, Kruskal-Wallis). In addition, 25 μ M OKG-0301 (Days 7, 9, 11), 2.5 μ M OKG-0301 (Day 11), and CDV (Days 5, 7, 11) produced fewer Positive Cultures/Total on the days indicated compared with CON ($P < 0.02$, Fisher Exact). Furthermore, 25 μ M OKG-0301 (5.67 ± 0.97 days), 2.5 μ M OKG-0301 (7.15 ± 2.11 days) and CDV (5.88 ± 1.36 days) reduced the Duration of Viral Shedding compared to CON (9.61 ± 2.87 days) ($P < 0.001$, ANOVA) for all treatments. Comparing only the OKG-0301 groups, 25 μ M OKG-0301 was significantly more effective than 2.5 μ M OKG-0301 for reducing daily titers and Positive Cultures/Total on Day 7 and shortening the Duration of Viral Shedding ($p \leq 0.05$).

Conclusions: 25 μ M OKG-0301 and 2.5 μ M OKG-0301 demonstrated significant antiviral efficacy compared with CON in the Ad5/NZW rabbit ocular model. The antiviral efficacy of the OKG-0301 groups was similar to that of the positive antiviral control, 0.5% CDV. OKG-0301 appears to be a promising candidate for a topical antiviral for adenoviral ocular infections and further development is indicated.

Commercial Relationships: Eric G. Romanowski, Okogen (F); Kathleen A. Yates, Okogen (F); Robert M. Shanks, Okogen (F); John E. Romanowski, Okogen (F); Regis P. Kowalski, Okogen (F) **Support:** Okogen, Inc.; NIH Core Grant EY08098; The Eye & Ear Foundation of Pittsburgh; RPB