On Monday, sessions at the ASRS 33rd Annual Meeting featured:

- AMD Neovascular 2
- Pediatric Retina-ROP
- Ocular Oncology
- Inflammatory and Infectious Diseases
- Hereditary Retinal Diseases and Genetics

Following are highlights from our team of *Retina Times* physician reporters.

AMD Neovascular 2

Reported by Glenn Yiu, MD, PhD
Sacramento, CA

Monday, July 13, 8:00-9:20 AM
Moderators: Susanne Binder, MD, and Jeffrey S. Heier, MD

Age-Related Macular Degeneration and Aspirin Use
Kent Small, MD

Despite recent publicity and awareness of several post-hoc epidemiological analyses questioning possible adverse effects of aspirin in AMD, the risk for AMD exacerbation with aspirin use is largely exaggerated. A meta-analysis and review of current literature showed that the number, size, and quality of studies supporting aspirin use are greater than the few studies suggesting possible adverse effect.

Major trials such as the Antithrombotic Trialists' Collaboration (ATT) showed that aspirin use reduces the risk of mortality, major coronary events, and ischemic stroke. Among AMD patients, the Blue Mountain Eye Study (BMES) suggested an increase in AMD in aspirin users, but did not reach statistical significance. The European Eye Study (EES) showed no association between aspirin use and early or late AMD.

In the Beaver Dam Eye Study, regular aspirin use 10 years prior to exam was associated significantly with wet AMD, but not with early AMD. In contrast, the Physicians' Health Study showed a possible benefit of aspirin use in preventing dry AMD. Given the lack of high-level evidence for stopping aspirin use in AMD, the author concluded that patients should continue taking their daily aspirin dose.

Influence of the Vitreomacular Interface on Treatment Outcomes in the Comparison of AMD Treatments Trials (CATT)
Thomas Ciulla, MD

This study was a post-hoc analysis of the association of vitreomacular interface (VMI) with treatment outcomes after anti-VEGF therapy in CATT. Of 1115 subjects with VMI status gradable on OCT, 1.8% had vitreomacular traction (VMT), 11% had vitreomacular adhesion (VMA), and 87.2% had neither. Although VMA and VMT are infrequent in the study, they are more common in young patients, men, and cigarette smokers.

VMA and VMT were not associated with visual acuity at baseline and showed no difference in visual acuity outcome or change in foveal thickness on OCT. However, eyes with VMA or VMT treated as needed required 2 more injections on average over 2 years.

Prospective, Multicenter Investigation of Aflibercept Treat-and-Extend Therapy for Neovascular Age-Related Macular Degeneration
Francis DeCroos, MD

A treat-and-extend protocol may reduce visit burden for patients with wet AMD, but has never been validated for aflibercept treatment of neovascular AMD. The 1-year data from the 2-year prospective clinical trial for treat and extend with aflibercept (ATLAS) enrolled a total of 40 patients treated at 4-week intervals, then extended by 2 weeks, up to a 16-week maximum, based on extension criteria including absence of 5 or greater letter loss, absence of macular fluid on SD-OCT, absence of new macular hemorrhage, and absence of leakage on FA if performed.

On average, subjects on this protocol showed 8.0-letter improvement in best-corrected visual acuity (BCVA) and 146.6-µm reduction in central retinal thickness. Mean treatment interval was 6.7 weeks, and mean injection number was 8.

Thus, a treat-and-extend protocol for aflibercept showed similar visual and anatomic outcomes compared with published reports for ranibizumab and bevacizumab, and has a satisfactory safety profile. Two-year results are pending.

How Do Large Pigment Epithelial Detachments Respond to Ranibizumab Treatment in Wet-AMD Patients?
David Eichenbaum, MD

An analysis of subjects with large pigment epithelial detachments (PEDs) in the HARBOR study for neovascular AMD showed that vision improved with ranibizumab 0.5 mg or 2.0 mg regardless of PED status at baseline, and that PED thickness decreased with treatment regardless of ranibizumab dose or regimen.

Subjects with the largest-quartile of PEDs (termed "extra-large" PEDs) were also effectively treated with ranibizumab 0.5 mg, monthly or PRN, but this treatment was associated with the majority of retinal pigment epithelium (RPE) tears.

Among eyes with PED at baseline, 44% of eyes with complete PED resolution developed atrophy, compared with 17% of eyes with partial PED resolution, suggesting a higher rate of atrophy seen in eyes with complete flattening of PED at month 24.

Factors Influencing Dose Accuracy and Variation of Anti-VEGF Drug Injections
Raymond Iezzi, MD, MS

Using a 1-mL tuberculin syringe may not be optimal for low-volume intraocular

injections. A comparison between injection of 50 µL of bevacizumab, ranibizumab, aflibercept, and de-ionized water using a 1-mL syringe and 32-gauge needle was performed using a microbalance capable of detecting a dose variation of 1/500th of a dose.

For 3 injecting physicians compared, there was significant intra- and inter-injector dose variation from the intended volume of 50 µL, with aflibercept being significantly underdosed compared with other agents. Aflibercept had the highest amount of bubble formation, likely due to increased protein concentration, and may account for underdosing of this drug.

En-Face Optical Coherence Tomography Imaging of Polypoidal Choroidal Vasculopathy (PCV) Diagnosed With Indocyanine Green (ICG) Angiography
Gregg Kokame, MD, MMM

While ICG is a useful modality for imaging polypoidal vessels seen in PCV, it is not always available or convenient compared with en-face OCT, which is noninvasive and takes advantage of conventional OCT data. The typical appearance is an inverted U-shape elevation of the RPE above Bruch's membrane with steep sides.

A case series of 100 eyes diagnosed with PCV by ICG was evaluated with Zeiss Cirrus HD-OCT (Carl Zeiss Meditec, Inc, Dublin, CA), which can segment a slab below the RPE. The author showed that PCV can be diagnosed and visualized well on both ICG and en-face OCT, with those with PED and prior PDT having slightly better visualization on en-face OCT. Although the rate of PCV identification was similar between the 2 modalities, the measured extent of the PCV complex is larger in en-face OCT in 65% of eyes.

Long-Term Vision and Anatomic Outcomes for Neovascular Age-Related Macular Degeneration (NVAMD) Patients in the Anti-VEGF Era
George Parlitsis, MD

This was an evaluation of long-term visual acuity and anatomic outcomes in a "real-life" multi-physician practice in 45 eyes with neovascular AMD treated with anti-VEGF therapy over an average follow up of 6.2 years. Mean baseline visual acuity was 20/73, with significant improvement at year 2.

But after an average of 23.4 injections over the 6-year follow up, the mean final visual acuity was 20/85, despite maintaining a significant decrease in macular thickness on OCT. The author postulated that this failure to maintain the initial vision gain may be due to undertreatment in the real-world setting or disease progression with the development of atrophy.

Monday, July 13, 9:20-9:40 AM
AMD Neovascular 2--Rapid-Fire Papers
Moderators: Susanne Binder, MD, and Jeffrey S. Heier, MD

Gene Therapy: The Next Frontier in the Management of Neovascular Age-Related Macular Degeneration (nAMD) and Other Acquired and Inherited Disorders
Szilárd Kiss, MD

Gene therapy with adeno-associated viruses (AAVs) is the next frontier in ocular diseases. AAVs are safe, non-pathogenic, non-replicating, and non-integrating, with

diverse serotypes having various tropisms for different cells types in the retina. Although viruses can be delivered intravitreally for retinal ganglion cells, they must be given subretinally to transduce photoreceptors or RPE, due to the internal limiting membrane (ILM) barrier.

Clinical trials are underway for AAV2 transduction of RPE65 gene for Leber congenital amaurosis. While 5 of 12 patients treated in London with subretinal AAV2/2 for RPE65 showed improved retinal sensitivity in the first year, there was a decline in vision at 3 years. Six-year follow-up from the US study of 3 of 15 patients showed a similar decline in visual improvement by year 6.

Clinical trials have also begun for gene therapy treatment of X-linked retinoschisis, cone-related diseases, retinitis pigmentosa, Stargardt disease, choroideremia, and neovascular AMD.

Intravitreal Bevacizumab for Choroidal Neovascularization Secondary to Age-Related Macular Degeneration: 5-Year Results of the PACORES Group
Lihteh Wu, MD

This was a retrospective case series of 292 eyes with exudative AMD treated with bevacizumab with mean 68.1-month (about 5-year) follow up in a "real world" usage setting in Latin America. Over 5 years, the average number of injections was 10.9, with most patients receiving 11 to 15 injections.

Although visual acuity improved in the first 12 months, there was progressive decline in gained vision over the 5-year follow up. These results are supported by long-term follow up of major clinical trials such as the SECURE, HORIZON, and SEVEN-UP studies. The authors speculated that this loss of efficacy may be related to undertreatment rather than tachyphylaxis or disease progression.

The Top 10 Practical Pearls From the HARBOR Trial of Ranibizumab in Neovascular (wet) Age-Related Macular Degeneration (wAMD)
Victor Gonzalez, MD

The author reviewed important findings of the HARBOR trial. First, quadrupling the ranibizumab dose to 2.0 mg did not lead to better vision. Both the monthly and the PRN regimen provided a rapid and sustained anatomic response. The study also evaluated low-luminance visual acuity and showed patients gaining nearly twice as much low-luminance vision as standard vision.

Differences between standard- and low-luminance vision at baseline also predicted treatment response. Interestingly, subretinal fluid is protective against atrophy development. PEDs decreased regardless of ranibizumab dose or regimen, with higher rates of atrophy in eyes that had complete flattening. Importantly, although some HARBOR patients are delayed vision gainers, 93% of the ranibizumab 0.5-mg PRN arm did not need monthly injections to maintain improved vision.

Pediatric Retina-ROP

Reported by Audina M. Berrocal, MD, and J. Michael Jumper, MD
Miami, FL and San Francisco, CA

Monday, July 13, 10:30-10:50 AM
Moderators: Audina M. Berrocal, MD, and Amir H. Kashani, MD, PhD

Telemedicine Diagnosis of Plus Disease in Retinopathy of Prematurity: Accuracy of Expert Versus Computer-Assisted Quantitative Vascular Analysis
Ashkan Abbey, MD

Dr. Abbey presented the Royal Oak, Michigan experience utilizing a proprietary computer program, ROPtool, to evaluate retcam photographs of premature infants. Semiautomated grading with ROPtool was found effective (highly sensitive and relatively specific) for detecting plus disease when compared with expert graders. Limitations of the study include poor-quality retcam images and the lack of a fully automated image analysis.

Neurodevelopmental Outcomes in Infants With Retinopathy of Prematurity and Bevacizumab Treatment
Wei-Chi Wu, MD, PhD

Dr. Wu presented the neurodevelopmental outcomes of children undergoing treatment for retinopathy of prematurity (ROP) with laser alone, intravitreal bevacizumab alone, and combined laser/bevacizumab.

No difference between the neurodevelopmental outcomes was seen between laser alone and intravitreal bevacizumab alone. Combined laser and intravitreal bevacizumab was associated with significant neurodevelopmental delay. This data further establishes developmental safety outcomes for ROP management.

Monday, July 13, 10:50-11:20 AM
Pediatric Retina-ROP--Expert Panel
Moderator: Philip J. Ferrone, MD

Fundus Pigmentation as a Risk Factor for Development of Retinopathy of Prematurity
Audina M. Berrocal, MD

Dr. Berrocal discussed the results of a multicenter, prospective study by the iROP Study Group in which 764 premature infants were screened. By multivariate analysis, birthweight, Hispanic ethnicity (parent reported) and medium/dark fundus pigmentation were all associated with a higher risk of developing any stage ROP. Interestingly, birthweight and light fundus pigmentation were correlated with treatment-requiring ROP.

Fluorescein Angiography for the Diagnosis and Management of Retinopathy of Prematurity
Michael Klufas, MD

Dr. Klufas presented an analysis of the impact of fluorescein angiography (FA) compared with color fundus alone in the grading and staging of ROP. Nine expert graders reviewed fundus photographs and FA images of 16 eyes in 8 premature infants.

With the addition of FA images, there was improved accuracy in diagnosing stage 2 or worse disease, stage 3 or worse disease, pre-plus or worse disease, and type-2 ROP. There was also improved intergrader agreement for diagnosis of treatment-requiring ROP. The study supported the benefit of FA in assessing ROP-related vasculature.

Retinal Detachments After Intravitreal Anti-VEGF Injections for Retinopathy of Prematurity
Antonio Capone Jr, MD

A retrospective review of 2 referral centers reported on 16 eyes of 11 infants with retinal detachment (RD) after anti-VEGF injection therapy for ROP. Mean gestational age was 24 weeks with a mean birthweight of 730 grams. All infants were diagnosed with advanced posterior ROP (APROP) at the time of anti-VEGF injection.

Twelve eyes demonstrated a progressive traction retinal detachment (TRD) with predominant circumferential tractional vectors noted akin to the "crunch" phenomenon noted previously with anti-VEGF injection. Fifteen of 16 eyes progressed to stage 4B or 5 ROP; 14 of 15 infants underwent surgery after which partial or complete reattachment was achieved in 11 (80%).

Local and Systemic Adverse Events After Intravitreal Bevacizumab in the Treatment of Retinopathy of Prematurity in a Nine-Year Period
Maria Martinez-Castellanos, MD

This was a multicenter study of systemic and local adverse events of 418 eyes of 262 preterm infants treated with intravitreal bevacizumab for ROP. The mean birth weight was 1338 grams with an average time of treatment at 30 weeks corrected gestational age.

Forty-seven (4.3%) systemic adverse events were reported including 3 deaths, 22 patients with psychomotor developmental retardation, 6 with respiratory distress syndrome, 9 with intraventricular hemorrhage, 1 with cerebellar hypoplasia and 1 dysmorphic syndrome.

Seventy-three (17.5%) local adverse events were recorded including 68 eyes with subconjunctival hemorrhage, 14 eyes with persistent avascular peripheral retina, 6 eyes with self-limited vitreous hemorrhage, 3 eyes with peripheral fibrous avascular membrane and 1 eye with subretinal hemorrhage.

Newborn Infant Global Universal Eye Screen Testing (GUEST) Study: Validation of Technique Approach
Darius Moshfeghi, MD

Dr. Moshfeghi reviewed the GUEST study that involved newborn (24-72 hours postpartum) screening of 89,478 images taken of 5669 infants in 3 countries. Screening identified retinal hemorrhages in 10% to 20% of newborns with foveal hemorrhages in 2% to 6%. Non-hemorrhagic pathology was identified in 2% of newborns. The GUEST study represents an effort at validating this potentially powerful screening tool.

Ocular Oncology

Reported by Prithvi Mruthyunjaya, MD
Durham, NC

Monday, July 13, 11:20 AM-noon
Moderators: Jay S. Duker, MD, and Gaurav K. Shah, MD

Application of Results of Cytopathological Analysis and Gene-Expression Profile in Clinically Diagnosed Posterior Uveal Melanomas (UM) Evaluated by FNAB
Zélia Corrêa, MD, PhD

Using clinical features, choroidal lesions can be categorized into one of 4 clinical categories. In a review of 275 patients with suspected UM evaluated by fine-needle aspiration biopsy (FNAB) for both cytopathology and gene-expression profile (GEP), cytology identified melanoma cells in 87% of tumors. Combining clinical and pathology features, algorithms were created to guide patient counseling, need for further treatment, and recommendation for entry into systemic-therapy clinical trials.

Iodine-125 Brachytherapy for Extra-Large Choroidal Melanomas: Benefit of Vitrectomy and Silicone Oil on Visual Acuity
Tara McCannel, MD, PhD

Large choroidal melanomas (>10 mm or ligand-binding domain [LBD] 16 mm) typically undergo enucleation per Collaborative Ocular Melanoma Study (COMS) guidelines. At the University of California-Los Angeles (UCLA), plaque brachytherapy (PBT) for "jumbo" melanomas (up to 20 mm in diameter) may be combined with pars plana vitrectomy (PPV) with short-term silicone oil (SO) tamponade (PBT + PPV/SO) to help attenuate radiation complications.

Of 41 cases with 1-year follow up, 22 cases received PBT alone, while 19 had PBT+PPV/SO. Overall, 98% eye retention was noted, with only 2 having local-treatment failures. Visual acuity was superior at final follow up for PBT+PPV/SO eyes vs PBT alone (20/150 vs 20/3170, respectively). Combining silicone oil tamponade to attenuate radiation damage may be a future strategy in these eyes.

Peripheral Retinal Perfusion Correlates With Radiation Retinopathy Status Following I-125 Brachytherapy for Uveal Melanoma
Prithvi Mruthyunjaya, MD

Wide field fluorescein angiography was performed in 65 patients with UM following plaque brachytherapy to quantify the degree of retinal nonperfusion. With 53 months follow up, progressive increase in the area of nonperfusion was noted and correlated with decline in visual acuity, severity of cystoid macular edema, and development of clinical radiation retinopathy. This quantifiable measure of radiation retinopathy may be useful to guide future treatment strategies.

Intravitreal Pharmacotherapy for Radiation Maculopathy (IRM Study): 5-year Follow-Up Detailing Treatment Extension and Enhanced Outcomes
Timothy Murray, MD, MBA

Radiation retinopathy (RR) can be detected by OCT in up to 99% of patients 5 years after iodine plaque brachytherapy (PBT). In the study, 139 patients followed for mean 5 years following PBT and presenting with RR were treated with frequent combination therapy with either intravitreal bevacizumab or triamcinolone acetonide at presentation.

Neovascular glaucoma and secondary enucleations were rare events and 50% of patients had final visual acuity greater than 20/50 at final follow up. Frequent pharmacotherapy treatments may alter the natural history of post-PBT RR.

Inflammatory and Infectious Diseases

Reported by Phoebe Lin, MD, PhD
Portland, OR

Monday, July 13, 1:15-2:15 PM
Moderators: Thomas A. Albini, MD, and Virgilio Morales-Canton, MD

Injectable Long-Acting Intravitreal Fluocinolone Acetonide Implant to Treat Non-infectious Intermediate, Posterior, or Panuveitis

Glenn Jaffe, MD

This paper discussed the results of an investigator-initiated IND, dose-randomized, dose-masked prospective study investigating 2 doses of an intravitreal fluocinolone acetonide (FA) implant injected in the clinic using a modified 25-gauge injector at 2 different doses: 0.5 µg/day and 0.2 µg/day, with release of steroid up to 3 years.

This implant was tested successfully in a preclinical model of uveitis in rabbits, and is composed of a polyimide tube with an FA core 3 mm in length. In the human study, patients with noninfectious intermediate, posterior, or panuveitis who required repeated injections or immunomodulatory therapy, and who had no history of an intraocular pressure steroid response, were included.

Eleven eyes of 11 patients were included in the study, with a mean uveitis duration of 7.3 years. These patients were followed for a minimum of 1 year, with an average follow up of 21 months. There were 17 recurrences in 8 eyes prior to implantation, and no post-implantation recurrences. Fellow eyes had 6 recurrences out of 10 eyes with pre-existing uveitis.

The study eyes had mean best-corrected visual acuity (BCVA) of 20/70 at baseline and 20/30 at 2 years *(P* = .028); 50% gained 3 or more lines of vision. Fellow eyes had unchanged vision or worse vision at follow up; 2/11 study eyes had elevated intraocular pressure (IOP), both eventually requiring incisional glaucoma surgery. Systemic therapy was reduced or eliminated in all patients who required this at baseline.

Treatment of Cytomegalovirus (CMV) Retinitis With Third-Party Donor-Derived CMV-Specific Cytotoxic T-lymphocytes

Mrinali Gupta, MD

Dr. Gupta presented 3 cases of treatment-refractory CMV retinitis in immunosuppressed individuals, at least 2 of whom had CMV resistance mutations UL97 and UL54 and were treated successfully with donor-derived CMV-specific cytotoxic T-lymphocytes (CTLs). This technique involves selection of a T-cell line from a library of cryopreserved donor T cells obtained from healthy CMV-seropositive individuals.

Patients are HLA-typed at high resolution, and donor cells are selected based on matching of at least 2 HLA alleles. Donor lines are restricted in their cytotoxicity to CMV epitopes presented by one of the matching HLA alleles. Treatments are given at 1x106 cells/kg CTLs IV weekly for 3 weeks with a 3-week hiatus between treatment cycles.

Two patients underwent 2 cycles of therapy. Patients were treated concurrently with systemic and intravitreal antivirals as needed. Follow up for these 3 patients ranged from 8 to 23 months. All patients had improved visual acuity in at least 1 eye at final

follow up, and none had recurrent retinitis. Two patients had uveitic cystoid macular edema during or after the infusion, but both self-resolved.

The Utility of 2z Ultra-Wide Fluorescein Angiography in the Management of Uveitis Patients
Sunil Srivastava, MD

This paper aimed to identify ultra-wide-field fluorescein angiography (UWFFA) findings in uveitis patients, to determine the impact on management of these findings, and to create an angiography measure of ocular inflammation. Around 18% of patients had peripheral vascular leakage, 13% had central leakage, 22.5% had diffuse leakage, and 5.9% had central and peripheral leakage.

Without UWFFA, 30% to 40% of eyes with leakage are missed. In patients with peripheral findings, management change was influenced by leakage on UWFFA in 27%, and in 19%, it was used to rule out inflammation.

The author mentioned that UWFFA leakage was 100% sensitive and 95% specific for active uveitis, although the retrospective study design means that UWFFA findings at the time of evaluation may have influenced the designation of active vs inactive.

This group also performed automated leakage analysis on UWFFA images and found a mean leakage-area percentage of 4.4% in active eyes compared with 0.9% in inactive eyes *(P* < .0001), with prospective studies to determine prognostic significance of these findings yet to be performed.

Analyses of SAVE-2: A Phase 2 Study to Assess the Safety and Efficacy of Two Doses of Intravitreal Sirolimus in Patients With Noninfectious Uveitis
Quan Nguyen, MD, MSc

Dr. Nguyen presented the interim analysis of the phase-2 study to assess safety and efficacy of 2 doses (group 1: 440 mg monthly vs group 2: 880 mg every 2 months) of intravitreal sirolimus in patients with noninfectious uveitis (SAVE-2 study). The primary endpoint was at 6 months, and showed decreased vitreous haze by 1 or more steps in 81.8% (group 1) and 92.9% (group 2) *(P* = .564).

Vitreous haze was decreased by 2 or more steps in 63.6% (group 1) and 50% (group 2) *(P* = .695). Among subjects with macular edema at baseline (n = 13), the mean change in foveal thickness was -89.42 µm in group 1 and +81.5 µm in group 2. There were no adverse events. In conclusion, both doses can decrease vitreous haze without causing ocular complications at 6 months.

Intravitreal Sirolimus Monotherapy Reduces the Corticosteroid Treatment Burden in Subjects With NIU of the Posterior Segment: SAKURA Study 1 Results
Pauline Merrill, MD

Dr. Merrill presented the results for the Phase-3 SAKURA-1 study to assess the safety and efficacy of sirolimus for noninfectious uveitis (NIU) of the posterior segment using 2 doses (440 or 880 mg every 2 months compared with a 44-mg control dose). The primary endpoint was a vitreous-haze score of 0 at 5 months. In the low-dose group, 22.8% met the primary endpoint compared with 10.3% in the control group *(P* = .025), and 16.4% in the high-dose group (NS).

The percentage of patients who met the secondary endpoint of vitreous-haze score of 0-0.5+ at 5 months was 52.6% in the low-dose group, 35% in the control group (*P* = .008), and 43.1% in the high-dose group (NS).

Only 1 patient in the high-dose group developed endophthalmitis. One patient in the low-dose group and 2 patients in the high-dose group developed sterile endophthalmitis; 8 (7%) in the low-dose group and 7 (6%) in the high-dose group developed uveitis. In conclusion, low-dose intravitreal sirolimus given every 2 months resulted in decreased inflammation by 5 months.

The Importance of Using Povidone-Iodine and Elimination of Topical Antibiotics for Intravitreous Injections: Update From the DRCR.net
Abdhish Bhavsar, MD

Dr. Bhavsar presented the rates of endophthalmitis in the DRCR.net Protocol H, I, J, N, S, T, and V studies. Consistent with the literature, there was an overall low rate of endophthlamitis without any preference for the type of injection given (bevacizumab vs ranibizumab vs aflibercept).

In 15% of injections during which povidone-iodine was not used, patients developed endophthalmitis. Not using povidone-iodine was a risk factor for endophthalmitis, while mode of povidone-iodine use and use of topical antibiotics were not.

Varicella Zoster Virus (VZV) Antigen Presence and Distribution in Giant-Cell Arteritis (GCA) Positive Temporal Artery (TA) Biopsies
Naresh Mandava, MD

Dr. Mandava reported that 74% (out of 82 GCA patients tested) had positive staining for VZV antigen using colorimetric immunohistochemistry staining of VZV using an anti-VZV antibody compared with 8% of control specimens. Staining was seen in the intima, media, adventitia and skeletal muscle, but there were skip lesions in which no staining was seen.

Negative studies in the literature may have been due to less-fine sectioning compared to this study. VZV DNA was seen by polymerase chain reaction (PCR) in 40% of GCA patients out of 45 patient specimens analyzed, and in the only normal subject tested similarly. The results imply an immunopathologic relationship between VZV and GCA.

Hereditary Retinal Diseases and Genetics

Reported by Joel Pearlman, MD, PhD
Sacramento, CA

Monday, July 13, 2:15-2:35 PM
Moderators: Netan Choudhry, MD, FRCS(C), and Jennifer I. Lim, MD

Effectiveness of Dexamethasone Intravitreal Implant in Refractory Macular Edema Due to Retinitis Pigmentosa
Cem Kucukerdonmez, MD

This paper reported on a small group of patients treated with Ozurdex (dexamethasone intravitreal implant, Allergan, Inc, Irvine, CA); the patients had cystoid macular edema (CME) due to retinitis pigmentosa (RP) resistant to topical carbonic anhydrase inhibitors for at least 6 months. The study was based on favorable, if short-lived

improvements in CME with intravitreal triamcinolone.

The authors found reduction in macular thickness over the first 3 months post-treatment that recurred at month 6 in most eyes. Visual acuity improved in all but 1 eye, even in the setting of recurrent macular edema. There were no significant intraocular pressure issues in any patients.

Whole-Exome Sequencing Identifies Rare Genetic Variants in Age-Related Macular Degeneration Patients
Eran Pras, MD

To find novel AMD-related genes, the authors performed whole-exome sequencing on 2 siblings from each of 2 families with early-onset AMD and discovered alleles of 2 genes related to the disease: a null mutation of hemicentin (HMCN1) and missense mutation of complement factor I (CFI).

Multiple genetic interactions can be illuminated by this technique. In one patient, an interaction between CFI and age-related maculopathy susceptibility 2 (ARMS2) may have led to a neovascular-AMD pathway rather than a geographic-atrophy pathway. The authors concluded that advances in next-generation genome sequencing may shed further light on the underlying genetics of AMD.

Pharmacology

Reported by Joel Pearlman, MD, PhD
Sacramento, CA

Monday, July 13, 2:35-3:10 PM
Moderators: Robert L. Avery, MD, and Baruch D. Kuppermann, MD, PhD

Pericentral Hydroxychloroquine Retinopathy in Korean Patients
Young Hee Yoon, MD

The authors reported on a novel pattern of hydroxychloroquine maculopathy in Korean patients; 4.1% of 218 Korean patients taking hydroxychloroquine were diagnosed with maculopathy. However, 89% of these patients had a pericentral pattern of atrophy rather than the more-familiar parafoveal pattern.

The investigators suggest that pericentral changes on OCT and autofluorescence may be the earliest signs of hydroxychloroquine toxicity in Korean patients. Detecting these abnormalities may require wide-field scanning and 30-2 visual-field testing.

Anti-Angiogenics in Iatrogenic Choroidal Neovascularization in Central Serous Chorioretinopathy
Jay Chhablani, MD

The authors suggest that choroidal neovascularization (CNV) related to the treatment of central serous chorioretinopathy (CSCR) may be more complex than originally thought. Laser-related CNVs were sensitive to subsequent treatment with anti-VEGF agents, requiring on average 3 injections. CNVs related to photodynamic therapy (PDT), however, tended to be anti-VEGF resistant and required further PDT for control.

Patients kept an average of 20/60 Snellen equivalent irrespective of the type of CNV. The authors suggest avoiding full-fluence PDT in the treatment of CSCR, as all patients

with CNV in the trial who had undergone initial PDT had full-fluence treatment.

MEK Inhibitor-Associated Subretinal Fluid
Marissa Weber, MD

The authors reported on 52 patients treated for metastatic cancer with the MEK inhibitor; 88% of patients developed subretinal fluid, some within an hour or 2 of treatment. Fluid accumulation was seen in multiple discrete areas, both subfoveally and along the vascular arcades in 64% of patients, with the remaining patients showing fluid either along the arcades or the subfoveal space.

Associated uveitis was not a common feature. Visual loss and subretinal fluid were reversible without additional treatment, and the authors concluded that potentially life-extending MEK-inhibitor treatment should not be withheld for visual reasons.

Bilateral Macular Neurosensory Retinal Detachment Associated With MEK Inhibitor Use for Metastatic Cancer: A Case Series and Review of the Literature
Seenu Hariprasad, MD

This paper presented 2 cases of MEK-inhibitor (pimasertib)-associated maculopathy somewhat more dramatic than those reported in the previous paper. Neurosensory detachment and cystoid macular edema associated with vision loss were seen in 1 patient 1 day after initiating treatment. No leakage was seen on fluorescein angiography.

Vision and anatomy returned to normal with discontinuation of therapy. A mechanism of action related to oxidative stress and down-regulation of aquaporin channels was suggested. The authors recommend fundus examination and OCT surveillance of patients on MEK inhibitors.

PRN Dexamethasone Implant for Macular Edema
Michel Farah, MD, PhD

The authors retrospectively reviewed the outcomes of 91 patients (97 eyes) treated as needed with Ozurdex for CME due to a variety of underlying etiologies. Most patients achieved good control with resolution of CME with a single injection over 6 months. Almost all eyes were controlled with 2 injections.

Vision improved from 0.89+/-0.61 logMAR at baseline to 0.71+/-0.63 logMAR. Adverse effects were not observed. The authors conclude that intravitreal dexamethasone implants are a reasonable option for treating CME from a variety of causes.

Clarification

Following is a more detailed version of a poster review by Michael A. Singer, MD, in Monday's *Retina Times* daily update:

Initial US Iluvien results and management considerations
Alexander M. Eaton, MD

Forty-one patients received Iluvien (fluocinolone acetonide intravitreal implant, Alimera Sciences, Inc, Alpharetta, GA) for refractory diabetic macular edema (DME).

Patients were seen at 2 weeks, 6 weeks, and 12 weeks to ascertain response to the implant.

Twenty-three patients completed 6 weeks of follow up; 9 completed the entire 12 weeks. Of the 23 patients at 6 weeks, 12 patients needed only monotherapy to control macular edema on OCT, while 11 patients required secondary supplementation using anti-VEGF agents.

In the 9 patients who completed the entire 12 weeks of follow up, 3 did well with monotherapy, while 6 additional patients required supplemental treatment with anti-VEGF medication.

This early cohort suggests that if early response to Iluvien is not observed, supplemental therapy with anti-VEGF may be helpful to achieve improvement of vision and reduction of macular edema on OCT. This improvement was better than anti-VEGF alone in most patients.

Watch for tomorrow's Retina Times *daily update covering the Tuesday sessions.*

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